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Title: An exploration of men's experience and use of treatments for erectile dysfunction (ED)

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Abstract

Erectile dysfunction (ED) is defined as the consistent inability to obtain and/or maintain a penile erection sufficient for satisfactory sexual performance and can have a negative impact on men's quality of life, as well as that of his partner. Successful treatment of ED can lead to increased sexual well-being and quality of life. There are a variety of treatments available, however, research suggests that adherence is suboptimal. Therefore, the studies presented in this thesis, are aimed at exploring the psychosocial barriers and enablers to ED treatment utilisation.

The research presented in this thesis drew on the MRC's framework for the design and evaluation of complex interventions and is of mixed methods design. Research includes: a systematic review of the literature; a qualitative interview study to explore patients' (n=10) experience of using treatment; and finally, a quantitative study in which patients' (n=116) beliefs about both their treatment and their condition were explored in a cross-sectional questionnaire study.

The results of this research indicated that, approximately one third of men, regardless of treatment modality, discontinue ED treatment. Both oral and injection therapy indicated the lowest level of treatment discontinuation. Men, on average used under half of the treatment they had been prescribed. The most prominent barriers to treatment utilisation was the negative impact treatment has on men's sense of masculinity, which was significantly associated with increased discontinuation. However, perceiving the condition as being caused by physiological problems was significantly associated with increased persistence. Finally, the perception of increased treatment necessity, related to a significantly higher frequency of sexual attempts. It is suggested that such beliefs may be amenable to change, which if addressed, may contain the possibility of improving ED treatment utilisation. Therefore, the findings of this

research lay the groundwork for future behaviour change interventions, aimed at supporting the successful use of ED treatment.

Introduction

The overall aim of the research presented in this thesis, was to explore the barriers and enablers of ED treatment utilisation and the extent to which they have the potential to influence men's decisions around treatment use.

Over the last 50 years there has been an increase in the extent to which a number of chronic diseases can be effectively treated using contemporary pharmacological management. This includes diseases such as hypertension, hypercholesterolemia, diabetes, depression, and cardiovascular disease (Krousel-Wood et al, 2014) as well as erectile dysfunction (ED), for which modern pharmaceuticals have been hailed as revolutionising treatment (Kirby et al, 2014).

Although modern treatments have improved in terms of their effectiveness, adherence to treatment in general has been reported as ranging from 0% to 100%, where the average rate is approximately 50% (Haynes et al, 2002). The wide range of reported rates has been suggested as being, related to methodological differences, operational definitions, the variety of adherence measures, treatment regimens, the variety of diseases and patient characteristics (Dimatteo, 2004). However, despite the variety of reported rates, low adherence to long-term therapy has been associated with a reduction of therapeutic success, reduced quality of life and higher health care service utilisation, treatment costs and even a higher risk of mortality with some conditions (WHO, 2003).

Early treatments for ED such as intracavernosal injections (ICI), urethral suppository (US) and vacuum erection devices (VEDs) have been described as lacking the ease that modern pharmaceuticals i.e., phosphodiesterase type 5 inhibitors (PDE5Is) offer (Conaglen & Conaglen,

2012). Despite such advantages, adherence to PDE5Is has been described as sub-optimal, typically involving a pattern of uptake followed by abandonment (Conaglen & Conaglen, 2012). There are many reasons that may contribute to men not using their ED treatment. Research has indicated, for example, that having to have a sexual schedule influenced by a medication regimen, the time interval between taking the medication and the onset of action as well as side-effects, dosing instructions and cost can all have an impact on whether men continue with treatment (Hackett, 2005). There are also psychosocial aspects to consider which influence medication taking for ED such as performance anxiety, depression, varying arousal patterns and misaligned expectations between patient and spouse (Althof, 2002a).

Althof (2002a) suggests that adherence to ED medication sits upon complex foundations whereby treatment is capable of producing an erection; however, getting men to make use of treatment regularly in sexual intercourse is rather more complicated. As a result, Althof (2002a) suggests considering treatment discontinuation from a biopsychosocial perspective. Successful ED treatment utilisation is important when we consider research that has revealed that treating ED successfully can lead not only to an increase in sexual well-being, but also an increase in overall life satisfaction (Fugl-Meyer et al, 1997). Research to date has explored barriers and enablers to ED treatment utilisation, however; there has been no synthesis of the research. This is important in the light of national guidelines for medication adherence (Nunes et al, 2009), which recognises that in order for health care professionals (HCPs) to be able to support patient adherence, a better understanding of the factors that influence patients' decisions is necessary.

Considering the points raised above, i.e. that there has not been any synthesis of previous research investigating barriers and enablers of ED treatment utilisation and secondly, that getting men to make use of ED treatment regularly in sexual intercourse is considered complex

(Althof, 2002a), a mixed methods approach i.e. exploratory sequential design (Creswell et al, 2011), was considered the most appropriate methodology for carrying out this research.

Using a mixed methods approach raises an important question which relates to this research and its epistemological lens. A constructivist approach focusses on understanding 'the world of human experience' (Cohen & Manion, 1994) and suggests that 'reality is socially constructed' (Mertens, 2005). It does not generally begin with a theory and instead 'generate(s) or inductively develop(s) a theory or pattern of meanings' (Creswell & Creswell, 2017). One of the major criticisms of the constructivist approach is that it diverges from scientific explanation models in terms of the need for hypothesis testing (Bendassolli, 2013). At the opposite end of the dichotomy the positivist approach, sometimes referred to as the 'scientific method' (Mackenzie & Knipe, 2006), focusses on testing theories and gathering evidence regarding theories (Bendassolli, 2013). However, a major criticism of the positivist perspective is that it can be restrictive of social inquiry. Although positivism focuses on the objectivity of the research process, post-positivism provides room for subjectivity and uses both qualitative and quantitative methods (Dawadi et al, 2021). The post-positivist perspective is considered as being representative of multiple perspectives (Nzabonimpa, 2018) embracing all forms of research and emphasis that what matters is the illumination of our understanding of the human experience (Smith, 1999).

Pragmatism is described as not being committed to any philosophical stance (Creswell & Poth 2016) but argues that the dichotomy of positivism and constructivism be abandoned and instead reality be considered as both singular and multiple (Dewadi et al, 2021) or pluralistic and oriented towards 'what works' and although pragmatism uses multiple methods, they should always be guided by research problems (Creswell & Plano Clark, 2011). Therefore, both objective

and subjective knowledge are considered important and research methods should be chosen based on whether they are the best method by which to approach a given research questions (Creswell & Poth 2016). Pragmatism, as a research paradigm, proposes that any approach to research should use the methodological approach that works best for the research problem being explored (Tashakkori & Teddlie 1998). As a result, pragmatism as an approach is often associated with mixed-methods or multiple-methods (Creswell & Clark 2017). Therefore, for the purposes of this research, it was considered that qualitative methods, through the use of interviews, would be necessary to identify factors which influence ED treatment utilisation. This would subsequently provide an explanation of how and why factors occur and the extent to which they have an effect (Pasick et al., 2009). The qualitative exploration could then be used to develop a questionnaire, which in turn would enable the use of quantitative methods to examine the pervasiveness of influential factors identified by the qualitative study and the identification of their central patterns of association (Creswell et al, 2011). As a result, this methodology enables one dataset to build on the results of the previous i.e. the quantitative study builds on the findings of the qualitative study. Therefore, a mixed-methods approach was considered the most appropriate way to address the aims of the research by combining the strengths of both qualitative and quantitative research (Creswell et al, 2011). This type of mixed methods design is referred to as an exploratory sequential design (Creswell et al, 2011) and was considered appropriate for this PhD thesis.

The Medical Research Council (MRC) guidelines for the design and evaluation of complex interventions suggest that in order to design an intervention of high quality and effectiveness, the selection of a theory upon which to base the intervention is necessary (Campbell et al, 2000; Craig et al, 2008). Therefore, prior to intervention design, it is necessary to undertake an exploratory study to gain a greater perspective and understanding of the potential theories, and

which surrounding issues influence an intervention of this nature (Campbell et al, 2007).

Therefore, this thesis describes a series of research studies (

Table 1: Summary of study titles and research designs

Study number	Title of study	Research design
Study 1	Rates of treatment discontinuation and barriers to adherence to treatment for erectile dysfunction – A Systematic Review	Systematic Review
Study 2	A qualitative exploration of Barriers and Enablers to ED Treatment Utilisation	Qualitative interview study
Study 3	Barriers and Enablers to Erectile Dysfunction Treatment and Their Effect on Utilisation	Cross-sectional, questionnaire study

) which are outlined below:

Table 1: Summary of study titles and research designs

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Study 1

To the authors knowledge, this was the first extensive and systematic database search and synthesis of the barriers and enablers which have the potential to impact ED treatment utilisation (See Chapter 3).

Study 2

This involved an in-depth, qualitative interview study which used a semi-structured interview guide based on the theoretical domains framework (TDF) (Michie et al, 2005 and Cane et al, 2012) in order to carry out an exploration of the barriers and enablers to ED treatment utilisation (See Chapter 5).

This research is not the first to use the TDF to investigate adherence to treatment. Recently, the TDF has been applied to investigations of treatment adherence in a variety of medical conditions, including; stroke (Crayton et al, 2017) cystic fibrosis (Arden et al, 2019) and cardiovascular disease (Easthall et al, 2019). However, based upon the systematic review in Study 1, the research presented within this thesis is the first to use a theoretical framework to gain insight into the psychosocial determinants of ED treatment utilisation.

Study 3

Using a quantitative cross-sectional study design, the findings from study 2 were then used to develop a questionnaire to investigate the impact barriers and enablers have, with regards to ED treatment utilisation (See Chapter 6). Study 3 includes the use of a novel questionnaire designed specifically for use with ED patients. The combination of studies 1, 2 and 3 lay the foundations to inform a theory-based intervention to promote adherence to ED treatment.

Abbreviations

AIDS - Acquired Immune Deficiency Syndrome

AMSTAR - A Measurement Tool to Assess Systematic Reviews

AS - Arterial Sclerosis

BEED-TQ - Barriers and Enablers to Erectile Dysfunction Treatment Questionnaire

BCTs - Behaviour Change Techniques

BHF - British Heart Foundation

BMQ - Beliefs about Medicines Questionnaire

BPH - Benign Prostatic Hyperplasia

CAD - Coronary Artery Disease

CB - Cerebrovascular Disease

CF - Cystic Fibrosis

CHD - Coronary Heart Disease

CINAHL - Cumulative Index to Nursing and Allied Health Literature

COPE - Coping Orientation to Problems Experienced

CPCC - Cambridgeshire and Peterborough Clinical Commissioning Group

CSM - Common Sense Model

CVA - Cardiovascular Accident

CVD - Cardiovascular Disease

DM - Diabetes Mellitus

DoH - Department of Health

ED - Erectile Dysfunction

GP - General Practitioner

HADS - Hospital Anxiety and Depression Scale

HCP - Health Care Professional

HMIC - Health Management Information Consortium

HIV - Human Immunodeficiency Virus

HRA - Health Research Authority

ICI - Intracavernosal Injection

IFG - Impaired Fasting Glucose

IGT - Impaired Glucose Tolerance

IHD - Ischemic Heart Disease

IIEF - International Index of Erectile Function

IJR - International Journal of Impotence Research

IO - Intrapelvic Operation

IPQ - Illness Perception Questionnaire

IPQ-R - Illness Perception Questionnaire Revised

IQR - Inter Quartile Range

HBM - Health Belief Model

LUTS - Lower Urinary Tract Symptoms

MCAR - Missing Completely at Random

MEMS - Medication Events Monitoring System

MeSH - Medical Subject Heading

MHF - Men's Health Forum

MI - Multiple Imputation

MRC - Medical Research Council

MUSE - Medicated Urethral System for Erections

NCF - Necessity Concerns Framework

NHS - National Health Service

NICE - National Institute for health and Care Excellence

NIH - National Institute of Health

NIHR - National Institute of Health Research

NR - Not Recorded

NSRP - Nerve Sparing Radical Prostatectomy

OaD - Once a Day

PAD - Peripheral Artery Disease

PALS - Patient Advice Liaison Service

PAQ - Persistence Adherence Questionnaire

PC - Prostate Cancer

PCA - Principle Components Analysis

PDE5I - Phosphodiesterase type 5 Inhibitor

PIS - Patient Information Sheet

PMAP - Pan Mersey Ap Committee

PP - Penile Prosthesis

PPI - Patient and Public Involvement

PRISMA - Preferred Reporting Items for Systematic Review and Meta-Analysis

PRN – Pro Re Nata

PS - Pelvic Surgery

QoL - Quality of Life

RCT - Randomised Controlled Trial

R&D - Research and Development

RP - Radical Prostatectomy

RPS - Radical Pelvic Surgery

RPSoGB - Royal Pharmaceutical Society of Great Britain

RT - Radiotherapy

SCI - Spinal Cord Injury

SCM - Social Cognitive Model

SCT - Social Cognitive Theory

SEAR - Self-Esteem and Relationship Questionnaire

SHIM - Sexual Health Inventory for Men

SNRI - Serotonin and Noradrenaline Reuptake Inhibitors

SRM - Self Regulatory Model

SPSS - Statistical Package for the Social Sciences

SSRI - Selective Serotonin Reuptake Inhibitors

TDF - Theoretical Domains Framework

TPB - Theory of Planned Behaviour

TRA - Theory of Reasoned Action

TTM - The Transtheoretical Model

UCLH - University College London Hospital

US - Urethral Suppository

UK - United Kingdom

VED - Vacuum Erection Devices

WFCCG - Waltham Forest Clinical Commissioning Group

WHO - World Health Organisation

1 Erectile Dysfunction – A Clinical Background

1.1 Chapter Overview

The following chapter will describe the pathophysiology and aetiology of erectile dysfunction (ED) and how it is diagnosed. It will summarise the prevalence of the condition, the various types of ED, how it affects individuals and their partners.

1.2 Definition

The term 'erectile dysfunction' is defined by the National Institute of Health (NIH) Consensus as the recurrent or consistent inability to obtain and/or maintain a penile erection sufficient for satisfactory sexual performance (NIH Consensus Conference, 1993).

1.3 Pathophysiology of Erectile Function

To achieve an erection, a complex process involving sexual stimulation, the central nervous system and a peripheral neuro-vascular pathway, involving hormones has to occur (Salonia et al, 2003). There are six integrated vascular processes that result in a penile erection (Dorey, 2000), which are as follows:

- Flaccidity
- Filling phase
- Tumescence
- Full erection
- Rigidity
- Detumescence

The flaccid phase is indicated by low blood flow and pressure. The sympathetic nervous system ensures that arteries are constricted and smooth muscle relaxed. In the event of sexual stimulation, the parasympathetic nervous system encourages vasodilation (Astbury-Ward, 2000). In the filling phase, tactile stimulus to the penis and genitalia as well as erotic stimuli

(visual, auditory, olfactory or imaginative) can produce a penile erection (Astbury-Ward, 2000). With the penis expanding and elongated, compression of the subtunical veins, which form a network between the inner and outer tunica albuginea (located in the subtunical space, Figure 1), against the tunica albuginea causes venous outflow to become reduced (the tumescence phase). The full erection stage is when intracavernous pressure rapidly increases. For complete rigidity, intracavernous pressure rises above diastolic pressure and blood outflow takes place with the systolic phase of the pulse. At this point no arterial flow takes place. Finally, in the detumescence phase a reversal of the above phases takes place, which is often after removal of erotic stimuli or ejaculation (Astbury-Ward, 2000) resulting in the contraction of the penile smooth muscles and arteries (Peate, 2007).

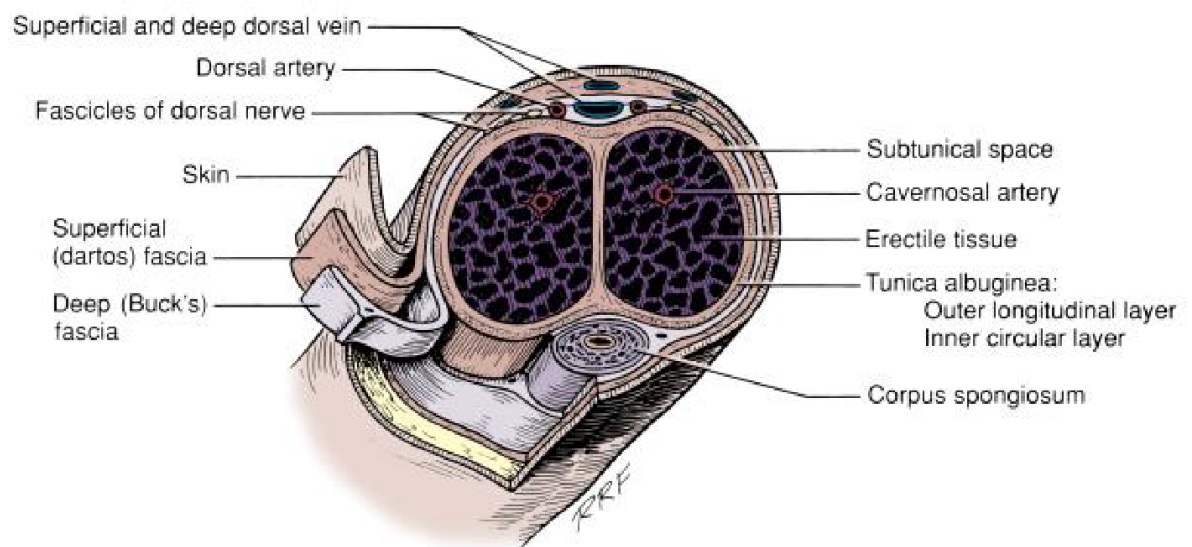


Figure 1: The anatomy of the penis (Walton, 2011 p4)

1.4 Aetiology of ED

A penile erection is a neurovascular phenomenon under psychological control; important abnormalities of erectile function are neurogenic (failure to initiate), arteriogenic (failure to fill) and venogenic (failure to store) (Morales et al, 1997). It has been suggested that ED can be categorised based upon its aetiology (See

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Study number	Title of study	Research design
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) and is broadly considered as relating to psychogenic, organic (neurogenic, hormonal, arterial, cavernosal, or drug-induced), or mixed psychogenic and organic (Lue, 2000), however, psychogenic factors are considered as likely to be involved to a certain degree in nearly all cases (Peate, 2007).

Table 2: A classification of the causes of ED

Causes of ED	
• Vascular	• Endocrine
• Psychogenic	• Iatrogenic
• Neural	• Cellular

Note: Adapted from Eardley (2000)

1.4.1 Neurogenic ED

The disruption of central neural networks or peripheral nerves involved in sexual function can cause ED and it has been estimated that approximately 10–19% of ED is of neurogenic origin (Siddiqui et al, 2012). There are many diseases of both the central and the peripheral nervous system (CNS & PNS respectively) that can result in ED (Table 3). Examples include; multiple sclerosis, temporal lobe epilepsy, Parkinson’s disease, stroke, Alzheimer’s disease, and spinal cord injury (Siddiqui et al, 2012). PNS diseases include cavernous nerve injury from, for example, radical pelvic surgeries such as radical prostatectomy, which has a high risk of neurogenic ED, however, contemporary surgical techniques such as nerve-sparing procedures during robot-assisted radical prostatectomy is considered one of the most important procedures for preserving both erectile function and lower urinary tract function after surgery (Mulhall, 2008; Haga et al, 2021). The risk of ED from spinal cord injury is dependent upon the severity of the injury. Typically, with high lesions there is the potential maintenance of reflex erections (through functioning reflex pathways), whereas, with men with low lesions there is a possibility of the maintenance of psychogenic erections (through functioning sympathetic pathways) (Eardley, 2002). Associated with neurogenic diseases are difficulties such as mobility, manual dexterity as well as urinary function which can be further deleterious to ED (Shamloul & Ghanem, 2013).

Table 3 Neurogenic causes of ED (adapted from Eardley, 2002)

Neurogenic ED	
Diseases of the central nervous system	• Multiple sclerosis • Spinal cord injury • Depression • Parkinson's disease • Cerebrovascular disease • temporal lobe epilepsy • Stroke • Alzheimer's disease
Diseases of the peripheral nervous system	• Cauda equine compression • Prolapsed inter-vertebral disc • Peripheral neuropathy (e.g. diabetes, alcohol) • Surgical injury to pelvic nerves

1.4.2 Vasculogenic ED

Vasculogenic ED is an umbrella term which is inclusive of arteriogenic (failure to fill), which relates to impaired arterial inflow, venogenic (failure to store) which relates to abnormality of corporal smooth muscle structure and/or responsiveness, as well as a combination of both i.e. arteriovenogenic (Mulhall et al, 2005). There are a variety of vasculogenic causes of ED (Table 4). For example, there is a high prevalence of ED reported in conjunction with vascular conditions including coronary artery disease (CAD) (Azab et al, 2018), hypertension (Koroglu et al, 2018), cerebrovascular disease (Ponholzer et al, 2010) and peripheral arterial disease (PAD) (Ugwu et al, 2016). For example, the prevalence of ED has been reported to be as high as 75% for individuals with CAD (Solomon, 2003; Montorsi et al, 2003; Kloner et al, 2003). The increased prevalence of ED in men with vascular conditions relates to atherosclerosis, a process involving the gradual build-up of fatty material inside arteries (**Error! Reference source not found.**). Although the exact causes of atherosclerosis are not known, it exacerbates over time and fatty deposits on artery walls build to the point that blood flow is constricted and flow to organs is subsequently constricted. It is systemic in nature, affecting all major vascular beds to the same

extent throughout the body and can affect any vessel from the aorta to the penile arteries (Eardley, 1999). The 'arterial size hypothesis' suggests that due to their size, penile arteries (1–2mm) become blocked by atherosclerotic plaque build-up before larger coronary arteries (3–4mm) (Jackson, 2013).

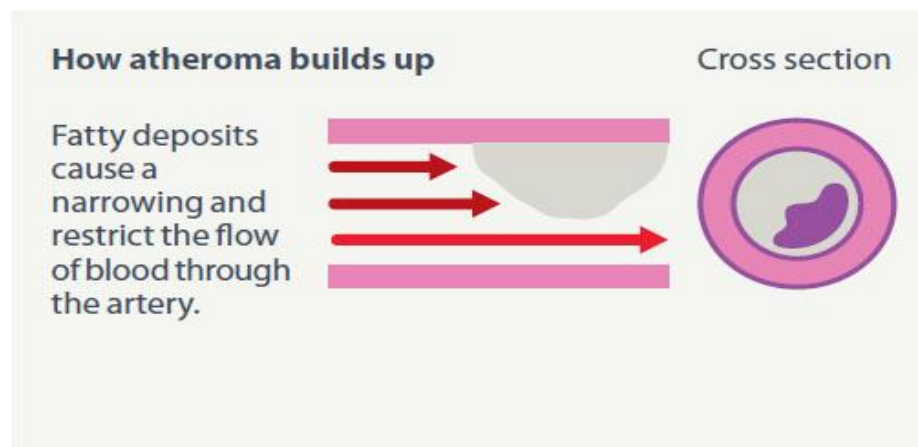


Figure 2: Build-up of atheroma (British Heart Foundation [BHF], 2014))

As a result of atherosclerosis, restricted blood supply can lead to relative ischemia (inadequate blood supply to an organ or part of the body) as well as impaired cavernosal (columns of erectile tissue) oxygenation. This, in turn can result in smooth muscle (responsible for the contracting of blood vessels) dysfunction and fibrosis (thickening/scarring of connective tissue) within the corpora. Both these changes are associated with veno-occlusive dysfunction i.e. blood leaks out of the veins in the penis too fast, decreasing blood pressure and thus interfering with achieving or maintaining an erection (Eardley, 1999). As a result, the arterial size hypothesis posits that ED be considered a marker for life-threatening conditions such as hypertension and hypercholesterolemia (Edwards et al, 2005).

Other vasculogenic causes of ED include, for example, arterial occlusion of the common penile artery in men who have sustained blunt pelvic or perineal trauma (e.g., from bicycling accidents)

(Levine et al, 1990). According to Lue (2000), veno-occlusive dysfunction, or failure of the veins to close during an erection, can cause ED through the formation of large venous channels draining the corpora cavernosa, degenerative changes to the tunica albuginea (as a result of Peyronie's disease, old age, or diabetes mellitus) or traumatic injury (penile fracture), structural alterations of the cavernous smooth muscle and endothelium, poor relaxation of trabecular smooth muscle (in anxious men with excessive adrenergic tone), and shunts acquired as a result of operative correction of priapism (Lue, 2000).

Table 4: Causes of Vasculogenic ED

Type of Condition	Factors
Arterial disorders	• Pelvic fracture associated arterial injury • Radiotherapy to pelvic malignancy • Aorto-iliac surgery
Abnormal venous channels	• Primary (congenital) • Following surgery for priapism • Following repeated urethral surgery
Failure of veno-occlusive mechanism	• Abnormal tunical function (e.g. due to aging, Peyronie's) • Reduced or abnormal smooth muscle (e.g. due to aging, renal failure)

Note: Adapted from Eardley, (2002)

1.4.3 Psychogenic ED

Psychogenic ED has been defined as the persistent inability to achieve and maintain an erection satisfactorily for sexual performance, owing predominantly and exclusively to psychological or interpersonal factors (Lizza & Rosen, 1999). A variety of factors can contribute to psychogenic ED, which can be divided into three groups; predisposing, precipitating and maintaining factors (Table 5) (Eardley, 2002). Epidemiologic studies have estimated that approximately 40% of men are afflicted by ED that is exclusively psychogenic in nature (Feldman et al, 1994; Caspari et al,

1999) this rate has been reported to be as high as 70% in men under 40 years (Karadeniz et al, 2004; Caskurlu et al, 2004).

Table 5: Predisposing, precipitating and maintaining factors

Factors contributing to psychogenic ED	
Predisposing factors	• Educational issues (e.g. poor sexual education) • Cultural issues (e.g. restricted upbringing) • Traumatic sexual experience • Lifestyle issues (e.g. marital, financial stress)
Precipitating factors	• Organic disorders • Extra-marital affairs • Unreasonable expectations • Depression and anxiety • Loss of partner (e.g. 'Widower's syndrome')
Maintaining factors	• Performance related anxiety • Diminished attraction to partner • Educational issues (e.g. poor sexual education) • Fear of intimacy

Note: Adapted from Eardley (2002)

1.4.4 Endocrine mechanisms for ED

Endocrine causes of ED include hypogonadism, diabetes mellitus, and thyroid dysfunction (Walczak et al, 2002). Endocrine disease frequently interrupts sexual function and sexual dysfunction potentially signals serious endocrine disease (Bhasin et al, 2007). Accurate prevalence rates of endocrine disorders in patients with sexual dysfunction from random, population-based samples have not been established and most reported data have been derived from selected clinic populations (Bhasin et al, 2007). However, a recent systematic review and meta-analysis, which included 145 studies, investigated the prevalence of ED in men with diabetes mellitus and reported a prevalence of 52.5% (Kouidrat et al, 2017).

Testosterone is essential to normal male sexual function, having an important part to play in both sexual drive and penile erections (Eardley, 2002). Androgens, such as testosterone, influence the growth and development of the male reproductive tract as well as secondary sex characteristics such as libido and sexual behaviour (Dean & Lue, 2005). Causes of reduced serum testosterone can essentially be classified into primary hypogonadism (where the disease is testicular) and hypogonadotropic hypogonadism, where the primary disease affects the pituitary or the hypothalamus (Eardley, 2002). Testosterone deficiency or hypogonadism has an effect on libido and less of a marked effect upon erectile function (Shamloul & Ghanem, 2013).

Veronelli et al (2006), explored the prevalence of ED in individuals affected by thyroid disorders such as hypothyroidism and hyperthyroidism compared to control subjects as well as patients at risk for ED as a result of obesity, diabetes mellitus, and the ageing process. ED was more prevalent in obese subjects (42%) and in patients affected by thyroid diseases (59%), than in controls (30%). In addition, ED was less prevalent in those with type 2 diabetes mellitus (81%).

1.4.5 Iatrogenic ED

A large number of drugs can impair sexual function and affect erectile function (Table 6). Antihypertensive and psychotropic drugs are the most prevalent drug classes involved in the development of ED (Outhoff, 2009).

Table 6: Common therapeutic and recreational drugs and their effects upon erectile function

Type of drug	Drug/class of drug	Effect
Major tranquillisers	Thioridazine	• Ejaculatory dysfunction
	Phenothiazines	• ED, loss of libido, ejaculatory dysfunction and priapism
	Butyrophenones	• ED and painful ejaculation
Antidepressants	Selective serotonin reuptake inhibitors	• Ejaculatory dysfunction
	Tricyclic antidepressants	• ED and loss of libido
Endocrine drugs	Steroidal antiandrogens e.g. cyproterone	• ED and loss of libido

Type of drug	Drug/class of drug	Effect
Antihypertensives	LHRH analogues	● ED and loss of libido
	Oestrogens	● ED and loss of libido
	Diuretics	● ED
	Adrenoceptor blockers	● ED
	Centrally acting agents e.g. α -methyl DOPA α -blockers	● ED, loss of libido, ● Ejaculatory dysfunction ● Retrograde ejaculation
Others	Cimetidine	● ED and loss of libido
	Digoxin	● ED
	Metoclopramide	● ED and loss of libido
Recreational Drugs	Phenytoin, carbamazepine	● ED and loss of libido
	Alcohol	● ED, arousal disorders, ejaculatory and orgasmic dysfunction
	Marijuana	● ED
	Amphetamine	● Loss of libido and ejaculatory dysfunction
	Opiates	● ED and loss of libido
	Cocaine	● ED
	Anabolic steroids	● ED and loss of libido

Note: Adapted from Eardley, (2002)

In relation to psychotropic drugs, the prevalence of ED for individuals taking antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) is estimated to be in the region of 30 to 50% and is a dose-related effect (Williams et al, 2006). However, establishing prevalence rates in this population can be difficult due to confounding factors such as the effects of mental illness itself, co-morbidities and cultural influences such as the expectations people have of their sexual performance as well as their willingness to discuss such issues with a physician which are suggested as potentially varying widely between different cultures (Outhoff, 2009; Montgomery et al, 2002).

Anti-hypertensive medication has the potential to cause/exacerbate ED by lowering blood pressure (Peate, 2007). Thiazide and thiazide-like diuretics, followed by β blockers have been shown to be most commonly associated with ED, however, α blockers, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are associated with having less of an effect on ED (Sica, 2004; Thomas et al, 2003). For example, in relation to diuretics, a prospective trial carried out on the general population found that using diuretics was associated with an increased risk of developing ED (RR = 1.3, CI 0.7-2.4) (Shiri et al, 2007). Similarly, a meta-analysis of 35,000 patients indicated that a significant risk of developing sexual dysfunction existed for patients using beta-blockers when compared to those taking a placebo, where the authors report that beta-blockers were associated with a small, significant annual increase in risk of reported sexual dysfunction (5 of 1000 patients, 95% CI 2-8) (Ko et al, 2002). However, the picture is not conclusive and it has been suggested that recent randomised, prospective trials have failed to confirm any negative effects of beta-blockers on ED (Baumhäkel et al, 2008). Further, 3rd generation beta-blockers such as nebivolol have been associated with improvements to erectile function. For example, hypertensive patients treated with atenolol, metoprolol or bisoprolol when switched to nebivolol (which has nitric oxide mediated vasodilatory properties) showed a 69% improvement in erectile function (Doulas et al, 2006).

1.4.6 Cellular causes of ED

Smooth muscle cells and endothelial cells are central to a penile erection. The vascular endothelial cells line the trabecular spaces of the cavernosal sinusoids and release a variety of vasoactive chemicals which control smooth muscle tone within the penis (Figure 3).

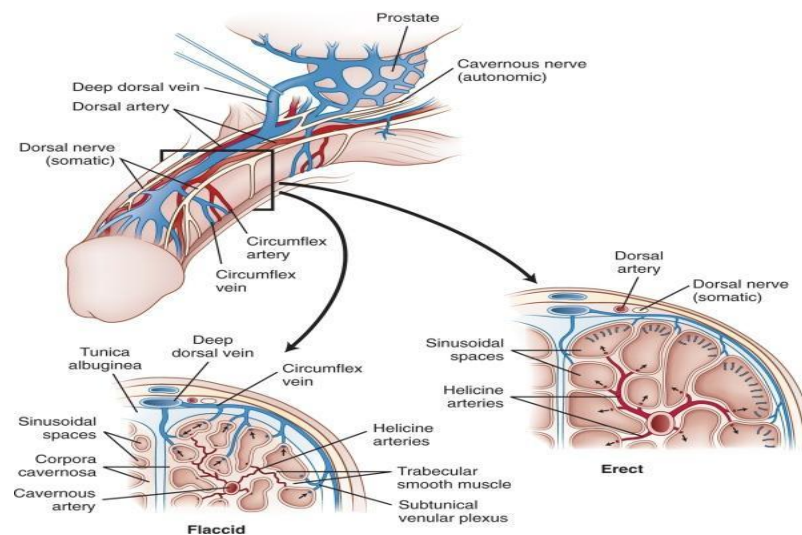


Figure 3: Penile anatomy (Nunes & Webb, 2012 p4)

The most important of these is nitrogen oxide (Eardley, 2002). Diseases such as diabetes mellitus can damage the endothelium and impair the vascular response of the penis. Diabetes causes structural changes in the endothelium which are accompanied by functional changes culminating in impaired smooth muscle relaxation (Cartledge et al, 2001; National Institute for health and Care Excellence [NICE], 2019). Atherosclerosis and aging can result in reduced penile smooth muscle, while renal failure can result in smooth muscle dysfunction. Malfunctions in smooth muscle can cause incomplete arterial dilatation, as a result, cavernosal relaxation fails to occur and the veno-occlusive mechanism fails (Eardley, 2002). Finally, if left untreated, ischaemic priapism, which is caused as the result of blood not being able to leave the penis, can results in smooth muscle necrosis followed by the development of fibrosis which manifests as ED (Ralph et al, 2009). The extent to which cellular ED is prevalent in comparison to other ED aetiologies is unclear.

1.5 Diagnosis of ED

The British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men (Hackett et al, 2018) suggests that initial assessment of ED should include the following:

- Original precipitating factor or factors (if identified)
- Predisposing factors (if identified)
- Maintaining factors (if identified)
- Any subsequent investigations
- Treatment interventions along with the response achieved
- An expression of tumescence and rigidity with quality of morning awakening erections, and spontaneous, masturbatory, or partner-related activity erections
- Sexual desire, ejaculatory timing, control, and orgasmic dysfunction
- Previous erectile capacity
- Issues around any sexual aversion or sexual pain
- Partner issues, e.g., low sexual desire, menopause, or gynaecological pain (Hackett et al, 2018)

The National Institute for Health and Care Excellence (NICE) suggest that the assessment of a man with ED should include the taking of a patient's history in terms of present and past erection quality, lifestyle (alcohol, smoking, illicit drug use) and previous treatments that have been tried (NICE, 2019). A focused physical examination including weight, waist circumference, heart rate and blood pressure, examination of genitalia may be required as well as subsequent investigations of serum lipid and fasting glucose levels (to calculate 10 year cardiovascular risk) and serum free testosterone. Both impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) are considered risk factors for diabetes mellitus (DM) and CVD where IFG is associated with higher risk and severe ED subsequently having a negative impact on both ones sexual life and overall health (Corona et al, 2012).

Diagnosing ED can involve a variety of diagnostic phases depending on the aetiology of the patient's ED (

Figure 4). The extent to which comorbidities such as atherosclerosis or diabetes may be influencing ED and whether there is any underlying cardiovascular condition also need to be ascertained. An investigation of the medications an individual may be taking may also reveal which, if any, are potentially contributing to ED. Ascertaining the above details will help to build a picture of the extent to which organic or psychogenic factors are involved (Shamloul, 2013; Hatzichristou et al, 2010).

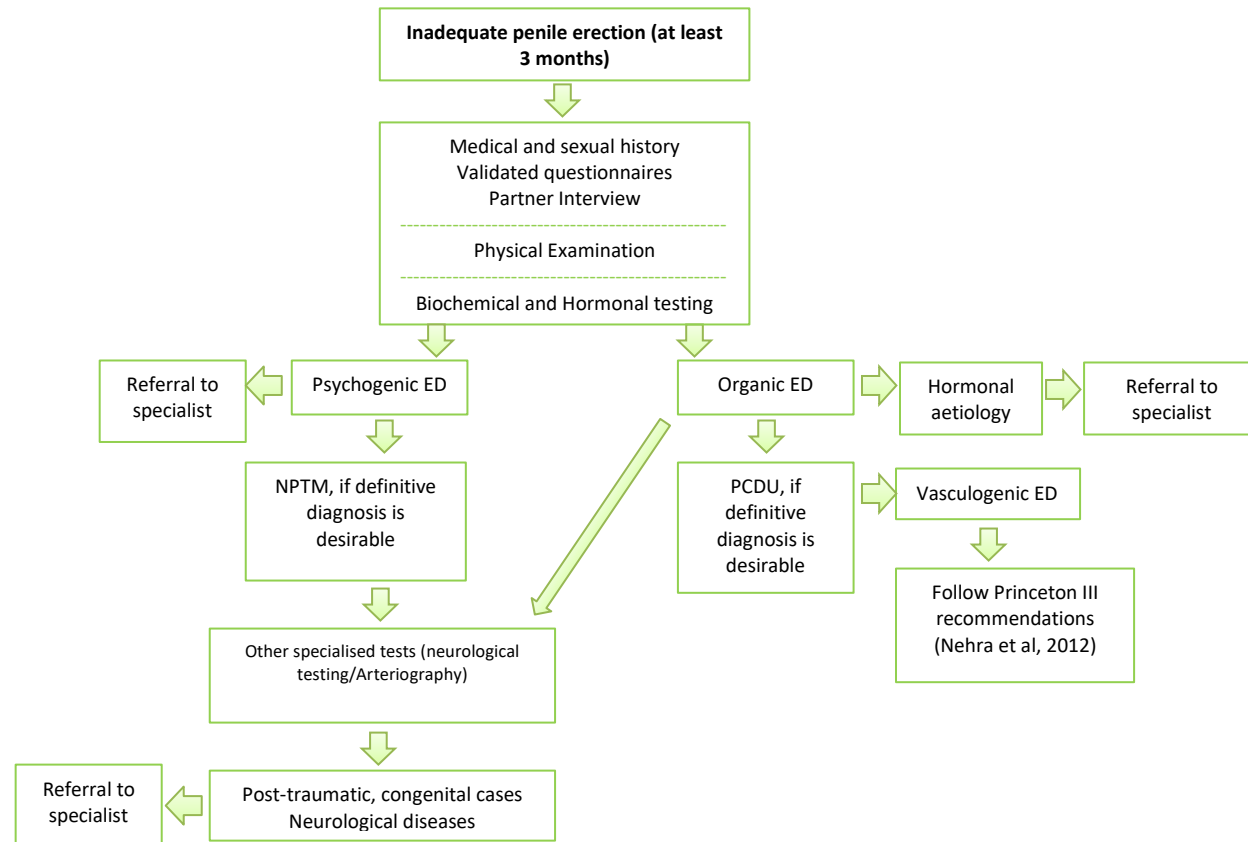


Figure 4: Stepwise algorithm for the initial assessment of men with ED (adapted from: Viigimaa, 2015)

Note: Nocturnal Penile Tumescence monitoring (NPTM). Penile Colour Doppler Ultrasound (PCDU)

1.5.1 Standardised questionnaires

Part of the diagnostic process can involve standardised questionnaires to both diagnose as well as establish the severity of ED (Viigimaa et al, 2015). The International Index of Erectile Dysfunction (IIEF) (Rosen et al, 1997) is a widely used psychometrically valid, reliable self-report tool for the evaluation of male sexual function (Rosen et al, 1997; Rosen et al, 2002). The IIEF consists of 15 items which correspond to five domains; erectile function (six items), orgasmic function (two items), sexual desire (two items), intercourse satisfaction (three items), and overall satisfaction (two items).

(Rosen et al, 2002). The IIEF has high sensitivity for detecting real treatment effects and has been adopted as the gold standard treatment outcome measure for clinical trials in ED (Rosen et al, 2002). Men complete the questionnaire by responding to each of the 15 items using a 5-point Likert scale. The total score is calculated and denotes the following ED classifications: no ED (IIEF total score, 26 to 30), mild (score 17 to 25), moderate (score 11 to 16), or severe (score 0 to 10) ED (Bal et al, 2007). The IIEF was originally designed for use in clinical trials and required simplification and abbreviation to be used as a diagnostic measure in clinical practice, which was the basis for the development of an abridged five-item version known as the Sexual Health Inventory for Men (SHIM) (Cappelleri et al, 2005).

The SHIM is an easily administered, validated, self-report diagnostic tool (Rosen et al, 1999). Each item of the SHIM is scored on a 5-point Likert scale. The total score is calculated and relates to five grades of severity: no ED (SHIM total score, 22 – 25), mild ED (17 – 21), mild to moderate (12 – 16), moderate (8 – 11), and severe ED (5 – 7) (59). Both the SHIM and the IIEF have been

translated into more than 30 languages, where the SHIM is widely used as a screening measure in clinical practice settings around the world.

1.5.2 Physiological testing

The use of biochemical and hormonal testing may be necessary for some patients and will depend on information ascertained from their medical history. Testing at this level enables the determination of the type of dysfunction and whether there is a need for any additional specialised testing; such as penile or pelvic blood flow, nocturnal penile tumescence and other blood tests (Viigimaa, 2015). It is suggested that all patients should undergo a fasting glucose test (to investigate for diabetes or to monitor diabetes) and lipid profile (to investigate abnormalities in lipids, such as cholesterol and triglycerides), as well as tests for testosterone deficiency which has a significant relationship with the presence of vasculogenic ED (Corona & Maggi, 2010; Sansone et al, 2014; Corona et al, 2008a)

The colour Doppler ultrasound is a specialised test and one which has been described as the cornerstone of the diagnostic workup for individuals with vasculogenic ED (Viigimaa, 2015). The test assesses cavernous artery inflow, which is a deep artery to the penis, as well as venous leakage, which occurs when penile veins are not able to constrict properly during an erection. Other tests include neurological testing which can be used to test somatic pathways (Shamloul & Ghanem, 2013); however such tests tend not to add any further details over and above the medical history, self-report questionnaires, physical examination and laboratory testing (Montorsi et al, 2010).

1.6 Prevalence of ED

A recent systematic review which focussed on population-based studies investigating the prevalence of ED indicated prevalence to be between 3 and 76.5% (Kessler et al, 2019). A previous

literature review carried out by the International Consultation Committee for Sexual Medicine, which drew on epidemiological studies from the USA, Europe, Australia, Canada, Iran, Morocco and Puerto Rico, reported the prevalence of ED to be 1–10% in men younger than 40 years, 2%–9% in men aged between 40 and 49 years, which increases to 20–40% in men aged 60–69 years and 50%–100% in men older than 70 years (Lewis et al, 2010). One study that used existing rates of ED prevalence to project future prevalence suggest that by the year 2025 there will be approximately 322 million men world-wide with the condition, which is a 152 million increase from 1995 (Aytac et al, 1999).

The most common organic cause of ED is vasculogenic, therefore, a higher prevalence of ED is evident in those suffering with vascular diseases. In a recent systematic review, men with ED were reported to have an increased risk of CVD mortality ([OR 1.43 (95% CI 1.00–2.05)]) (Kessler et al, 2019). For those suffering with CAD, ED prevalence rates range from 47–75% (Montorsi et al, 2003; Jackson et al, 2010; Montorsi et al, 2006), which has largely been attributed to the effects of atherosclerosis (Johannes et al, 2000). In patients with essential hypertension (where the cause of hypertension is unknown), the prevalence of ED in those untreated ranges between 17–79%. For men receiving blood pressure-lowering treatment, ED prevalence is between 25 – 72% and for normotensive men between 7 – 24% (Doumas et al, 2006; Bulpitt et al, 1976; Croog et al, 1988; Bener et al, 2007; Baumhäkel et al, 2008).

1.7 Impact of erectile dysfunction

1.7.1 Quality of Life

Both clinical and epidemiological studies have indicated a strong link between ED and QoL and it has been shown that men with ED have significantly poorer QoL than age-matched men from the general population (Litwin, 1999; Guest & Gupta, 2002). ED can lead to anxiety, relationship strain, loss of self-esteem and self-confidence (Althof, 2002a; Jonler, 1995, Taylor, 1997), which is associated with a profound negative impact on both the man as well as his partner (McMahon, 2019). Finally, ED has been shown to contribute significantly to 20% of relationship breakdowns (Taylor, 1997).

1.8 Help-seeking

Research has shown that a large proportion of individuals do not seek help for sexual problems in general. In a study consisting of 742 male participants, 45.2% did not seek any help at all, whether from a partner, friend, the internet or from a health care professional (HCP) for their sexual problems (Laumann et al, 2009). In fact, 75.7% of men had not sought help from a HCP. The most common reasons for not consulting a doctor included; believing that the problem was not a serious one, waiting for the problem to go away and belief that it was a normal part of the aging process. Less than 5% reported embarrassment as a reason for not seeking any help (Laumann et al, 2009). However, in one research study, in 218 men with ED, 74% reported embarrassment as a reason for not wanting to discuss the issue with their urologist. Twelve percent believed it was part of the natural aging process and 5% did not believe the problem was worthy of attention. Of the men who had not spoken to a HCP about their condition, 82% reported that they would have liked their primary-care physician to have initiated a discussion about ED during their routine visit (Baldwin et al, 2003). It is suggested that because of individual reluctance and cultural issues associated with ED, it is likely that many patients remain

undiagnosed and untreated, therefore, prevalence is likely to be underestimated (Basu & Ryder, 2004).

When men do seek help for ED there are many treatments available. It is suggested that, similar to many medical conditions, lifestyle modifications can have a positive impact on ED. However, men presenting with ED want their HCP to help with measures that can have an immediate impact. The options for management beyond behaviour modification include phosphodiesterase type 5 inhibitors (PDE5I), Intracavernosal vasoactive drug injection therapy (ICI), Intraurethral suppositories, vacuum erection devices (VED), penile prosthesis as well as psychosexual counselling. These will be considered in more detail in the following chapter (Chapter 2).

2 Treatment for Erectile Dysfunction and its Utilisation

2.1 Chapter Overview

This chapter will consider what treatments are available for men who suffer with ED and will also consider what barriers exist in relation to using such treatment. Therefore the main areas of focus will be:

- Pharmacological and non-pharmacological treatment for ED
- Adherence, persistence and discontinuation terminology and their application to ED treatment utilisation
- Intention and unintentional non-adherence
- Barriers to medication adherence in relation to ED

2.2 Primary Care Management

The British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men (Hackett et al, 2018) suggests that the primary goal in the management of ED is enabling the individual or couple to enjoy a satisfactory sexual experience. The following steps are integral to this aim;

- Identifying and treating any curable causes of ED.
- Initiating lifestyle change and risk-factor modification.
- Providing education and counselling to patients and their partners.

NICE guidelines for the treatment of ED (NICE, 2019) suggest starting with improvements in lifestyle measures such as weight loss, smoking cessation, reducing alcohol consumption as well as drug treatment. Overall, NHS expenditure on ED is approximately £144m per year (Department of Health [DoH], 2014). Prescribing treatment on the NHS to patients with ED has

been modified in recent years. Figure 5 provides an algorithm for clinical decision making with regards to prescribing treatment.

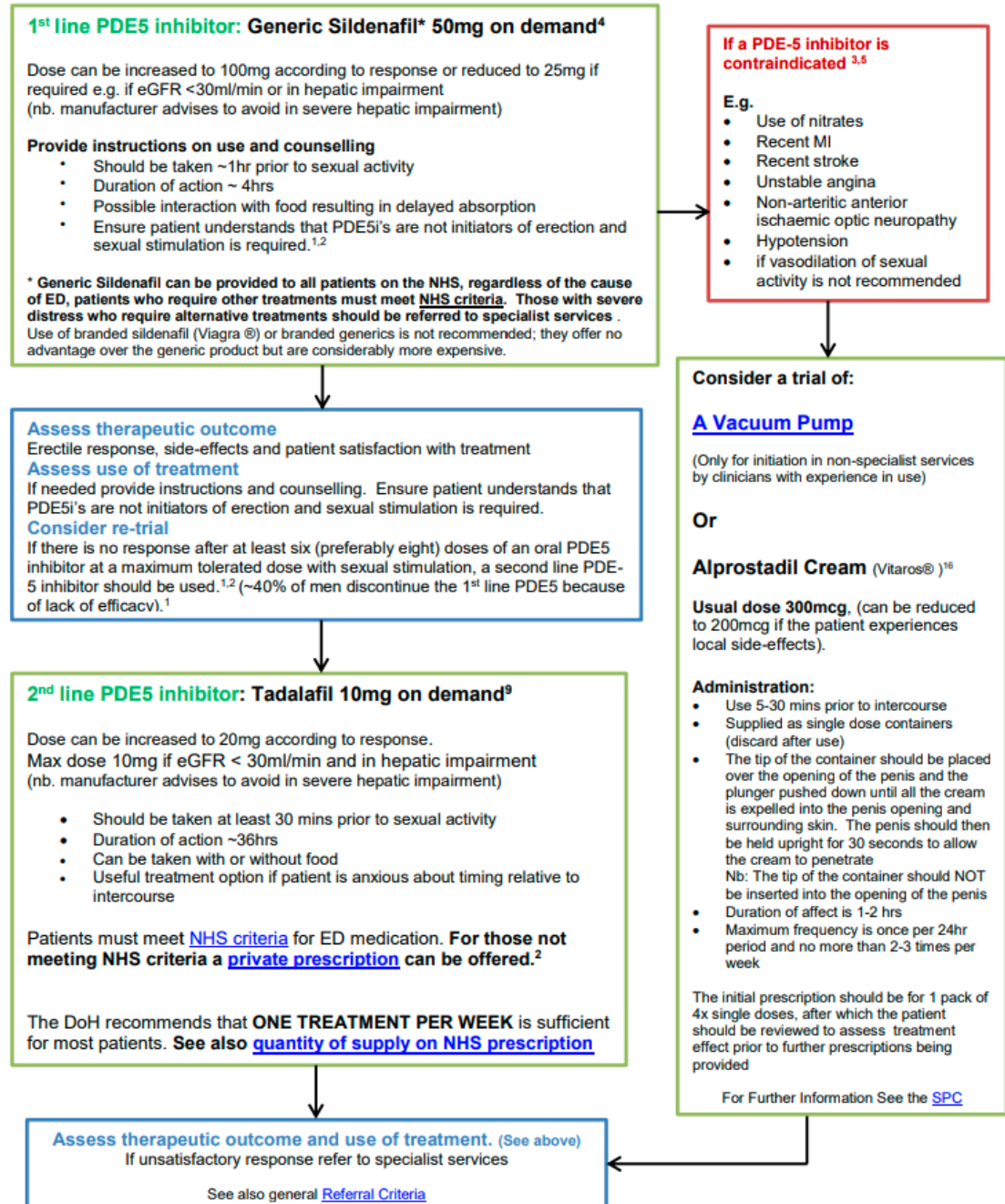


Figure 5: Erectile Dysfunction Guidance (McKernan, 2015)

Available treatments, as indicated in Table 7 can be considered as pharmacological as well as non-pharmacological. These will be considered in more detail in the following sections.

2.2.1 Pharmacological treatments

Phosphodiesterase type 5 inhibitors (PDE5Is)

The first-line drug treatment for ED is Phosphodiesterase type 5 inhibitors (PDE5Is) and constitute the most common pharmacological treatment for the condition (Table 7). Usually a low dose is titrated up until it is effective. The individual will try 8 doses with sexual stimulation before being classified as a non-responder (NICE, 2019). The Department of Health (DoH) recommends that consideration of the frequency of treatment needs to take place on a case-by-case basis. The guidelines were however based on the sexual attitudes and lifestyle survey (Johnson et al, 1994), which indicates that the average frequency of sexual intercourse in the 40-60 age range is once a week, therefore the DoH advises doctors to prescribe using this as a guideline (NHS Executive, 1999).

When administered, PDE5Is are rapidly absorbed after oral administration (Corona et al, 2011). However, they need to be used in conjunction with mental and physical sexual stimulation to work effectively (Tomlinson, 2016). PDE5Is differ with respect to the duration of time to onset, currently there are four types of PDE5I: tadalafil, sildenafil, avanafil and vardenafil (Steggall et al, 2021). All of the PDE5Is are available 'on-demand' (taken prior to a sexual encounter) except for tadalafil once-daily which was introduced in 2009 available in 2.5mg and 5mg strengths. It is recommended that the choice of an appropriate drug should be based on both the patient and his partners' preference, whilst being guided by an appropriate HCP (Hatzimouratidis & Hatzichristou, 2005) Clinical trials data illustrate that PDE5Is have a high level of efficacy and have shown, for example, that patients using sildenafil citrate when compared to a placebo, show higher rates of intercourse attempts, which in one study were 83% vs 45% respectively (Fink, 2002).

There are a number of treatment options other than oral medications, which include intracavernosal injections, intra-urethral treatment (pellets as well as cream i.e. Vitaros) and vacuum pumps (Table 7). Depending upon comorbidities, treatments vary. For example, a man with CVD prescribed nitrates (a vasodilatory drug to treat angina) would be unable to take PDE5Is due to the risks of profound hypotension (Corona et al, 2008b) and therefore would be prescribed an alternative treatment. It is estimated that approximately 25-50% of patients do not respond to PDE5Is within 12 months of prescription and therefore second line treatments are available in such instances (Porst et al, 2012).

Intracavernosal vasoactive drug injection therapy (ICI)

Some patients experience medical contraindications with PDE5I therapy, such as concurrent nitrate use, where PDE5I use may cause a sudden decrease in systemic blood pressure. Others cannot tolerate the side effects of the medication such as headaches, dizziness, and vision and hearing changes. In addition, 11%–44% of patients have been found to be therapeutic non-responders to PDE5Is (Sommer, 2004). Therefore, second line treatments are available which include intracavernosal vasoactive drug injection therapy (ICI), which is an on-demand treatment which involves self-injecting the penis with vasodilators such as papaverine hydrochloride, phentolamine mesylate, alpha-1, alpha-2 selective adrenergic receptor antagonist or alprostadil (brand name: Caverject), a synthetic prostaglandin E1 (PGE1), or a combination of these (Costa, 2012).

Intraurethral suppository (US)

Another on demand treatment which involves a different method of delivering alprostadil is the use of an intraurethral suppository (US) such as Medicated Urethral System for Erections (MUSE®), which involves the patient inserting a pellet of alprostadil into the urethra approximately 10 minutes before sexual intercourse. The patient is required to use an applicator

to insert the pellet into the urethra. When the pellet is in place it is dissolved and absorbed by the urethral mucosa (the innermost layer of the urethra) and then enters the corpora (cavernous body of the penis) (Peate, 2007).

Non-pharmacological treatments

Non-pharmacological interventions include vacuum devices, penile implants and pelvic floor retraining as well as psychosexual counselling (Steggall, 2021).

Vacuum Erection Devices

The vacuum erection device (VED) draws blood into the penis by creating a vacuum, when the blood is trapped in the intra and extra corporal compartments a constriction ring is used to maintain the effect (Peate, 2007), A VED requires manual application approximately 5-10 minutes prior to sexual intercourse.

Pelvic floor retraining

Organic causes of ED generally point to neurologic, vascular, or endocrine systems. Pelvic floor muscle function may be involved in the enhancement of blood flow to the penis. Exercises to strengthen muscles involved in facilitating and maintaining the erection can help to reduce blood from escaping (venous leakage) from the penis. Research has demonstrated that pelvic floor retraining has been utilised successfully in comparison to for example surgery for venous leakage, where in a randomised comparison of the two treatment options, 42% of participants were sufficiently satisfied with the outcome of pelvic floor retraining and subsequently refused surgery (Claes & Baert, 1993).

Surgery

When all other alternatives for ED treatment have been tried and exhausted, surgical treatment, such as penile implants, can be an option; however, the incidence of morbidity and complications is significantly greater than other treatment modalities (Carson et al, 2002). Penile implants provide penile rigidity and an erectile size that stimulates a normal physiological erectile state which can be activated prior to sexual intercourse (Woodworth et al, 1991). However, the nature of such implants carries the possibility of infection and mechanical failure (Peate, 2007).

Psychosexual Therapy

Psychosexual therapy is tailored to the individual patient depending on their needs. This could be related to difficulties with the relationship with their partner, problems with intimacy and lack of sexual experience which may serve to increase anxiety which can manifest as ED. As a result psychosexual treatments range from simple sex education to attempting to improve communication between the man and his partner as well as cognitive and behavioural therapy. Psychosexual therapy is often combined with pharmacotherapy for ED (McMahon, 2014). It has been indicated that psychosexual therapy can be effective in the short term but less effective over a longer time period (Melnik et al 2011).

Table 7: Commonly used treatment options for ED

Treatment		Dosage guide	Time to onset (hours)	Contraindications	Mode of action	Mode of action
Avanafil (Spedra)		100 mg initially, then dose adjust depending on response. Range is 50–200 mg as needed	$\frac{1}{4}$	Concurrent use of nitrates; recent myocardial infarction, unstable angina or stroke; ischaemic optic neuropathy, hypotension; do not use with nicorandil (lowers blood pressure), some antibiotics, and grapefruit juice		Phosphodiesterase type-5 inhibitor, increases blood flow to penis
Sildenafil (Viagra)/sildenafil	citrate	25–100 mg, need 6–10 doses before benefits seen; regular dosing helps to reduce performance anxiety	1	As above		As above
Tadalafil (Cialis)		10–20 mg, need 6–10 doses before benefits seen; regular dosing helps to reduce performance anxiety; Tadalafil 2.5–5 mg daily dosing (takes around seven days to	$\frac{1}{2}$ to 2	As above		As above

	build up a therapeutic level)				
Vardenafil (Levitra®)	5–20 mg, need 6–10 doses before benefits seen; regular dosing helps to reduce performance anxiety	1/3	As above		As above
Medicated Urethral System for Erections (MUSE®): intraurethral alprostadil (prostaglandin E1)	250–1000 µg, essential to massage the intra-urethral medication for up to 10 minutes	1/3	Sickle cell disease or bleeding disorders		Increases blood flow to penis
Vitaros (contains alprostadil)	3 mg/g applied to the tip of the penis	Takes 5–30 mins to work	As above		As above
Intracavernosal injection of alprostadil (prostaglandin E1) – Caverject®, Caverject® dual chamber or Viridal Duo®	2.5–60 µg essential to provide full teaching of injection technique and support/discuss patient anxieties	¼	Warfarin, bleeding disorders		Increases blood flow to penis
Vacuum devices	Important to teach correct technique and reinforce that the vacuum needs to be created slowly	1/3	None, but must be competent to remember to remove the constriction ring within 30 minutes		Non-pharmacological, drawing blood into the corpus cavernosum under pressure. Blood held in

						place by constriction band
Surgery (protheses)	Various prostheses available	¼	Depends on fitness for surgery			Prosthesis – artificial implants replace the corpus cavernosum. Erection then possible ‘on demand’
Psychosexual therapy (behavioural programme with counselling of underlying issues)	Weekly or regular attendance with ‘homework’	n/a	Lack of acceptance, culturally unacceptable			Breaks pattern of failure, removes anxiety and restores confidence

Note: Adapted from Steggall et al, 2021

Prescription guidelines

Prescription guidelines denote that on-demand oral PDE5Is are likely prescribed for most men, whereas, once daily treatment is normally reserved for men who engage in frequent intercourse or regard sexual intercourse spontaneity as a key treatment goal (McMahon, 2019). In addition, although the DoH uses the average frequency of sexual intercourse to be once a week based on the sexual attitudes and lifestyle survey (Johnson et al, 1994), it is suggested that GPs, in exercising their clinical judgement, may also consider it appropriate to prescribe more than one treatment a week (Hackett et al, 2008). In addition to the treatment routes available to patients within the NHS, in November 2017, Viagra Connect was made available without prescription over the counter from pharmacies in the UK. It has been suggested that all men, irrespective of known or unknown comorbidities should be directed to pay for Viagra Connect tablets from a pharmacy if they are willing and able (Medicines and Healthcare Products Regulatory Agency [MHRA], 2017; Taylor et al, 2019). However, this approach has been criticised for potentially undermining 25 years of research which has established the foundations regarding ED as an independent CVD risk factor necessitating comprehensive investigation and management within primary care (Hackett et al, 2020).

As previously indicated, PDE5Is are considered the frontline treatment for ED. It has been suggested that PDE5Is are strongly preferred over other ED treatment options (Hackett, 2005), however, adherence to PDE5Is is considered suboptimal (Conaglen & Conaglen, 2012). In order to consider the problem of adherence to ED treatments, first we will consider the term 'adherence', as well as other terms used to describe treatment utilisation in more detail in the following sections.

2.3 Treatment Adherence

2.3.1 Terminology: Compliance, Adherence, Persistence and Concordance

Terminology to describe a patient's medication-taking behaviour, has changed over time (Cramer et al, 2008). This change relates to a shift from doctor-centred care to patient-centred care. In conjunction, the terminology has evolved to reflect this (Edelmann, 2000). The term 'patient compliance' was introduced in 1975 as an official Medical Subject Heading (MeSH) in the US National Library of Medicine (Blackwell, 1992; 1998). The term has evoked criticism due to the implication that the patient is to passively follow the doctor's orders (Stimson, 1974). Non-compliance is therefore the failure or refusal to comply with HCPs instructions, which implies disobedience on the part of the patient (Vermeire et al, 2001). A term which is often considered an evolution of the term compliance is the term 'adherence', which has been defined by the World Health Organisation (WHO) as;

'the extent to which a person's behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider' (WHO, 2003).

The term was introduced, in an attempt to reduce the amount of power HCPs are attributed, in their relationships with patients (Vermeire et al, 2001) and implies that HCPs have a responsibility to form a therapeutic relationship with their patients. Despite intending this term to be less judgemental than non-compliance, the terms non-adherence and poor adherence are still loaded with the inferences that patients are not taking their medicine according to the prescribed regimen (Howard, 2008). Essentially, poor adherence still implies that HCPs hold greater power than patients with regards to making decisions that could affect patients' lives (Kyngäs et al, 2000).

Generally, adherence is accepted as a less judgemental term than compliance, yet it still holds implicit assumptions of practitioner power and their better judgement. Subsequently, in 1997, the Royal pharmaceutical Society of Great Britain (RPSoGB) recommended a new term, 'concordance' (RPSGB, 1997), as the most appropriate term to describe the relationship between prescriber and patient. The term concordance, which is a relatively recent term and predominantly used in the UK, differs from previous terms by relating to patients' behaviour and describing the process and outcome of a medical consultation (Horne et al, 2005). The term concordance is the subject of much debate and is still regarded as a relatively novel concept. It was originally defined as:

"a new approach to the prescribing and taking of medicines. It is an agreement reached after negotiation between a patient and a health care professional that respects the beliefs and wishes of the patient in determining whether, when and how medicines are to be taken. Although reciprocal, this is an alliance in which the health care professionals recognise the primacy of the patient's decisions about taking the recommended medications" (Horne et al, 2005 p33).

Other terms relating to the notion of adherence include the term 'discontinuation' which refers to the abandonment of treatment and is defined as:

"the failure to enter a treatment programme, premature termination of therapy and incomplete implementation of instructions (including prescriptions)" (Blackwell, 1976 p153).

Similarly, the term non-persistence, a term that is usually used in tandem with non-adherence is also used in research and refers to patients who start taking their medicine and then for some reason cease taking them without advice from their HCP. Persistence, therefore, has been defined as:

“the extent to which a patient continues to follow treatment advice without a break and without stopping” (Cramer, 2008).

To summarise, patients have been considered as either submitting (compliance) or agreeing (adherence) to decisions made by HCPs. Concordance considers both parties as *equal partners* in relation to health care decision making. The term, therefore, acknowledges that noncompliance can be a rational response to a patient’s personal perception of the illness and treatment.

It has been suggested that there are essentially two lenses through which medication taking is considered (Horne et al, 2006). The first can be considered the biopsychosocial or the ‘scientific/clinical’ approach, which predominantly focuses on clinical aspects and involves categorising patient behaviour i.e. what patients *actually do*, with prescribed medication and the extent to which this reflects what they were advised to do by the prescriber. The second is considered the ‘normative’ agenda, which has a more psychosocial focus and leans towards the interaction between patient and healthcare provider, focussing on understanding what is *good and right* about the prescribing and taking of medication. The term compliance reflects the first agenda by attempting to ascertain the degree to which a patient’s behaviour matches the prescriber’s advice. However, it neglects the normative agenda and most objections to the term seem to stem from this (Horne et al, 2006). The term adherence seeks to address the normative agenda through its recognition that the patient is free to decide whether to adhere to the HCPs

recommendations; developing the definition of compliance by emphasising the need for agreement. Concordance relates to both the process of prescribing consultations (e.g. considering patients' views and negotiating treatment options) and their outcome (e.g. shared agreement) making a valuable contribution to the debate and highlighting that good prescribing should entail a process of negotiation between patient and practitioner.

2.3.2 Terminology and Treatment for Erectile Dysfunction

Although the above terms encompass, to one degree or another, aspects of using treatment for ED, it is important to highlight the difficulties of applying these terms to ED treatment utilisation. Most ED treatments are taken 'on-demand' (PRN) i.e. taken when needed, although once daily (OaD) ED treatments do exist. In relation to PRN ED treatments there is no regimen that has to be followed in order to prevent the possibility of ill-health. Therefore, a specified or recommended regimen against which to measure usage patterns i.e. compliance, adherence, concordance or persistence will not necessarily exist. In relation to PDE5Is, for example, the DoH recommend that consideration of the frequency of treatment should take place on a case-by-case basis (NHS Executive, 1999). However, this is guided by the sexual attitudes and lifestyle survey (Johnson et al, 1994), which indicates that the average frequency of sexual intercourse in the 40-60 age range is once a week, therefore the DoH advises doctors to prescribe using this as a guideline. With the difficulty with regards to the appropriateness of terminology to describe the problem of ED treatment utilisation in mind, the following sections will consider non-adherence in general before moving onto consider which potential barriers exist in relation to ED treatment utilisation.

2.3.3 Intentional and Unintentional Non-Adherence

Reasons for non-adherence vary from person to person and it has been suggested that there are as many as 200 factors identified as having the potential to influence adherence (Meichenbaum

& Turk, 1987; Haynes et al, 1976) which stem from the patient, health care provider and health care system (Miller et al, 1997).

At the patient level, non-adherence is largely categorised as either intentional or unintentional (Horne, 1997). The authenticity of these distinctions is supported by a large body of evidence (Wroe, 2002). Intentional non-adherence is understood as a conscious process in which a patient makes an active deliberate choice to miss a dose of their medication (Horne, 1997). On the other hand, unintentional non-adherence is a passive process where specific barriers prohibit adherence in such as forgetfulness or carelessness (Gadkari & McHorney, 2012). Estimates of unintentional non-adherence to medication vary considerably and are reported as ranging from 20% to over 50% (Lowry et al, 2005; Sewitch et al, 2003; Rees et al, 2010; Barber et al 2004; Wray et al, 2006, Julian et al, 2009, Sahm et al, 2009, Daleboudt et al, 2011; Saratsiotou et al; 2011; Unni & Farris, 2011 and Lindquist et al, 2012).

2.3.4 Adherence to ED Treatment

In relation to ED treatment utilisation, successful treatment is important when we consider research that has revealed that treating ED successfully can lead not only to an increase in sexual well-being, but also an increase in overall life satisfaction (Fugl-Meyer et al, 1997). Improvements in psychological status, self-esteem and perceived relationship quality can be achieved by improving sexual function through the use of treatment (Turner et al, 1992; Costa et al, 2013; McCabe et al, 2011; Rosen et al, 2004b; Shabsigh et al, 2001; Williams et al, 1998). In addition, successful ED treatment has been shown to play an important role in adherence to other medications prescribed for comorbid conditions. Research examining men's prescription claims for antihypertensive, oral hypoglycaemic, lipid lowering or antidepressant medication, 12 months before and 12 months after individuals were first prescribed sildenafil citrate for ED

found that in the period after sildenafil citrate was prescribed, adherence to all comorbid medications increased significantly (McLaughlin et al, 2005). This suggests that if ED is managed successfully then there is not only a potential to increase sexual well-being and overall life satisfaction, but also potentially improve the management of other comorbid conditions.

However, despite the various ED treatment options, patient utilisation of ED treatments has been described as sub-optimal, typically involving a pattern of uptake followed by abandonment (Conaglen & Conaglen, 2012). PDE5Is are considered the frontline treatment for ED and it is suggested that they are strongly preferred over other ED treatment options (Hackett, 2005). However, with this in mind, adherence to PDE5Is is still suboptimal (Conaglen & Conaglen, 2012).

Althof (2002b) suggests that the reasons for ED treatment discontinuation can be divided into “absolute” and “relative”. Absolute reasons include, for example: medical problems, lack of efficacy and side-effects. Relative reasons relate to, for example, the effects of the medication being perceived as less than anticipated, a lack of spontaneity, a decrease in libido, a disharmonious relationship with one’s partner as well as comorbidities (Ströberg, 2007; Hackett 2002; Hackett 2005; Pescatori, 2006; Althof, 2002a). Althof (2002b), provides a broad perspective on the issue of non-adherence in relation to ED treatments by suggesting that:

“Discontinuation of treatment may be considered the end result of an extended process that began months before the patient, with or without partner, presented for evaluation”.

Althof (2002b) highlights that clinicians all too often take a limited, organ-focussed view and suggests that giving men firm erections is relatively straightforward in the wake of contemporary ED treatments. However, the issue that is more complicated, as well as being a challenge, is how

to encourage men to make use of treatment regularly for sexual activity. Althof (2002b) suggests that such a constricted view potentially omits the following:

- (1) Patient variables, such as performance anxiety, depression, unrealistic expectations, or unconventional sexual arousal patterns
- (2) Partner variables, such as health status or a disinterest in sexual activity as well as an inability to resume sexual activity if such circumstances have prevailed
- (3) Interpersonal nonsexual variables, such as the quality of the couple's overall relationship
- (4) Interpersonal sexual variables, such as interval of sexual abstinence or sexual scripts (cognitive schema that instruct people how to understand and act in sexual situations)
- (5) Contextual variables, such as current life stresses with finances, children, parents, or occupation

Althof (2002b) also suggests five potential reasons for psychological resistance to treatment that may impact upon discontinuation:

- (1) The length of time the couple were asexual before seeking treatment
- (2) The man's approach to resuming a sexual life with his partner
- (3) The partner's physical and emotional readiness to resume sexual relations
- (4) The meaning for each partner of using a medical intervention to enable intercourse
- (5) The quality of the nonsexual aspects of the relationship

Althof (2002b) has suggested that the most influential ways in which to encourage men to make use of treatment regularly for sexual activity are to address factors relating to the man and his partner (i.e. performance anxiety, depression and a disinterest in sexual activity), interpersonal nonsexual variables (i.e. the quality of the couple's overall relationship), interpersonal sexual

variables (i.e. the interval of sexual abstinence), and contextual variables (i.e. current life stresses with finances, children, parents, or occupation). The prevalence of each factor outlined by Althof (2002b) and their strength in relation to influencing ED treatment utilisation has not been established. Therefore, an exploration of the barriers and enablers individuals may encounter, is considered a necessity in order that it is possible to understand what can be done to address the problem of adherence in this patient population. The concept of adherence is unusual when considered in conjunction with ED, as unlike other conditions, treatments are predominately taken on-demand, the utilisation of which will depend on both the man and his partner which adds the context of treatment use a couple's intimate relationship.

2.3.5 Measuring adherence in ED

Measuring ED treatment utilisation poses a challenge for researchers, particularly because treatments are predominantly PRN, such as tadalafil, which is prescribed for the majority of patients (Hackett, 2005). The recommendations set out by the Department of Health provides a benchmark against which prescribing occurs and is based on the sexual attitudes and lifestyle survey (Johnson et al, 1994), which indicated that the average frequency of sexual intercourse for those 40-60 years old was once a week (NHS Executive, 1999). As a result, the DoH states that '*... one treatment per week will be appropriate for most patients*' (NHS Executive, 1999 p4). However, guidelines around prescribing are flexible and attempt to tailor both the type and dose of ED medication to the man's particular needs. Treatment utilisation, in relation to on-demand treatment will therefore not necessarily have a rigid prescribing regimen against which dosages taken by the patient can be compared.

When researchers are faced with measuring treatment utilisation in an ED population, two problems arise. The first relates to the that outlined above, i.e. the difficulty associated with measuring treatment which is used on-demand and does not have a rigorous treatment regimen

against which patient usage patterns can be contrasted. The second relates to the real-world practicality of measuring treatment utilisation in this population. Currently, there are, for example, a number of validated generic measures of treatment adherence (Garfield et al, 2011), however, to the author's knowledge, there are no specific or tailored measures of ED treatment utilisation.

2.4 Summary

For men, ED is a prevalent sexual problem, associated with reduced QoL. Treatments for ED include pharmacological (i.e. PDE5Is) as well as non-pharmacological interventions (i.e. VEDs). NICE guidelines suggest that attempts to improve erectile function should involve a combination of reducing risk factors and drug treatment. Adherence to pharmacological and non-pharmacological treatments is therefore key to improving erectile function. Contemporary treatment for ED is regarded as highly effective resulting in improved erections indicated by significantly improved scores on standardised questionnaires such as the IIEF, allowing most men with ED to partake in sexual intercourse (Hackett, 2005).

However, the problem of non-adherence is described as difficult to detect by healthcare providers and concealed by patients (Horne et al, 2005). PDE5Is are suggested as being preferred over other ED treatment options (Hackett, 2005), however, adherence in relation to PDE5Is is still suboptimal (Conaglen & Conaglen, 2012) and represents a missed opportunity to experience the positive effects of successful treatment. This includes improvements in quality of life, psychological status, social functioning, self-esteem, social and familial roles, perceived relationship quality and both satisfaction and perception of one's own sex life (Turner et al, 1992; Costa et al, 2013; McCabe et al, 2011; Rosen et al, 2004b; Shabsigh et al, 2001; Williams et al, 1998 and Fugl-Meyer et al, 1997).

The complexity of measuring treatment utilisation in this population has been considered. It has been highlighted that ED has a significant impact on both patients and their partner. Intentional non-adherence highlights the fact that patients' beliefs about their medication can play a big role in their decision about whether to take it. It is now commonly accepted that psychological and social factors play an important role in a person's illness experience, health choices and outcomes (Weinman & Petrie, 1997).

The objective of this thesis is to understand what barriers and enablers to ED treatment utilisation exist and the extent to which they influence ED treatment utilisation with a view to laying the foundations for the development of an intervention to improve treatment utilisation in this patient population. The MRC guidelines for the design and evaluation of complex interventions are built on the premise that designing an intervention of high quality and effectiveness involves the selection of a theory upon which to base the intervention (Campbell et al, 2000; Craig et al, 2008). However, prior to intervention design it is important to carry out an exploratory study, in order to gain a greater perspective and understanding of the potential theories as well as the surrounding issues influencing an intervention of this nature (Campbell et al, 2007). Therefore, this thesis will involve mixed methodology to explore the problem of ED treatment utilisation and will involve the following stages:

Study 1: An exploration of this research area, by carrying out a systematic review to explore the existent literature, in order and to understand what is known about adherence to ED treatment. This will be the focus of the following chapter (Chapter 2).

Study 2: An in-depth, qualitative interview study with two objectives:

- i) Through the use of semi-structured qualitative interviews carry out an exploration of the barriers and enablers to ED treatment utilisation using a theoretical framework for behaviour change
- ii) Based on the findings of the first objection, develop a questionnaire to explore barriers and enablers to ED treatment utilisation which can subsequently be used in Study 3.

Study 3: A quantitative cross-sectional study to explore and identify what factors are associated with ED treatment utilisation, using a theoretically informed approach i.e. building on study 2 through the use of a theoretically informed questionnaire aimed at exploring the barriers and enablers to ED treatment utilisation.

To date, there has been no attempt to synthesise research concerned with ascertaining the reasons for decisions to discontinue with ED treatment. The following chapter will therefore consist of a systematic review of the existent literature concerned with barriers and enablers to ED treatment utilisation as well as ascertaining rates of treatment utilisation.

3 Study 1. Barriers to and enablers of adherence to treatment for erectile dysfunction – A Systematic Review

3.1 Chapter Overview

It has been suggested that, despite the variety of treatments currently available to treat ED, there is a problem with regards to adherence and long-term satisfaction with treatment (Panach-Navarrete et al, 2017). Reasons for non-adherence have been described as being related to factors such as, side-effects, not wanting a sexual schedule dependent on a treatment regimen, the delayed response between i.e., taking medication and its effect, as well as the financial cost of treatment (Hackett, 2005). Psychosocial explanations are suggested as including performance anxiety, depression, varying arousal patterns and misaligned expectations between a man and his partner (Althof, 2002b). A number of studies have investigated barriers and enablers to ED treatment utilisation, however to date there has been no synthesis within individual treatment types. This is important considering national guidelines for medication adherence (Nunes et al, 2009) recognise that in order for HCPs to support patients, a better understanding of factors that influence patients' decisions regarding treatment utilisation is necessary. Therefore, the aim of this systematic review was to identify barriers and enablers to ED treatment utilisation and the extent to which they influence men's decisions to utilise their treatment.

3.2 Aim

The primary aim of this review is to identify barriers to and enablers of ED treatment utilisation.

3.3 Objectives

The objectives of this review are to:

- (i) Carry out an extensive and systematic database search to investigate factors which have the potential to impact ED treatment utilisation
- (ii) (ii) Synthesise any resultant data that emerges to establish rates of adherence to treatment for ED

3.4 Methods

3.4.1 Protocol and registration

The protocol was registered on PROSPERO (reference CRD42015023341). This systematic review has been reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix 1), which consists of a 27-item checklist and a four-phase flow diagram (Liberati et al, 2009). The PRISMA guidelines were primarily developed to improve the reporting quality of systematic reviews and meta-analyses (Shea et al, 2002). In an evaluation of the effectiveness of the PRISMA guidelines, utilization of the PRISMA statement was associated with an increase in both the quality of reporting and its associated methodological quality (Panic et al, 2013). Further, the quality of the review improves the likelihood that its design will generate unbiased results (Moher et al, 1995). In order to ensure the quality of the review with regards to this aspect, 'A measurement tool to assess systematic reviews' (AMSTAR) was utilised (Appendix 2). This checklist is reported as having good reliability, construct validity and feasibility (Shea et al, 2009). Therefore, the AMSTAR checklist was used to inform the overall quality of the present review.

3.4.2 Eligibility criteria

Types of publications

Papers were included if they were:

- published in English
- published in a peer reviewed journal

3.4.3 Information Sources

Searches were carried out across the following electronic databases on 30th July 2015 with no impediment in relation to publication date.

Using the online access provider OVID:

- AMED (Allied and Complementary Medicine)
- Cochrane Central Register of Controlled Trials
- Embase
- HMIC (Health Management Information Consortium)
- Health Technology Assessment
- MEDLINE®

Using the online access provider EBSCO:

- CINAHL plus with full text
- PsychARTICLES
- PsychINFO

E-alert functions for both Ovid and EBSCO were utilised to capture any studies that might be of relevance after the date of the initial search.

3.4.4 Search

The search utilised English language key words and MeSH terms, coupled with Boolean logical operators. Search terms included all known medical terms for ED such as ‘erectile dysfunction’, ‘impotence’ and ‘male erectile disorder’. Terms related to treatment utilisation included, ‘adherence’, ‘compliance’, ‘uptake’ as well as terms related to adherence and cessation of medication taking. Barriers to medication adherence included ‘psychological barrier’ and ‘medication belief’. A detailed database search strategy can be found in Appendix 3.

3.4.5 Study Selection

Types of studies

Studies utilising qualitative, quantitative, or mixed methodologies of primary research were included. Articles were excluded if they were:

- a systematic review
- a meta-analyses
- conference proceedings
- commentary articles or letters

Types of participants

Studies were included if they recruited men:

- with a diagnosis of ED made either by a relevant HCP (i.e., a GP or urologist) or using a validated diagnostic tool, such as the IIEF or SHIM

- whose ED was investigated in isolation or in conjunction with comorbid diseases
- age ≥ 18 years
- who had been prescribed pharmacological or non-pharmacological treatment for ED

Types of treatment

Studies that investigated pharmacological as well as non-pharmacological treatments were included which were:

- PDE5Is
- Urethral suppositories
- ICIs
- Only prescription non-pharmacological treatments i.e., penile prosthesis and VEDs were included. However, pelvic floor exercises and psychosexual counselling were not included

Types of outcome measures

- A measure of ED treatment utilisation which was either validated or non-validated

AND

- reported barriers and/or enablers to ED treatment utilisation; including demographic, clinical (participant and treatment-related), behavioural, emotional, social, or psychological factors, however measured

Studies identified by the search strategy were imported into Thomson Reuters Reference Manager v12.0 and all duplicate records were removed. The titles and abstracts of resultant studies were independently screened for inclusion against the eligibility criteria by the author and another researcher. Upon consensus, full text versions of the selected articles were

acquired, and a further assessment of inclusion made by the author and another researcher. At both stages any disagreements were discussed and if agreement was not reached, a member of the supervisory team was referred to resolve any disagreement. Where ambiguities existed that derived from the studies themselves, the author was contacted to acquire necessary information and resolve discrepancies.

3.4.6 Data Collection Process

Data were extracted using a standard data extraction form (Appendix 4) which was adapted from the Cochrane Data Extraction Form (Higgins et al, 2019). The data extraction sheet collected information including:

- name of the author/s
- country in which the research was carried out
- year of publication
- title of the paper
- study design
- demographic data
- clinical information (i.e., presence of comorbidities, ED severity, duration of ED)
- level of adherence/persistence/discontinuation, how measured and whether validated/non-validated
- barriers and enablers to ED treatment utilisation
- data analysis techniques employed

3.4.7 Synthesis of results

Quality of evidence

In order to assess the quality of each study, the quality index QualSyst (Kmet et al, 2004) was used. This quality assessment tool was selected for several reasons. Firstly, the authors provide extensive and comprehensive instructions with regards to how to use the assessment tool. Secondly, the scope of the current review is broad in nature potentially involving a variety of study methodologies. The quality assessment tool was therefore identified as being appropriate due to its ability to cater for quantitative, qualitative, and mixed-method study designs. This is achieved through the provision of two separate validated scoring systems; a quantitative scale and a qualitative scale (Appendix 5).

The assessment tool considers key areas of a given study such as the appropriateness of a study's objective, rationale, methodology and their subsequent impact on the study's results and conclusions. For example, quantitative studies were assessed for the appropriateness of the study design (i.e., whether it was evident and appropriate), whether the outcome measure was robust and clearly defined, whether the analytical methods were described, justified and appropriate and whether the conclusions were supported by the results.

Qualitative studies were assessed using the QualSyst 10-item validated checklist where each item is scored on a range from 0 to 2 depending on the degree to which the specific criteria were met ("yes" = 2, "partial" = 1, "no" = 0). Items not applicable to a particular study design are marked "n/a" and are excluded from the calculation of the mean summary score. Quantitative studies were assessed using the validated 14-item checklist. Again, each item is scored on a range from 0 to 2 ("yes" = 2, "partial" = 1, "no" = 0) and then a mean summary score is calculated in the same way as the qualitative check list i.e., summing the total score obtained across the

items and then dividing by the maximum possible score (Kmet et al, 2004). Total scores obtained through the QualSyst assessment tool were converted to percentages to reflect the quality of each study enabling comparisons between studies where <50% indicates that the study is limited in terms of quality, 50–70%: adequate; 71–80%: good and a score of >80%: strong (Greenwood & Smith, 2015; Johnson et al, 2016). The quality assessment process was carried out in full by the author. Ten percent of the papers were quality checked by a second researcher. For any discrepancies, members of the supervisory team were at hand to act as an arbitrator and facilitate agreement.

Data synthesis

The scope of the current review was wide and therefore it was anticipated that; included studies would be heterogeneous, in terms of their methodological approaches and with regards to treatment type. Therefore, the current review is narrative in nature and considered the most appropriate method of synthesising both qualitative and quantitative evidence (Mays et al, 2005).

To achieve the aims of the current review, the following data were tabulated: demographic attributes of the studies (e.g. country of origin, utilised study designs, treatment type; participant characteristics (clinical aspects such as ED severity and duration); rates of treatment utilisation recorded in conjunction where a given studies terminology i.e. adherence/persistence and discontinuation (including the methods by which data were captured) and the reported barriers to ED treatment utilisation. Tabulating the results permitted data synthesis and common themes across studies to emerge. Treatment barriers and enablers were classified as either demographic, clinical, psychological, social, or behavioural. The frequency of a particular barrier or enabler was calculated across studies as well as the means

by which it was explored i.e., using descriptive or inferential statistics. These are presented in the following section and reported in accordance with the PRISMA checklist (Appendix 1).

3.5 Results

3.5.1 Literature search results

After duplicate records were removed, a total of 2,585 potential papers were identified for inclusion. After removal of irrelevant records, 76 studies were identified for full text screening. A total of 45 full papers, published between 1991 and 2014, were included in the current review (Figure 6).

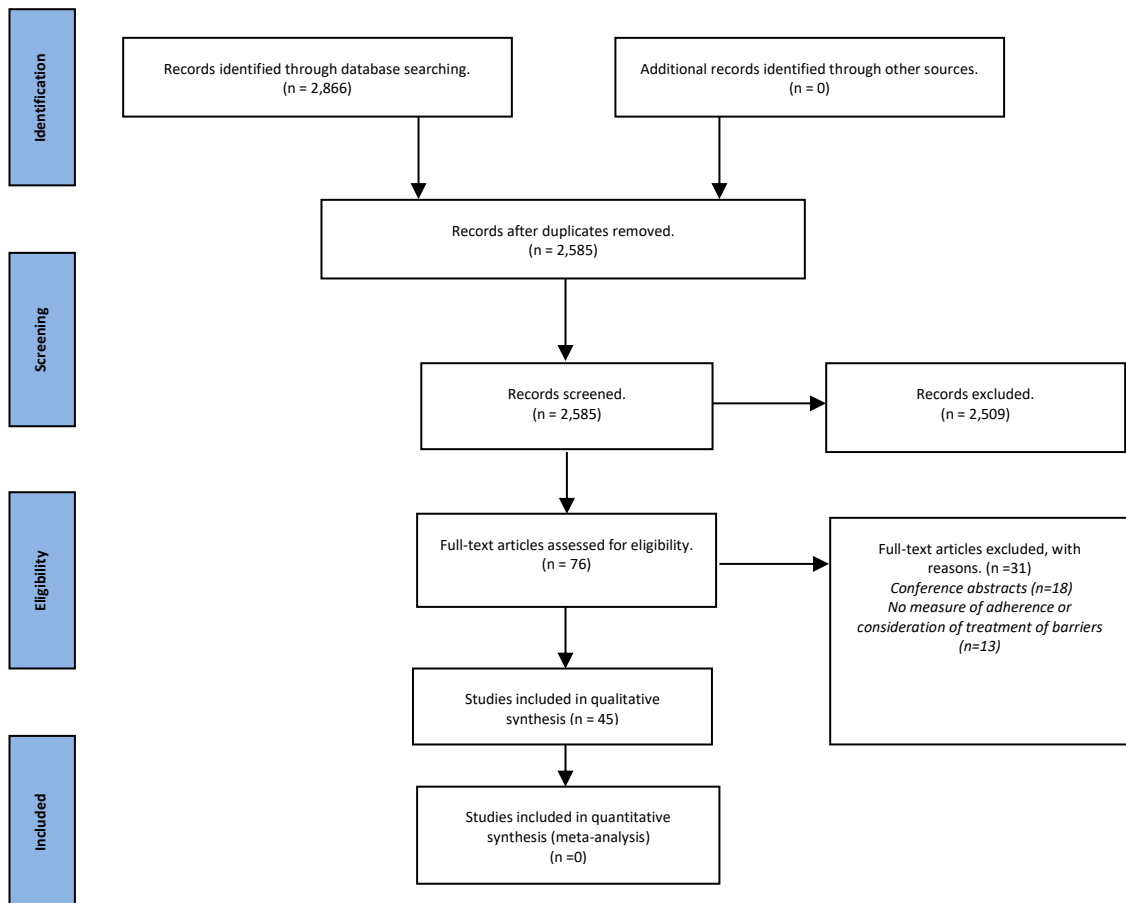


Figure 6: PRISMA flowchart

3.5.2 Publication characteristics

Country

Almost one third of studies were conducted in the USA (n=14, 31.1%), followed by Italy (n=4, 8.9%), South Korea (n=3, 6.7%), Portugal (n=2, 4.4%) and the Netherlands (n=2, 4.4%) (Table 8). There were also 8 (17.8%) that were multicentre studies taking place in more than one country. Only one study included participants from the UK, which was a multicentre study including other European countries (Buvat et al, 2013). The rest of the studies (n=12, 26.7%) were carried out in individual countries and included, N. Ireland, Germany, Finland, Switzerland, Greece, Portugal, Norway, Brazil, Turkey, Japan, New Zealand and Sweden.

Study design

All studies utilised a quantitative design except one study which used a mixed methods design, incorporating both a quantitative and qualitative component; however results to the qualitative aspect of the study were presented using frequency data and therefore the results were interpreted quantitatively (Carvalho et al, 2014). There were two studies of quasi-experimental design (Buvat et al, 2013; Ricardi et al, 2010) and only one randomised controlled trial (RCT) (Incrocci et al, 2003). For the non-randomised studies, the majority used a prospective longitudinal research design (n=34). The remainder of the studies utilised cross-sectional study designs (n=7) (Table 8).

Sample size

The number of participants included in each study varied greatly. The smallest sample size was a cohort of 30 participants (Armstrong et al, 1994) who were included in a prospective cohort study focusing on PDE5Is and the largest sample size included 1,567 participants who were recruited for a 12 month follow-up study of men receiving Tadalafil (Roumeguere et al, 2008). The median number of participants was 287.

Treatment type

Studies varied regarding the treatment they focussed on. Thirteen studies focussed on ICI therapy, one of which also investigated participants who had penile prosthesis. Three focussed on urethral suppositories; and the remainder (n=29) on PDE5I medication (Table 8). Of the 13 studies concerned with ICI therapy, the majority were carried out between 1991 and 1999 (n=9). Studies that investigated urethral suppositories were carried out between 2001 and 2007 and the one study that focussed on penile prosthesis was carried out in 1998. Only one study that focussed on PDE5Is was carried out prior to the year 2000 and the rest (n = 28) between 2001 and 2014.

Treatment dose

Of the 45 studies, 24 specified participants' dosing regimen, which included studies involving participants who were using a fixed dose as well as studies of participants on flexible dosing (i.e. dose titration).

3.5.3 Analysis techniques

Less than half (n=20) of the studies examined whether there was a statistically significant relationship between potential barriers/enablers and treatment utilisation using inferential statistics, such as multivariate logistic analysis or Cox proportional hazards model. The remaining 25 studies reported only descriptive statistics such as percentages or total numbers of participants reporting a particular barrier or enabler as influencing their treatment utilisation (Table 8).

3.5.4 Quality of the Studies

Studies included in this review varied with regards to their quality, as denoted by the Quallsyst assessment tool. Quality ranged between 41 and 100% (see Figure 7). Using the aforementioned quality classifications; 7 studies were limited in their overall quality (i.e., scored <50), 20 were deemed adequate (scored between 50–70%), 4 were good (scored between 71–80%) and 14 were strong (scored >80%). Studies that derived lower scores on the QualSyst assessment tool typically did so for similar reasons, including not defining their outcome measure/s adequately; leaving room for subjectivity; not reporting information on power calculations, sample or effect sizes and not controlling for confounding variables.

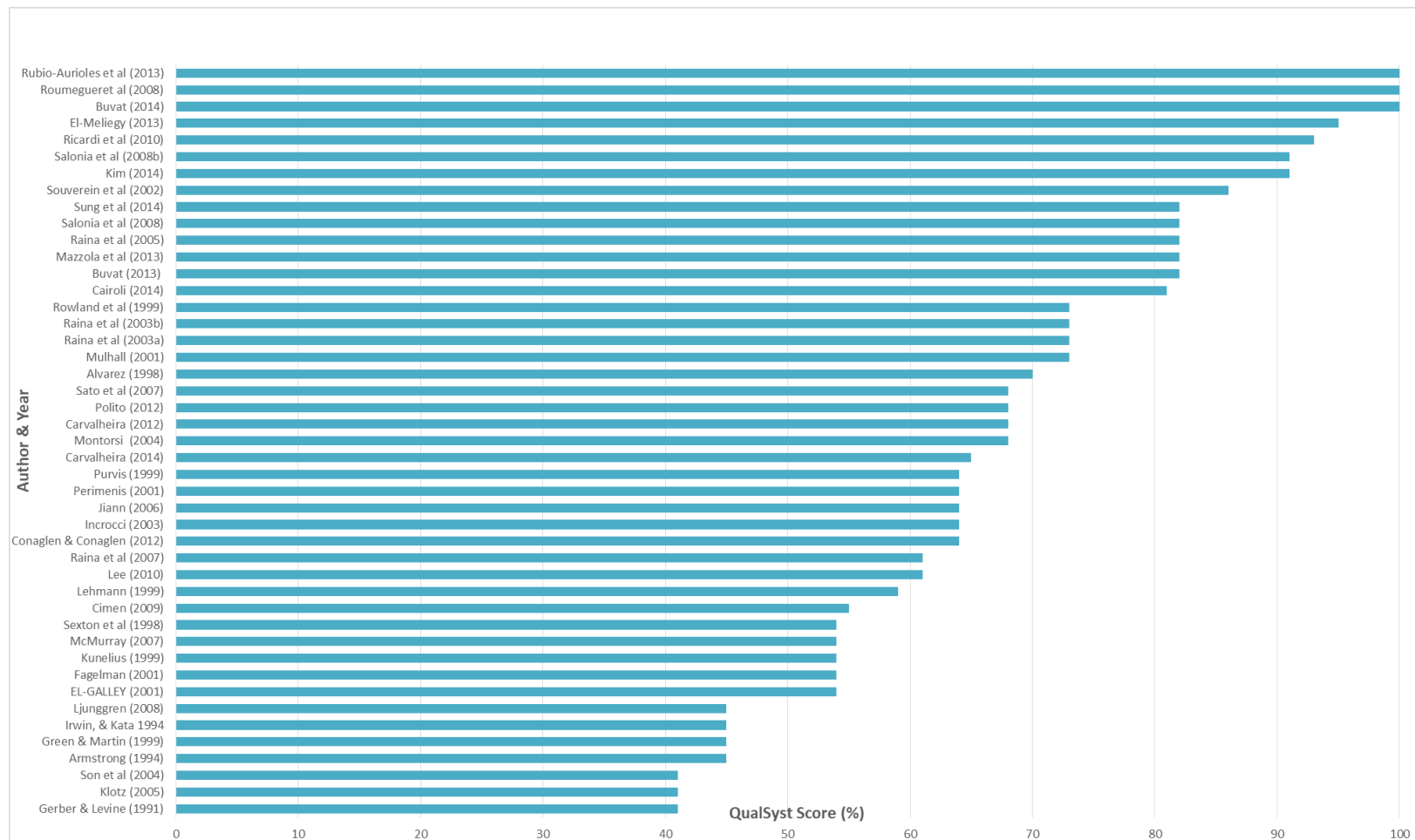


Figure 7: Study quality as determined by QualSyst

Table 8: Study Characteristics

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
ICI treatment						
Alvarez et al (1998)	Europe, South Africa	To evaluate the long-term safety and efficacy	Prospective cohort study	Aprostadil 20 mg/mL	6 months	848
Armstrong et al (1994)	N. Ireland	To identify factors contributing to patient drop- out from an ICI programme.	Cross-sectional	NR	n/a	30
Gerber & Levine (1991)	USA	To investigate erectile response, pain after injection and frequency of use.	Prospective Cohort Study	Aprostadil: 5, 10 or 20 mcg's	M=7 months (2-28 months)	72
Irwin & Kata (1994)	USA	To determine acceptance and durability of treatment.	Prospective cohort study	Aprostadil (mean dosage) = 23 ug (range 5-30 ug).	6 months	60
Kunelius et al (1999)	Finland	To assess the long-term outcome of treatment and overall patient satisfaction with their sexual life.	Prospective cohort study	NR	36 months	69
Lehmann et al (1999)	Switzerland	To clarify the reasons why experience with self-injection therapy for ED shows high dropout rates.	Prospective cohort study	Alprostadil 2-mL	M=16 (3-64 months)	86
Perimenis et al (2001)	Greece	To compare patient compliance with treatment and the dosages used for the management of impotence.	Prospective cohort study	Aprostadil initially 5 – 10 ug	84 months	40
Polito et al (2012)	Italy	To assess the rate of compliance in the first 6 months of a rehabilitation protocol for patients undergoing RRPP.	Prospective cohort study	Alprostadil initially 2 – 3 mcg	6 months	273

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Purvis et al (1999)	Norway	To examine the impact of treatment on libido, ejaculatory control, quality of life and treatment dependency in men with erectile failure. Furthermore to assess the drop-out rate and reasons for dissatisfaction with the technique.	Cross-sectional study	Aprostadil (10 ± 20mg), papaverine-phentolamine (15 mg; 0.5 mg) and Trimix (10 mg Aprostadil; 15mg papaverine; 0.5 mg phentolamine).	n/a	766
Raina et al (2003a)	USA	To investigate drug efficacy in patients following RP.	Prospective cohort study	Aprostadil alone (10 or 20 mg/ml in normal saline), high-dose triple therapy (20 mg/ml Aprostadil +1 mg/ml phentolamine +30 mg/ml papaverine), or low-dose triple therapy (5.88 mg/ml Aprostadil +0.59 mg/ml phentolamine+ 17.65 mg/ml papaverine).	M=14.5 months	102
Rowland et al (1999)	USA	To explore satisfaction with and dropout from ICI use.	Prospective cohort study	NR	M=9 months	119
Sexton et al (1998)	USA	To compare the long-term outcomes of both penile prostheses and ICI therapy and determine the reasons for discontinuation.	Prospective cohort study	NR	M=37 months (PP) M=63 months (ICI)	130

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Sung et al (2014)	Korea	To investigate the rate of withdrawal and its associated reasons.	Prospective cohort study	Trimix (a mixture of prostaglandin E1 18 ug, papaverine 48 mg and phentolamine 2 mg in 2 mL of distilled water).	18 +/- 23.9	294
PDE5Is						
Buvat et al (2013)	France, Greece, Portugal, Germany, UK	To evaluate the effects of initiating treatment with Tadalafil OaD, Tadalafil PRN, or sildenafil PRN on treatment utilisation.	Quasi experimental	(1) Tadalafil OaD, 5 mg OaD (2) Tadalafil PRN, 10 mg PRN (3) Sildenafil PRN, 50 mg PRN	median = 4.3 months median = 5.5 months median = 2.2 months	770
Buvat et al (2014)	Germany, France, Italy, Greece	To evaluate treatment continuation, effectiveness and tolerability of Tadalafil OaD.	Prospective cohort	Tadalafil OaD 5-mg	6 months	778
Cairol et al (2014)	Brazil	To characterize persistence and adherence to PDE5I on-demand therapy over 6 months	Prospective cohort study	NR	6 months	104
Carvalho et al (2014)	Portugal	(i) To characterize the way men use PDE5I and (ii) analyse treatment utilisation, identifying the factors that influence PDE5I use.	Cross-sectional Study	NR	n/a	148
Cimen et al (2009)	Turkey	To retrospective evaluation of ED patients who were recommended a PDE5I treatment in terms of patient satisfaction.	Cross-sectional Study	NR	n/a	345

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Conaglen & Conaglen (2012)	New Zealand	To evaluate factors influencing adherence to, or discontinuation of, oral ED medications.	Prospective cohort study	NR	12 months	155
Mazzola et al (2013)	USA	To explore the link between erection hardness and treatment adherence.	Prospective cohort study	Sildenafil, 100 mg	17 +/- 4 months	186
El-Galley et al (2001)	USA, Saudi Arabia	To evaluate the long-term efficacy of Sildenafil	Prospective cohort study	NR	24 months	200
El-Meliegy et al (2013)	Saudi Arabia Egypt, United Arab Emirates, USA	To assess on-demand PDE5I treatment persistence and adherence over 6 months in men with ED.	Prospective cohort study	NR	6 months	493
Fagelman et al (2001)	USA	To evaluate the efficacy, side effects, renewal patterns and other relevant practice issues related to the use of sildenafil.	Prospective cohort study	Sildenafil 50 mg, increasing to 100 mg if necessary.	6 – 12 months	164
Green and Martin (2000)	USA	To evaluate the efficacy and safety of sildenafil in patients with ED caused by spinal cord injury and multiple sclerosis.	Prospective Cohort Study	NR	M=21 months	40
Incrocci et al (2003)	Netherlands	To determine the efficacy of Sildenafil citrate in patients with ED after three-dimensional conformal external beam radiotherapy.	RCT	50 mg for 2 weeks increasing to 100 mg if necessary.	24 months	50
Jiann et al (2006)	Taiwan	To assess treatment compliance and reasons for dropout.	Cross-sectional Study	NR	M=36 months	434
Kim et al (2014)	Korea	To identify characteristics of ED patients who discontinued PDE5I medication.	Cross-sectional Study	NR	n/a	485

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Klotz et al (2005)	Germany	To determine the rate of abandonment of sildenafil therapy and assess the reasons for abandonment.	Prospective cohort study	Sildenafil 50 or 100 mg	6 months	234
Lee et al (2010)	USA	To evaluate factors that affect discontinuation in men after nerve sparing RAP.	Prospective cohort study	Sildenafil citrate (100 mg) three times a week or Tadalafil (20 mg) three times a week.	6 months)	53
Ljunggren et al (2008)	Sweden	To study long-term compliance among patients who were treated according to a “three-drug regime” i.e. able to try all 3 PDE5I medications.	Cross sectional study	NR	M=27 months	138
McMurray (2007)	USA	To assess the safety and effectiveness of flexible doses of Sildenafil	Prospective cohort study	Flexible-doses (25, 50, and 100 mg) of Sildenafil.	48 months	979
Montorsi et al (2004)	Italy, Belgium, Netherlands, Germany, Spain, Canada, Argentina, Mexico, USA	To assess the long-term safety and tolerability of tadalafil for patients with ED.	Prospective cohort study	Initial dose was 10 mg (Tadalafil) taken as needed	18-24 months	493
Carvalho et al (2012)	Portugal	(i) To analyse discontinuation rates of PDE5Is; (ii) to identify predictors of discontinuation; and (iii) to study the reasons for discontinuation using a qualitative methodology	Mixed methodology	NR	36 months	327

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Raina et al (2003b)	USA	To evaluate the long-term effect and safety of sildenafil citrate for the treatment of ED.	Prospective cohort study	Starting dose was 50 mg, which was titrated to 100 mg if necessary.	36 months	48
Ricardi et al (2010)	Italy	To compare the efficacy and safety of Tadalafil PRN 20-mg (arm A) with Tadalafil 5-mg OaD (arm B) in patients with ED following radiotherapy for prostate cancer.	Quasi experimental	Tadalafil 20 mg PRN (arm A) or Tadalafil 5 mg OaD (arm B)	3 months	52
Roumeguere et al (2008)	Austria/Belgium/Denmark/Greece/Iceland/Netherlands/Norway/Sweden	To determine the effectiveness of Tadalafil and the factors associated with the continuation of treatment for ED.	Prospective cohort study	Tadalafil 10 or 20 mg	12 months	1567
Rubio-Aurioles et al (2013)	Brazil, Mexico, Venezuela	To investigate the factors that may be predictive for PDE5I persistence and adherence.	Prospective cohort study	NR	6 months 6 months	511
Salonia et al (2008a)	Italy	To explore whether the educational status may have a significant impact on the delay before seeking first medical help and compliance with a suggested PDE5I.	Prospective cohort study	Sildenafil 50 mg, Vardenafil 10 mg or Tadalafil OaD 10 mg.	=/< 24 months)	231
Salonia et al (2008b)	Italy	To assess acceptance of and discontinuation rate from ED treatment in patients after bilateral nerve-sparing radical retro-pubic prostatectomy.	Prospective cohort study	NR	18 months	51
Sato et al (2007)	Japan	To study the dropout rate for use of sildenafil after initial prescription and during successful treatment to clarify their risk factors.	Prospective cohort study	NR	36 months	322

Author, year	Country	Study Aim	Design	Dose	Follow-up (months)	n
Son et al (2004)	Korea	To investigate the reasons for discontinuations of Sildenafil after the successful restoration of erectile function.	Prospective cohort study	Flexible Sildenafil doses; 25-100 mg according to patients need and side effects	6 months	156
Souverein et al (2002)	Netherlands	Sildenafil utilization was evaluated in men with ED. Further, some determinants of Sildenafil discontinuation were identified.	Prospective cohort study	NR	M=18 months	317
Intraurethral suppository						
Mulhall et al (2001)	USA	To determine the consistency of a successful response to a urethral suppository (Aprostadil)	Prospective cohort study	Aprostadil 1000 mg	M=9 months	68
Raina et al (2007)	USA	To obtain baseline and follow-up data of 54 patients who used medicated urethral system for erection for ED associated with RP.	Prospective cohort study	Aprostadil 125 ug or 250 ug of urethral suppository.	M=9 months	56
Raina et al (2005)	USA	To assess whether early introduction of Aprostadil after RP results in a shorter recovery time for the return to functional erections and successful sexual activity.	Prospective cohort study	Aprostadil 250 mg flexible to 500 or 1000 mg dose of urethral suppository, if needed	M=27 +/- 14 months	54

Note: ICI: Intracavernousal Injection; OaD: Once a day; PDE5I: phosphodiesterase type 5 inhibitor; PRN: on demand; RP: radical prostatectomy; RAP: robot-assisted prostatectomy; RRPP: radical retro-pubic prostatectomy.

3.5.5 Participant Characteristics

The 45 papers provided data relating to 12,849 participants from a wide variety of demographic stratifications (Table 9).

Demographics

Age

The majority of studies (n=41, 91.1%) provided information on men's mean age, which ranged from 40.4 to 69.1 years.

Ethnicity

Only four studies provided information on participants' ethnicity (Buvat et al, 2013; Buvat et al, 2014; Conaglen & Conaglen, 2012; McMurray, 2007). Based on these studies, between 67.2% and 97.8% of study participants were classified as white/Caucasian.

Relationship status

Only seven studies reported participants' relationship status (see Table 9). Studies employed a variety of adjectives to describe relationship status, making comparisons between studies difficult. However, between 61.5 – 96% of men across these studies were described as having some form of intimate partner, which included being 'married', 'partnered', 'living together' or 'cohabiting'.

Educational status

A similar issue was found regarding educational status. The majority of participants across the eight studies that provided information regarding education status, had been educated to secondary, tertiary or university level (Table 9).

Employment status

Only two studies reported detailed information on participants' employment status in which participants classified as employed ranged from 59% (Buvat et al, 2014) – 84.5% (Kim et al, 2014).

Clinical characteristics

Diagnosis of ED

There were 18 studies that provided information regarding how ED had been diagnosed. The most common method of ED diagnosis was the taking of patients' medical or sexual history (n=14), in which some also incorporated a physical examination (n=8) or some form of laboratory testing (n=7). Four studies used the IIEF or the SHIM (see chapter 1, 'Standardised Questionnaires' for a full description).

ED Aetiology

Eighteen studies provided data on ED aetiology where, studies indicated that between 21.8 - 86% of participants were classified as having organic ED, 11 - 36.3% as having psychogenic ED and 15 - 51% as having mixed ED (n=10) (Table 9).

ED duration

Eighteen studies provided data on ED duration, which ranged from 12 – 60 months.

Severity of ED

Nineteen studies (42.2%) used the International IIEF or the SHIM to assess ED severity. In these studies, there were a higher proportion of men with moderate ED (45 - 61.7%) than those with mild or severe ED (Table 9).

Co-morbidities

Eighteen studies provided data on patient comorbidities, the most prevalent of which were hypertension and diabetes. Hypertension was reported as being present in 9.4 to 51.9% of men and diabetes in 5.3 to 42.4%. Other conditions included cardiovascular disease (CVD) (1.3-34.5%), dyslipidaemia (5.4-38%) and obesity (9.5-28.8%) (Table 9).

Additional Medications

Three studies provided information regarding concurrent medications (Conaglen & Conaglen, 2012; Purvis et al, 1999; Souverein et al, 2002), of which two studies reported that antihypertensive medication was the most commonly reported medication to be taken alongside treatment for ED (Purvis et al, 1999; Souverein et al, 2002).

Table 9: Participant Characteristics

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
ICI treatment									
Alvarez et al (1998)	52(NR)	NR	NR	NR	NR	NR	Neurogenic: 118 (14) Vasculogenic: 215 (25) Psychogenic: 268 (32) Diabetes: 94 (11) Other: 30 (3.5) Mixed causes: 123 (15)	54	NR
Armstrong et al (1994)	50.5(NR)	NR	NR	NR	NR	NR	NR	NR	NR
Gerber & Levine (1991)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Irwin & Kata (1994)	64(NR)	NR	NR	NR	NR	NR	NR	NR	NR
Kunelius et al (1999)	60.5(NR)	NR	NR	NR	NR	NR	Vasculogenic: 30 (28) Psychogenic: 31 (29) Neurologic: 8 (7)	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Lehmann et al (1999)	58 (10)	NR	NR	NR	NR	NR	Organic: 52 (60) Mixed: 23 (27) Psychogenic: 11 (13)	NR	NR
Perimenis et al (2001)	54.85(NR)	NR	NR	NR	NR	NR	NR	28	NR
Polito et al (2012)	64.6 (6.5)	NR	NR	NR	NR	NR	NR	NR	M=No ED (=/ $\geq$ 20): 212 (77.6%)
Purvis et al (1999)	57(NR)	NR	NR	NR	NR	NR	Vascular: 33% Idiopathic: 31% Psychogenic: 26% Neurologic: 7% Endocrine: 3%	NR	NR
Raina et al (2003a)	60.4 (6.3)	NR	NR	NR	NR	NR	NR	NR	Sev: 68%
Rowland et al (1999)	58(NR)	NR	NR	NR	NR	NR	NR	41	NR
Sexton et al (1998)	58.5(NR)	NR	NR	NR	NR	NR	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co- morbidities, n (%)	ED Aetiology, n (%)	ED Duratio n, months (sd)	ED severity – IIEF n(%)
Sung et al (2014)	61.8 (7.9)	NR	NR	NR	NR	Diab: 82 (27.9) Hyp: 118 (40.1) CVD: 37 (12.6) CVA: 11 (3.7), Previous RP: 198 (67.3), NSRP: 72 (36.4), Previous pelvic RT: 31 (10.5)	NR	NR	NR
PDE5I medication									

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Buvat et al (2013)	53.03 (11.66)	White 753 (97.8), Black/African American 10 (1.3), Multiple 1 (0.1)	NR	NR	NR	Hyp: 266 (34.5), Hyperl: 137 (17.8), Diab: 142 (18.8), BPH: 68 (8.8), Dys: 42 (5.4), Osteo: 36 (4.7), Dep: 36 (4.7), Anx: 30 (3.9)	Tadalafil OaD Psychogenic: 54 (21.0) Organic: 56 (21.8) Mixed: 125 (48.6) Unknown: 22 (8.6) Tadalafil PRN Psychogenic: 59 (23.4) Organic: 65 (25.8) Mixed: 106 (42.1) Unknown: 22 (8.7) Sildenafil PRN Psychogenic: 62 (23.8) Organic: 66 (25.3) Mixed: 111 (42.5) Unknown: 22(8.4)	23.3	Mi 300 (38.9), Mod 261 (33.9), Sev 204 (26.5)

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Buvat et al (2014)	57 (NR)	Caucasian 523(67.2), Other 4(0.5)	Married 639(65.9), Partnered/living together 120(12.4)	Full-time 532(54.7) Part-time 42(4.3) Pensioner/retired 341(35.0) Student 12(1.2) Unemployed/unable to work 41(4.2) Other 15(0.5)	No formal education 14(1.4) Primary school 256(22.6) Secondary school 415(42.7) University/post graduate 270(27.8) Unknown 17(1.7)	CVD: 268 (34.5), Hyp: 260 (33.4), Dysl: 144 (18.5), Diab: 124 (15.9) PS: 89 (11.4), BPH: 49 (6.3), Hypog:12 (1.5)	Mixed: 443 (45.7) Organic: 286 (29.5) Psychogenic: 172 (17.8) Unknown: 68 (7.0)	<3 n=55 (7.1%) 3-12 n=231(29.7%) ≥12 n=490(63.1%)	Mi 160 (20.6), Mod 411 (53.0), Sev 204 (26.3)

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Cairol et al (2014)	57.8 (10.9)	NR	NR	NR	Primary education 34 (33.3) Secondary education 37 (36.3) Tertiary education 14 (13.7) University education 14 (13.7) Postgraduate education 2 (1)	Hyp: 54 (51.9), Diab: 25 (24.0), Ob: 10 (9.6), CAD: 4 (3.8), BPH: 7 (6.7), LUTS: 5 (4.8), Hyperl: 13 (12.6)	Mixed: 48 (47.1) Organic: 37 (36.3) Psychogenic: 16 (15.7)	24	Mi 13 (13.8), Mod 58 (61.7), Sev 23 (24.5)
Carvalheira et al (2014)	55.8 (11.11)	NR	Married: 61.5% Divorced/separated: 20.3% Single: 12.2% Common law: 4.1% Widowed: 2.0%	NR	Undergraduate 58.1% Graduate 33.8% Postgraduate 8.1%	NR	Venogenic:31% Arteriogenic: 23% Psychogenic: 18% Iatrogenic: 13% Neurogenic: 8% Diabetic: 7%	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Cimen et al (2009)	56 (11.2)	NR	NR	NR	NR	Diab: 21.7%, Hyper: 16.1%, CVD: 4.7%	NR	27.7	NR
Conaglen & Conaglen (2012)	55.85 (8.59)	Maori or Pacific Islander 8 (5.1) Caucasian/European 128 (82.6) Mixed Ethnicity 11 (7) Other 8 (5.1)	NR	NR	NR	NR	NR	NR	NR
Mazzola et al (2013)	61 (22)	NR	Partnered: 63%	NR	NR	Hyper: 36%, Dys: 38%, CAD: 16%, Diab: 15%	NR	26	Mi 25%, Mod 45%, Sev 30%,

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co- morbidity, n (%)	ED Aetiology, n (%)	ED Duratio n, months (sd)	ED severity – IIEF n(%)
El-Galley et al (2001)	58 (10)	NR	NR	NR	NR	NR	Radical prostatectomy: 25 Neurogenic impotence: 12 Arterial insufficiency: 26 Diabetes mellitus: 19 Diagnosed venous leak: 7 Clinical venous leak: 9 Peyronie's disease: 6 Other: 47	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
El-Meliegy et al (2013)	49.6 (12.03)	NR	NR	NR	Primary education 25 (5) Secondary education 55 (11.16) Tertiary education 99 (20) University education 248 (50.3) Postgraduate education 47 (9.5) No formal education 19 (3.8)	Hyp: 222 (45), Diab: 209 (42.4), Ob: 104 (28.8), BPH: 105 (21.3) LUTS: 110 (22.3), Hyperl: 169 (34.3)	Tadalafil Psychogenic: 66 (19.3) Organic: 133 (38.9) Mixed: 125 (36.5) Unknown: 18 (5.3) Sildenafil Psychogenic: 14 (18.4) Organic: 32 (42.1) Mixed: 18 (23.7) Unknown: 12 (15.8) Vardenafil Psychogenic: 9 (12.2) Organic: 30 (40.5) Mixed: 28 (37.8) Unknown: 7 (9.5)	18	Mi 78 (15.8), Mod 259 (52.5), Sev 155 (31.5)
Fagelman et al (2001)	54.1(NR)	NR	NR	NR	NR	NR	NR	44	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co- morbidity, n (%)	ED Aetiology, n (%)	ED Duratio n, months (sd)	ED severity – IIEF n(%)
Green & Martin (2000)	40.4(NR)	NR	NR	NR	NR	NR	Multiple sclerosis: 7 Spinal cord injury: 33 Quadriplegics: 13 Paraplegics: 20 Complete injuries: 14 Incomplete injuries: 19	NR	NR
Incrocci et al (2003)	68(NR)	NR	NR	NR	NR	Diab and/or Hyp 13%	NR	NR	NR
Jiann et al (2006)	66.8 (9.8)	NR	NR	NR	NR	NR	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Kim et al (2014)	53.6 (11.8)	NR	Marriage/Co-habit: 416 (85.8) Bereavement: 11 (2.3), Divorce: 14 (2.9) Separation: 13 (2.7), Bachelor: 25 (5.2), Others: 6 (1.2)	White collar 153 (31.5) Blue collar 102 (21.0) Self-employed/Ser vice 155 (32.0) Others/No job 75 (15.5) No answer 0 (0.0)	No education 1 (0.2) Elementary 11 (2.3) Middle school 29 (6.0) High school 162 (33.4) University 238 (49.1) Post-graduate 42 (8.7) No answer 2 (0.4)	Diab: 58 (12.0) Hyp: 102 (21.0) Dys: 39 (8.0), Ob: 46 (9.5), CAD: 14 (2.9), BPH: 119 (24.5), Arthritis: 13 (2.7), Herniated nucleus pulposus: 17 (3.5), Digestive disorder: 25 (5.2)	Psychogenic: 176 (36.3) Organic: 309 (63.7)	<5 years: 276 (56.9) 5–9 years: 125 (25.8) 10–14 years: 48 (9.9) = />15 years: 12 (2.5) Don't know/No answer: 24 (4.9)	Mi: 47.0%, Mod: 46.2%, Sev: 6.8%
Klotz et al (2005)	60.5(NR)	NR	NR	NR	NR	Hyp: 40%, Diab: 16%	Organic: 202 (86)	NR	M=M _i -Mod 17
Lee et al (2010)	57.8 (7.0)	NR	NR	NR	NR	NR	NR	NR	Median=M _i 22

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Ljunggren et al (2008)	60 (7)	NR	NR	NR	NR	NR	Organic: 40 (32%) Psychogenic: 23 (18%) Mixed: 64 (50%)	60	NR
McMurray (2007)	58.2(NR)	White: 873 (89.2), Black: 68 (6.9), Asian: 8 (0.8), Other: 30 (3.1)	NR	NR	NR	Hyp: 272 (27.8), Diab: 213 (21.8), Hyperl: 139 (14.2), IHD: 83 (8.5)	Organic: 72 Mixed: 17 Psychogenic: 11	54	NR
Montorsi et al (2004)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Carvalheira et al (2012)	56.30 (11.44)	NR	Married: 65.4% Divorced/separated: 18.3% Single: 10.4% Common law: 3.1% Widowed: 2.8%	NR	<Ninth grade 9.2 Ninth grade 20.4 High school 28.3 Degree 34.9 Master's degree 3.6 PhD 3.6	NR	Venogenic :79 (24.2) Arteriogenic: 75 (22.9) Iatrogenic: 62 (19.0) Psychogenic: 50 (15.3) Diabetic: 40 (12.2) Neurogenic: 21 (6.4)	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Raina et al (2003b)	NR	NR	NR	NR	NR	NR	NR	NR	Sev: 68%
Ricardi et al (2010)	69.1(NR)	NR	NR	NR	NR	NR	NR	12	Sev: 88.9%
Roumeguere et al (2008)	56.5 (11.1)	NR	Currently has a partner 1504 (96)	NR	NR	CHD: 157 (10), Hyp: 674 (43), Diab: 360 (23), Anx/Dep: 219 (14), LUTS: 266 (17), Pros: 78 (5), Ob: 376 (24), PS: 47 (3)	Organic :28% Mixed: 51% Psychogenic: 21%	>12	N: 78 (5), Mi: 517 (33), Mod: 392 (25) Sev: 580 (37)

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Rubio-Aurioles et al (2013)	53.2 (12.4)	NR	NR	NR	Primary education 106 (20.8) Secondary education 123 (24.2) Tertiary education 110 (21.6) University education 143 (28.1) Postgraduate education 24 (4.7)	Hyp: 157 (30.7), Diab: 106 (20.7), Ob: 95 (18.6), BPH: 81 (15.9), LUTS: 75 (14.7), Hyperl: 62 (12.2)	Mixed: 232 (45.6) Organic:168 (33.0) Psychogenic: 94 (18.5)	20	Mi: 114 (22.8), Mod: 272 (54.3) Sev: 115 (23.0)
Salonia et al (2008b)	53; 10.3 51.4; 13.5	NR	NR	NR	High educational status: 168 (72.7) Low educational status: 63 (27.3)	NR	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Salonia et al (2008a)	51.8 (12.7)	NR	No stable sexual relationship: 38 (16.45) Stable sexual relationship >12 months: 193 (83.5)	NR	NR	NR	NR	NR	M=Mi-Mod: 13.75
Sato et al (2007)	NR	NR	NR	NR	NR	Diab: 55 (5.3), Hyp: 102 (9.4), CVD: 13 (1.3), IHD: 2 (0.2), AS: 6 (0.6), CBD: 20 (1.9), Dep: 19 (1.8), SCI: 12 (1.2), PC: 19 (1.8), IO: 17 (1.6)	NR	NR	Mi: 291 (28.1), Mod: 352 (34.0), Sev: 393 (37.9)
Son et al (2004)	54.6(NR)	NR	NR	NR	NR	BPH: 33 (21), Diab: 26 (17), Hyp: 17 (11) CVA: 4 (3), Others: 4 (3)	NR	28.8	M-Mod: 16.23 (mean)

Author, year	Age (yrs), Mean(SD)	Ethnicity n (%)	Relationship status n (%)	Employment n (%)	Education n (%)	Co-morbidities, n (%)	ED Aetiology, n (%)	ED Duration, months (sd)	ED severity – IIEF n(%)
Souverein et al (2002)	57.2 (10.74)	NR	NR	NR	NR	NR	NR	NR	NR
Intraurethral suppository									
Mulhall et al (2001)	46.5 (14.6)	NR	NR	NR	NR	Diab: 11% , Hyp: 29%, Hyperch: 21%, A History of cigarette smoking: 31%	NR	NR	NR
Raina et al (2007)	55.6 (3.78)	NR	NR	NR	NR	NR	NR	NR	Sev: 19.65 (mean)
Raina et al (2005)	63.7 (5.6)	NR	NR	NR	NR	NR	NR	NR	Sev: 68%

Note: Anx: anxiety; AS: Arterial sclerosis; BPH: Benign prostatic hyperplasia; CAD: Coronary artery disease; CBD: Cerebrovascular disease; CHD: Coronary heart disease; CVA: Cardiovascular accident; CVD: cardiovascular disease; Dep: depression; Diab: diabetes; Dys: Dyslipidaemia; Hyperch: Hypercholesterolemia; Hyp: hypertension; Hyperl: hyperlipidaemia; Hypog: Hypogonadism; IHD: Ischemic heart disease; IO: Intrapelvic operation; LUTS: Lower Urinary Tract Symptoms; M: mean; Mi: mild; Mod: moderate; N: normal; NR: Not recorded; NR; Ob: obesity; Osteo: Osteoarthritis; PC: Prostate cancer; PS: Pelvic surgery; RP: radical prostatectomy; RPS: radical pelvic surgery; RT: radiotherapy; Sev: severe; SHIM: Sexual health inventory for men; NSRP: Nerve sparing radical prostatectomy; Pros: Prostatectomy; SCI: Spinal cord injury; Sev: Severe

3.5.6 Study Design

Studies varied in their design and included cross-sectional, prospective cohort, quasi-experimental and randomised control trials. Designs that incorporated a follow-up period varied from 3 to 48 months. There did not appear to be any relationship between the length of follow up and rates of treatment utilisation. One might posit that the longer the follow up, the higher the chance of discontinuation, however, there was no evidence to support this notion (Table 8).

3.5.7 Follow-up period

Studies that included a follow-up period varied with regards to the duration of follow-up, where the shortest follow-up interval looked at medication taking behaviour over a 3-month period, the longest over 7 years. Even though it might be expected that a longer follow up period would be indicative of higher rates of discontinuation, no such pattern emerged with regards to any of the included ED treatments (Table 8).

3.5.8 Definitions of Adherence, Persistence and Discontinuation

Studies included a wide variety of operational definitions that extended beyond simply adherence and included the terms persistence and discontinuation however, many studies did not provide any operational definitions (n=31) (see Table 10). Where definitions were stated, they varied for example, in relation to the term *adherence*, one study defined participants as adherent, if they had taken at least 70% of the prescribed dose (Ricardi et al, 2010), whereas another defined it as taking medication over the last 4 weeks (Lee et al, 2010). Due to the lack and heterogeneous nature of definitions and in order that synthesis was possible, a top-down application of concept definitions was agreed by the co-authors post-hoc. The definitions provided in chapter 2 were employed (see section 2.3.1).

Therefore, studies that claimed that they measured adherence, but were not explicit with regards to their operational definition, could only be categorised as measuring persistence as it was not possible to determine to what extent medication regimes were being followed. Studies that were explicit with regards to their operational definition were also interpreted and categorised according to the definitions outlined above, the result of which can be seen in (Table 8).

3.5.9 Measures of treatment utilisation

There were 15 studies (33.3%) which provided an explicit definition of adherence, persistence, or discontinuation. Based on the definitions outlined above, it was determined that 39 (86.7%) studies measured discontinuation as an outcome measure (Table 10). One study measured adherence only and defined adherence as taking at least 70% of prescribed doses, which was calculated under the assumption that arm A, who were supplied 2 tablets per week, were taking the whole supplied medications (at an average of twice weekly) and arm B were taking it daily. (Ricardi et al, 2010). Two studies utilised a measure of persistence only and 3 studies measured both persistence and adherence using the Persistence Adherence Questionnaire (PAQ). The PAQ is an unvalidated measure, (Rubio-Aurioles et al, 2013; El-Meliegy et al, 2013; Cairoli et al, 2014) and classifies adherence as taking the most recent dose in accordance with one's prescription and persistence as taking ≥ 1 dose of medication in the last 4 weeks.

Thirty-seven studies (82.2%) provided details of the method used to measure adherence, persistence, or discontinuation. Methods included consultations (n=5), chart reviews (i.e., previously recorded clinical data) (n=2), prescription renewal (n=2), telephone survey (n=3), interviews (n=4), patient diary (n=2). However, the most common method was the use of self-

report questionnaires (n=19); of these, seven studies used a questionnaire designed specifically for the study and 12 studies did not state the questionnaire source. Rates of treatment utilisation were presented as a percentage. None of the studies included in this review used a validated measure of adherence.

3.5.10 Treatment Utilisation

PDE5Is

Rates of discontinuation for PDE5I treatment ranged between 13.8 – 76%, rates of treatment adherence ranged from 59.6 -100% and rates of persistence from 64.9 - 100% (). Follow up periods ranged from 2.2 – 48 months. Out of the 29 studies, 20 utilised a prospective cohort design, two were quasi experimental, five cross-sectional, one mixed methodology and one was an RCT.

ICI

Discontinuation rates for ICI ranged from 18.6 to 79.9%. These studies varied regarding the length of follow up, ranging from 6 to 84 months. Two of these studies were cross-sectional and all other studies utilised a prospective longitudinal cohort design. For example, three studies had a follow-up period of 6 months (Alvarez et al, 1998; Polito et al, 2012; Irwin & Kata, 1994) where rates of discontinuation were 34, 60 and 18.6% respectively. There were no studies that reported rates of persistence or adherence in relation to ICI treatment.

Urethral Suppositories US)

Three studies focussed on urethral suppositories for ED, in which rates of discontinuation ranged from 32–69%. All the studies were a prospective cohort design where follow up periods were 9 months (mean) (Mulhall et al, 2001; Raina et al, 2007) and 27 +/- 14 months (Raina et al, 2005).

There was no pattern with regards to rate of discontinuation and length of follow-up. For example, two studies had a follow-up period of 9 months (Mulhall et al, 2001; Raina et al, 2007) and the third a follow up period of 27 months (Raina et al, 2005) with rates of discontinuation were 69, 32 and 52% respectively.

Penile Prosthesis

The only study of penile prosthesis followed patients over a 65-month period; the reported discontinuation rate was 30% (Sexton et al, 1998).

Table 10: Adherence to Treatment

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
ICI treatment				
Alvarez et al (1998)	NR	PD	After each injection: date, time, volume of injection and dose were recorded by the patient.	34% (D)
Armstrong et al (1994)	NR	SRQ	Qs: covering home injection use including period of time.	64% (D)
Gerber & Levine (1991)	NR	Cons	Qs: covering frequency of prostaglandin E1 use.	72% (D)
Irwin & Kata (1994)	NR	NR	Monthly follow-up visits to evaluate patients' acceptance and usage pattern.	60% (D)
Kunelius & Lukkarinen (1999)	NR	SRQ	Qs: aspects of sexual function and possible problems with Aprostadil self-injection.	46%.4 (D)
Lehmann et al (1999)	NR	Int & Cons	Qs: covering the number of injections used.	20% (D)
Perimenis et al (2001)	NR	NR	NR	42.5% (D)
Polito et al (2012)	NR	NR	NR	18.6% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Purvis et al (1999)	NR	SRQ	NR	38.6% (D)
Raina et al (2003a)	NR	SRQ, CR	Data collected: treatment effect, frequency of use, duration of erection following penile injections and side effects.	52% (D)
Rowland et al (1999)	NR	SRQ	Qs: items pertained to how ICI was used, its effectiveness, and the patients' general satisfaction.	40% (D)
Sexton et al (1998)	NR	NR	NR	ICI:59%(D) PP:30%(D)
Sung et al (2014)	NR	TS	Qs: multiple responses.	79.9% (D)
PDE5I medication				
Buvat et al (2013)	NR	Cons	NR	Tadalafil OaD:52% (D) Tadalafil PRN:42% (D) Sildenafil PRN:67% (D)
Buvat et al (2014)	D = days to switch or discontinuation	Cons	A telephone follow-up call was performed if a patient had no visit within 4–6 months after baseline.	13.8% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Cairolí et al (2014)	P= $\geq$ 1 dose in last 4 weeks A= most recent dose in accordance with prescription	PAQ	Qs: drug administration, dosing compliance, erectile function, sexual performance/satisfaction, relationship status.	70.2% (A) 69.2% (P)
Carvalho et al (2014)	P=Continued use	SRQ	Qs: demographics, type of PDE5i and frequency of use, other previous treatments, side effects, expectations regarding the treatment, and partner involvement	100% (P)
Cimen et al (2009)	NR	Int	Qs: PDE5 inhibitor usage status (current using/stopped using), patient satisfaction, reasons of treatment interruption (inadequate efficacy, treatment expenses, adverse effects, etc.), drug shift (interchange between different PDE5 inhibitors) and satisfaction with the new drug were interrogated.	32.8% (D)
Conaglen & Conaglen (2012)	D=stopping medication taking	Int	Qs: details of frequency of usage and reasons for discontinuation of use.	33% (D)
Mazzola et al (2013)	D=stopping medication taking	NR	Qs: regarding continued use of PDE5Is.	67% (P)
El-Galley et al (2001)	P=Continued use	TS	NR	48% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
El-Meliegy et al (2013)	P= $\geq$ 1 dose in last 4 weeks A= most recent dose in accordance with prescription	PAQ	NR	59.6% (A) 64.9 (P)
Fagelman et al (2001)	D=Prescription renewal	SRQ, Int	Qs: demographics, comorbid conditions, duration of ED, length of time taking sildenafil, number of tablets taken, maximum dose, efficacy, safety, satisfaction, and others.	38% (D)
Green & Martin (2000)	NR	Quest	At follow-up clinic visits or telephone interviews.	32.5% (D)
Incrocci et al (2003)	NR	SRQ	Qs: current sexual functioning and use of sildenafil.	76% (D)
Jiann et al (2006)	NR	SRQ	Qs: marital status, ED duration, frequency of sexual intercourse, history and current status of usage.	57% (D)
Kim et al (2014)	D=not taken PDE5i in the past 1 year	SRQ	Qs: characteristics and treatment of ED.	23.9% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Klotz et al (2005)	D=no 2 nd prescription within 6 months	PR	NR	31% (D)
Lee et al (2010)	D=treatment cessation at 2/6 months	NR	Compliance measured at two different time points: at 2 months and again at the 6 month follow-up after.	72% (D)
Ljunggren et al (2008)	NR	Int	Qs: current treatment, frequency of use, change of treatment, reason for change, and reason for discontinuation.	14.2% (D)
McMurray (2007)	NR	PD	Compliance was assessed by medication diaries and by continued study participation.	40% (D)
Montorsi et al (2004)	NR	Cons	NR	21% (D)
Carvalheira et al (2012)	NR	SRQ	Qs: quantitative and qualitative variables and including frequency and duration of PDE5 use.	48.9% (D)
Raina et al (2003b)	NR	CR	Data collected: drug efficacy, dose, frequency, compliance, return of erections, new side effects.	27% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Ricardi et al (2010)	A=taking at least 70% of doses	NR	NR	Arm A (20-mg tadalafil PRN): 86% (A) Arm B: (tadalafil 5-mg OaD): 100% (A)
Roumeguer e et al (2008)	D=not using treatment in past 4 weeks.	Quest	Qs: Tadalafil utilisation in the past 4 weeks: the number of tablets, dosage, and tolerance were recorded.	16% (D)
Rubio-Aurioles et al (2013)	P $\geq$ 1 dose taken within the last 4 weeks A= most recent dose taken according to original instructions	PAQ	PAQ administered to patients at 1, 3, and 6 months after treatment initiation.	67.5% (A) 66.5% (P)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Salonia et al (2008b)	NR	Cons	Data gathered included patient compliance with the suggested PDE5.	42% (D)
Salonia et al (2008a)	NR	SRQ	Patients were asked to complete a multiple-choice GAQ	72.6% (D)
Sato et al (2007)	NR	SRQ, Int, Cons	NR	48% (D)
Son et al (2004)	NR	TS, CR	Compliance to medication and the reason for discontinuity were reviewed by chart or surveyed by telephone.	34.6% (D)
Souverein et al (2002)	D = (1) no refills in 12 months; (2) switched treatment or (3) 6 months between the last refill and the end of follow-up.	PR	Sildenafil use during follow-up was assessed using information on the number of Sildenafil refills during follow-up	45% (D)
Intraurethral suppository				
Mulhall et al (2001)	NR	SRQ	Qs: to determine whether they were continuing to use MUSE as a treatment.	69% (D)

Author, year	Definition (A,P,D)	Method	Adherence measure	% Adherent (A), persistent (P) discontinued (D)
Raina et al (2007)	NR	NR	NR	32 (D)
Raina et al (2005)	NR	CR	Data gathered: treatment effect, frequency of use, duration of erection following treatment and side effects.	52 (D)

Note: CR: chart review; Cons: consultation; Int: interview; NR: not reported; PAQ: persistence adherence questionnaire; PD: patient diaries; PR: prescription records; Qs: questions; Quest: questionnaire; SRQ: self-report questionnaire; TS: telephone survey; Y: year

Assessment of barriers and enablers of treatment utilisation

Overall, none of the studies (n=45) used a validated measure or a theoretical approach to investigate the barriers and enablers to treatment utilisation. However, of the 45 included studies, 39 (86.7%) provided details of their method for assessing the barriers and enablers to treatment utilisation (Table 10).

The most common method of assessment was unvalidated questionnaires (n=20); 15 used this method exclusively and five used them in conjunction with other methods. Three of these used the PAQ. Other methods included telephone surveys (n=6), consultations (n=6), patient interviews (n=1), prescription records (n=1), and patient diary entries (n=1). There were another four that used a combination of these methods (Table 10).

Most studies did not provide information on the items within the questionnaires or how questions were posed to participants. Some studies indicated that questionnaire items were closed i.e., participants responded by selecting multiple choice answers (n=5), while others utilised questions that were open ended (Carvalheira et al, 2014; Carvalheira et al, 2012).

Twenty-five studies reported barriers and enablers to ED treatment utilisation using only descriptive statistics, where results were presented as proportions of participants either continuing with, or ceasing ED treatment for a particular reason. Less than half (n=20) of the studies examined whether there was a statistically significant relationship between potential barriers/enablers and rates of treatment utilisation.

Table 11: Measurement of Barriers and enablers of treatment utilisation

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
ICI treatment			
Alvarez et al (1998)	PD	Reasons for discontinuation were collected monthly.	Descriptive: Patients were asked about reasons for discontinuation and the percentages of patients reporting a particular reason for discontinuation were reported.
Armstrong et al (1994)	SRQ	A questionnaire was sent to patients who had failed to attend follow-up appointments. Reasons for withdrawal from treatment were collected via predefined questions asking reasons for discontinuation.	Descriptive: Percentages of patients reporting a particular reason for discontinuation.
Gerber and Levine (1991)	Cons	Patients returned for evaluation 1 and then every 3 months and were questioned regarding erectile response, pain after injection and frequency of ICI use.	Descriptive: Reasons for discontinuation were reported as a total percentage or participants reporting a particular reason for discontinuation across the cohort
Irwin & Kata (1994)	Cons	Patients were given monthly follow-up visits scheduled to evaluate the patients' acceptance and usage patterns	Descriptive: Data with regard to reasons for discontinuation were collected and subsequently presented as a percentage of total participants reporting a particular reason for discontinuation.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Kunelius et al (1999)	SRQ	Patients with ED who had been started on ICI treatment were invited to a check-up after three years. Patients were sent a questionnaire prior to their appointment.	Descriptive: Reasons for discontinuation were collected retrospectively and reported as percentages across the entire participant cohort.
Lehmann et al (1999)	Int, Cons	The evaluation protocol covered objective and subjective variables which included barriers to treatment use.	Descriptive: The percentages of both those who had discontinued and those who had continued were compared on a variety of demographic and clinical variables. Inferential: Patients who had continued with treatment were compared with those who discontinued therapy on a variety of demographic and clinical variables using Student's <i>t</i> test, Mann-Whitney <i>U</i> test, or Fisher's exact test, as appropriate.
Perimenis et al (2001)	NR	NR	Descriptive: Data with regards to discontinuation were compared between two groups: one of those with diabetes and one group without. The overall number of patients discontinuing for a particular reason were reported.
Polito et al (2012)	SRQ	Patients were administered a questionnaire if they had decided to interrupt the treatment. The questionnaire contained multiple choice questions including: lack of, disappointment with the effects / Injection pain/ Problems with the injection (difficulty/fear) / Cost of the drug.	Descriptive: Reasons for discontinuation were reported across all patients retrospectively and presented using percentages.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Purvis et al (1999)	SRQ	Participants were sent a questionnaire with a stamp addressed envelope. Twenty-eight questions were asked which were multiple choice in the majority of cases.	Descriptive: Participants who were still using treatment were compared to those who had ceased treatment on a number of factors and presented using percentages. In addition reasons for discontinuation across the cohort of patients who had discontinued were reported using overall percentages of participants for each reason.
Raina et al (2003a)	NR	NR	Descriptive: The number of patients discontinuing treatment for multiple reasons was calculated as a percentage of the total.
Rowland et al (1999)	SRQ	Participants completed a questionnaire at follow up which had a section for participants who had discontinued ICI treatment.	Descriptive: Reasons for discontinuation were presented as percentages of overall participants indicating a particular reason. Inferential: Initially bivariate analyses was used (for example, simple correlation, Chi square, t-tests) and where variables suggested relationships ($P < 0.10$) to the outcome variable they were then considered for inclusion in a multivariate logistic regression analysis.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Sexton et al (1998)	TS	Follow-up telephone interviews were conducted with all patients to determine level and frequency of sexual activity, current form of therapy, and reasons for discontinuing therapy, side effects and overall satisfaction.	Descriptive: Overall percentages of participants discontinuing for a given reason were provided. Inferential: Chi-square analysis was used to compare outcome data among subgroups of patients. Student's t test was used to compare means. Kaplan- Meier survival curves were used to estimate treatment longevity among patients using ICI versus penile prostheses.
Sung et al (2014)	TS	At the follow up telephone interview participants were asked about reasons for discontinuation. The questionnaire included questions focussed on withdrawal from ICI treatment and its reason.	Descriptive: Percentages of participants were recorded against pre-defined multiple-choice options for discontinuation. Inferential: Two-tailed Student's t-test was employed for the comparison of means between those that continued and those that discontinued. Statistical significance was assessed based on a two-sided $p < 0.05$.
PDE5Is			

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Buvat et al (2013)	Cons	Time to discontinuation was measured by the number of days from randomization up to discontinuation of randomised treatment. Secondary outcomes included the proportion of patients who switched and discontinued treatment, switching patterns and reasons for switches and discontinuations.	Descriptive: Reasons for discontinuation were presented as a percentage of overall patients reporting a particular reason for discontinuation. Inferential: Time to discontinuation of treatment was estimated using the Kaplan–Meier product-limit method. The primary analysis compared each of the two tadalafil groups vs. sildenafil PRN using a Cox proportional hazard model with factors for treatment group, baseline IIEF-EF score, and country. Reasons for discontinuation from treatment were compared using Fisher’s exact test.
Buvat et al (2014)	Cons	Patients who initiated or switched to tadalafil OaD at baseline but switched or discontinued this treatment during the observation were followed up until the end of the 6-month observation period. A telephone follow-up call was performed if a patient had no visit within 4–6 months after baseline.	Descriptive: Treatment switching patterns and reasons for switches or discontinuations were presented as a percentage of patients discontinuing treatment for a given reason. Inferential: Time to discontinuation was estimated using the Kaplan–Meier product-limit method. Additional exploratory analysis investigated the association between time to discontinuation of tadalafil OaD and selected baseline factors using a Cox proportional hazards model.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Cairolì et al (2014)	SRQ, clin, demog data	A questionnaire administered at 1, 3, and 6 months post baseline.	Descriptive: Baseline data was used to look at persistence, adherence and discontinuation at 6 months where participants who were persistence, adherent or had discontinued were compared using percentages. Inferential: To identify factors associated with persistence and adherence, a multivariate logistic regression model was used to analyse data for the complete study population.
Carvalheira et al (2014)	SRQ	A 29-item questionnaire including open ended questions with regards to utilisation of PDE5Is.	Descriptive: A phenomenological approach was taken. Data with regard to reasons for discontinuation presented qualitatively. This data was then used to provide a quantitative interpretation where overall percentages were given for reasons for discontinuation.
Cimen et al (2009)	SRQ	Patients were called by phone and asked to answer questions on the phone including questions regarding reasons for discontinuation.	Descriptive: Reasons for discontinuation were presented as overall percentages of patients discontinuing treatment for a given reason. Inferential: Cost of treatment was the only variable that was presented with a level of significance.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Conaglen & Conaglen (2012)	Int	The interviewer followed a question schedule that sought details of frequency of usage and preference for the drugs available to participants. Reasons for that choice, or for discontinuation of use, were also sought.	Descriptive: Data with regard to reasons for discontinuation was presented descriptively using overall percentages of participants and their given reasons for discontinuation.
Mazzola et al (2013)	Cons	On follow-up, patients were questioned regarding continued use of PDE5.	Inferential: Multivariable analysis was conducted to define predictors of continued sildenafil Use.
El-Galley et al (2001)	TS	Participants were contacted by telephone. Patients who ended treatment were asked about the main reason for discontinuation.	Descriptive: Reasons for discontinuation were presented as descriptive data and overall percentages of patients reporting a particular reason for discontinuation were reported.
El-Meliegy et al (2013)	SRQ, clin/demog data	Outcomes were assessed at baseline and at 1, 3, and 6 months after treatment initiation.	Descriptive: Demographics and baseline characteristics were described using summary statistics for patients who were persistent at 6 months versus patients who were non persistent Inferential: A logistic regression model indicated factors significant at the 10% level and used stepwise model reduction excluding factors with $p > 0.05$.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Fagelman et al (2001)	SRQ	At follow-up visits, the patients were given a questionnaire and then interviewed	Descriptive: Reasons for not renewing treatment were reported based on the first and second follow up visit and were presented as the total percentages of patients reporting a particular reason for discontinuation.
Green and Martin (2000)	SRQ / TS	The initial forty patients were followed for a two-year interval either by follow-up clinic visits or telephone interviews.	Descriptive: Data was presented descriptively by providing the total number of participants reporting a particular reason for discontinuation.
Incrocci et al (2003)	SRQ	Patients who had participated in the trial were sent a questionnaire to evaluate their current sexual functioning and to ask about sildenafil use.	Descriptive: Data was presented descriptively by providing the total number of participants reporting a particular reason for discontinuation.
Jiann et al (2006)	SRQ	Participants were mailed a questionnaire which used multiple choice questions regarding reasons for discontinuation.	Descriptive: Reasons for discontinuation were presented as percentages of participants indicating pre-defined multiple-choice reasons for discontinuation. Inferential: A comparison was made between those who had continued and those who had discontinued. Data were analysed using χ^2 test and t-test. The level of significance was considered as $P < 0.05$.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Kim et al (2014)	SRQ	A questionnaire was distributed to participants regardless of the effect (success or failure). The questionnaire had multiple choice questions regarding discontinuation.	Descriptive: Data were presented as percentages of overall participants reporting a particular reason for discontinuation. Inferential: Socio-demographic characteristics influencing compliance were analysed using univariate and multivariate analyses where discontinuation vs continuation were dependent variables. Univariate analysis was used to look at the difference between those that continued and those that discontinued and were compared using the chi-square test or, if necessary, the Fisher's exact test. A multivariate logistic analysis was used to investigate factors found to be significant by the univariate analysis.
Klotz et al (2005)	TS	Abandonment of therapy was defined as not asking for a second prescription within 6 months of receiving the first prescription for sildenafil. Afterwards, the reasons for abandonment were determined by a telephone survey.	Descriptive: Reasons for discontinuation were presented as a percentage of overall participants indicating a particular reason for discontinuation.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Lee et al (2010)	TS	Reasons for discontinuing PDE5I therapy were recorded by asking each patient, 'Have you been consistently taking your medication as prescribed?' and, 'How long have you been consistently taking your medication?' A negative response was followed by the question, 'Why did you stop taking the (PDE5I type) medication?' The answer was then categorized according to the four most frequent responses: high cost, side-effects, effect below expectations, and other.	Descriptive: Reasons for discontinuation were presented using overall percentages. Inferential: Reasons for discontinuation were analysed using Fisher's exact test. A Student's T-test and Wilcoxon-Mann-Whitney test were used to analyse participant's demographic and clinical data. A one-way ANOVA F-test and a Kruskal-Wallis test was used to compare men who were initially noncompliant with those who remained compliant throughout, and those who changed from compliant to noncompliant after 2 months.
Ljunggren et al (2008)	TS	Participants were contacted by telephone and asked questions regarding reasons for discontinuation.	Descriptive: Data with regard to reasons for discontinuation was presented as the total number of patients reporting a particular reason for discontinuation.
McMurray (2007)	NR	Effectiveness was assessed by asking, at yearly intervals or at discontinuation, questions relating to adverse events and changes in dosing or to temporary or permanent discontinuation were recorded.	Descriptive: Data with regard to reasons for discontinuation was presented descriptively by indicating the total number of participants reporting a particular reason for discontinuation.
Montorsi et al (2004)	Cons	At patient visits, blood pressure and pulse, adverse events, concomitant medications and the reason for dose modification were recorded.	Descriptive: The total numbers and percentages of participants indicating a particular reason for treatment discontinuation were presented.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Carvalho et al (2012)	SRQ	A telephone interview involving a comprehensive, detailed questionnaire which included two open ended questions: (i) How did you take the inhibitor? And (ii) What reasons led you to stop medication?	Descriptive: Demographic and qualitative reasons for discontinuation were presented for three groups: those that discontinued at 1-3, 4-12 and >12 months using the total percentage of patients according to each category. Regarding open-ended questions, transcribed data were organized into categories and a content analysis was performed. Inferential: A logistic regression was conducted to assess whether age, aetiology, side effects, partner's involvement in the treatment, and partner's level of sexual activity could predict PDE5 discontinuation. A chi-square test was used to test the association between ED aetiology and discontinuation rate. Significant effects were assumed for $P < 0.05$.
Raina et al (2003b)	SRQ	A questionnaire which focussed on sexual satisfaction of the patients' spouses/partners 3 years after the first survey to assess long-term efficacy and compliance.	Descriptive: Reasons for discontinuation were presented as the total number and percentage of Bilateral NS, Unilateral NS and Non-NS who had discontinued for a particular reason.
Ricardi et al (2010)	NR	NR	Descriptive: Reasons for discontinuation were presented as the total number of participants indicating a particular reason for discontinuation.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Roumeguere et al (2008)	SRQ	At 1, 6, and 12 months, patients completed the IIEF-EF domain questionnaire, EDITS and the relationship questionnaire, and indicated whether tadalafil was used in the previous 4 weeks. If it was used, the number of tablets, dosage, and tolerance were recorded. If tadalafil was not used, the patients indicated from a series of predefined reasons for discontinuation.	Descriptive: Data with regard to reasons for discontinuation was presented descriptively as the total percentage of patients indicating a particular reason for discontinuation. Inferential: Multivariate logistic regression was used to identify the factors as statistically significantly associated with treatment continuation at 12 months
Rubio-Aurioles et al (2013)	SRQ, clin/demog data	Patients provided assessments of drug administration and dosing compliance, erectile function, sexual performance and satisfaction, and relationship status at 1, 3, and 6 months following the initiation of treatment.	Descriptive: Clinical and demographic differences as well as rates of adherence and persistence between groups who were taking tadalafil, sildenafil and vardenafil were provided as the total number and percentage of participants falling into each category. Inferential: To identify the factors that were associated with persistence and adherence, a multivariate logistic regression model was used.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Salonia et al (2008b)	Clin, demog data	Patients were subdivided into two groups according to their compliance: group 1 included patients who answered “yes” to the question, “Do you still use the therapy that has been previously prescribed to you?” and group 2 included patients who answered “no” to the same question.	Descriptive: Descriptive statistics for the 9-month follow-up parameters (demographic and clinical factors) in both compliant and noncompliant patients were compared by providing the total number and percentage of participants falling into each category. Inferential: Univariate and multivariate logistic regression analysis were used to address patients’ compliance with the suggested PDE5 treatment across the whole sample.
Salonia et al (2008a)	SRQ	At the 18-month follow-up, patients were also asked to complete a multiple-choice global assessment questionnaire (GAQ) regarding specific reasons for eventual therapy discontinuation.	Descriptive: Data with regard to reasons for discontinuation was presented as the total number and percentage of participants indicating a particular reason for discontinuation.
Sato et al (2007)	Clin, demog data	Reasons for discontinuation were not asked about due to privacy concerns of the authors, however, significant risk factors for the dropout during successful treatment were analysed.	Inferential: Significant risk factors for the dropout during successful treatment were analysed by the Cox proportional hazards model. In this model, dropout was a dependent variable; independent variables were the pre-treatment age, IIEF-5 score, and status of comorbidities.
Son et al (2004)	TS, CR	Six months after the first sildenafil prescription, compliance to medication and the reasons for discontinuation were reviewed by chart or surveyed by telephone.	Descriptive: Data with regard to reasons for discontinuation was presented descriptively using the total number and percentage of participants indicating a particular reason for treatment discontinuation.

Author, year	Measure of barriers and enablers	How barriers and enablers to treatment utilisation were measured	Analysis
Souverein et al (2002)	PR	The date of sildenafil discontinuation was defined as the last sildenafil prescription date plus the number of tablets dispensed.	Inferential: Relative risk (RR) estimates for discontinuation of sildenafil and 95% confidence intervals (CI) were calculated using Cox proportional hazards analysis. Other potential determinants of sildenafil discontinuation were included in a multivariate Cox regression model.
Intraurethral suppository			
Mulhall et al (2001)	SRQ	Patients from the study group were interviewed during office follow-up visits in a prospective manner to determine whether they were continuing to use MUSE as a treatment. Those who had discontinued therapy were asked to complete a questionnaire regarding the reasons for stopping. Answers were multiple choice.	Descriptive: Data with regard to reasons for discontinuation were presented descriptively using the total percentage of participants reporting a particular reason for treatment discontinuation.
Raina et al (2007)	NR	NR	Descriptive: Several reasons for treatment discontinuation and the number of participants reporting a particular reason are indicated.
Raina et al (2005)	NR	NR	Descriptive: Several reasons for treatment discontinuation and the total number and percentage of participants reporting a particular reason are indicated.

Clin: clinical data; CR: chart review; Cons: consultation; demog: demographic data; Int: interview; NR: not reported; PD: patient diaries; PR: prescription records; SRQ: self-report questionnaire; TS: telephone survey; Y: year

3.5.11 Barriers and enablers to ED medication adherence and persistence

Definitions of barriers and enablers

A wide range of barriers and enablers were reported by the 45 studies included in this review. In order to synthesise the data in relation to the barriers and enablers of adherence, persistence and discontinuation, broad categories emerged, and the data was categorised according to the following six categories (Table 12):

- Demographic factors - age, gender, ethnicity, education
- Clinical factors - those relating to the nature of the condition such as its aetiology, ED severity and duration as well as factors related to ED treatment which included e.g., side-effects and the efficacy of medication
- Psychological and cognitive factors - individual-level processes and meanings that influence mental states such as coping, depression, stress and beliefs about illness and treatment
- Social factors - general factors at societal level concerned with social structure and social processes that impinge on the individual, such as having a sexual partner and intimate relationship, factors such as sexual, social, emotional, recreational, and intellectual aspects of a relationship
- Behavioural factors - observable behaviours, which can be objectively measured such as physical activity, as opposed to internal events such as thinking

The findings in each category are reported below.

Demographic factors

Sixteen studies examined the relationship between demographic factors and the utilisation of PDE5Is (n=12) or ICI treatment (n=4) (Table 12).

Age

Age was investigated as a factor affecting treatment utilisation in 16 studies, 12 on PDE5Is and 4 on ICI therapy (Table 12).

Of the twelve studies focussed on PDE5Is, eleven used inferential statistics. Of these, six found that age did not significantly influence treatment utilisation (Kim et al, 2014; Lee et al, 2010; Cairoli et al, 2014; Jiann et al, 2006; Salonia et al, 2008a; Sato et al, 2007), however, three reported significantly higher rates of discontinuation for men aged over 60 (Roumeguere et al, 2008; Souverein et al, 2002) and over 65 (Buvat et al, 2014). Conversely, two studies reported that older men were significantly more persistent and adherent than younger men (El-Meliegy et al, 2013; Carvalheira et al, 2012). One descriptive study reported higher rates of persistence in younger men (Rubio-Aurioles et al, 2013). Studies were similar in terms of the number of participants and length of follow-up.

Four studies considered the effects of age on adherence to ICI treatment, of these, three used inferential statistics (Lehmann et al, 1999; Rowland et al, 1999; Sung et al, 2014) and one descriptive (Purvis et al, 1999). In all cases age was not indicated as being associated with rates of treatment utilisation.

Education

Five studies investigated the relationship between level of education and PDE5I utilisation (Kim et al, 2014; Cairoli et al, 2014; Rubio-Aurioles et al, 2013; El-Meliegy et al, 2013; Salonia et al, 2008a). Although various terminology was used, studies using descriptive statistics reported that, higher levels of education were associated with increased persistence and adherence (Rubio-Aurioles et al, 2013; El-Meliegy et al, 2013). Where inferential statistics were used, two

studies reported significantly higher levels of persistence with regards to those with higher levels of education (Kim et al, 2014; Rubio-Aurioles et al, 2013; Salonia et al, 2008a). However, one of these studies indicated that this relationship was non-significant when using multivariate analysis rather than univariate (Salonia et al, 2008a). Further, one study investigated education in finer detail comparing for instance those with postgraduate or university education with those with no formal education. No significant differences in terms of treatment utilisation emerged (Rubio-Aurioles et al, 2013).

Employment

Three studies investigated the effects of employment on PDE5I utilisation; two indicated that being employed full-time was associated with significantly higher rates of adherence when compared to being employed part-time, retired, or unemployed (Cairolì et al, 2014; El-Meliégy et al, 2013). Similarly, significantly higher rates of persistence were indicated for those in full-time employment compared to being unemployed or retired (El-Meliégy et al, 2013). However, there was evidence to suggest that relationships were not significant according to one study (Buvat et al, 2014). Studies were of similar quality across the board according to the QualSyst tool (Figure 7) and utilised both multi logistical regressions and Cox proportional hazards models to control for confounding variables such as age.

Religion

One study reported that being Catholic compared to Protestant, Buddhist or other religions was significantly related to discontinuing PDE5Is (Kim et al, 2014).

Other demographic factors

Participant's height, residential area, occupation, ethnic background, and number of children were reported as not having a significant impact on treatment utilisation (Kim et al, 2014; Cairoli et al, 2014).

Clinical Factors

All forty-five studies examined the relationship between one or more clinical factors and treatment utilisation, twenty-eight (62.2%) focussed on PDE5Is; thirteen on ICI treatment, three on US and one on PP (Table 12).

Treatment ineffectiveness

Thirty-two studies indicated that ineffectiveness has an impact on treatment utilisation, eighteen focussed on PDE5Is, ten on ICI treatment, three on US, as well as one which focussed on PP (Table 12).

Seventeen studies, which used descriptive statistics, reported that between 2 and 75.7% of men (median 34%) discontinued PDE5Is due to self-reported ineffectiveness, related to hardness and duration of erection. Fishers exact test was used by one study which indicated that significantly higher discontinuation rates of sildenafil on-demand medication was attributable to perceived ineffectiveness (erection duration) when compared to tadalafil OaD and tadalafil PRN treatment. However, no significant differences were found between the various PDE5Is in relation to hardness of erection (Buvat et al, 2013).

In relation to ICI treatment, it was reported that inadequate erectile response was a reason for discontinuation. Ten studies used descriptive statistics and one used inferential statistics.

Descriptive statistics indicated that between 8–64.7% (median 33%) of men discontinued due to ineffectiveness. Additionally, self-reported ineffectiveness was reported as having a statistically significant relationship with higher rates of discontinuation (Rowland et al, 1999).

Three studies which utilised descriptive statistics reported that between 29.6-73% (median 29.6%) of men discontinued urethral suppositories due to ineffectiveness, as the treatment lacked consistency and led to insufficient erections. A total of 4.7% of men reported prosthesis malfunction as a reason for discontinuation (Sexton et al, 1998).

Perceived side-effects

Sixteen studies on PDE5Is, 11 on ICI treatment, two on US and one on PP indicated the impact of side effects and their influence on ED treatment utilisation (Table 12). Many studies reported 'side effects' as a general term without further clarification however, where details were provided, typical side effects of PDE5I medication included, priapism (Carvalheira et al, 2014), adverse effects of the drug (Cimen et al, 2009) such as headache and rhinitis (Klotz et al, 2005), Peyronie's disease (El-Meliegy et al, 2013; Fagelman et al, 2001) and chest pain (Fagelman et al, 2001). In 16 studies that used descriptive statistics between 4.0 - 36% (median 16.6%) of men discontinued PDE5Is due to side effects. Three studies also used statistical analysis. One reported a non-significant relationship between experiencing side effects when using tadalafil once daily, tadalafil on demand and sildenafil on demand and treatment utilisation (Buvat et al, 2013). Contrary to these findings, higher rates of persistence were associated with increased incidence of adverse events in one study (Giann et al, 2006). Finally, one study reported that men who reported side effects to their HCP were less likely to discontinue treatment (Carvalheira et al, 2012) (see Table 12).

Typical side-effects for ICI treatment included distortion of the penis (Armstrong et al, 1994), pain caused by the injection (Irwin & Kata, 1994; Polito et al, 2012; Gerber & Levine, 1991; Kunelius et al, 1999), bleeding from the injection site (Lehmann et al, 1999), fibrosis in the penile shaft (Kunelius et al, 1999; Lehmann et al, 1999) and priapism (Raina et al, 2003). In the 9 studies that used descriptive statistics, between <1.0 and 45% (median 5.7%) of men discontinued ICI treatment due to side-effects. There were 2 studies which used statistical analysis where one reported significantly higher rates of discontinuation due to side-effects (Rowland et al, 1999). However, the second study, a 3-month prospective follow-up study, reported a non-significant relationship (Lehmann et al, 1999).

Urethral pain and/or burning were related to discontinuation of US, however, this was only reported by 4 men in each of two studies focused on US, where the total cohort was 54 and 56 participants respectively (Raina et al, 2007; Raina et al, 2005). Finally, infection and erosion were reported to be responsible for 9.4% of overall participants' discontinuation of penile prosthesis (Sexton et al, 1998).

Treatment Spontaneity

Six studies reported that between 3.7-9.5% of men using PDE5Is (Kim et al, 2014; Carvalheira et al, 2012; Son et al, 2004), 16.1-18.3% of those using ICI treatment (Sexton et al, 1998; Sung et al, 2014) and 49% of those using US (Mulhall et al, 2001) decided to discontinue their treatment due to the treatment lacking spontaneity (i.e. treatment requires an element of planning). In relation to PDE5Is, only one study indicated what type of PDE5I participants were using, therefore it is not possible to decipher whether there are differences between various PDE5Is in this respect.

3.5.12 Specific to PDE5I medication

History of ED utilisation

Out of two studies which considered the effects of previously using treatment for ED, one study indicated significantly higher rates of persistence for those with a history of utilisation (Souverein et al, 2002), however, the second study did not find the relationship to be significant (Sung et al, 2014).

Types of PDE5I medication

Two studies reported on different types of PDE5I medication and its effects on treatment utilisation, but neither found any statistically significant differences in persistence or adherence between vardenafil, sildenafil or tadalafil. (El-Meliegy et al, 2013; Rubio-Aurioles et al, 2013).

Men who continued to use PDE5I treatment when compared to those who had discontinued indicated significantly higher rates of indicating that treatment was effective at 1 month post prescription, having tried treatment titration (Giann et al, 2006) as well as trying doses greater than 50mg (Roumeguere et al, 2008; Giann et al, 2006).

Duration of effectiveness

In one study, participants reported that the short window of action in which sildenafil PRN is effective, was a reason for significantly higher rates of discontinuation when compared with tadalafil OaD and tadalafil PRN (Buvat et al, 2013).

Slow onset of action

Participants reported slow onset of action of PDE5Is as a reason for discontinuation in two studies (Buvat et al, 2013; (Buvat et al, 2014), however, there was no significant relationship with rates of treatment utilisation in either study.

Inconvenience and embarrassment in relation to ED Treatment

Inconvenience and embarrassment around obtaining treatment and forgetting to obtain PDE5Is were also reported as reasons for discontinuation by two studies (Carvalheira, 2014; Jiann, 2006), although like the factors mentioned above, evidence was sparse and affecting only a small percentage of study participants (Table 12).

Averse to oral medication

One study reported that 4.7% of men discontinued due to an aversity to taking oral medication (Carvalheira et al, 2014) and 23.4% reported that they discontinued due to the medication causing personal conflict, although conflict in this instance was not defined by the authors (Montorsi et al, 2004).

3.5.13 Specific to ICI treatment

There were nine studies that utilised descriptive statistics to report on aspects of ICI administration, such as: inability, difficulty, unwillingness or fear of self-injections, needle phobia or the effort to prepare and inject ICI treatment. These factors were reported as reasons for discontinuation by 2-35.2% (median 21.5) of men. One study reported that men who had difficulty with the administrative procedure, indicated statistically significant higher rates of discontinuation (Lehmann et al, 1999).

One study reported that different methods of ICI administration such as Manual Injection (d-penn) was associated with increased persistence when compared to the semi-automatic B-D injector, likewise, higher rates of persistence were indicated for Trimix as opposed to

papaverine-phentolamine and for Prostaglandin E1 as opposed to papaverine-phentolamine (Purvis et al, 1999) (Table 12).

3.5.14 Related to ED

ED Aetiology

Evidence was not clear with regards to any association between ED aetiology and treatment utilisation (see Table 12). There were five studies which focussed on PDE5Is. One study using descriptive statistics indicated that higher rates of persistence were evident for participants who had psychogenic ED rather than organic ED (Rubio-Aurioles et al, 2012), where one study indicated significantly higher rates of persistence for those with psychogenic compared to organic ED (Kim et al, 2014). In addition, those with venogenic as opposed to arteriogenic, diabetic or iatrogenic ED reported statistically significant higher rates of medication persistence (Carvalho et al, 2012). However, 2 studies did not find a statistically significant relationship between ED aetiology and utilisation of PDE5Is (Buvat et al, 2014; Cairoli et al, 2014). ED aetiology was reported as not influencing ICI treatment utilisation (Rowland et al, 1999).

ED severity

Nineteen studies used either the IIEF or the SHIM as a diagnostic tool to indicate the severity of ED (see section 1.5.1). Seven studies, all of which focussed on PDE5Is, investigated the effects of ED severity on treatment utilisation. Five found that a lower SHIM score or having mild or moderate ED was associated with significantly higher rates of persistence (Roumeguere et al, 2008; Rubio-Aurioles et al, 2014; El-Meliegy et al, 2014; Salonia et al, 2008b; Sato et al, 2007) and adherence (Rubio-Aurioles et al, 2014) compared to those with severe ED. However, two studies did not find such relationships (Buvat et al, 2014; Cairoli et al, 2014). A further study used the erection hardness scale (EHS) and found significantly higher rates of PDE5I persistence in

conjunction with a shift of 2 or more points, or a score of 4 on the EHS which indicates improved erectile function (Mazzola et al, 2013). In relation to ICI treatment, significantly higher rates of persistence were found in men who experienced penile rigidity adequate for sexual intercourse (Sung et al, 2014).

ED duration

Five studies considered the effects of ED duration on PDE5I medication taking (see Table 12), however, results were unclear. Whilst one study found that both persistence and adherence were not significantly related to ED duration (Cairolì et al, 2014), most studies suggested that both shorter (Rubio-Aurioles et al, 2014; Jiann et al, 2006) and longer ED duration (Kim et al, 2014; El-Meliegy et al, 2013) were associated with significantly higher rates of PDE5I persistence and adherence. Studies were similar in terms of cohort size (range 434 - 511) and length of follow up (6 months). Mean duration of ED symptoms were reported to be <5 years, except in one study in which it was 31 years.

Comorbidities

Nine studies investigated the effect of comorbid conditions on treatment utilisation of PDE5Is, 3 on ICI treatment and 1 on penile prosthesis (Table 12). Studies that utilised descriptive statistics indicated that comorbid conditions were a reason for PDE5I discontinuation by 4%-11% (Ljunggren et al, 2008; Klotz et al, 2005; Son et al, 2005) of participants. However, a higher proportion of those with hypertension were reported to be both more persistent and adherent (El-Meliegy et al, 2013).

Where studies used statistical analysis and were specific with regards to the type of comorbidity, participants with CAD were significantly more likely to discontinue PDE5Is (Cairolì et al, 2014).

However, participants who had undergone pelvic surgery (Roumeguere et al, 2008), had a BMI of ≥ 23 or who weighed more ($71.93\text{kg} \pm 8.55$ compared to $69.37\text{kg} \pm 8.95$) (Kim et al, 2014) reported significantly higher rates of persistence to PDE5Is (Roumeguere et al, 2008; Kim et al, 2014). Conversely, there were four studies which reported a non-significant relationship between comorbid conditions and rates of PDE5I adherence and persistence (Buvat et al, 2014; Kim et al, 2014; Lee et al, 2010; Cairoli et al, 2014).

In relation to ICI treatment 3.4% and 5.5% of overall study participants discontinued treatment due to comorbid conditions (Sexton et al, 1998; Gerber & Levine, 1991). However, one study reported comorbidities as not having a significant effect on rates of treatment utilization (Sung et al, 2014). The one study that investigated the effects of comorbid conditions on penile prosthesis treatment utilisation reported that 2.3% of overall participants discontinued due to comorbid conditions (Sexton et al, 1998).

Other conditions and treatments

One study explored the effect of other medications and treatments on PDE5I utilization. Treatment for incontinence, antidepressants, nitrate therapy and the use of insulin were associated with significantly higher rates of PDE5I discontinuation, whereas the use of lipid-lowering drugs was reported as being related to significantly higher rates of persistence. Antihypertensive agents, oral anticoagulants, low dose acetylsalicylic acid and benign prostatic hyperplasia products were shown to have a non-significant relationship with treatment utilization (Souverein et al, 2002). In addition, according to one study, 6% of men who discontinued PDE5Is reported that they did so due to believing it more important to treat other conditions (Kim et al, 2014).

In relation to ICI treatment, unrelated medical events (Alvarez et al, 1998) and deteriorating health (Armstrong et al, 1994) were associated with ICI discontinuation, whereas a low response to psychophysiological screening was related to significantly higher rates of ICI discontinuation (Rowland et al, 1999).

Other clinical factors

One study indicated that having an initial ED diagnosis by a urologist as opposed to a GP was associated with significantly higher rates of PDE5I discontinuation (Buvat, 2013). In addition, one study indicated that a lack of spontaneous erections prior to using ICI treatment and co-existing premature ejaculation were associated with significantly higher rates of ICI discontinuation (Rowland, 1999).

Psychological and Cognitive Factors

Eleven studies explored one or more psychological or cognitive factors, nine of which focussed on PDE5Is and three on ICI treatment (Table 12).

Beliefs about treatment

Lacking confidence in PDE5I medication was reported by two studies (Buvat et al, 2013; Buvat et al, 2014) as being responsible for a small percentage of men who decided to discontinue PDE5I treatment (0.8 – 1.9%), however, statistical analysis utilised by one study indicated the relationship to be non-significant (Buvat et al, 2013).

Drug dependency

Five studies found that 2.8-31% (median 7.4%) of men had decided to discontinue PDE5Is due to fear of drug dependency (Carvalho, 2012) or not wanting their intimate relationship to

become dependent on medication (Buvat et al, 2013; Buvat et al, 2014; Kim et al, 2014; Son et al, 2004). There was a significantly higher rate of discontinuation in conjunction with not wanting one's intimate relationship to depend on medication for those taking Sildenafil 'on demand' compared to those taking tadalafil 'once daily' (Buvat et al, 2013).

Fear of side effects

Four studies reported that fear of side-effects was a reason for PDE5I discontinuation. Fear of side effects in general and harm to the heart was reported by 4-15.7%-of men discontinuing PDE5Is (Carvalho et al, 2014; Son et al, 2004; Carvalho et al, 2012).

Sexual performance

Qualitative data suggested greater PDE5I persistence was associated with the perception that treatment would help to avoid and/or improve bad performance (Carvalho et al, 2014).

Treatment regime preference

Two studies investigated the effects of 'on demand' treatment and those taken 'once daily'. One utilised statistical analysis to report that those taking tadalafil 'once daily' were significantly more likely to discontinue due to 'not wanting to take a pill every day' compared to those taking sildenafil 'on demand' (Buvat et al, 2013). Conversely, men taking either sildenafil or tadalafil 'on demand' who preferred to take a pill every day exhibited significantly higher rates of discontinuation compared to those taking tadalafil 'on demand' (Buvat et al, 2013).

Satisfaction and disappointment

In relation to ICI treatment, disappointment with the treatment was associated with increased rates of discontinuation according to two studies (Polito et al, 2012; Perimenis et al, 2001).

Conversely, satisfaction was related to significantly higher rates of persistence (Lehmann, 1999) and where participants reported that they would recommend treatment to a friend, significantly higher rates of persistence were found (Polito et al, 2012).

Psychosocial well-being

A small number of studies reported individual psychosocial factors as influencing treatment utilisation. Persistence to PDE5Is, according to participants, was associated with their psychological and emotional state (Carvalheira et al, 2014), i.e., participants reported the need to take treatment when their emotional state was affected by hassles and problems.

A lack of self-esteem or self-confidence was given as a reason for PDE5I discontinuation and significantly higher rates of persistence to ICI treatment were associated with higher levels of self-esteem (Lehmann et al, 1999). However, these studies did not define what was meant by self-confidence or self-esteem or whether it was related to ED, comorbid conditions, sexual relationships, taking the treatment or indeed if it was more general in nature.

Social factors

Thirty-five studies reported a relationship between social factors and ED treatment utilisation. Twenty-two studies focussed on PDE5Is, nine on ICI treatment, two on US and one on PP (see Table 12).

Cost

Men reported the high personal financial cost of treatment as a reason for treatment discontinuation according to sixteen studies on PDE5I medication (Carvalheira et al, 2014; Incrocci et al, 2003; Roumeguere et al, 2008; Green & Martin, 2000; Buvat et al, 2014; Conaglen & Conaglen, 2012; Kim et al, 2014; Ljunggren et al, 2008; Lee et al, 2010; Rubio-Aurioles et al,

2013; Klotz et al, 2005; Carvalheira et al, 2012; Cimen et al, 2009; Fagelman et al, 2001; Jiann et al, 2006; Son et al, 2004), three studies focussed on ICI treatment (Sexton et al, 1998; Gerber & Levine, 1991; Sung et al, 2014) and one focused on US (Mulhall et al, 2001). Of those who had discontinued treatment; 3.7 - 63% of those taking PDE5Is, 4.6 - 5.5% of those using ICI treatment and 36.5% of men using US had done so due to the high personal cost of treatment. However, none of the studies used statistical analysis to explore the relationship. These included studies from the USA, Portugal, Sweden, South Korea, Taiwan, Turkey, Italy, New Zealand as well as several multicentre studies.

Relationship status

Having a partner was associated with increased persistence to PDE5I medication (Mazzola et al, 2013). Whereas not having a partner or a stable relationship was associated with medication discontinuation for; PDE5Is (Roumeguere et al, 2008; Green & Martin, 2000; Conaglen & Conaglen, 2012; Raina et al, 2003), ICI (Armstrong et al, 1994; Irwin & Kata, 1994; Sexton et al, 1998; Raina et al, 2003) and for penile prosthesis treatment (Sexton et al, 1998). However, all studies investigated this relationship using descriptive data to inform their conclusions.

In relation to PDE5I treatment, marital status (Kim et al, 2014; Cairoli et al, 2014; Salonia et al, 2008a), living with a partner (Kim et al, 2014) as well as the length of one's marriage or relationship (Kim et al, 2014; Rowland et al, 1999; Salonia et al, 2008a) were reported as having a non-significant relationship with PDE5I utilisation. However, a longer duration of living with a partner was related to a significantly higher rate of PDE5I discontinuation (Buvat et al, 2014). Finally, having a partner who was more than 10 years younger was related to significantly higher rates of persistence to PDE5Is according to one study (Mazzola et al, 2013), however, a further study found no such relationship (Kim et al, 2013).

Intimate Relationship factors

Factors related to a couples' intimate sexual relationship were explored by twenty-four studies, where fifteen focused on PDE5Is (Kim et al (2014); Carvalheira et al (2012); Jiann et al (2006); Fagelman et al (2001); Ljunggren et al (2008); Salonia et al (2008); Cimen et al (2009); Klotz et al (2005); Son et al (2004); Carvalheira et al (2014); Conaglen et al (2012); El-Galley et al (2001); Buvat et al (2014); Roumeguere et al (2008); Green et al (1999); Raina et al (2003b); Mazzola et al (2013); Salonia (2008b); Cairoli et al (2014); Buvat et al (2013), seven on ICI treatment (Irwin & Kata, 1994; Sexton et al, 1998; Gerber & Levine, 1991; Kunelius et al, 1999; Lehmann et al, 1999; Rowland et al, 1999; Sung et al, 2014) and one each on US (Raina et al, 2007) and PP (Sexton et al, 1998).

The sexual relationship

Loss of libido, or interest in the sexual relationship, was the most common factor related to couples' intimate relationships reported by 1.3-45% of men as a reason for discontinuation. According to ten studies focused on PDE5Is (Carvalheira et al, 2014; Kim et al, 2014; Ljunggren et al, 2008; Klotz et al, 2005; Carvalheira et al, 2012; Cimen et al, 2009; Fagelman et al, 2001; Montorsi et al, 2004; Son et al, 2004). In relation to ICI treatment 6.9 – 30% reported that they discontinued (Irwin & Kata, 1994; Sexton et al, 1999; Gerber & Levine, 1991; Sung et al, 2014). Finally, 8.9% and 6.9% of participants who had discontinued urethral suppositories and penile prosthesis, respectively (Raina et al, 2007; Sexton et al, 1998) (Table 12).

A partner's lack of interest in the sexual relationship (Kim et al, 2014; Klotz et al, 2005; Jiann et al, 2006; Salonia et al, 2008b), a lack of emotional readiness for restoration of sexual activity (Kim et al, 2014; Son et al, 2004) and conflict within one's relationship (Carvalheira et al, 2014;

Conaglen & Conaglen, 2012; El-Meliegy et al, 2013) were all reported as reasons for discontinuing PDE5Is. Lower levels of satisfaction with one's sexual relationship were associated with significantly higher rates of ICI discontinuation (Rowland et al, 1999). Conversely, a better-quality sexual relationship was associated with significantly higher rates of ICI treatment persistence (Lehmann et al, 1999).

Partners perception of treatment

Four studies reported that discontinuation was due to a partner's difficulty in accepting PDE5I (Buvat et al, 2013; Carvalheira et al, 2014; Roumeguere et al, 2008; Buvat et al, 2014) as well as ICI treatment (Kunelius & Lukkarinen, 1999). The percentage of men discontinuing either PDE5Is or ICI treatment due to a partner's difficulty in accepting treatment was low (Buvat et al, 2013). However, a partner's satisfaction with ICI treatment and where partners were involved in the use of PDE5I treatment, significantly higher rates of persistence were evident (Carvalheira et al, 2012; Lehmann et al, 1999).

Behavioural Factors

Seven studies examined behavioural factors and their effect on treatment utilisation, of which six focused on PDE5Is (Carvalheira et al, 2014; Roumeguere et al, 2008; Kim et al, 2014; Carvalheira et al, 2012; Mazzola et al, 2013; Salonia et al, 2008b) and one on ICI treatment (Rowland et al, 1999) (Table 12).

Help-seeking

One study investigated the impact of help-seeking behaviour and taking PDE5Is. Using inferential statistics, the study reported that the length of time before seeking help for ED was not significantly related to rates of discontinuation (Salonia et al, 2008a).

Sexual opportunity

Two studies used descriptive statistics and reported that a lack of opportunity for sexual intercourse with one's partner was a reason for up to 11.5% of men's decisions to discontinue PDE5Is (Carvalho et al, 2014; Carvalho et al, 2012).

Number of sexual attempts and Masturbation

Less frequent masturbation was related to significantly higher levels of ICI treatment discontinuation (Rowland et al, 1999). A greater number of sexual attempts in the first month of treatment and a higher rate of pre-treatment sexual activity were both associated with significantly higher rates of PDE5I persistence (Roumeguere et al, 2008; Mazzola et al, 2013).

Levels of exercise

One study reported a non-significant relationship between levels of exercise and PDE5I treatment utilisation (Kim et al, 2014).

Table 12: Treatment barriers and enablers

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
Demographic	Age			
	Being of older age	PDE5I	(-): Rubio-Aurioles (2013)	(0): Kim et al (2014) ,Salonia (2008b),Cairolì (2014),Jiann (2006),Lee et al (2010) ,Sato et al (2007) (-): Buvat (2014),Roumeguere (2008),Souverein (2002) (+): Carvalheira (2012),El-Meliegy (2013)
		ICI		(0): Lehmann (1999),Rowland (1999),Purvis (1999)
	Education			
	Higher level of education	PDE5I		(0): Cairolì (2014),El-Meliegy (2013) (+): Kim et al (2014) ,Salonia (2008b),Rubio-Aurioles (2013)(P, not A),
	Employment			
	Being in FT employment	PDE5I		(0): Buvat (2014) (+): Cairolì (2014) (A, not P),El-Meliegy (2013)(A/P),
Clinical	Related to Treatment			
	Medication Ineffective	PDE5I	(-): Carvalheira (2014), Conaglen (2012), Buvat (2014), McMurray (2007), Buvat (2013), Carvalheira (2012), Roumeguere (2008), Rubio-Aurioles (2013), Jiann (2006), Lee (2010), El-Galley (2001), Fagelman (2001), Green (1999), Incrocci (2003), Ljunggren (2008), Montorsi (2004), Raina (2003b), Salonia (2008)	Buvat (2013); - Hardness of erection (0): Tad OaD Vs Sild PRN Vs Tad PRN - Duration of erection: (0): Tad OaD vs. Tad PRN (+): Tad OaD sig increased P compared to Sild PRN (+): Tad PRN sig increased P compared to Sild PRN
		ICI	(-): Sexton (1998), Sung (2014), Alvarez (1998), Armstrong (1994), Gerber (1991), Kunelius (1999), Perimenis (2001), Polito (2012), Raina (2003a),	(-): Rowland (1999)
		US	(-): Mulhall (2001), Raina (2005), Raina (2007)	
		PP	(-): Sexton (1998)	
	Side-effects/Fear of side-effects	PDE5I	(-): Carvalheira (2014), Buvat (2014), McMurray (2007), Kim et al (2014), Roumeguere (2008), Lee (2010), El-Galley (2001), Fagelman (2001), Incrocci (2003), Ljunggren (2008), Cimen (2009), Klotz (2005), Ricardi (2010)	(0): Buvat (2013) (between PDE5Is) (+): Carvalheira (2012); (Men who reported side-effects were less likely to discontinue treatment) (-): Jiann (2006)

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
		ICI	(-): Sexton (1998), Sung (2014), Armstrong (1994), Gerber (1991), Kunelius (1999), Perimenis (2001), Polito (2012), Raina (2003a), Irwin (1994)	(0): Lehmann (1999) (-): Rowland (1999)
		US	(-): Raina (2005), Raina (2007)	
		PP	(-): Sexton (1998)	
	Medication lacks spontaneity	PDE5I	(-): Kim (2014), Carvalheira (2012), Son (2004)	
		ICI	(-): Sexton (1998), Sung (2014)	
		US	(-): Mulhall (2001)	
	Specific to PDE5I Treatment			
	Initial treatment	PDE5I		(0): Cairoli (2014)
	Having a history of ED treatment utilization	PDE5I		(0): Sung (2014) (+): Souverein (2002)
	Using; Tadalafil/Sildenafil or Vardenafil	PDE5I		El-Meliegy (2013); (0): Tad Vs Sild (0): Tad Vs Sild (+): Using Sild at initial prescription rather than Vard Rubio-Aurioles (2013); (0): Sild Vs Vard (0): Sild Vs Vard (0); (+): Tad sig increased utilisation compared to Sild (P/A)
	Able to tolerate treatment at 1 month	PDE5I		(+): Roumeguere (2008); Having good toleration for treatment after 1 month was associated with sig continued utilisation.
	Higher incidence of trying dose titration	PDE5I		(+): Jiann (2006)
	Having a dose greater than Purvis (1999)mg	PDE5I		(+): Jiann (2006)
	Short window of time in which the drug is effective	PDE5I		Buvat (2013); (0): Tad OaD Vs Tad PRN (+): Tad OaD sig increased utilisation compared to Sild PRN (P) (+): Tad PRN sig increased utilisation compared to Sild PRN
	Slow onset of action	PDE5I		(0): Buvat (2013) (Tad OaD Vs Sild PRN Vs Tad PRN)
	Specific to ICI Treatment			
	Administration	ICI	(-): Sexton (1998), Rowland (1999), Sung (2014), Alvarez (1998), Armstrong (1994), Gerber (1991), Polito (2012), Raina (2003a), Irwin (1994)	(-): Lehmann (1999)
	Type of vasoactive substance	ICI		(-): Rowland (1999)
	Disposable 1ml syringe	ICI	(0): Purvis (1999)	

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
	Fully automatic RFSU pistol	ICI	(0): Purvis (1999)	
	Manual Injection (d-penn) as opposed to semi-automatic BD pistol	ICI	(0): Purvis (1999)	
	Using papaverine-phentolamine (15 mg; 0.5 mg)	ICI	(0): Purvis (1999)	
	Using;Low dose Aprostadil (0 ± 10 mg)/High dose Aprostadil (0 ± 20 mg)/TRIMIX/D-penn Aprostadil	ICI	(0): Purvis (1999)	
	Condition Specific Factors			
	Aetiology	PDE5I	(+): Rubio-Aurioles (2013) (psychogenic associated with continuation)	(0): Buvat (2014), Cairoli (2014) (-): Kim et al (2014) (psychogenic associated with discontinuation) (+): Carvalheira (2012) (venogenic associated with continuation compared to arteriogenic /diabetes/iatrogenic)
		ICI		(-): Rowland (1999) (ED including an organic component)
	Having more severe levels of ED	PDE5I		(0): Buvat (2014), Cairoli (2014), Lee (2010) (-): Roumeguere (2008), Salonia (2008b), El-Meliegy (2013), Rubio-Aurioles (2013), Sato et al (2007)
	A shift of =/> 2 or a score of 4 on the erection hardness score (EHS)	PDE5I		(+): Mazzola et al (2013)
	Shorter Duration of ED symptoms	PDE5I		(-): Kim et al (2014) (+): Rubio-Aurioles (2013) (≥ 4 years versus <1 year; P=+, A=0),El-Meliegy (2013) (<1 year P=0, A=+), Jiann (2006) (0): Cairoli (2014) (P=0, A=0)
	Comorbidities			
	Due to the effects of co-morbidities	PDE5I	(+): El-Meliegy (2013) (Hypertension) (-): Ljunggren (2008), Klotz (2005) (tumor/hip prosthesis),Son (2004)	(0): Buvat (2014), Lee (2010) (BMI score/Charlson Comorbidity Index score). Kim et al (2014) ; (0): Number of comorbidities/Stress/Smoking/alcohol (+): Sig increase in utilisation by those of higher weight and those with a BMI of ≥ 23 Cairoli (2014); (0): Diabetes Mellitus/Dyslipidemi/Hypertension/Depression (+): Those with Coronary artery disease had sig higher rates of utilisation. (+): Roumeguere (2008) (Sig increase in utilisation by those with pelvic surgery)

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
		ICI	(-): Sexton (1998), Gerber (1991)	(0): Sung (2014) (diabetes mellitus/hypertension/cardiovascular disease/cerebrovascular attack/previous radical pelvic surgery including prostatectomy and cystectomy/unilateral or bilateral nerve sparing prostatectomy/previous pelvic radiotherapy)
		PP	(-): Sexton (1998)	
	Illness (ongoing health issues, deteriorating health or recent injuries or operations)	PDE5I	(-): Conaglen (2012), Roumeguere (2008)	
		ICI	(-): Alvarez (1998), Armstrong (1994)	
	Other medications and treatments			
	Due to other Medications and Treatments	PDE5I	(-): Kim (2014)	Souverein (2002); (-): incontinence materials/antidepressants/nitrate therapy/Insulin (0): antihypertensive agents/oral anticoagulants/low dose acetylsalicylic acid/benign prostatic hyperplasia products (+): Lipid-lowering drugs
	Other clinical factors			
	Type of physician	PDE5I		Buvat (2013); (0): Endocrinologist/diabetologist/urologist/Other (+): diagnosed by a GP rather than a urologist sig higher utilisation.
	-Presence of erections prior to treatment -Low response during psychophysiological screening (investigation of pharmacological effects on sexual response). -Lack of spontaneous erections	ICI		(-): Rowland (1999)
	Penile rigidity adequate for sexual intercourse	ICI		(+): Sung (2014)
	Premature ejaculation	ICI		(-): Rowland (1999)
Psychological and Cognitive Factors	Treatment Related Beliefs			
	Lack of confidence in medication	PDE5I	(-): Buvat (2014)	(0): Buvat (2013) (Tad OaD/Tad PRN/Sild PRN)
	Fear of drug dependency	PDE5I	(-): Carvalheira (2012)	
	Fear that medication is harmful for the heart	PDE5I	(-): Carvalheira (2014), Carvalheira (2012)	
	Averse to taking medication	PDE5I	(-): Carvalheira (2014)	
	Medication caused personal conflict	PDE5I	(-): Montorsi (2004)	
	Don't want to take a pill everyday	PDE5I	(-): Buvat (2014)	Buvat (2013); (0): Tad PRN vs Sild PRN (-): Tad OaD sig increased discontinuation compared to Tad PRN/Sild PRN
	Prefer a pill every day, not on demand	PDE5I		Buvat (2013); (0): Tad PRN vs Sil PRN

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
				(+): Tad OaD sig increased utilisation compared to Sild PRN/Tad PRN
	Not willing for sex life to depend on medication/medication controls sex life	PDE5I	(-): Buvat (2014), Kim (2014), Son (2004)	Buvat (2013); (0): Tad PRN vs Sild PRN (0): Tad OaD vs. Tad PRN (-): Sild PRN sig increased discontinuation compared to Tad OaD
	Inconvenience/embarrassment in obtaining medication	PDE5I	(-): Carvalheira (2014), Jiann (2006)	
	Forgetting to buy or to get medical prescription	PDE5I	(-): Carvalheira (2014)	
	Satisfaction with treatment	ICI		(+): Lehmann (1999)
	Disappointed with treatment	ICI	(-): Perimenis (2001), Polito (2012)	
	Would recommend treatment to a friend	ICI		(+): Lehmann (1999)
	Psychosocial Well-being			
	Lack of self-confidence/self-esteem	PDE5I	(-): Carvalheira (2014), Roumeguere (2008)	
		ICI		(-): Lehmann (1999)
	Improve Sexual performance	PDE5I		(+): Carvalheira (2014)
	To improve psychological and emotional state	PDE5I	(+): Carvalheira (2014)	
Social	Cost of Treatment			
	Cost	PDE5I	(-): Conaglen (2012), Carvalheira (2014), Buvat (2014), Kim et al (2014), Carvalheira (2012), Roumeguere (2008), Rubio-Aurioles (2013), Jiann (2006), Lee (2010), Fagelman (2001), Green (1999), Incrocci (2003), Ljunggren (2008), Cimen (2009), Klotz (2005), Son (2004)	
		ICI	(-): Sexton (1998), Sung (2014), Gerber (1991),	
		US	(-): Mulhall (2001)	
	Related to Partner and Intimate relationship			
	Loss of libido/interest in sex	PDE5I	(-): Kim (2014), Carvalheira (2012), Jiann (2006), Fagelman (2001), Ljunggren (2008), Salonia (2008), Cimen (2009), Klotz (2005), Son (2004)	
		ICI	(-): Sexton (1998), Sung (2014), Gerber (1991), Irwin (1994)	
		US	(-): Raina (2007)	
		PP	(-): Sexton (1998)	

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
	Partner lack of interest in sexual relationship	PDESI	(-): Kim et al (2014), Jiann (2006), Salonia (2008), Klotz (2005) (+): Carvalheira (2014)	
	Lack of emotional readiness for restoration of sexual activity	PDESI	(-): Kim (2014), Son (2004)	
	Higher level of Partners sexual activity	PDESI		(0): Carvalheira (2014)
	Conflicts within one's relationship	PDESI	(-): Carvalheira (2014), Conaglen (2012), El-Galley (2001)	
		ICI	(-): Sung (2014)	
	Low satisfaction with sex life	ICI		(-): Rowland (1999)
	Better quality of sexual relationship	ICI		(+): Lehmann (1999)
	Person within the dyad who most often initiated sexual activity	ICI		(0): Rowland (1999)
	Partner Related			
	Partner's difficulty in accepting treatment	PDESI	(-): Carvalheira (2014), Buvat (2014), Roumeguere (2008)	(0): Buvat (2013)
		ICI	(-): Kunelius (1999)	
	Partner satisfaction with treatment (reported by patient)	ICI		(+): Lehmann (1999)
	Partner aware of and involved in the use of treatment	PDESI		(+): Carvalheira (2014)
	Having no partner	PDESI	(-): Conaglen (2012), Roumeguere (2008), Green (1999), Raina (2003b)	(+): Mazzola et al (2013) (having a partner)
		ICI	(-): Sexton (1998), Armstrong (1994), Raina (2003a), Irwin (1994)	
		PP	(-): Sexton (1998)	
	Marital Status/Relationship Status	PDESI		(0): Kim et al (2014), Salonia (2008b), Cairoli (2014)
		ICI		(0): Rowland (1999)
	Living with partner	PDESI		(0): Kim et al (2014)
	Longer duration of living arrangement	PDESI		(-): Buvat (2013)
	Length of marriage/relationship	PDESI		(0): Kim et al (2014), Salonia (2008b)
		ICI		(0): Rowland (1999)
	Geographical distance from partner	PDESI	(-): Carvalheira (2014)	
	Partner being of younger age (=>10 years younger)	PDESI		(0): Kim et al (2014) (+): Mazzola et al (2013)
	Partners illness	ICI	(-): Kunelius (1999)	

	Barrier / Enabler	Treatment Type	Descriptive results	Inferential results
Behavioral	Help seeking			
	Length of time before seeking help for ED	PDE5I		(0): Salonia (2008b)
	Personal behavior			
	Lower frequency of masturbation	ICI		(-): Rowland (1999)
	Related to sexual relationship			
	Lack of opportunity for sexual intercourse	PDE5I	(-): Carvalheira (2014), Carvalheira (2012)	
	Pre-treatment sexual activity (=/>4 times per month)	PDE5I		(+): Mazzola et al (2013)
	Greater No of sexual attempts in the first month of treatment	PDE5I		(+): Roumeguere (2008)
	Life style			
	Level of exercise	PDE5I		(0): Kim et al (2014)

Key: A=adherence; OaD=Once a day; P=persistence; PRN=On demand; Sild=Sildenafil; Tad=Tadalafil; Vard=Vardenafil; (-) = Barrier to treatment utilisation; (+) = Enabler of treatment utilisation; (0) = Not significant

3.6 Discussion

The primary aim of this systematic review was to explore the barriers and enablers to ED treatment utilisation. The results to this review are based on an extensive and systematic database search, explicit inclusion criteria, as well as a clear approach to collecting and synthesising data, combined with an assessment of quality.

The most reported reasons for treatment discontinuation across treatment modalities, were treatment ineffectiveness and treatment side-effects. Other widely reported factors included loss of libido and the cost of treatment. Overall, there were no clear patterns of association between rates of treatment utilisation and sample size, study design or country in which the study took place.

Data on rates of treatment utilisation were synthesised. Rates of adherence and persistence were available only for PDE5Is and ranged from 59.6-100% and 64.9-100% respectively. It was, therefore, only possible to compare discontinuation rates across treatments. Overall, the highest rate of discontinuation was 79.9% for ICI therapy and the lowest 13.8% for PDE5Is. The median rates of discontinuation across the treatment modalities correspond with previous research, indicating that, in relation to medication in general, approximately 50% of individuals do not adhere to their medication regimen (Haynes et al, 2002).

A total of 45 articles were reviewed. Most focused on PDE5Is, of which the majority were carried out after 2000 which is likely to be related to the recent advent of PDE5Is and their use as the first line of treatment for ED (NICE, 2019). Less than a quarter of studies were explicit, regarding their definition of treatment utilisation and where definitions were provided, variation existed.

Findings support a previous call for the standardisation of medication adherence definitions, which would enable more accurate comparisons between studies (Cramer et al, 2008).

Results indicated a wide variation in discontinuation rates, both within, and between different treatment modalities. It has previously been suggested that methodological differences, operational definitions, type of adherence measure, treatment regimens, the variety of comorbidities and patient characteristics are potential reasons for the variety of reported rates of adherence to treatment in general (Dimatteo, 2004). In relation to this review, there was significant heterogeneity in terms of methodological designs, country as well as participant and clinical characteristics. There was an absence of reliable and validated measures in respect to both ED treatment utilisation as well as barriers and enablers to ED treatment utilisation. Many studies utilised self-report methods such as author-developed questionnaires, patient diaries, as well as semi-structured interviews. Across studies there was a lack of sufficient detail with regards to the questions asked and response options. For example, it was unclear in many of the included studies if participants were given open-ended questions or if they were provided with a selection of multiple-choice questions, which have the potential to influence participant responses. There were however, a few exceptions, where some studies provided a copy of the instrument increasing transparency (Carvalho et al, 2014; Purvis et al, 1999; El-Meliegy et al, 2013; Polito et al, 2012).

Self-report measures offer a simple and convenient way of measuring a given construct such as adherence. However, they can suffer from response bias, which involves a participants' motivation to present themselves in a positive light, in this case, to appear more persistent or adherent. Self-report methods not only rely on the participant to be truthful with regards to their responses, but also to be accurate regarding their recall of events (Paulhus, 2002). This can

include accurate recall of when they took their last treatment dose and potentially why treatment was discontinued. In a review of adherence measures, those that were self-report, such as questionnaires and diaries, were found to be consistent with objective methods, such as electronic pill counts. However, the review indicated that the use of interviews were less consistent (Garber et al, 2004). Therefore, the method used has the potential to dictate to some degree how participants respond to a given question. However, it has been highlighted that each method has its own advantages and disadvantages and that there is no 'gold standard' adherence measure (Wagner et al, 2001).

There are, in existence, a variety of validated treatment adherence measures (Garfield et al, 2011). However, none have been designed specifically for ED. Existing measures may not be suitable for assessing ED treatments which are predominantly taken on demand. The PAQ was used in three studies included in this review; and although not validated, it is potentially the first step towards developing a tool specific for use with ED. This finding echoes the call for simple, valid, and reliable methods for detecting the prevalence and types of non-adherence necessary to build effective targeted adherence interventions (Garfield et al, 2011).

Studies included in this review were retrospective with regards to investigating reasons for treatment discontinuation. The use of a retrospective study design for exploring reasons for discontinuation harbours the possibility that the associations found could be explained by other variables (Euser et al, 2009). Therefore, future research would benefit from exploring barriers to treatment utilisation prospectively, subsequently having fewer potential sources of bias and confounding variables.

3.6.1 Demographic Factors

In line with previous research, this review found limited support regarding the influence of patients' demographic characteristics (Ockene et al, 2002). The effects of age on treatment utilisation, for example, were inconsistent. However, a small number of studies indicated that a higher level of education was associated with significantly higher rates of PDE5I persistence and adherence falling in line with research related to other chronic conditions (Delamater et al, 2001). In addition, being employed full-time was associated with significantly higher rates of persistence and adherence to PDE5Is compared to those employed part-time, or who were unemployed or retired. Studies controlled for the effects of age which as a result added to the robustness of the finding. However, the cost of medication, an important factor linked with treatment discontinuation, was not controlled for. Being employed full-time is potentially linked to a higher rate of income when compared to being employed part-time or being retired. Therefore, the extent to which levels of employment and the cost of treatment overlap is not known.

3.6.2 Clinical Factors

Experiencing treatment as being less effective than expected, has previously been indicated as a reason for discontinuation (Hackett, 2002). This systematic review found treatment ineffectiveness to be the most widely reported clinical factor associated with discontinuation across all treatment modalities. Conversely, when treatment was reported as effective, increased medication persistence was reported. There was however, a lack of operational definitions with regard to 'ineffectiveness' which potentially refers to different characteristics of a given treatment. Future research would benefit from exploring individual perceptions of ineffectiveness, which could enable HCPs to support men in selecting the most appropriate

treatment, dose, and method of administration, thereby potentially reducing the chances of discontinuation.

Treatment side-effects were widely reported as a reason for discontinuation. Drug side-effects have previously been identified as being a reason for discontinuation of ED treatment (Hackett, 2002). Importantly, one study found that when side-effects were reported to a relevant HCP, significantly higher rates of persistence were found. It was not reported whether any action was taken by the HCP to facilitate this outcome, however, prescription guidelines in relation to PDE5Is suggest a starting dose which is then adjusted according to response and side effects (Wespes et al, 2006).

3.6.3 Social Factors

The most prevalent social factor related to treatment discontinuation across treatment modalities was the cost of treatment. This related to participants against which treatment charges were levied and supports previous research which has established that financial cost to the individual is a salient issue in relation to treatment discontinuation (Hackett, 2005).

In the UK, for example, the DoH provided guidance in 1999, which restricted prescription of ED treatments to those patients who meet specific criteria, meaning that, for example, those men with ED who also have diabetes, multiple sclerosis or Parkinson's disease could receive treatment on the NHS for ED (NHS Executive, 1999). If a patient did not meet such criteria, they incurred a personal cost for treatment. However, with the advent of cheaper medicines becoming available (NHS, 2019), in 2014, legislation was introduced removing the restrictions on NHS prescribing generic sildenafil, enabling HCPs the ability to prescribe generic sildenafil for all men with ED on NHS prescription (CPCC, 2018). More recently, sildenafil has also been made

available in UK pharmacies for men who wish to purchase the treatment over-the counter (PMAP, 2019). However, it was not within the scope of this review to investigate the various routes of ED treatment procurement across various healthcare systems. Studies which reported cost as barrier to treatment were from a wide variety of countries including: New Zealand, Portugal, Germany, France, Italy, Greece, South Korea, Portugal, Austria, Belgium, Denmark, Iceland, the Netherlands, Norway, Sweden and more. Suffice to say, high personal cost with regards to ED treatment relates to the wider social and economic environments which deserve attention from further research to explore the extent and the strength of the relationship to treatment discontinuation as none of the studies included in this review utilised statistical analysis, to investigate the effect of treatment cost on treatment utilisation.

It has been previously suggested that re-establishing erectile function and re-establishing a satisfying sexual interaction with a partner are fundamentally different objectives and when the latter is not met, discontinuation of treatment is likely (Riley, 2002). Loss of libido was a widely reported social factor impacting upon discontinuation. However, the term libido can be considered as having a wide variety of meanings and as a result, potential overlaps with behavioural factors such as less frequent masturbation which was related to significantly higher rates of discontinuation to ICI treatment, as well as a greater number of sexual attempts in the first month of PDE5I treatment use.

In addition, loss of libido was potentially underreported. This is because factors such as a lack of emotional readiness for restoration of sexual activity and conflict within one's relationship could potentially be related to a loss of libido. In addition, both ED and a loss of libido are symptoms of testosterone deficiency (Wu et al, 2010). This is an important consideration when it is considered that none of the studies reported potential causes of low libido in their participants.

The causes of low or a lack of libido are important considerations for HCPs when providing treatment for ED as successful treatment of other conditions such as testosterone deficiency may influence successful treatment with regards to ED.

The importance of the quality of one's intimate relationship and its effects on ED treatment utilisation has been highlighted by Althof (2002b), who suggests that a couple's physical and emotional readiness to resume sexual activity, the period of time in which the couple have not been sexually active prior to seeking treatment, the man's approach to resuming a sex life with his partner and the partner's physical and emotional readiness to resume sexual intercourse are important influential components related to treatment utilisation (Althof, 2002b). In all instances, data related to libido was self-reported, measured using non-validated measures and not subjected to any statistical analysis. Therefore, there is scope for further research to address these issues, which would enable a more in depth and thorough investigation of the relationship between libido and discontinuation.

3.6.4 Psychological and Cognitive Factors

The number of studies that considered psychological factors and their impact on ED treatment utilisation were limited in number (n=12). This was surprising considering that, for example, ED in many instances is considered as being caused by psychogenic factors. Not being willing to allow one's sex life to depend on medication was the most frequently reported psychological reason for discontinuation. As this review has considered, adherence to treatment for ED will partially relate to how treatment is perceived by the man requiring treatment. However, this review also draws attention to the additional component of men's partners' acceptance and satisfaction with ED treatment and its potential effect on treatment utilisation. Evidence from this review suggests that higher rates of discontinuation of PDE5Is and ICI treatment were

related to the negative perceptions of men's partners in relation to treatment as well as an inability to accept treatment as part of sexual relations. Conversely, when partners were satisfied with, for example ICI treatment, higher rates of persistence were reported. A large body of research exists which highlights the importance of patient beliefs about their condition and its respective treatment (Horne et al, 2001; Horne et al, 2010; Horne et al, 2013), which have been found to predict adherence in a variety of chronic conditions (Weinman & Petrie, 1997). Although socio-demographic factors are important in enabling the identification of patients who may be at high risk of discontinuing their treatment, psychological and cognitive factors are amenable to change and therefore can be targeted by psychological interventions to improve adherence (Horne et al, 2005). There were a wide range of different beliefs reported by men as reasons for discontinuing their ED treatment, however, none of the studies included in this review utilised psychological theory to assess beliefs in a systematic way. Research could therefore benefit from employing psychological theory to advance our understanding of the effect of psychological and cognitive factors on ED treatment utilisation.

3.6.5 Implications for Future Research

The methods used to ask men about barriers and enablers to treatment utilisation varied considerably. The use of open-ended questions may result in some barriers or enablers being under reported if they are not asked about specifically. Future studies would benefit from using research methodology that is prospective in nature coupled with the use of validated measures. In addition, analysis of results using multivariate statistics would enable causes to be established rather than associations.

This review indicates psychological factors related to ED treatment utilisation and psychological factors have the potential of being amenable to change, providing an opportunity to

understand motives for health-related behaviours (Hagger & Orbell, 2003). As mentioned above, research in the field of ED could potentially benefit from employing psychological theory to advance our understanding of ED treatment utilisation, creating a theoretical foundation for intervention development. A framework that highlights the importance of illness perceptions on behaviour and health outcomes is the Self-Regulation Model (SRM) (Leventhal et al, 1980). It posits that when individuals are faced with a health threat, they develop cognitive and emotional illness representations which will determine associated coping strategies such as adherence to treatment (Glattacker et al, 2012). Beliefs specific to treatment have also been given consideration through what has been termed the Extended Self-regulatory Model (Glattacker et al, 2012; Horne, 1999), which includes the Necessity-Concerns framework (NCF) (Horne, 1997). This posits that individuals carry out a cost benefit analysis in which the extent to which they believe they need a medication is weighed against any concerns they may have when consciously deciding whether to take medication or not (Donovan & Blake, 1992). The importance of patients beliefs about treatment in the context of ED has been demonstrated, for example, by Silvestri et al (2003), who explored men's use of beta-blockers. One group of participants, group A, were given beta-blockers but were not told any information about the drug they were provided. Group B, on the other hand, were informed about the drug but not its side-effects and group C were given details of the drug and its effects on erectile function. After 3 months, the incidence of ED was 3.1% in group A, 15.6% in group B and 31.2% in group C ($P < 0.01$). Men reporting ED were entered into a second phase of the study and given Sildenafil and a placebo, both of which were reported as equally effective in reversing ED (Silvestri et al, 2003). This study highlights the importance of treatment perceptions and their potential impact on treatment utilisation.

To identify salient psychological factors and subsequently the key determinants of ED treatment utilisation, the use of relevant theories and models of health-related behaviour could potentially help to understand what barriers and enablers predict treatment utilisation (Riekert et al, 2013). Horne et al (2005) suggests that psychological factors which are amenable to change can be targeted by psychological interventions to improve adherence. However, prior to intervention design it is important to carry out an exploratory study to gain a greater perspective and understanding of the potential theories, as well as the surrounding issues influencing such an intervention (Campbell et al, 2007). Therefore, an explorative study focussed on the barriers and enablers to ED treatment utilisation, in the form of a series of semi-structured qualitative interviews would be a necessary first step in this process and will be the focus of Study 2 (Chapter 5).

3.6.6 Implications for practice

The rates of treatment discontinuation identified in this review indicate that ED treatments are underutilised and as a result not achieving their full therapeutic benefit. This has important implications for both men and their partners considering research has shown that improving sexual function using treatment, has the potential to improve sexual well-being, perceived relationship quality, psychological status, self-esteem as well as overall life satisfaction (Fugl-Meyer et al, 1997; Turner et al, 1992; Costa et al, 2013; McCabe et al, 2011; Rosen et al, 2004b; Shabsigh et al, 2001; Williams et al, 1998).

This review indicated that most prevalent reasons for discontinuation across all treatment modalities were perceived side-effects, as well as perceiving the treatment as ineffective. Where men report that their treatment is ineffective, there is an opportunity for prescribers to seek to identify and clarify any misconceptions patients may have in relation to their relevant treatment.

This would provide the opportunity to explore patients' beliefs about treatment as well as the opportunity to change treatments or alter doses in line with any insights that arise. This in turn could potentially increase ED treatment utilisation. Additionally, exploring the quality of patients' intimate relationships may indicate the necessity for additional treatments such as psychosexual counselling, which could potentially work in conjunction with prescribed treatments and subsequently increase utilisation. In summary, exploring patients' beliefs in relation to treatment is important, considering research that indicates the importance of individuals' beliefs about treatment, which are considered as being potentially amenable to change. This highlights the potential importance for HCPs to explore illness and treatment beliefs with patients which in turn may benefit aspects of treatment utilisation.

3.6.7 Limitations

This review has a number of limitations which will be considered below.

Study Quality

The quality of findings from any systematic review, relies in part, on the quality of the studies included. Although study quality varied, 60% were classified as either having limited or adequate quality according to the QualSyst assessment tool. In general, there was an under-reporting of important participant data such as ED duration, ED severity, relationship status, levels of employment and education as well as comorbidities. As a result, conclusions drawn in relation to these factors are made on a limited number of studies restricting the generalisability of results.

Representativeness of the sample

Studies included in this review have demonstrated the impact of some demographic and clinical factors on ED medication taking behaviour. However, in general there was an under reporting

of important participant data. For example, a minority of studies provided data on ED duration, severity of ED, relationship status, employment, and education as well as medications used for conditions other than ED. As a result, conclusions drawn in relation to factors that have the potential to effect ED medication taking behaviour are made on a limited number of studies

Potential biases in the review process

This review was guided by the AMSTAR checklist, which highlights the importance of publication bias. The inclusion of only published manuscripts means that results of this review are potentially impacted by publication bias. In addition, available resources dictated that the search was limited to articles published in English only.

Factor Definitions

Due to the nature of some of the barriers and enablers to treatment utilisation, allocation to one of the overarching themes was not always straight forward. For example, side-effects can be clinical, but as demonstrated by the study outlined above by Silvestri et al (2003), they are also likely to have a psychological component and therefore straddle both classifications. Further, lack of libido was a term used by some studies, whereas other studies used terms such as 'no longer sexually active' which may or may not be equivalent. Therefore, in the absence of explicit definitions there is inevitably a level of ambiguity with regards to the interpretation of the results in relation to such factors.

Operational Definitions

There were a wide range of operational definitions for adherence, persistence and discontinuation employed by the included studies. Only 11 of the 45 studies were explicit regarding the definition used and even when definitions were provided, there were variations across studies. This posed a problem about interpreting study findings, as well as comparing and

contrasting study results. To overcome this hurdle, a top-down process was used, whereby definitions were imposed by the author (see section 2.3). Studies were grouped according to these definitions, however, there remains the possibility for interpretative errors to have occurred. Standardising definitions of medication adherence could be of benefit to the scientific community and would permit easier comparisons if implemented (Cramer et al, 2008).

3.6.8 Conclusions

When managed effectively, ED treatment can lead to an increase in sexual well-being as well as increased overall life satisfaction (Fugl-Meyer et al, 1997) among other factors. However, this review has identified rates of treatment discontinuation across all treatment modalities that potentially hinder such improvements. There were several socio-demographic and clinical factors that could be used to identify the type of men that may be more susceptible to non-adherence or discontinuation. However, there were a range of factors relating to patient beliefs which are potentially amenable to change and have the potential to improve treatment utilisation and subsequently sexual well-being as well as overall life satisfaction. Beliefs relating to perceived ineffectiveness, associated treatment side-effects as well as a plethora of factors related to the patient and his partner and their respective intimate relationship, have the potential to be targeted by future interventions with a view to improving treatment utilisation.

One of the important findings of the current systematic review, was the absence of theoretical models across the included studies for exploring barriers and enablers to ED treatment utilisation. Subsequently, the following chapter (Chapter 4) will consider what theoretical models are available and appropriate for exploring barriers and enablers to ED treatment utilisation with a view to selecting an appropriate model for further exploration in this thesis.

3.6.9 Systematic Review Update

The current chapter consists of a systematic review of published literature identified by database searches conducted in July 2015. Subsequently, an updated database search was conducted in August 2018, when the systematic review was being prepared for publication. This identified an additional five studies; however, the addition of these studies did not change the conclusions of the review. The systematic review was published in the International Journal of Impotence Research (IJIR) in 2020 (Williams et al, 2021) (*Appendix 6*).

4 Adherence and Theoretical Frameworks for Behaviour Change

4.1 Chapter Overview

The systematic review (Chapter 3), found that research on the barriers and enablers to using ED treatment lacked theoretical models to explore this issue. Therefore, this chapter will consider what theoretical models are available and appropriate for exploring adherence to medication and ED treatment utilisation specifically.

4.2 Background: The Advent of Behaviour Change Research

Engel highlighted the importance of the interaction between biological, psychological, and social factors (Engel, 1977; 1981), which harbour the potential to impact upon thoughts, feelings, culture, and environment and ultimately a person's behaviour. As a result, the subsequent 'biopsychosocial' approach attempts to *understand the person within the context of their life* (Forshaw, 2002). In relation to ED medication, it has been suggested that discontinuing treatment may be best explained from a biopsychosocial perspective in order that a broader view, rather than simply efficacy, education, or adverse event profiles, can be considered (Althof, 2002b).

The use of theory to inform research, such as understanding behaviour, is an important consideration as it provides a foundation for intervention development and evaluation. Theory, is able to provide an organising description of a system that accounts for what is known, and explains and predicts phenomena (Davis et al, 2015). As a result, it encompasses the ability to identify key determinants of health behaviour and can have predictive capabilities for future

health actions (Riekert et al, 2013). The use of theory is also a way to summarize available evidence, make predictions in novel contexts and provide a framework from which to design, evaluate, and refine interventions (Davis et al, 2015; Noar & Zimmerman, 2005; Prestwich et al, 2015). This is important considering the findings of the systematic review (Chapter 3) which indicated that, to date, studies that have investigated ED treatment utilisation have not used theory to underpin their research.

The use of theory to inform research can be advantageous. A systematic review and meta-analysis of internet-based health promotion strategies found that more extensive use of theory was associated with statistically significant increases in effect size ($p=0.049$) with regards to behaviour (Webb, 2010). Conversely however, a recent systematic review of systematic reviews which involved a synthesis of all published randomized controlled trials (RCT) and meta-analyses (Dalgetty et al, 2019) indicated that there was no increase in effectiveness for theory-based compared to non-theory-based interventions. Dalgetty et al (2019) propose that their results may relate to methodological and reporting issues at study and review level that may not reflect the true utility of theory. They suggested that instead of focussing on the utility of theory to increase effectiveness, the promotion of theory use may benefit from considering the benefits of using theory as stemming from a multifaceted approach i.e. using theory enables the identification of key determinants of health behaviour and enables predictive capabilities for future health actions.

4.3 Health Psychology Theories and Their Utilisation for Improving Adherence

According to Holmes et al (2014), the biomedical literature focuses on patient and disease characteristics as predictors of suboptimal adherence and such an approach has been criticised and described as being flawed due to variable selection often being based on availability rather than theoretical foundations (Steiner, 2010). Health behaviour research has consistently shown

the importance of patients' beliefs, motivations, and planning abilities as fundamental explanatory variables with regards to treatment utilisation (Jackson et al, 2014). Theories that come out of this tradition are called social cognition theories or models (SCMs) (Bosworth et al, 2006).

SCMs were developed by social psychologists to explain and predict behaviour and behaviour change (Conner & Norman, 2005). SCMs were developed on the premise that people's social behaviour is best understood by examining their beliefs about their behaviour in a social context i.e., their social perceptions and representations (Rutter & Quine, 2002). Subsequently, they attempt to model the way in which cognitions influence behaviour. Therefore, social cognitive approaches to behaviour highlight the importance of the role of interpreting information from the social context and the cognitive processes that determine whether or not, an individual engages with a given behaviour (Rodham, 2010). Fiske and Taylor (1991) define social cognitions as thoughts or cognitions which exist between observable stimuli and a subsequent response.

There are a variety of SCMs, which have been used to predict adherence to medications (Munro et al, 2007). These include the health belief model (HBM) (Becker 1974; Rosenstock, 1988), the theory of reasoned action (TRA) (Fishbein, 1967), the theory of planned behaviour (TPB) (Ajzen, 1991), the self-regulatory model (SRM) (Leventhal et al, 1992); the extended SRM (Glattacker et al, 2012; Horne, 1999), and, to a lesser extent, the transactional model of stress and coping (Folkman et al, 1984).

The behaviour on which the current research focuses is utilisation of ED treatment and therefore it is necessary to ascertain which SCMs are most relevant to modelling and predicting such behaviour. Although several SCMs have been utilised in adherence research, the following

section will include the most pertinent models based on a literature review which focussed on ascertaining what recent meta-analyses, reviews and systematic reviews have been carried out which focus on the use of psychology models and theories in research on adherence to medication (Munro et al, 2007; Holmes et al, 2014; Conn et al, 2015; Conn et al, 2016; Patton et al, 2017). The following theoretical models were included across the 5 reviews: the health belief model (n = 5/5 reviews), the transtheoretical model (n = 4/5 reviews), the self-regulation model (SRM) (n = 4/5 reviews), social cognitive theory (n = 4/5 reviews) and the theory of planned behaviour (TPB)/theory of reasoned action (TRA) (n = 3/5 reviews). These models will be considered in the following sections.

4.3.1 The Health Belief Model

The HBM was one of the first SCMs and (Figure 8) highlights the importance of health beliefs in determining whether an individual engages with protective health behaviours (Becker, 1974). The model proposes that if an individual perceives themselves to be at risk and they perceive the risk to be severe, they will act appropriately to reduce the risk using a process whereby the individual weighs up the benefits and barriers of the behaviour necessary to reduce the risk. Figure 8 provides a visual representation of the model which considers the likelihood of an individual engaging in a health-related behaviour is determined by the individual's perception of the following six variables:

- ***Perceived susceptibility*** – perceived risk for contracting the health condition of concern
- ***Perceived severity*** – perception of the consequence of contracting the health condition of concern
- ***Perceived benefit*** – perception of the good things that could happen from undertaking specific behaviours

- ***Perceived barriers*** – perception of the difficulties and cost of performing behaviours
- ***Cues to action*** – exposure to factors that prompt action

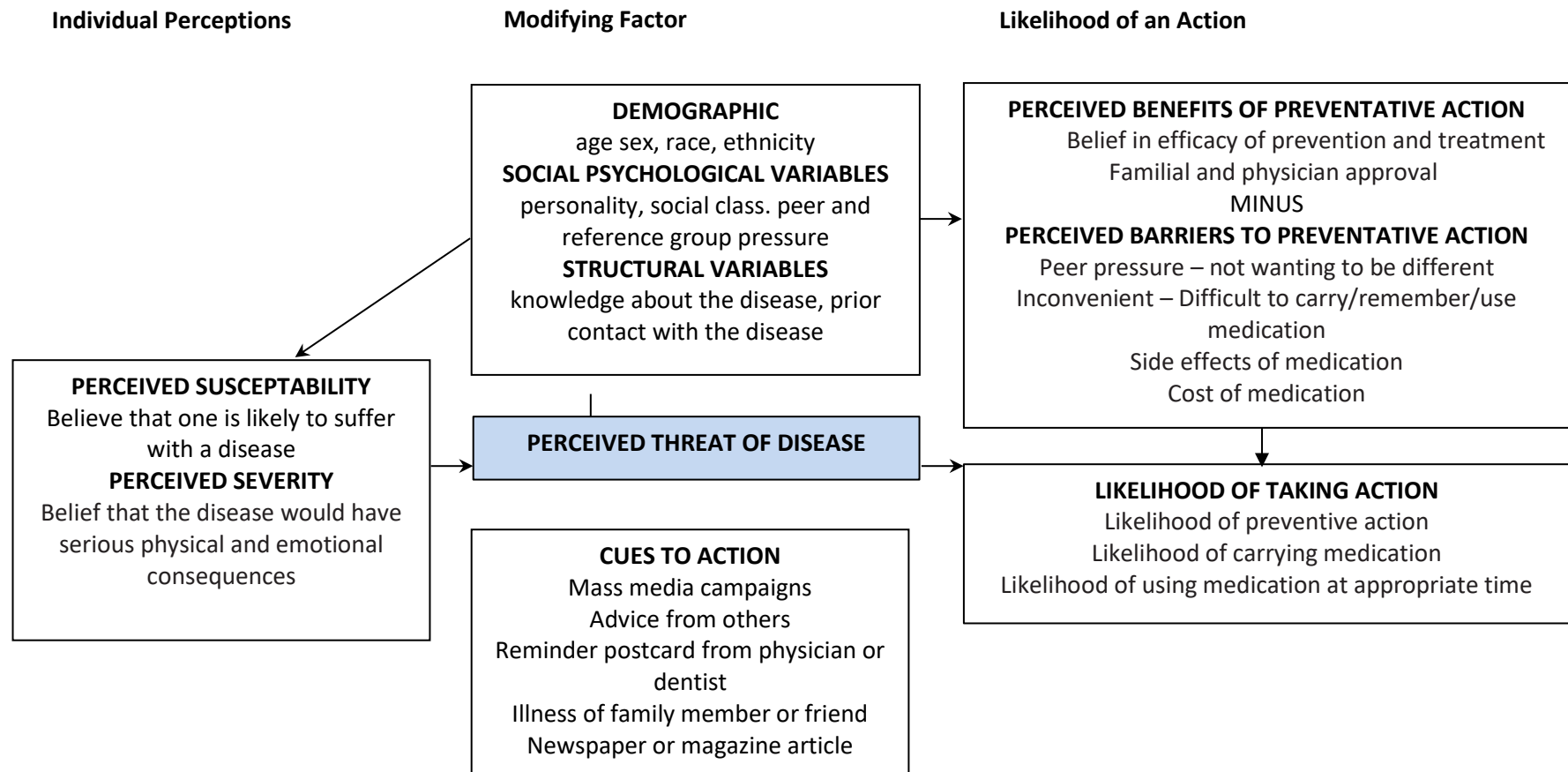


Figure 8: The Health Belief Model; adapted from Rosenstock (1974)

Arrows in the above depiction of the HBM indicate relationships between constructs. Individual beliefs can be modified by factors such as knowledge and sociodemographic factors which can influence health perceptions. Health beliefs create the major constructs of the HBM i.e., susceptibility, severity, benefits, barriers, and self-efficacy. The HBM has the capacity to identify constructs that lead to outcome behaviours. However, it has been suggested that relationships between and among these constructs are not defined and therefore are unclear. As a result, this ambiguity has led to differences regarding how HBM has been used, where some studies have attempted to establish each of the major dimensions as independent, whereas others have tried multiplicative approaches (Champion & Skinner, 2008).

There have been several meta-analyses carried out to investigate the effectiveness of individual HBM components in predicting behaviour (Carpenter, 2010; Harrison et al, 1992; Janz & Becker, 1984; Zimmerman & Vernberg, 1994). A review carried out by Janz and Becker (1984) indicated that barriers, benefits, and susceptibility were good predictors of behaviour, however, severity was not. The review does not provide precise estimates of the strength of the relationships between the variables. A review carried out by Zimmerman and Vernberg (1994), considered the HBM model as a whole, rather than in relation to the effects of each variable on behaviour and indicated that the HBM is only a weak predictor of behaviour. A review carried out by Harrison et al (1992) indicated that in relation to retrospective studies, substantially larger effect sizes were reported compared to prospective studies, suggesting the HBM is perhaps not as good at predicting future behaviour. Carpenter's (2010) analysis reported that both the constructs; perceived barriers and perceived benefits, are consistently the strongest predictors of behaviour. In line with the other reviews considered above, the study indicates that the HBM,

although used as a theoretical basis to inform the design of interventions to change behaviour, evidence for its predictive power is weak.

Application of the HBM to Treatment Adherence

A systematic review and meta-analysis of adherence interventions for adults with hypertension, carried out by Conn et al (2015), included three studies which used the HBM as a theoretical basis for intervention. They found only a small overall effect size of the HBM, reported as 0.152, however, the authors caution the interpretation of these results and highlight the small number of studies included which utilised the HBM. However, more support for the utility of the HBM is offered by a systematic review focussed on medication adherence interventions that target subjects with adherence problems (Conn et al, 2016), reported that where studies used single theories as their basis, the largest effect sizes were evident for interventions based on the HBM (0.477). However, in contrast to these findings, Holmes et al (2014) carried out a systematic review with a view to identifying the empirical evidence for the utility of SCMs at predicting adherence to medication. Results indicated limited support for the utility of the HBM. HBM constructs failed to reach statistical significance and where statistical significance was reached, constructs explained only a limited proportion of the variance in adherence. In contrast to the findings of Conn et al, (2016) i.e., that the HBM when used as a single theory, larger effect sizes are evident, Holmes et al (2014) indicate that the prediction of adherence increased when the HBM was used in conjunction with the theory of planned behaviour and self-efficacy.

Based on the reviews outlined above, there is support for both the use of the HBM as an individual theory (Conn et al, 2016), although, Holmes et al (2014) indicate that the prediction of adherence increased when the HBM was used in conjunction with the other theories. Jones et al (2014) carried out a systematic review with the aim of identifying interventional studies

using the HBM as their theoretical basis and included eighteen interventional studies which utilised the HBM. The review reported that 14 (78%) of the included studies indicated significant improvements in adherence and 7 (39%) indicated moderate to large effects. However, the authors report that on closer inspection only three studies used the HBM in its entirety, only five measured model constructs pre-and post-intervention and only one study offered mediation analysis of HBM constructs. Therefore, the authors conclude that the improvements were not necessarily due to the application of the model or to HBM constructs, challenging the utility of the HBM for interventions designed to promote adherence behaviour. Further, a systematic review carried out by Patton et al (2017), which aimed at determining the effectiveness of theory-based interventions for improving medication adherence in older adults, reported that even when the HBM was coupled with the additional construct 'self-efficacy' no statistically significant improvements in adherence were reported. Therefore, the evidence for the utility of the HBM as a stand-alone model or in conjunction with other models are limited.

Finally, a review which was carried out by Munro et al (2007) focussed specifically on health behaviour theories and their application to long-term treatment adherence and sites several criticisms of the HBM and its appropriateness to be used in conjunction with research focussing on adherence. It is pointed out that relationships between the variables are not explicit (Stroebe & de Wit, 1996) and that no definitions have been articulated for the individual components or offered in relation to transparent rules related to combining components (Armitage & Conner, 2000). The HBM also assumes that variables affect health behaviour directly and remain unmoderated by behavioural intentions (Stroebe, 2000). Finally, important determinants of health behaviour, such as the positive effects of negative behaviours and social influence, are not included (Stroebe & de Wit, 1996; Stroebe, 2000). Munro et al (2007) suggest that when

applying this theory to long-term medication adherence, it is important to consider the influence of socio-psychological factors such as cultural beliefs.

To the authors' knowledge, the HBM model has not been used to investigate ED treatment utilisation. The reviews outlined above indicate that the predictive power of the HBM is weak, however, there are additional criticisms which question the HBM's suitability for investigating ED treatment utilisation. Firstly, it has been suggested that difficulty exists when applying the HBM to the problem of adherence which exists in its lack of fluidity and flexibility, whereby the HBM implies a one-off decision or cost-benefit analysis of whether to engage in particular health related behaviour (Horne et al, 1999). Secondly, the model assumes that individuals are rational processors of information, failing to account for the influence of emotions, where emotions are likely to be pertinent with regards to ED treatment utilisation. For example, one of the key findings from the systematic review carried out in Study 1 (Chapter 3) was the importance of the quality of a couple's intimate relationship where libido was indicated as one of the most prevalent factors associated with treatment discontinuation. Thirdly, the model assumes that 'health' is a highly valued concern for most individuals and that cues to action are widely prevalent and this has been criticised for focussing on the individual, neglecting social and environmental factors. This is an important consideration for ED treatment utilisation which is highly dependent on social and environmental factors i.e., the interaction between a man and his partner in order that the treatment is likely to be utilised. Therefore, the HBM is unlikely to be a model sufficient for exploring the problems associated with ED treatment utilisation.

4.3.2 Theory of Reasoned Action (TRA) and the Theory of Planned Behaviour (TPB)

The Theory of Reasoned Action (TRA) (Ajzen & Fishbein, 1980; Fishbein & Ajzen, 1975) was developed to better understand relationships between attitudes, intentions, and behaviours

(Fishbein, 1967). The TRA is based on the assumption that an individual's intention is an immediate determinant of behaviour and intention is predicted from a combination of attitude and social (subjective) normative factors (Andrew Smith & Biddle, 1999). The TRA assumes that most socially relevant behaviours are under volitional control. It considers an intention to perform a given behaviour is influenced by the individual's attitudes towards the action and therefore involves positive or negative beliefs as well as evaluations in relation to the outcome of the behaviour. It is also posited that behaviour is influenced by subjective norms which include the perceived expectations of others who are considered important and the motivation for a person to comply with others perceived wishes (Fishbein & Ajzen, 1975). Behavioural intention, it is contended, then results in action. Over time, the TRA was often used for the study of behaviours which included control as a variable factor and therefore, the successor of the TRA which incorporates volitional control is the theory of planned behaviour (TPB) (Figure 9) (Ajzen, 1985, 1991).

Both the TRA and TPB (Ajzen, 1985) differ from the HBM in that they account for social influences such as the phenomenon of what friends and family may think, or what is perceived as 'normal', and considers individuals perceived pressure to please others. The TRA and TPB propose that *intentions* are the single most important determinant of behaviour. Subsequently, the TRA and TPB consider that intentions precede behaviours where intentions are envisaged as being shaped by attitudes towards the behaviour and subjective norms (Ajzen, 1991).

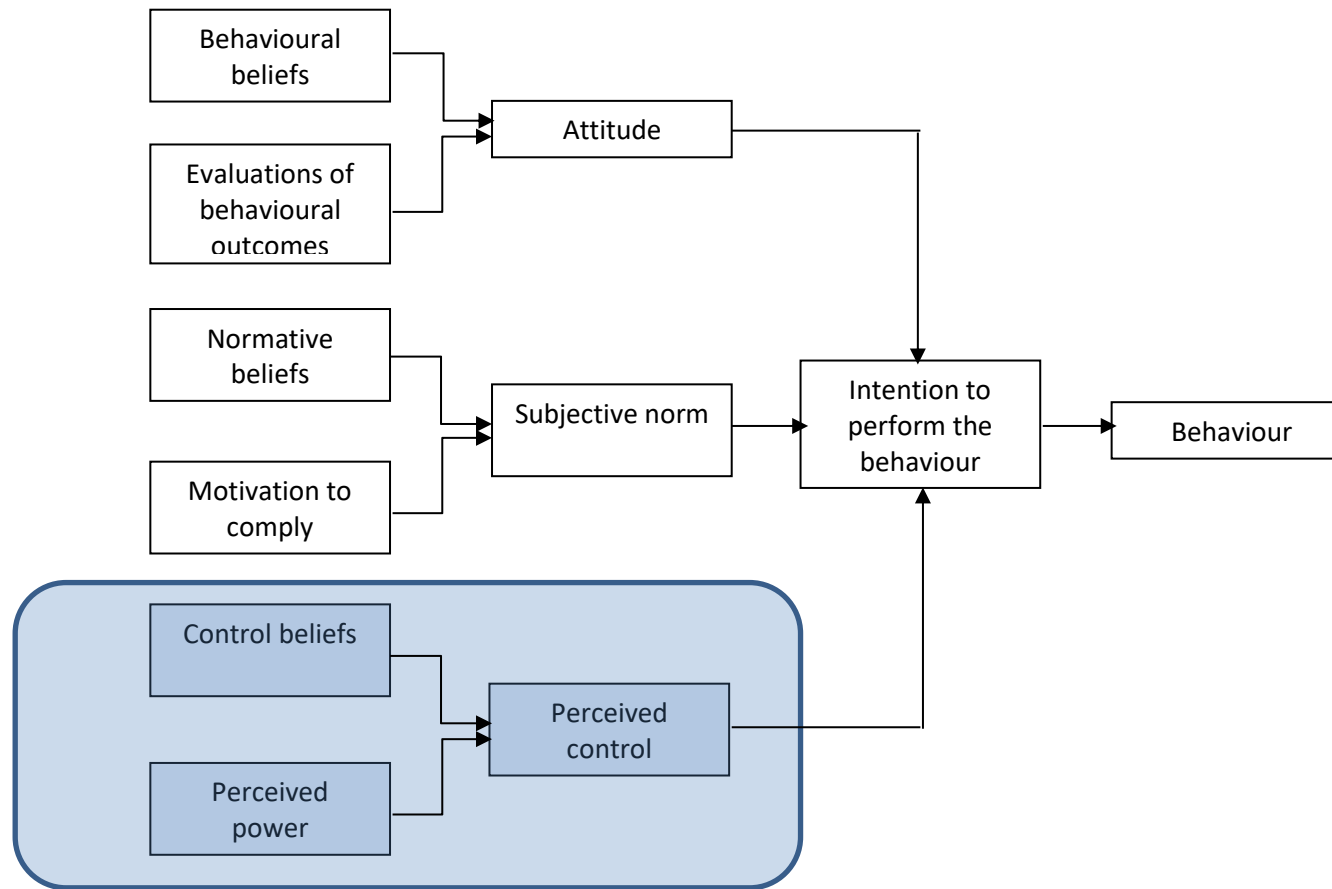


Figure 9: Theory of Reasoned Action (TRA) and Theory of Planned Behaviour (adapted from Montano & Kasprzyk, 2015).

Note: The image in its entirety represents the TPB whereas the upper area represents the TRA.

The TPB has been found to be effective in relation to predicting a range of health intentions and behaviours. The TPB has been used to explore, for example, dietary behaviours, physical activity, condom use, drug use, and health screening behaviours (Armitage & Conner, 2001; Hagger et al, 2002; McEachan et al, 2011). It has also been used to explore adherence to behaviours such as diet (Sainsbury & Mullan, 2011), exercise (Blanchard et al, 2008), and taking medication in acute illnesses such as urinary tract infections (Ried & Christensen, 1988) and chronic illnesses such as HIV (Vissman et al, 2013).

A meta-analysis of the efficacy of the TPB included 185 independent studies and found that TPB constructs accounted for 27% and 39% of the variance in behaviour and intention, respectively. Additionally, where behavioural measures were of a self-report nature, the TPB accounted for 11% more of the variance in behaviour than objective or observed measures (Armitage & Conner, 2001). A meta-analysis of 206 studies by McEachan et al (2011) indicated that behaviour type moderated the model i.e., physical activity and diet behaviours were better predicted (23.9% and 21.2% variance explained, respectively) than behaviours such as safer sex and abstinence from drugs (between 13.8 and 15.3% variance explained). However, neither of these reviews included any studies focussed on treatment utilisation, which will be considered below.

Application of TPB to Treatment Adherence

The TPB has predominantly been applied to the problem of medication adherence as opposed to the TRA. For example, a meta-analysis carried out by Rich et al (2015) examined the TPB as a predictor of treatment adherence in chronic illness. The analysis included 27 studies covering a variety of chronic illnesses including diabetes, heart disease, hypertension, HIV, coeliac disease, psychiatric illnesses, breast cancer, organ transplantation, epilepsy, lymphoma, obesity, and

insomnia (Rich et al, 2015). Results indicated that the constructs of the TPB accounted for 33% and 9% of the variance in intentions and behaviour respectively with regards to treatment adherence. Attitudes, subjective norm, and perceived behavioural control were found to be statistically significant predictors of adherence intention and intention was found to be a statistically significant predictor of treatment adherence. Perceived behavioural control was the strongest predictor of intention and was reported as having significantly larger effects than attitude and subjective norm. Effect sizes between the TPB components and adherence ranged from 0.22 to 0.51, which were considered to be in the small-to-medium range. The authors concluded that focusing solely on the TPB variables to predict and develop interventions to alter adherence is likely insufficient (Rich et al, 2015). They indicate that while the TPB does indeed contribute to our understanding of treatment adherence in chronic illness, the TPB neglects factors beyond patient-related factors, for example, social and economic, therapy related and health system factors (WHO, 2003). The authors conclude that any theory focussed on predicting adherence behaviour must be able to accommodate such multifaceted components. Similar to the criticism of the HBM, the TPB, as suggested by WHO et al (2003) neglects social, economic and health system factors. The systematic review carried out in study 1 (Chapter 3) indicated the importance of both a couple's relationship being integral to treatment utilisation and indicated that cost of treatment was also a prevalent factor associated with discontinuation. Although there is no research which has used the TPB to investigate treatment utilisation to ED treatment, on this basis it is considered that the TPB would not be sufficient for investigating ED treatment utilisation.

4.3.3 Transtheoretical Model

The Transtheoretical model (TTM), also known as the stages of change model, was developed in 1983 by Prochaska and DiClemente (Prochaska & DiClemente, 1983) and was based on the

analysis of different theories of psychotherapy (Prochaska & Norcross, 2013). It is an integrative model of behaviour change as it combines key constructs from other theories. The central construct of the model is the Stages of Change which involves a phenomenon occurring over time. The TTM considers change as a process which involves a series of five stages (see below). However, the model also includes a series of independent variables i.e., the 'processes of change' which involves both the covert and overt activities that people use to progress through the stages. The 'decisional balance' construct which involves an individual's weighing of the pros and cons in relation to change and the Self efficacy/Temptation construct which involves situation specific confidence in relation to coping with e.g., a high-risk situation without relapsing to their unhealthy or high-risk habit (Velicer et al, 2000).

1. Pre-contemplation – an individual is unaware of a need to change or is unwilling to change, they will not be thinking about changing their behaviour and will not be interested in any help to do so.
2. Contemplation – the individual becomes aware of the consequences of their current behaviour and their personal susceptibility and begin to weigh up the costs and benefits of changing the behaviour. Whilst thinking about the behaviour, they are not yet fully committed to changing it.
3. Preparation – the individual has made the decision to change their behaviour and intends to do so in the near future. This is the period of psychological preparation for change, small changes may be tried first to ease the behavioural transition.
4. Action – the individual implements the plans made in the preparation stage and attempts to change their behaviour, though the risk of relapse is high.
5. Maintenance – the individual develops strategies to maintain their new behaviour and resist temptations which would prompt relapse.

The TTM is the most widely applied stage model and assumes that different cognitions take precedence at different stages of change. It recognises that individuals change their behaviour in a gradual and frequently non-linear fashion. The model hypothesizes a number of stages and

processes that people move through which can involve relapsing and revisiting earlier stages before a successful outcome (Prochaska & DiClemente, 1983; Sutton, 2000). An integral part of the model involves the individual's perception of the advantages and disadvantages of a given behaviour considered crucial for behaviour change (Prochaska, 1994).

Application of TTM to Treatment Adherence

According to Munro (2007), the TTM has received support from healthcare practitioners over the years, however, it has received less direct research support for its efficacy (Michie & Abraham, 2004; Brawley et al, 2000). A systematic review and meta-analysis aimed at exploring the effectiveness of interventions to improve medication adherence in hypertensive patients (Conn et al, 2015) reviewed 6 studies which used the TTM. The overall effect size, which related to post-intervention differences between treatment and control participants, was small (0.118). However, the authors suggest that given the small number of samples contributing to each of the pooled effect sizes, these findings should be considered with caution.

Conn et al (2016) carried out a systematic review focussed on exploring medication adherence interventions that target individuals with adherence problems. This included 14 studies which used the TTM as the basis for intervention. Effect sizes were calculated for treatment versus control groups, and a small effect size of 0.334 was reported for interventions that used the transtheoretical model. Patton et al (2017) carried out a systematic review in an attempt to determine the effectiveness of theory-based interventions aimed at improving medication adherence in older adults. The review included the TTM and reported that basing interventions on the TTM did not lead to statistically significant improvements in medication adherence.

Criticisms of the TTM are multifaceted. For example, Munro (2007) brings into question the coverage, definitions and descriptors of the stages that constitute the model. Other criticism has been voiced by Bandura (2000) who suggests that the TTM violates the three basic assumptions of stage theories i.e.; qualitative transformations across discrete stages, invariant sequence of change as well as non-reversibility. Further, it has been proposed that the model's stages potentially exist on a larger continuum of change (Bandura, 1997; Sutton, 1998) and Sutton (2000) argues that the stages included in the TTM are logically flawed because the time periods ascribed to each stage are arbitrary. Sutton also suggests that there is a need for more attention to measurement, testing issues and definition of variables and causal relationships. As a result, it is suggested that the TTM provides little information on how people change and why only some individuals succeed (Armitage & Conner, 2000).

The TTM has not been used to explore ED treatment utilisation. An important criticism which is to be considered in conjunction with the model's potential use in this area is that the complexity of human functioning is too multifaceted to fit into separate, discrete stages (Bandura, 1997). ED treatment is used in the context of a man and his partner, therefore the extent to which multifaceted human functioning is likely to be involved in any decision relating to the utilisation of ED treatment is increased and therefore further making the TTM unsuitable for the exploration of treatment utilisation in this context.

4.3.4 Social Cognitive Theory

Social cognitive theory (SCT) evolved from social learning theory and describes learning as being affected by cognitive, behavioural as well as environmental factors, which are intricately and reciprocally connected (Bandura, 1991). The key principle of behaviour change is considered as the continuous, dynamic interaction between the individual, the environment and behaviour.

According to SCT, human motivation and action are extensively regulated by forethought. The theory posits a number of important factors that influence behaviour (Figure 10).

According to SCT, motivation (intention or goal) to engage in a given health behaviour is the result of three types of expectations. Firstly, expectations about possible outcomes if no action is taken (i.e., current personal risk); secondly, the consequences of carrying out preventive measures; and thirdly, the individual's ability to carry out a preventive behaviour successfully. Risk perceptions (situation-outcome expectations) are considered to be the risks an individual feels e.g. when presented with a given illness. Outcome expectations are considered to be the beliefs an individual holds, about both the positive and negative consequences of carrying out a preventive behaviour, in relation to a given illness. Self-efficacy is considered to be an individual's subjective perception of their ability to perform a given behaviour; which refers to both technical aspects (knowledge of how to successfully carry out the behaviour) and personal aspects (the belief in one's ability to perform behaviour regularly) (Schüz et al, 2006).

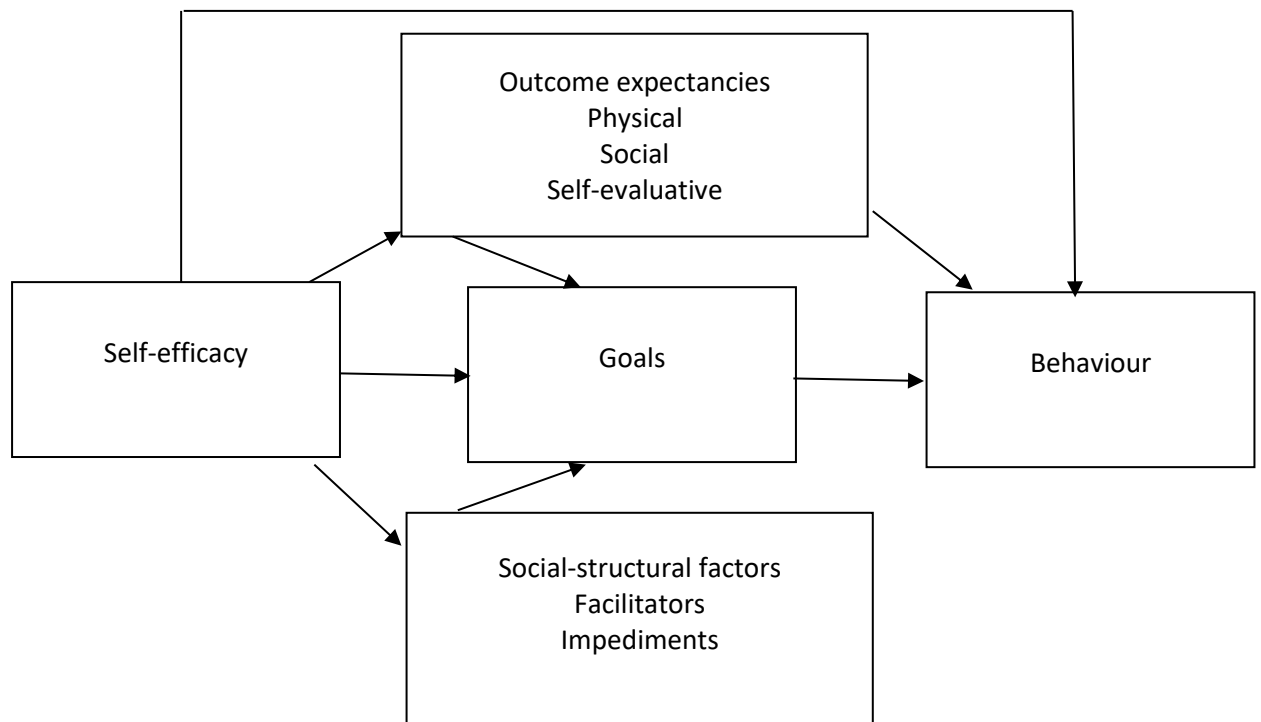


Figure 10: Illustration of social cognitive theory (Bandura 2000)

The SCT posits that, while knowledge of health risks and benefits are considered a prerequisite to change, additional self-influences are necessary for a change in behaviour to occur (Bandura, 2004), where self-efficacy plays a central role in behaviour change. Outcome expectancies involve the positive or negative effects of carrying out a given behaviour which may have social connotations such as social approval or disapproval with regards to a particular action. A further important aspect of SCT relates to perceived enablers and impediments and their impact on behaviour. This is of particular interest with regards to the current research, given the central focus of the research is the exploration of potential barriers and enablers to ED treatment utilisation. Bandura (2004) suggests that behaviour change may rely on the reduction or elimination of barriers and that a given behaviour is likely to be enacted if the individual has self-efficacy to carry out a given behaviour i.e., they perceive they have control over the outcome

and that there are few external barriers. In relation to ED treatment utilisation, a man is likely to use his ED treatment if confident that he can successfully use it, that the treatment will work and that there is an opportunity for intimacy with a respective partner.

Application of SCT to medication adherence

The systematic review of interventions to enhance adherence to hypertension medication by Conn et al (2015) included 7 studies that used the SCT as the foundation for their interventions. Effect sizes were calculated for treatment versus control groups, where the overall effect size for interventions which used the SCT was small. As with the other theories included in this review, the authors exercise caution when considering the results due to the small number of studies contributing to each of the pooled effect sizes. A further meta-analysis carried out by Conn et al (2016) indicated a similarly small effect size, despite including 31 studies. The authors concluded that interventions based on theory such as the SCT, although statistically significant, had a modest effect on medication adherence. Patton et al (2017) carried out a systematic review to determine the effectiveness of theory-based interventions aimed at improving medication adherence in older adults. The review only included one study which utilised SCT. Although the authors report that none of the included studies made optimal use of theory it was reported that the study utilising SCT as the foundation (Barnason et al, 2010) for its intervention led to a statistically significant difference in self-reported adherence. The authors report that social-structural factors which impacted upon behaviour were personal factors (e.g., motivation) and environmental factors (e.g., assistance from others).

To the authors' knowledge, the SCT has not been used in research to explore ED treatment utilisation. In a systematic review which explored the use of SCT in chronic health condition interventions it was reported that only 52% of interventions considered self-regulation an

important component of the theory (Tougas et al, 2015). A key component of the SCT is motivation (intention or goal) to engage in a given health behaviour and as such is focussed on the individual. In relation to treatment for ED, the extent to which treatment is used will depend on both the man and his partner and as such they may not have aligned goals and therefore motivation towards behaviour, therefore, the SCT is limited in this respect to the exploration of ED treatment utilisation.

4.3.5 Leventhal's self-regulation model

The Self-Regulation Model (SRM), also known as the Common Sense Model (CSM), is a social cognition model which aims to explain how an individual copes with an illness. Self-regulation is defined as:

‘mental and behavioural processes by which people enact their self-conceptions, revise their behaviour, or alter the environment so as to bring about outcomes in line with their self-perceptions and personal goals’ (Fiske & Taylor, 1991).

Leventhal et al (1992) developed the SRM, which is a framework for understanding the self-regulation processes by which people make sense of their experience of a given illness. The notion of self-regulation is that it is a dynamic process incorporating feedback from the appraisal of coping efforts which are considered influential with regards to cognitive representations and emotional responses (Leventhal et al, 1980, 1984, 1992). See Figure 11 below.

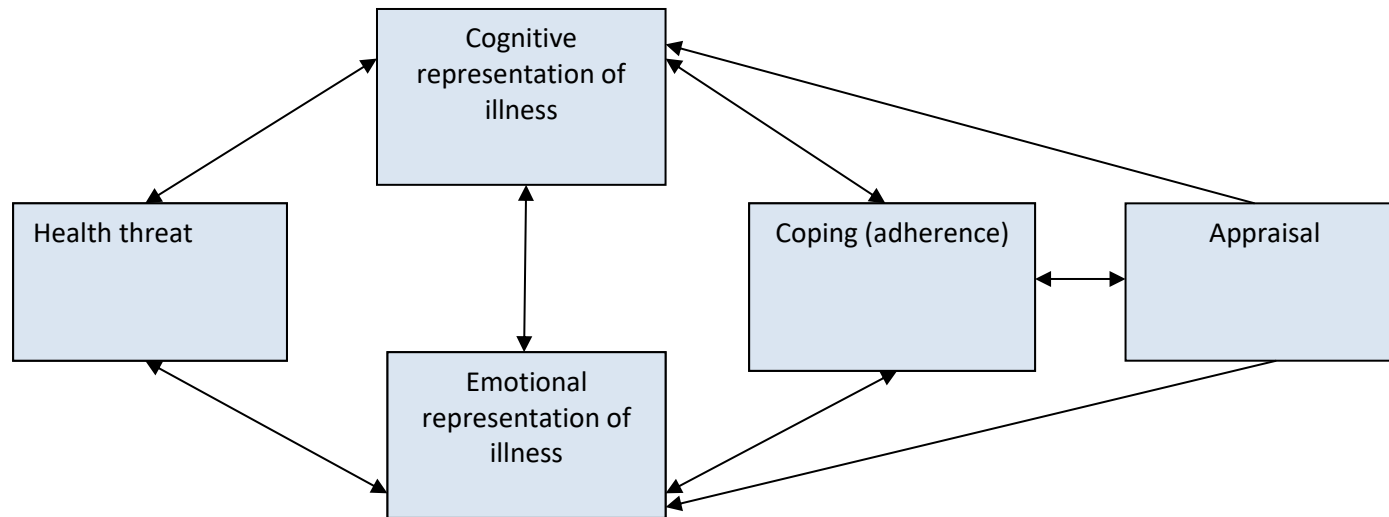


Figure 11: Self-regulation model of illness cognitions and emotions (Leventhal et al, 1984)

Illness-related cognitions are thought to be guided by information from peoples' social environment including doctors or family, cultural knowledge of the disease, the individual's current perceptions as well as an individual's previous experiences of the illness (Leventhal et al, 1984; Leventhal et al, 1980). This is why the model is sometimes referred to as the common-sense model i.e., patients will engage in a particular health protective behaviour if it makes common sense and falls in line with their illness perceptions and beliefs (Leventhal et al, 1984). Illness cognitions (represented by 'cognitive representation of illness' in Figure 11) lie along five broad cognitive dimensions (Table 13).

Table 13: Self-Regulation Model Illness Representations (Leventhal et al, 1992)

DIMENSION	DESCRIPTION
Identity	The label given to an illness, either via a practitioner's diagnosis or self-diagnosis, which can be influenced by prior experiences
Timeline	Individual's perception of how long an illness will last, based on own assumptions or information from health professionals
Perceived cause	Personal beliefs about what may have caused the illness, may also be based on personal experience
Consequences	How an individual thinks the illness will impact on their life
Curability and controllability	Whether the individual believes their illness can be treated and the outcome of their illness can be controlled

As mentioned above, the SRM considers people's beliefs about their illness as both cognitive and emotional (Leventhal et al, 1980) and that they are formed simultaneously through a parallel process (Leventhal et al, 1980). Emotional representations are the feelings that arise in response to the illness, for example, anger, anxiety or depression (Diefenbach & Leventhal, 1996; Leventhal et al, 1992). The emotional response to having a medical condition, although independent, is suggested as being able to 'interact with and/or be part of the cognitive'

representation (Leventhal et al, 1992). Intrinsic to the model is the assumption that individuals adopt a problem-solving approach (Leventhal, 1980). Individuals are regarded as dealing with illness and related symptoms in very much the same way as any other problem. In the presence of, or threat of, an illness, individuals are regarded as being motivated to engage in activities to resolve such a threat (Rodham, 2010).

Illness beliefs have been shown to influence peoples physical, social, and psychological functioning as well as coping and self-management behaviours (Fortune et al 2000; Hagger & Orbell, 2003; Heijmans, 1998; Horne & Weinman, 2002; Leventhal et al, 1992; Meyer et al, 1985). Adherence can be considered a self-management behaviour, therefore, it is suggested that medication adherence will be influenced, for example, where individuals consider their illness to be chronic, serious and that treatment for the condition is thought to be important (Hampson et al, 1994).

The SRM involves the following distinct processes which occur when a person is diagnosed with an illness or is informed of a health threat:

- (1) Interpretation (both cognitive and emotional), which leads to
- (2) Coping, problem-focussed or emotion-focussed which is followed by
- (3) Appraisal, checking if the method of coping is effective (Leventhal et al, 2010).

During the interpretation phase, aspects of the five dimensions (Table 13) create a cognitive illness representation. An emotional response is also evoked during this phase as the implications of an illness have the potential to lead to anxiety, stress as well as fear. In the second phase, the individual will begin to act upon their interpretation of the illness in an attempt to cope. In the third phase, the individual is considered as assessing their chosen coping strategies and deciding whether to continue or adopt an alternative strategy. However, it has been

suggested that some individuals opt instead for an avoidant strategy or indeed they may only know and use one coping strategy (Forshaw, 2002).

Table 13: Self-Regulation Model Illness Representations (Leventhal et al, 1992)

DIMENSION	DESCRIPTION
Identity	The label given to an illness, either via a practitioner's diagnosis or self-diagnosis, which can be influenced by prior experiences
Timeline	Individual's perception of how long an illness will last, based on own assumptions or information from health professionals
Perceived cause	Personal beliefs about what may have caused the illness, may also be based on personal experience
Consequences	How an individual thinks the illness will impact on their life
Curability and controllability	Whether the individual believes their illness can be treated and the outcome of their illness can be controlled

There are two theorised processes of coping: *problem-focussed coping* and *emotion-focussed coping*, which can occur simultaneously (Leventhal et al, 1984). Problem-focussed coping consists of making efforts to modify the problem at hand and typically includes generating options to solve the problem, evaluating pros and cons and subsequently implementing steps to solve the problem (Lazarus & Folkman, 1984). This might involve e.g., seeking advice from friends, family, or healthcare providers or, in relation to adherence, using prescribed treatment. On the other hand, emotion-focussed coping is conceptualised as aiming to manage the emotional distress associated with the situation (Lazarus & Folkman, 1984). This can include strategies such as denial, focusing on and venting of emotions, positive reinterpretation of events as well as seeking out social support (Baker & Berenbaum, 2007). The effectiveness of emotion-focussed coping depends on the particular strategy employed (Carver, Scheier, & Weintraub, 1989). The predominant view in the literature is that emotion-focussed coping processes are considered maladaptive (Baker & Berenbaum, 2007).

The SRM has been suggested as perhaps the most appropriate model for investigating low adherence to medication (Munro et al, 2007). The SRM benefits from being a dynamic model, i.e., it is capable of accounting for the continuously changing nature of an individual's appraisal of their ability to cope with a health threat or illness resulting from increases in knowledge and understanding for example. This is relevant to adherence as adhering to a medication regimen is considered a coping strategy i.e., it is a way of managing the illness. The model theorises that patients are more likely to be adherent in relation to their medication if they have a coherent model of their illness i.e., one which makes sense to them and which they can employ to cope with an illness. As the model's name suggests, the SRM views people as going through a continual process of self-regulation (appraisal of their resources for coping and action plans) in order to manage their illness. The application of the model to adherence to medication will be considered below.

Application of SRM to Treatment Adherence

Many studies have shown empirical support for the SRM, with associations between illness perceptions and adherence. Hagger & Orbell (2003) carried out a meta-analytic review which included 45 empirical studies with the aim of assessing the relationship between illness cognitions and coping strategies and the relationship between illness cognitions and illness outcomes. Results indicated a significant positive relationship between the construct cure-control i.e., the belief that a given illness can be treated and the outcome controlled and problem-focused coping-specific behaviour (Hagger & Orbell, 2003), however, the review did not focus specifically on adherence and was carried out over a decade ago.

With this in mind, a more recent systematic review carried out by Jones et al (2016) focussed specifically on the effectiveness of interventions using the SRM to improve adherence behaviour. The review identified nine studies that used the SRM in intervention design to improve adherence behaviours. Of these nine studies, six reported statistically significant improvements in adherence behaviours and three demonstrated large effects on improving adherence behaviours. There was one intervention study (Petrie et al, 2002) which significantly changed participants' illness perceptions, however, this was true only for the cure/control construct which the authors interpret as providing evidence that this construct is potentially important for interventions aimed at improving adherence behaviours in chronic conditions. As a result, the authors conclude that adherence behaviours could be improved where interventions targeted cure/control perceptions.

Further, a systematic review and meta-analysis carried out by Brandes & Mullan (2014) did not find strong support for the SRM as the review carried out by Jones et al (2016). Brandes & Mullan (2014) included 30 studies aimed specifically at examining the role of illness beliefs in predicting adherence. The review included a range of adherence behaviours including medication adherence and found that the effect sizes for the SRM mental representation constructs with regards to adherence ranged from 0.02 to 0.12. The small effect sizes indicates that the relationships between the different mental representations of the SRM and adherence are very weak. As a result, the authors conclude that the SRM may not be the most appropriate model to use in predictive studies of adherence (Brandes & Mullan, 2014).

Similar findings to that of Brandes & Mullan (2014), Aujla et al (2016) carried out a systematic review and meta-analysis which included 21 studies, in order to determine whether the SRM can prospectively predict adherence to self-management behaviours (including; attendance,

medication, diet and exercise) in adults with acute and chronic physical illnesses. The authors found that illness belief domains that emerged as significant predictors of adherence to self-management behaviours were: identity; timeline acute–chronic; consequences; personal control; treatment control; cure-control; and illness coherence. However, the effect sizes ranged from 0.04 to 0.13, indicating weak predictive relationships between individual illness belief domains and adherence to self-management behaviours. Therefore, predictive relationships between individual illness belief domains, outlined by the SRM, and adherence to self-management behaviours for adults with acute or chronic physical illnesses, are weak according to Aujla et al (2016), reflecting the findings of Brandes & Mullan, (2014) outlined above.

4.3.6 Extended SRM – Necessity Concerns Framework

Aujla et al's (2016) systematic review and meta-analysis outlined above indicated the potential importance of treatment beliefs as a mediating factor with regards to medication adherence. Holmes et al (2014) carried out a systematic review in an attempt to identify the empirical evidence for the application of a variety of models at predicting patient adherence to medications. The review included the SRM, where the authors report that beliefs about the necessity of medicine as well as concerns about medicines, indicated significant associations with adherence. This falls outside of the parameters of the SRM as a model in its strictest form. Furthermore, Hagger et al (2017) carried out a meta-analysis which included 254 empirical studies and had several aims, one of which was to explore the inter-correlations among illness representation dimensions, coping strategies, and illness outcomes of studies which had utilised the SRM. The analysis highlighted a growing body of research which, in addition to measures of illness representations, has included measures of treatment beliefs. Hagger et al (2017) analysis included 18 such studies, where results indicated that individuals with strong beliefs in relation to the necessity of medication and fewer concerns with regards to its use, have better

medication adherence independent of illness perceptions. This has involved the addition of treatment beliefs to the SRM and has been termed the extended model of illness self-regulation (Horne & Weinman, 2002) and was proposed by Horne (1999). Hagger et al (2017) highlight the unique effects of beliefs about medication and the importance of including treatment beliefs in the revised SRM or the extended model of illness self-regulation (Hagger et al, 2017).

Horne & Weinman (2002) used the extended SRM in a study in relation to adherence to medication for asthma. The study found two groups of beliefs to be associated with adherence to medication: beliefs about the necessity of taking medication and concerns about the medication. Therefore the extended SRM incorporates the Necessity-Concerns Framework (NCF) (Horne, 1999) (Figure 12), which posits that people undertake a cost-benefit analysis with respect to their treatment, where their own beliefs about the necessity of their medication for improving or maintaining their health are weighed against their concerns about possible adverse effects (Horne & Weinman, 1999), which ultimately impacts their adherence behaviour.

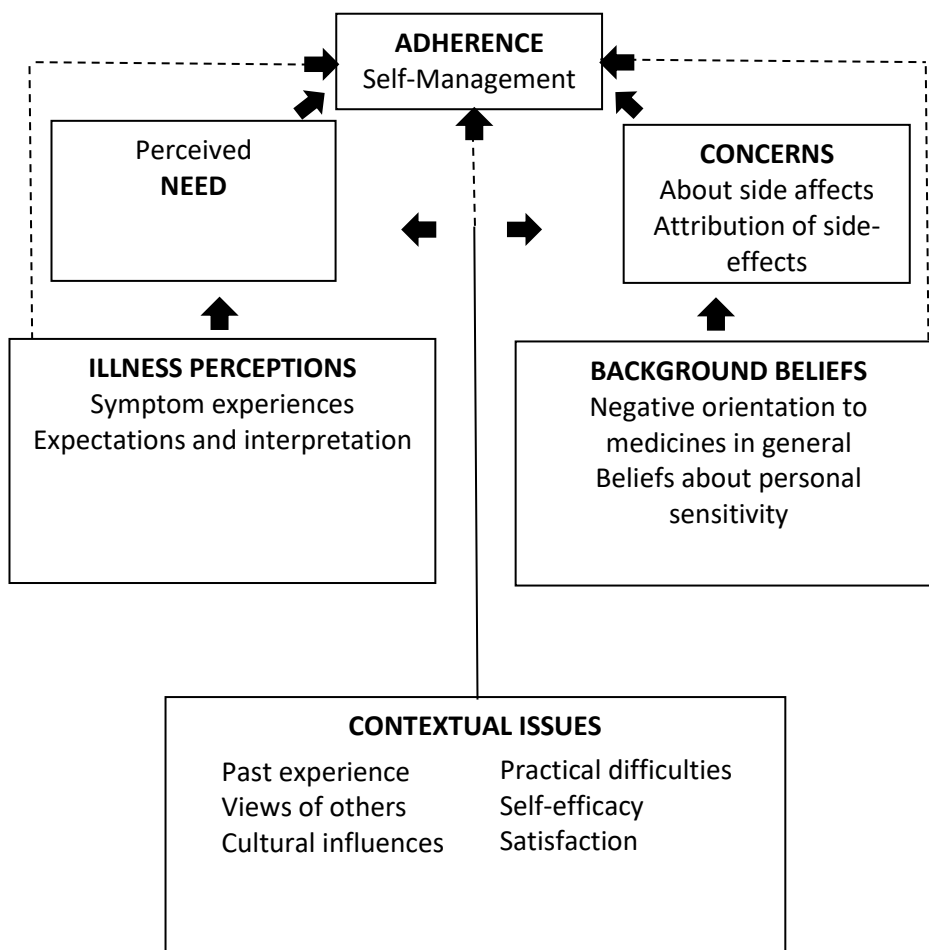


Figure 12: Necessity Concerns Framework (adapted from Horne et al, 2006)

Application of the Necessity Concern Framework to Treatment Adherence

A systematic review of 20 years of empirical research carried out by Holmes et al (2014) sought to explore the application of models from social cognitive theory, self-regulation theory and social support theory with regards to predicting patient adherence to medication. In relation to components of the NCF, results indicated significant associations with adherence for beliefs about the necessity of medicine; reported by 8 of 9 studies. In addition, significant associations were reported for concerns about medicines; reported by 7 of 8 studies. The authors report that

the following factors: symptoms, medication concerns, medication necessity and distrust, were found to predict up to 24% of the variance in adherence to antiretroviral therapy.

Foot et al (2015) carried out a meta-analysis focussed on whether beliefs in the necessity of medicine, concerns about medicine and the necessity–concerns differential are correlated with medication adherence in a variety of medical conditions. The necessity–concerns differential is a score derived from the Beliefs about Medicines Questionnaire (BMQ) which consists of two five-item scales, which assesses patients’ beliefs about the necessity and their concerns relating to a given treatment.

The BMQ concern score is subtracted from the BMQ necessity score to generate a necessity–concerns differential (Neame & Hammond, 2005). Ninety-four papers were included in the analysis. The overall effect size for necessity, concerns, and the necessity–concerns differential, was 0.17, 0.18 and 0.24 respectively all of which were significant ($p < 0.0001$). The authors conclude that the effect sizes were mostly small comparable to other predictors of adherence such as the relationship between adherence and physician communication as well as adherence and perceived illness severity. However, necessity and concern beliefs and the necessity–concerns differential were correlated both with medication adherence on a population level as well as across the majority of included conditions.

Horne et al (2013) carried out a meta-analytic review to assess the utility of the NCF in explaining non-adherence to prescribed medicines. The authors found that across studies, higher adherence was significantly associated with stronger perceptions of necessity of treatment and fewer concerns about treatment. The authors suggest that the NCF is potentially useful for understanding patients’ evaluations of prescribed medicines. It is noted that the magnitude of

the aggregate effect sizes indicates that, for each standard deviation increase in relation to necessity beliefs, the odds of adherence increase by a factor of 1.7, whereas for each standard deviation increase in concerns, the odds of adherence decrease by a factor of 2.0. It is concluded that by taking account of patients' treatment necessity beliefs, as well as their treatment concerns, has the potential to enhance the quality of prescribing by helping clinicians to engage patients in treatment decisions and therefore potentially supporting adherence to prescribed treatment regimens.

There is support for the use of the SRM as a basis for intervention design to improve treatment adherence which relates to the empirically supported relationship between the SRM constructs i.e. patients' illness and treatment representations and treatment adherence (Heurtin-Roberts & Reisin, 1992; Horowitz et al, 2004; Meyer et al, 1985). The extension of the SRM to include perceptions of treatment has been shown to be particularly predictive of treatment adherence (Horne et al, 1999) and potentially improves the models utility with regards to treatment adherence prediction. A further advantage of the SRM is that an individual's illness and treatment representations are dynamic and individuals are considered to be active problem solvers with regards to their own health. The dynamic nature of the model means that as behaviour or experiences change (e.g. treatment use), beliefs are updated and revised (Leventhal et al 2010; Wearden & Peters, 2008).

The dynamic characteristics of the SRM and NCF is potentially important when considering ED treatment utilisation, as this capacity enables the possibility for individuals illness and treatment beliefs to be considered as changeable. This is likely to be important when considering that treatment perceptions in this instance will possibly relate to both those of the man and his partner and therefore changes in perceptions with regards to illness and treatment are possible.

As indicated by the research outlined above, the SRM and the NCF have been used in conjunction to investigate adherence across a number of illnesses, however, to the author's knowledge research to date has not employed these theoretical models to investigate ED treatment utilisation. However, the SRM offers potentially important constructs relating to the way in which men may interpret their ED e.g., identity, timeline, perceived cause, consequences, curability, and controllability. The addition of the NCF offers the ability to include individual's perceptions in relation to their treatment, which is of particular importance to this thesis i.e., the exploration of barriers and enablers to ED treatment utilisation. Therefore, although the SRM and the NCF have not been used in relation to ED treatment utilisation, they are potentially more comprehensive than other models considered in this chapter.

4.4 Model Selection and Associated Difficulties

SCMs have been widely used as a basis to health behavioural intervention and have been used to examine the predictors of health-related behaviours, including adherence to treatment by examining the determinants of behaviour as well as predicting future behaviour. In general, SCMs suggest that human functioning can be explained by the interactions of behaviour, personal, and environmental factors. SCMs seek to promote individual's responsibility for their health and therefore encourage both decisions and action to perform a health behaviour on the basis of individual risk perception, perception of severity as well as the importance of self-efficacy to change behaviour (Abdulrahman et al, 2019).

However, there are a number of criticisms of SCMs. For example, by Sutton (1998) who suggests that even though SCMs are designed to predict behaviour, they leave much of the variance in behaviour unexplained. They have also been criticised for being incapable of representing change as a process that occurs over time, relating to single point decisions about

recommendations for maintaining health (Horne & Weinman, 1998). However, it is important to note that, as mentioned above, the SRM is considered a dynamic model capable of representing change (Leventhal et al 2010; Wearden & Peters, 2008). Ashing-Giwa (1999), suggests that SCMs do not address socio-cultural aspects sufficiently. In relation to ED, interpersonal relationships as well as sexual relationships are likely to be influenced by e.g. cultural backgrounds. Bhavsar & Bhugra (2013), suggest that, for example, attitudes to sex and the perceived role of sexual activity are strongly influenced by cultural values and culturally determined gender roles. Further, they suggest that cultural values affect attitudes towards sexual variation and that culture defines what is considered deviant behaviour. Bhavsar & Bhugra (2013), indicated the importance of being aware of cultural influences on sexual behaviour which includes the notion of power relationships in terms of sex and gender.

Norman & Conner (1996) have criticised SCMs for the existence of overlapping variables between different models and in a similar vein, Armitage & Conner, 2000 indicate the potential to resolve such overlap through the amalgamation of individual models to form a more comprehensive model. In relation to using SCMs to explore barriers and enablers, Francis et al (2009) suggests that there are potentially at least two problems. Firstly, it is not possible to use all the potentially relevant theories to investigate the behaviour which is being targeted for change. Secondly, there is no systematic basis on which to select the most relevant, important, or useful theories for exploring a particular behaviour. Francis et al (2009) suggest that one possible method is to take a more inclusive approach to selecting theory which involves a comprehensive set of theoretical construct domains, such as the Theoretical Domains Framework (TDF), (Michie et al, 2005). This has the potential to enable the identification of the domains most relevant to a behaviour such as adherence to treatment. This will be explored further in the following section.

4.4.1 The Theoretical Domains Framework (TDF)

Michie and colleagues (2005), developed The Theoretical Domains Framework (TDF) in the context of understanding professional behaviour change. Michie et al (2005) involved 18 experts in health psychology theory, 16 international health service researchers with expertise in implementation research and 30 delegates at a health psychology conference in a multi-stage consensus approach over a 14-month period to develop a theoretical framework that could be used in implementation research. They used a six-stage consensus approach which involved:

- i) identifying theories and theoretical constructs relevant to behaviour change
- ii) simplifying the resulting constructs into overarching theoretical domains
- iii) evaluating the importance of selected theoretical domains
- iv) conducting an interdisciplinary evaluation and synthesis of the domains and constructs
- v) validating the domain list
- vi) piloting interview questions relevant to the constructs and domains (Cane et al, 2012)

The resulting framework was derived from the integration of 33 theories and 128 constructs from behavioural theory culminating in 12 theoretical domains useful for categorising barriers and enablers to specific behaviours (Table 14).

Table 14: Behavioural domains of the Theoretical Domains Framework (TDF)

TDF Constructs	Description
Knowledge	an awareness of the existence of something
Skills	ability or proficiency acquired through practice
Social/professional role and identity	represents a set of behaviours and displayed personal qualities of an individual in a social or work setting
Beliefs about capabilities	characterised as an acceptance of the truth, reality or validity about an ability, talent, or facility that a person can put to constructive use
Beliefs about consequences	Beliefs that relate to the acceptance of the truth, reality, or validity about the outcomes of a given behaviour in a given situation.
Motivation and goals	mental representations of outcomes or end states that an individual wants to achieve
Memory, attention and decision processes	the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour
Social influences	interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours
Emotion regulation	complex reaction pattern, involving experiential, behavioural, and physiological elements, by which

TDF Constructs	Description
	the individual attempts to deal with a personally significant matter or event
Behavioural regulation	aspects of beliefs that are aimed at managing or changing objectively observed or measured actions
Nature of the behaviour	The ways in which the behaviour at hand is routine or a habit or indeed the opposite i.e., breaking of a habit. This can also relate to a direct experience or a past behaviour.

In 2012, the TDF was refined following a comprehensive, three-step validation process resulting in the refined but expanded model containing 14 domains and 84 component constructs (Cane et al, 2012). The refined framework provides explicit behavioural domain definitions and was informed by the use of the American Psychological Association's Dictionary of Psychology. Further refinements to the TDF are summarised in Table 15 .

Table 15: Summary of key changes to updated TDF

Nature of change	Rationale
Motivation and goal's domain separated into 'intentions' and 'goals'	Domain split to differentiate between 'goals' which focus on a preferred outcome or end state and 'intentions' which concern the resolve to initiate or terminate a behaviour.
Beliefs about consequence's domain split into two domains, one retaining the original name and one termed 'reinforcement'	Domain split to differentiate between 'reinforcement' which focuses on the constructs of associative learning and 'beliefs about consequence's which focuses purely on beliefs.
'Beliefs about capabilities' domain split into two domains, one retaining the original name and one termed 'optimism'	Domain split to differentiate between 'optimism' which concerns a general disposition and 'beliefs about capabilities' which focuses on specific capabilities

Nature of change	Rationale
'Behavioural regulation' domain clarified	Clarification enables focus on self-regulatory processes
Nature of the behaviours domain removed	Analysing the nature and influences of behaviour are two distinct processes

Atkins et al (2017) suggest six steps involved in using the TDF which are summarised below:

- 1) **Select and specify the target behaviour/s:** the first step is to ascertain the specific behaviour of interest by considering the behaviour in the context in which they are performed. This involves an exploration of the key behaviours and any interdependent behaviours related to the individual as well as the behaviours of others.
- 2) **Select the study design:** choosing appropriate study design will depend on the research question which will depend on the state of knowledge in the particular field of interest. If little is known about a specific problem qualitative interviews may be more useful allowing researchers to gain in-depth understanding which can be helpful when, for example, developing a theory-informed intervention.
- 3) **Decide the sampling strategy:** The target population will need to include those that will be adopting the behaviour. These could be individuals (e.g., clinicians, patients, students, or members of the public), dyads (e.g., clinicians and patients; teachers and students) or teams (e.g., teams of clinicians and managers or business workgroups). The organisational level at which change is proposed to occur could be at different levels, e.g., individual, team, organisation, or population levels.
- 4) **Develop interview schedule:** Questions should focus explicitly on the target behaviour. The number of domains covered as well as the number of questions within each domain will depend on the target behaviour. It is advised that the language used to develop a schedule is relevant to the target population. This can be checked by piloting any interview schedule in order to check comprehension. Typically, the interview schedule should use open questions for each of the theoretical domains, which can then be followed by a series of prompts to explore concepts more deeply. Questions do not need to be asked in any specific order and flexibility is encouraged with regards to the order in which domains are covered to promote the natural flow of the conversation.
- 5) **Collect the data:** Data collected using the TDF can be carried out by one or more of the following mediums: interviews, surveys, observation, and documentary analysis.
- 6) **Analyse the data:** Data can be analysed both deductively i.e., using the TDF to generate a framework for content analysis, as well as inductively i.e., by generating themes which are then considered in relation to TDF domains.

The TDF has been used to facilitate implementation of health care interventions (French et al, 2013; Tavender et al, 2014; Dyson, 2013), for example, it has been used to develop behaviour

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change interventions for the management of acute low back pain (French et al, 2012). The TDF has also been used to carry out theory-based process evaluation (Cane et al, 2012; French et al, 2013; Curran et al, 2013). For example, the TDF has been used to identify barriers to the implementation of best practice guidelines in schizophrenia (Michie et al, 2007); to identify barriers and enablers to the incorporation of evidence based guidelines in acute low back pain (McKenzie et al, 2008; McKenzie et al, 2010); to classify the behavioural determinants of blood transfusion practices in health care (Francis et al, 2009a; Francis et al, 2009b); to understand what facilitates and inhibits midwives' behaviour to implement guidelines to assist pregnant woman with smoking cessation (Beenstock et al, 2012); to investigate the barriers and enablers to the implementation of physical activity guidelines for midwives when advising obese pregnant women. Further, the TDF has been used to inform guidelines for following e.g. hand hygiene behaviours in hospital workers (Dyson , 2011) as well as guidelines for safety behaviours related to the positioning of nasogastric tubes (Taylor, 2013b). The following section will consider the application of the TDF specifically to treatment adherence.

Application of TDF to Treatment Adherence

Francis et al (2012) identified 133 papers which cite the TDF and included 21 studies which utilised the TDF. The research included seventeen studies which investigated the behaviour of health professionals as well as four that investigated health-related behaviour of members of the public (Francis et al, 2012). The TDF was used to investigate behaviours relating to tobacco cessation, immunisation of health care workers, weight management, hand hygiene as well as self-management in osteoarthritis. The research provided good evidence that the TDF has considerable breadth and cross-disciplinary impact in relation to health-related behaviour (Francis et al, 2012).

An example of the way in which the TDF has been used to define the content of an intervention to change patients' adherence to treatment for bronchiectasis (McCullough et al, 2015). The study identified barriers and enablers of patients' adherence behaviour in bronchiectasis using the TDF. It was indicated that eight of the 14 TDF domains were perceived to influence patients' behaviours: Knowledge, Skills, Beliefs about capability, Beliefs about consequences, Motivation, Social influences, Behavioural regulation, and Nature of behaviour. The study identified 12 theory-derived behaviour change techniques (BCTs) to form an intervention for bronchiectasis.

Arden et al, (2019) used the TDF to explore and identify the factors affecting adherence to nebulizer treatment in adults with Cystic Fibrosis (CF). The study involved 18 qualitative interviews and indicated that factors influencing adherence included all 14 domains of the refined TDF (Cane et al, 2012). The authors describe the study as enabling the systematic assessment of participants beliefs related to adherence and enabled comparisons between participants with different levels of adherence (Arden et al, 2019). Similarly, Voshaar et al (2016) used the refined TDF (Cane et al, 2012) to identify barriers and enablers to treatment for inflammatory rheumatic diseases which were evident across ten domains of the TDF. The authors conclude that the TDF was an appropriate framework for systematically assessing factors which have the capacity to influence treatment utilisation for inflammatory rheumatic diseases. Finally, Presseau et al, (2017) used the TDF to conduct a series of semi-structured interviews to explore barriers and enablers to adhering to treatment for post-myocardial infarction. Similar to the above studies, the refined TDF (Cane et al, 2012) was used to identify key barriers and enablers which were reported as existing in the domains: Beliefs about Consequences, Memory, Attention, Decision Processes, Behavioural Regulation, Social Influence and Social Role.

Through its amalgamation of theoretical models, the TDF provides a simple framework which enables researchers to identify key barriers and enablers of health-related behaviours. This approach has been applied to a variety of health behaviours and in a variety of different ways. It is important to highlight that the TDF is a theoretical framework rather than a theory and as a result it does not propose testable relationships between elements but provides a theoretical lens through which to view the cognitive, affective, social, and environmental influences on behaviour. This can be considered one of its limitations. SCMs specify relationships between model components, whereas the TDF does not. The TDF can therefore be considered as not attempting to replace such theories, but instead offers a viable alternate approach (Francis, 2009a). This is demonstrated in research such as that carried out by Islam et al (2012) which used the TDF as a basis to systematically select relevant theories and models to inform future research.

4.5 Summary

As demonstrated throughout this chapter, the use of a theoretical approach to research in adherence related behaviour is an important consideration. A number of theories have proliferated over time and each with their own strengths and weaknesses. This offers a plethora of theories, models, and frameworks to choose from when considering the exploration of treatment utilisation. As a result, researchers are faced with a multitude of theories which have been described as fragmented, and often offering contradictory evidence (Munro et al 2007). There is a need for theoretical integration (Stewart & Klein, 2016) and an appropriate and widely used integrative framework identified in relation to the focus of this thesis exists in the TDF (Michie et al, 2005; Cane et al, 2012). Atkins et al (2017) suggest that the TDF may be suitable to guide data collection using, for example, interviews, focus groups, structured observation and questionnaires designed to identify barriers and enablers to change. In addition, Taylor et al,

(2013a) highlighted that the TDF is amenable to adaptation for specific behaviours whilst also offering a degree of flexibility with regards to its application (Taylor, 2013a). Therefore, both the original TDF (Michie et al, 2005) and the subsequent updated version (Cane et al, 2012) can be considered important frameworks offering potential for use in behaviour change and implementation research. With this in mind, the TDF could be considered a suitable framework for use in the exploration of the barriers and enablers to ED treatment utilisation. Whilst the TDF has been applied to numerous health behaviours and promising work has emerged to utilise the TDF to identify barriers to behaviour change. To date, the TDF has not been applied to ED treatment utilisation. An important step to take towards improving ED treatment utilisation would be to use the TDF to identify barriers and enablers to ED medication utilisation. This thesis will attempt to lay the groundwork for future development of a theory-based adherence intervention targeted at resolving identified barriers and enhancing enablers of adherence.

The following chapter describes Study 2, a qualitative exploration of the barriers and enablers men experience in relation to ED treatment utilisation. The chapter will describe, in detail, the use of the TDF to identify barriers and enablers to ED treatment utilisation and to develop a tailored questionnaire for investigating non-adherence to ED treatments in Study 3.

5 Study 2. A qualitative exploration of Barriers and Enablers to ED Treatment Utilisation

5.1 Chapter Overview

One of the findings of the systematic review reported in Chapter 3 was that the included studies neglected to utilise a theoretical foundation upon which to base their exploration of ED treatment utilisation. Chapter 4 therefore, considered which theories are available to inform adherence research and considered which are likely to be the most suitable for exploring the problem of ED treatment utilisation. This chapter describes a theoretically informed qualitative study which utilised the TDF in a series of interviews (n=10) to identify barriers and enablers to ED treatment utilisation. The Chapter also details how the interview findings were used to develop a questionnaire to examine salient barriers and enablers to ED treatment utilisation quantitatively, for use in study 3 (reported in Chapter 6).

5.2 Introduction

The systematic review in study 1 (chapter 3) found that across 45 studies, the reported rates of discontinuation ranged from 13.8-76% for PDE5Is, 18.6-79.9% for intracavernosal injection (ICI) treatment, 32-69% for urethral suppositories (US) and 30% with regards to penile prosthesis (PP), indicating that interventions are needed to help men with ED to make the most of their treatment. The review suggested that the most prevalent barriers to ED treatment utilisation were treatment ineffectiveness, side effects, the quality of men's intimate relationships and treatment cost. Importantly, out of the 45 included studies, none used theoretical models or frameworks as the foundation for exploring the barriers and enablers to ED treatment utilisation.

To the author's knowledge there have not been any qualitative, theory-based explorations of the barriers and enablers to ED treatment utilisation. Prior to intervention design, it is important to carry out an exploratory study, in order to gain a greater perspective and understanding of potential relevant theories (Campbell et al, 2007). Therefore, this necessitates the use of qualitative research, as it enables the investigation of people's attitudes and motivations (Keats, 1999) as well as an in-depth understanding of the target behaviour which is important when laying the groundwork for theory-informed interventions (Atkins et al, 2017).

The use of theoretical models in intervention development is advocated by the Medical Research Council (Campbell et al, 2007) as well as the National Institute for Health and Care Excellence (NICE, 2021), in order to increase the likelihood that interventions will be effective. The utilisation of social cognition models (SCM) has received criticism for the existence of overlapping variables between models (Norman & Conner, 1996; see 4.4). Therefore, it has been suggested that a potential resolution to this problem exists in the amalgamation of individual models to form a more comprehensive one (Armitage & Conner, 2000). The Theoretical Domains Framework (TDF; Michie et al, 2005; Cane et al, 2012) is an integrative framework offering a potential solution to the aforementioned problem, as it is considered to be a comprehensive framework (Huijg et al, 2014). Qualitative studies which have utilised the TDF indicate that the framework enables the exploration of barriers and enablers to treatment utilisation (McCullough et al, 2015; Arden et al, 2019; Voshaar et al, 2016; Pesseau et al, 2017). Therefore, the TDF was considered to be the most appropriate framework for investigating treatment utilisation for the current research. The framework is broad in its approach and offers a comprehensive set of theoretical construct domains suitable for the exploration of ED treatment utilisation. It has also been used to explore barriers and enablers to adherence in conditions

including bronchiectasis (McCullough et al, 2015), Cystic Fibrosis (Arden et al, 2019), inflammatory rheumatic diseases (Voshaar et al, 2016) as well as post-myocardial infarction (Presseau et al, 2017).

An important consideration of using the TDF in qualitative research relates to the extent to which the research is driven by theory i.e. whether it is top-down and deductive in nature, or alternatively, whether it is bottom-up and driven by the data or the patterns of meaning that may emerge from the analysis. Using the TDF involves primarily deductive analysis, i.e. the TDF uses a framework to guide the qualitative data analysis. However, it also utilises inductive analysis, i.e. after the deductive analysis is completed, inductive analysis is used to generate themes which are based on their respective domain (Atkins et al, 2017; See 5.6.7). Atkins (2017) indicates that this approach has been used as the basis for designing questionnaires to collect quantitative data, enabling the testing of hypotheses generated by the qualitative analysis. Therefore, this approach to qualitative analysis, i.e. one that is both deductive and inductive in its approach, was considered a suitable method for achieving the goals of the qualitative study (Study 2) as well as the wider goals of this PhD thesis.

5.3 Aims

The overall aim of this study was to identify barriers and enablers that men experience to utilising their ED treatment.

5.4 Objectives

The objectives of this study were to:

1. Carry out in-depth, semi-structured interviews using an established theoretical framework for behaviour change, to explore barriers and enablers to ED treatment utilisation

2. Use the findings to develop a questionnaire to explore barriers and enablers to ED treatment utilisation which can be used in Study 3, a quantitative cross-sectional study (reported in Chapter 6)

5.5 Research question

What barriers and enablers do men with ED experience using treatment for the condition?

5.6 Methodology

5.6.1 Study Design

This study used face-to-face, semi-structured interviews.

5.6.2 Participants

Men meeting the following inclusion and exclusion criteria were approached to take part in the study:

- Aged ≥ 18 years
- Received an official ED diagnosis by a relevant HCP e.g. via their GP or Urology clinic.
- Either A) Prescribed or using ED treatment OR B) prescribed ED treatment in the past but subsequently discontinued treatment. Treatments could include; PDE5Is, ICI, US, a VED or PP
- Able to read and speak English

5.6.3 Setting

Men were recruited from specialist ED clinics within the urology services at Barts Health NHS Trust and University College London Hospitals NHS Foundation Trust (UCLH).

5.6.4 Interview schedule

The interview schedule used a combination of the original (Michie et al, 2005) and the refined version of the TDF (Cane et al, 2012). The interview schedule included ‘nature of the behaviour’ from the original TDF, plus all 14 domains from the refined version of the TDF. The inclusion of the domain ‘nature of the behaviour’ was considered important, as the domain is described as being constituted by behaviour, considered habitual or routine and this is important considering utilisation of ED treatment is likely to involve habits as well as routines which may relate to, for example, a couples routine around sexual intimacy which may or may not have a habitual aspect to it. Overall, the interview schedule was compiled of fifteen constructs (Table 16).

Table 16: Theoretical Domains used in this study

Domain	Definition
Knowledge	An awareness of the existence of something
Skills	An ability or proficiency acquired through practice
Social/Professional Role and Identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting
Beliefs about Capabilities	Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use
Optimism	The confidence that things will happen for the best or that desired goals will be attained
Beliefs about Consequences	Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus
Intentions	A conscious decision to perform a behaviour or a resolve to act in a certain way
Goals	Mental representations of outcomes or end states that an individual wants to achieve
Memory Attention and Decision Processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives
Environmental Context and Resources	Any circumstance of a person’s situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour
Social Influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours
Emotions	A complex reaction pattern, involving experiential, behavioural, and physiological

Domain	Definition
	elements, by which the individual attempts to deal with a personally significant matter or event
Behavioural Regulation	Anything aimed at managing or changing objectively observed or measured actions
Nature of the behaviour	Any behaviour that is considered a habit, routine, automatic or a direct experience or a past behaviour

In a similar vein to other studies which have used the TDF to develop an interview schedule (e.g. McSherry et al, 2012, Atkins et al, 2017), the TDF constructs (outlined above) were used to compile a series of questions based on salient issues from study 1 and the wider literature. In order to utilise the TDF for Study 2, the six steps outlined by Atkins et al (2017) were followed (See section 4.4.1). Interview question phraseology was informed by other adherence studies that have used the TDF (i.e. Nicholson et al, 2014, McSherry et al, 2012).

TDF domain descriptions were used to develop questions. Subsequently, the questions were reviewed by two clinical urologists, two health psychologists and two men with ED for comprehension and face validity. The questions were revised and then circulated to the group for a second time to ensure that feedback had been satisfactorily incorporated. The final questionnaire included 34 questions covering the above 15 TDF domains (Appendix 7). In addition there were 4 general questions about the participants' current treatment for ED. The final interview schedule can be found in Appendix 7. For each participant, self-reported demographic data was captured which included: age, level of education, sexual orientation and relationship status. In addition, self-reported clinical data was also captured, which included; the duration and severity of ED, comorbidities, current treatment and a question about current treatment use.

5.6.5 Procedure

Recruitment took place between September 2016 and January 2017. Prior to men attending their out-patient clinic appointment, the nurse specialist reviewed the patient list and identified those men who met the inclusion criteria.

The nurse specialist or urologist introduced the study when the patient presented in clinic and asked if they were interested in taking part. If they expressed an interest then the nurse or clinical specialist introduced the participant to the researcher, who then explained the study further and provided them with a patient information sheet (Appendix 8). Patients who wished to take part in the study were subsequently asked to complete a consent form (Appendix 9).

Men who agreed to take part in the study were given the option of being interviewed on the same day as their appointment. If this was not possible, an alternative date was arranged. Interviews were carried out by the author, either face-to-face or on the telephone.

5.6.6 Sample Size

Maximum variation or heterogeneous purposeful sampling is a qualitative sampling technique which enables identification and selection of information-rich cases. Additional advantages reside in its effective use of limited resources (Patton, 2002). Central to the method is the identification of individuals or groups of individuals especially knowledgeable or experienced in relation to the phenomenon to be focussed on (Cresswell & Plano Clark, 2011). Using this technique ensured that there was a mix of participants who had used or were using PDE5Is, ICI, US, VEDs or PP. This was achieved through consultation with respective clinicians and specialist nurses at both Barts and UCLH urology clinics to identify men based on their respective treatments to ensure all relevant treatment types were included.

Data saturation in qualitative research is considered as the point at which additional participants do not provide any further insights (Fusch & Ness, 2015). It has been suggested that this phenomenon often occurs at around 12 participants in homogeneous groups (Guest et al, 2006). Therefore, the study aimed to recruit approximately 12 participants, however, this was used as a guide and participants would be recruited until data saturation.

5.6.7 Analysis

Interviews were transcribed verbatim by the author. Analysis was conducted using a process previously used to analyse qualitative data derived from the TDF (Patey et al, 2012; Islam et al, 2012). This involved the following steps.

Coding

Open coding using a line by line process was used to analyse the transcripts. To ensure integrity of the analysis process, two coders (PW, HM) independently coded the first two interviews. The coders used the TDF domain descriptions outlined in Table 16 in order to be able to allocate quotes (i.e. sentences or sentiments relating to a particular domain) to a specific TDF domain. Using the 15 TDF domains outlined previously (Michie et al, 2005; Cane et al, 2012), quotes were allocated to the most appropriate domains, with some quotes allocated to more than one domain if appropriate. Quotes that did not fall under the domains of the TDF were discussed by the two coders, where a third coder (KM) was consulted to reconcile any differences. It was found that in some instances there were quotes that that did not fit into the TDF domains. This was a result of the TDF domains being explicitly related to treatment related beliefs and their impact on treatment utilisation. It was evident that there were, in addition to treatment related beliefs, illness related beliefs that participants reported as having an important influential

impact on treatment utilisation (Table 16). As a result it was decided that these beliefs fell under the domains of the self-regulation model (SRM; See 'Relevant SRM Illness Representations' section below).

The two coders compared results and any differences were resolved through discussion. Where necessary again consultation with a third coder (KM) brought about consensus. Finally, in order to ascertain interrater agreement, the methods set out by Islam et al (2012) which involved using the last four interviews to ascertain interrater agreement at the domain level. The method involves ascertaining the level of both partial (i.e. two coders identified the same quote but put them in different domains) and complete agreement (both coders identified the same quote and put them in the same domain). This is carried out by comparing the quotes allocated to each of the TDF domain by each coder of the coders. Agreement was considered high if both coders allocated 80% - 100% of quotes to the correct domain; moderate if it was between 55-70% and low if it was 55% and below. Therefore, based on comparing the coding of each coder, complete agreement across domains i.e. where both coders identified the same quote and allocated it to the same domain ranged from 36.6% to 95.8%. Partial agreement, i.e. where both coders identified the same quote but put them in different domains ranged from 2.5% – 46%. (See Table 18).

Generating specific beliefs

Once the interview transcripts had been coded into the TDF domains, the author and a second researcher (HM) generated belief statements which were considered as representative of specific underlying beliefs within domains. Again, where necessary, consultation with a third coder (KM) enabled consensus. A belief statement represents a collection of responses with a similar underlying theme related to the target behaviour (Francis et al, 2009). As a result a belief

statement was worded to convey a meaning that was common to multiple quotes. To quantify belief statements, the number of quotes were recorded as well as the number of participants that uttered a given belief statement (Table 19).

Identifying key domains

Key domains, in other words those considered most important with regards to ED treatment utilisation, were identified through consensus discussion between the two researchers (PW, HM) and where any discrepancies occurred they were considered in conjunction with a third researcher (KM). Three factors were considered when identifying key domains:

- Frequency of the beliefs across interviews
- The presence of conflicting beliefs i.e. variability in the views among participants and conflicting viewpoints expressed within a participant;
- Evidence of strong beliefs that may impact on the behaviour.

5.6.8 Ethics

Ethical approval was obtained from the sub-committee of the North East Newcastle and North Tyneside 1 Research Ethics Committee (Ref. No. 16/NE/0333). Once a favourable opinion was received, research and development approval was requested and obtained from Barts Health NHS Trust (ref. no. 011603) and UCLH (ref. no. 207576).

5.7 Results

5.7.1 Participants

A total of fifteen men were asked to take part in the study, all 15 provided signed consent and ten completed an interview. The reasons for drop out were: being unable to arrange a suitable date and time that was convenient for the participant (n=4), and revoking consent due to no longer wishing to participate (n=1). These 10 interviews were carried out between January and March 2017. Three of the interviews were carried out in a dedicated room within the hospital clinic and seven over the telephone. The interviews were conducted and audio-recorded by the researcher. They took, on average, 45 minutes (range: 20 – 70 minutes) to complete.

Participant characteristics are reported in Table 17. With regards to their age ranges, the youngest participant was in the 21-30 year old age bracket and the oldest was in the 71-80 years of age bracket. Men were most likely to be 51–60 years old (n=4) (Table 17). Five participants were currently using ED treatment and five had ceased to use treatment. The severity of ED ranged from mild to severe where most were suffering with mild to mild-moderate ED (n=6). The average duration participants had been suffering with ED was 5.1 years (sd=2.68). All participants were heterosexual and half of the participants were married (n= 5). Nearly all men had tried PDE5Is (n=9), however, 2 had tried PDE5Is as well as ICI and VED (n=1) or ICI and US (n=1). Finally, one participant had tried a VED and had then undergone PP. Four men did not have any co-morbidities; CVD (n=2), hypertension (n=1), diabetes (n=1), hypertension and diabetes (n=1), asthma (n=1) were the most common.

Table 17: Participant demographic data

Participant	Age	Level of education	Sexual Orientation	Relationship Status	ED duration	ED Severity	Comorbidities	Treatment	Currently Using Treatment
1	51 – 60	GCSE	Heterosexual	Married	2 y	Mild	None	PDE5I	No
2	21 – 30	Undergraduate	Heterosexual	Partner	5 y	Mild to Moderate	None	PDE5I	No
3	41 – 50	Undergraduate	Heterosexual	Married	3 y	Severe	None	PDE5I	No
4	61 – 70	Postgraduate	Heterosexual	Single	10 y	Mild	CVD	PDE5I	Yes
5	51 – 60	Undergraduate	Heterosexual	Married	8 y 4 m	Severe	HypT	PDE5I, ICI, VED	Yes
6	41 – 50	Undergraduate	Heterosexual	Married	8 y	Severe	HypT, Diab, Obes	PDE5I, US, ICI	Yes
7	51 – 60	GCSE	Heterosexual	Divorced	4 y	Severe	Diab	VED, PP	No
8	21 – 30	A Levels	Heterosexual	Single	3 y	Mild to moderate	None	PDE5I	Yes
9	71 – 80	GCSE	Heterosexual	Widower	4 y	Mild to Moderate	CVD	PDE5I	Yes
10	51 – 60	GCSE	Heterosexual	Married	4 y	Mild	Asth	PDE5I	No

Asth: Asthma; CVD: cardiovascular disease; HypT: Hypertension; Diab: Diabetes; Obes: Obesity

5.7.2 Interrater reliability

Although Islam et al (2012) do not indicate what an acceptable level of interrater agreement is, according to Atkins (2012), reliability between two coders is acceptable if 60% agreement is achieved. The domains with the highest agreement between the research team were *optimism, beliefs about capabilities, reinforcement and skills* (75-95.8%). Moderate agreement was evident for the domains *beliefs about consequences, social professional role and identity, social Influence, behavioural regulation, knowledge, memory attention and decision processes* and *emotion* (55.5-70%). The lowest levels of agreement were evident for *goals, intentions* and *environmental context and resources* (36.6-53.5%) (Table 18).

Table 18: Percent agreement across interviews and domains

Domain	Complete Agreement	Partial Agreement
Optimism	95.80%	2.50%
Beliefs about capabilities	75%	10%
Reinforcement	77.70%	14.40%
Skills	75%	25%
Beliefs about consequences	70%	17.30%
Social/professional role and identity	66.60%	33.30%
Social Influences	61%	25.70%
Behavioural regulation	58.30%	27.50%
Knowledge	58.20%	33.30%
Memory, attention and decision processes	57.50%	40%
Emotion	55.50%	22.20%
Goals	53.50%	46%
Intentions	51.40%	44%
Environmental context and resources	36.60%	37%

5.7.3 Relevant TDF Domains

A total of 68 beliefs across 14 TDF domains were identified (Table 19). The following section reports the belief statements and their categorisation within each of the TDF domains. There

were no belief statements elicited from the domain 'nature of the behaviour'. Therefore, of the 15 TDF domains, 14 contained relevant beliefs statements. Discussion between the research team involved the consideration of the salience of belief statements. Therefore, this included the frequency of elicited quotes according to the qualitative interviews in conjunction with the findings from the systematic review (Study 1) in order to ascertain the salience of a belief statement (Table 19). The following sections will consider the TDF domains in order of frequency starting with the TDF domain that elicited the highest frequency of quotes.

Table 19: TDF Domains and Belief Statements

Domains & Belief statements	N° of Participants	N° of Quotes
Beliefs about consequences (TDF)	10	170
<i>A small daily dose of ED medication is more effective than a larger dose</i>	1	1
<i>ED medication can cause pain due to not having used my penis for a long period of time</i>	1	4
<i>I do not always need to take my treatment for ED in order to achieve an erection adequate for sexual intercourse</i>	4	9
<i>I experience medication side-effects (e.g. headaches, facial flushing, pain, Peyronie's disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of taking my ED medication</i>	9	47
<i>I use a pump to grow my penis to a normal size and use injection therapy to maintain my erection</i>	1	1
<i>My ED treatment does not live up to my expectation</i>	1	1
<i>My ED treatment enables me to have a sexual relationship with my partner</i>	9	26
<i>My ED treatment improves my ability to get an erection</i>	9	22
<i>My ED treatment is quick to work upon taking it</i>	4	5
<i>My ED treatment works every time I take it.</i>	9	39
<i>My partner becomes frustrated when my ED medication does not work</i>	1	1
<i>My partner does not like using ED treatment for the intimate aspects of our relationship</i>	1	1
<i>Taking ED medication makes my sex life less spontaneous</i>	6	16
<i>Taking my treatment for ED is a necessity rather than a choice</i>	5	8
<i>The effect of my ED treatment (i.e. duration of erection) does not last long enough</i>	5	13
Social Influence (TDF)	10	95
<i>I feel encouraged by my doctor or nurse to take my ED medication</i>	9	18
<i>I feel encouraged by my partner to take my ED medication</i>	10	44
<i>I feel that there is a taboo around ED medication</i>	2	2
<i>I have informed my partner that I use ED medication</i>	4	8
<i>I know other men who take medication for ED</i>	5	7
<i>I know who to contact if I had any issues with my ED medication</i>	4	4
<i>If I wanted to change my ED medication or alter my dose I would speak to a doctor or nurse first</i>	2	2
<i>My doctor or nurse has provided me with adequate instructions about how to take my ED medication correctly</i>	6	16
Goal (TDF)	10	60
<i>I aim to have a sex life that does not rely on medication.</i>	7	23

Domains & Belief statements	N° of Participa nts	N° of Quo tes
<i>I would like to maintain or regain an intimate sexual relationship with my partner</i>	6	8
<i>My aim is to find a more natural or holistic solution to my ED</i>	2	15
<i>My aim is to use my treatment for ED as a rehabilitative measure</i>	2	5
<i>My partner and I are trying for a baby</i>	1	1
<i>Taking my ED medication as prescribed is high on my list of priorities</i>	9	10
Intention (TDF)	9	44
<i>I intend to take my medication in the future</i>	7	19
<i>If I think sex is likely then I take my ED medication in preparation</i>	7	20
<i>If I want to be sure that I will be able to perform I will take my ED medication</i>	2	3
Environmental context and Resources (TDF)	9	43
<i>A lack of privacy makes it difficult to take my ED medication</i>	1	2
<i>I am able to obtain more ED tablets if I need them</i>	2	6
<i>I can easily get hold of a prescription for ED medication</i>	4	7
<i>I find it difficult to pay for my ED medication</i>	9	21
<i>I have sought alternative treatments for my ED outside of the NHS</i>	2	5
<i>Work makes it difficult to take my ED medication</i>	2	2
Behavioural Regulation (TDF)	9	39
<i>I ensure I have access to my ED medication in case I need it</i>	2	5
<i>I ensure that I take my ED medication as prescribed (e.g. on an empty stomach)</i>	2	2
<i>I have a plan or pattern with regards to taking my ED medication</i>	9	25
<i>I take my ED medication as part of my daily routine</i>	2	8
<i>I take my ED medication before every sexual encounter</i>	2	2
Knowledge (TDF)	10	37
<i>I know how my treatment for ED works</i>	1	3
<i>I know how to take my ED medication, as prescribed, in order for it to work effectively</i>	10	33
<i>I know the possible side effects of my ED medication</i>	2	2
<i>If I needed to change the way I take my ED treatment I would know how to go about doing this</i>	1	1
Social, Professional role and Identity (TDF)	9	20
<i>Having ED affects the way I feel about myself</i>	3	3
<i>I am too young to be relying on treatment to achieve an erection</i>	1	2
<i>Sexual intimacy is important to me</i>	2	2
<i>Taking medication for ED has a negative impact on my masculinity</i>	6	11
Optimism (TDF)	7	19

Domains & Belief statements	N° of Participants	N° of Quotes
<i>I am hopeful that new medication will become available to me</i>	1	1
<i>I am optimistic about being able to take my ED medication</i>	4	6
<i>I am optimistic that my ED medication will make my ED better</i>	4	13
Memory, attention and decision process (TDF)	9	16
<i>Decisions about whether to take my treatment for ED are difficult to make</i>	6	7
<i>I can't remember my ED medication dosage</i>	1	3
<i>I never forget to take my ED treatment</i>	6	6
Beliefs about capabilities (TDF)	8	14
<i>I feel confident that I am able to take my ED medication</i>	8	14
Emotion (TDF)	6	13
<i>Having my sex life depending on ED medication is depressing</i>	1	2
<i>I am anxious about whether the ED medication will be effective</i>	1	1
<i>I feel embarrassed about having to use treatment for ED</i>	1	1
<i>My ED medication makes me feel confident</i>	4	8
<i>My mood dictates whether I take my ED medication</i>	1	1
Skills (TDF)	3	8
<i>I have learnt when to take my ED medication from experience (e.g. in relation to food and alcohol consumption)</i>	1	1
<i>I have not been able to use my pump effectively</i>	1	4
<i>The more I practise using my pump the easier it is to use</i>	1	2
Reinforcement (TDF)	4	5
<i>Being able to have an enjoyable sex life encourages me to take my ED medication</i>	2	3
<i>The more my ED medication works the more I want to use it</i>	2	2

Beliefs about consequences (TDF)

This domain elicited the most quotes (n=170) and across all participant interviews (n=10), generating 15 belief statements. The most notable belief statement within the beliefs about consequences domain related to treatment side-effects. Across nine of the interviews there were 47 quotes that related to one or more ED treatment related side-effects all of which had the potential to influence treatment utilisation. Side-effects were also an important factor to emerge from the systematic review (Study 1). For PDE5Is side-effects included; headaches, facial flushing, dry mouth, pain to the penis and a hangover sensation. In relation to ICI, reported side-effects included pain at the injection site, aching sensations in the penis and Peyronie's disease.

The pump was associated with causing pain to the penis and the penile implant was associated with scar tissue and pain resulting from relevant surgery. The effect of side-effects on treatment utilisation is highlighted in the following quote;

'I'm not really at this point prepared to... be strictly adherent to how you would take the drug and I'm not prepared to have the side effects, so therefore I will stop taking it...' (P-03)

Belief statements relating to perceiving ED treatment as not effective were also considered pertinent to ED treatment utilisation based on the frequency with which they occurred throughout the qualitative interviews, treatment ineffectiveness was also a pertinent factor to emerge from the systematic review (Study 1). Nine interviewees (39 quotes) reported that their treatment was not necessarily effective every time they took it. For example:

'it was a bit of a shock when I read it and it said it takes about an hour to kick in and even then it's you know, you don't get an instant reaction err... erection or anything like that you actually then have to have the feeling which is possibly why.... It is not working well for me' (P-10)

One participant reported that the lack of efficacy in relation to PDE5Is led to the decision to change to ICI treatment:

'It just seemed to be err... the efficacy wasn't as good so that's why I went to... to thingy... Caverject...' (P-06)

Five men felt that the effects of ED medication did not last as long as they would have liked (n participants = 5, n quotes =13);

'now one of the reasons I looked at Tadalafil rather than a traditional Viagra, was well it could carry on working for 12 hours which I never really got... any of the benefits from where the only thing that carried on for 12 hours was the head ache!' (P-03)

ED treatment was also experienced as having a positive effect on enabling men to have a sexual relationship with their partner (n participants = 9, n quotes = 26);

'the consequences are if I don't take the ED drug... then... there is a strong likelihood that without doing anything else the ED problems will continue and our sex life will pretty much... not exist, not in terms of penetrative sex...' (P-03)

There were a number of quotes relating to the effects of treatment on reducing the spontaneity of participants' sex lives. Themes relating to this statement were evident in 16 quotes across 6 interviews.

'like I say I find the whole thing is a bit... lacking in spontaneity so... it seems more like a chore than a... a... moment of passion really if you know what I mean' (P-01)

Social Influence (TDF)

Social influence was mentioned by all 10 participants across 95 quotes. A total of 8 belief statements were generated. Based on discussion within the research team to consider the frequency of beliefs as well as evidence from the systematic review (Study 1), 4 belief statements were considered salient.

The systematic review highlighted, for example, the importance of partners being involved in and aware of ED treatment or where men's partners felt satisfied with ED treatment increased utilisation was reported. According to the interviews, all men felt a level of encouragement by their partner to use their respective ED medication or not (n participants = 10, n quotes = 44) and a majority by their healthcare team (n participants = 9, n quotes = 18). For example, some men experienced a high level of encouragement;

'I mean, because my wife is pretty good like that if I say, and because you know, if I say you know I want to make love she is always a 'yea come on then let's go for it', so sometimes I'll just take the tablets and just come up to her and she's always like 'yea yea come on then let's go for it' (P-07)

However, some men felt less encouraged by their partner to use their ICI treatment and VED, as opposed to medication.

'She came to one... and err... it was the one in which the doctor suggested right lets go up to the next level, let's think about injections and I went up to the nurse on my own for the, for the injections and came back with the packages and... and etc... we tried... I don't think she liked the idea of me sticking a...a needle in my penis... she is a nurse herself and she still doesn't like the idea' (laughs) (P-05)

'Ermm... again the tablets she doesn't mind... the pump she is a little confused as to what I am doing with that ermm... and I have explained it to her but... you know if I go upstairs and say that's what I am doing erm... yea... not that she's verbally negative about it' (P-05)

On the other hand, some participants felt that, overall, the utilisation of treatment was simply down to the individual;

'It's only you that manages it... it's you that decides when to take it, it's on your own accord... once you've got your prescription... whatever, you've got it... no one is going to force you to take' (P-02)

'I mean... I don't think... my wife directly influences... me as such... around taking the treatment, so it's not like her saying; 'you should take the tablet so that we can have sex', it's not really that dynamic in our relationship so no, it's just me primarily...' (P-03)

In relation to feeling encouraged by one's HCP, most men reported positive affirmations. However, one participant had experienced both ends of the spectrum as demonstrated by the following quotes;

'certainly what encouraged me last week was the, the... male... nurse there demonstrating it on me and, and being really encouraging and positive; 'I can see this working, you are responding well to it, I can see that you haven't had an erection in a long, long time but you are responding to it'... so those sorts of positive reinforcements really... matter...' (P-05)

'She was quite erm... demeaning... not demeaning... she was just 'you are very lucky to have this'... etc, etc...' (P-05)

There were a number of participants who indicated beliefs (n participants = 4, n quotes = 8) related to informing one's partner that ED treatment was being used, as mentioned previously, this was highlighted by the systematic review. Most men had informed their partner that they

use treatment for ED, however, one participant who had a penile prosthesis had not. He explained this in the following quote:

Participant: *'How can I put this, she's Portuguese and her English is not top notch... so I, I wouldn't be able to explain it to her so it's best just not to say nothing'... (laughs)*

Interviewer: *'So at the moment she is not aware of it?'...*

Participant: *'Nope, nope'* (P-07)

Based on the frequency of the belief (n participants = 6, n quotes = 15), men's belief that their healthcare team had provided them with adequate instructions about how to take their ED medication correctly was deemed relevant, for example:

'Well I think... the first err... prescription I was given the doctor gave me some advice, but it was only when I came up to the hospital yesterday that err... the consultant said that I have to take it on an empty stomach and nobody had told me that previously...' (P-01)

Goal (TDF)

Across all ten participants, 60 coded quotes resulted in a total of six belief statements. Three of these belief statements were considered salient. Men were asked on a scale of one to five to what extent is using treatment for ED a priority. Across nine interviews (10 quotes) men described the extent to which using treatment for ED was considered high on their lists of priorities. The responses ranged from it being low priority all the way through to being a very high priority due to the essential nature of the treatment in promoting a good relationship between the participant and his partner. The following quotes demonstrate the variety of responses to this question;

'so my motivation at the moment is low because I don't have the means to... to do it so I suppose it would be about a 3 or 4 because I don't have the means to'... (P-05)

'Erm... I think 3 at the moment is the... priority erm... because I, the reason I picked 3 is because it's not the highest of things in your life as a priority... you know... if you are younger, quite a bit younger, I am 58, whereas when you are younger in your life it is most probably a 5 and you know when you get older it goes down to a 2 and a 1 like an 80 year old... so about 3 at the moment because I still feel young so I still want to be able to have the intimacy with my wife'... (P-10)

'Err... well I'd say yes; number 5 definitely because it's absolutely crucial for my future really, it's an important part of my life, I want to have a partner or partners in my life, you know, and err... I want to make sure that I am fit and ready for that, you know, and that's all aspects of it... Your body really... so very important' (P-09)

Two further beliefs statements constituted a strong desire to move away from ED medication so their sex life did not have to rely on medication as well as moving towards a more natural or holistic method of ED management. The first belief statement, which is represented by 23 quotes across 7 participant interviews, related to aiming to have a sex life that does not rely on treatment, exemplified by the following statement:

'I wish I wasn't taking it... I'd knock it on the head... so I'm open to taking, I'm open to taking ED drugs in the short term, now whether this applies to this question or not... I don't... I don't want to see basically from here forth my sex life revolving around taking a tablet 3 hours before I have sex, even if it works, for me that is very depressing'. (P-03)

Considered similar to the above belief statement; ‘my aim is to find a more natural/holistic solution to my ED’, this sentiment was constituted by 15 quotes (n participants = 2) and exemplified by the following:

‘... so for example now... what I am doing with the Tavistock Clinic which is psychosexual if they were saying this is something that you should try as a part of a combined therapy... here are some things that are non-pharmaceutical in terms of ... technique’s or things that I want you to try and then as part of that experimentation let’s... you know... try taking this drug at that point so it would be kind of more like a combined therapy thing rather than just.. You self-administer when, you know, you want to try for sex and go from there... that would... does that make sense?’ (P-03)

Intention (TDF)

Three belief statements were generated from 44 quotes across 9 interviews. Two of the belief statements were considered salient. The first related to intentions to use treatment in the future. Participants had both negative and positive intentions with regards to the prospect of using treatment in the future (7 participants, 19 quotes):

‘so I would be prepared to take an ED drug for a period of time to get our sex life back on track... and then I’d be looking to stop it... It’s tough to be thinking I’d be taking it for the rest of my sex life type thing...’ (P-03)

‘Well I will use it for as long as I can and... or as long as I am sexually active...’ (P-04)

The second belief statement, mentioned by the majority of men (n participants = 7, n quotes = 20) related to using treatment in anticipation of a sexual encounter i.e. there was an intention to use treatment prior in order to engage in sexual intimacy:

'If I think that a sexual encounter is likely... in an evening... I will take it before the meal that might be taking place that evening... I might have it with a cup of tea or even a cup of tea and a biscuit at tea time'... (P-04)

Environmental context and resources (TDF)

There were a total of 43 quotes related to this domain, across nine interviews. This generated 6 belief statements. The combination of evidence from the review and the interviews culminated in two salient belief statements. The difficulty experienced by men having to pay for their ED medication was the most frequently reported belief statement (n participants = 9, n quotes = 21), which was also a salient barrier to treatment utilisation that emerged from the systematic review (Study 1). Participants were of differing ages and had a variety of comorbidities. Therefore, participants had very different experiences with regards to paying for treatment:

'No I'm 60 now so, it's free isn't it... prescriptions free now...' (P-01)

However, one participant's decisions around whether to use medication related heavily to the cost of purchasing treatment and the extent to which he considered this to be worthwhile:

'They're the main two yep... and actually to be honest... the cost... because Tadalafil is not a.... I can't remember how much it is.... It ends up being about £15 a tablet... yea... so when I was talking about the premeditated nature and the level of anxiety to say right

well... if I take it of my own accord to try and maintain the spontaneity... a) I've got the side effect b) I've burnt £15 for no good reason because I'm getting headaches for 24 hours and burnt £15 for the pleasure of it...' (P-03)

Subsequently, the same participant reported that due to the cost in combination with the perceived side-effects he ultimately made the decision to cease using the treatment:

'I'm not using the treatment because... to be fair, it's quite expensive to get it anyway...'
(P-02)

The following statement indicates the potential overlap with regards to the cost of ED treatment and the decision to seek alternative treatment for ED outside of the NHS. This was indicated by two men (n quotes = 5), exemplified in the following quote:

'There is also another device which I erm... I purchased erm, these things are not available on the NHS which is fair enough I mean I don't expect them to be... it's a sort of vibrational system, a special American thing... and err... so I bought one of those as well so I use that to stimulate the blood vessels in the penis erm... and that seems to be having some impact...' (P-09)

Behavioural regulation (TDF)

A total of 5 belief statements were generated within the behavioural regulation domain, representing 39 quotes, across 9 of the 10 interviews. The most salient belief statement related to having a plan or a pattern as well as not having a plan with regards to using ED treatment (n

participants = 9, n quotes = 25). There were, for example, participants who did not necessarily have a plan in relation to using treatment:

'so that makes it something that you're like well do I or do you not... so that's often I think why... you know... you've had half a bottle of wine and you're probably a little bit more relaxed... ah fuck it I'll... try it and see what happens type of thing...' (P-03)

Other participants described the necessity to have a plan that would facilitate the use of treatment:

'It's... err... You've just got to plan... like I say you've to... to plan it, it's not... it's like a military exercise as opposed to just err.... A run of the mill sort of... intercourse session, it's almost like going back to the days when you were planning to have a child, it's like you know... right the hormones are all in place lets go for it!' (P-10)

Knowledge (TDF)

Overall there were 4 belief statements within the 37 related quotes across all 10 interviews. The vast majority of these quotes (n quotes = 33) related to participants beliefs with respect to knowing or not knowing how to take their ED medication in order for it to work. For example:

'I've heard that... I've heard don't take it with alcohol or this that... I've heard that... but... I have taken it once with alcohol and it worked fine... I might be lucky I don't know... someone else might take it with alcohol and it might not work for them...' (P-02)

'I think probably once or twice I have tried to take it in the correct conditions... sometimes it has worked and sometimes it hasn't... now, whether there's a complete correlation

between the large steak and half a bottle of wine... and being very tired and it not working... I haven't really considered it... because I think the side effects had become something that was like right well... I'm not really at this point prepared to... be strictly adherent to how you would take the drug and I'm not prepared to have the side effects, so therefore I will stop taking it...' (P-03)

The above statement demonstrates the relationships between domains and this impacts on the decision to use treatment. The participant has knowledge around how to successfully use the treatment; however, due to the experience of side-effects, the treatment would still be used although not necessarily in a way that would maximise its effectiveness.

Social, professional role and identity (TDF)

In total there were 20 quotes across 9 of the interviews, and 4 belief statements were generated. The research team considered evidence from the systematic review. The review indicated that not being willing for one's sex life to depend on medication and believing that medication controls one's sex life were associated with increased rates of discontinuation. Therefore, the belief statement considered most relevant related to six men's (n quotes = 11) belief that taking medication for ED had a negative impact on their sense of self. This is demonstrated in the following example of the effect that ED treatment had on the participant's sense of masculinity:

'Oh yea... erm... yea of course it does... you know the fact that I have to rely on pharmaceuticals I have to rely on a physical pump... the idea of a physical pump and a ring just to maintain an erection is quite emasculating'.... (P-05)

This was not always the case, other men reported that they did not feel that ED treatment affected their self-identity:

'...it hasn't affected me thinking that... I'm less of a man because I have to take it, it's just it's my age and it's what the situation that I'm in that I've had to deal with you know...'

(P-10)

Optimism (TDF)

Seven of the interviews generated 19 quotes which were represented by 3 belief statements. There were belief statement which related to feeling optimistic about treatment improving their ED, reported by four men (n quotes = 13), was considered the most salient and is exemplified by the following quote:

'even when I could get an erection before, and nobody can last for ages and ages, but now I am going to be able to... I'm hoping... it will be even better than before!' (P-07)

Memory, attention and decision process (TDF)

There were 15 quotes which were evident across 9 of the interviews, generating 3 belief statements. The salient belief statement in this domain related to men finding the decision to use ED treatment as a difficult one (n participants = 6; n quotes = 7). For example:

'Erm... I guess it is difficult because... because I think that all of the downsides of taking it, so the cost, the premeditated nature and side effects, versus well I'd really like to have... an enjoyable sexual encounter with my wife today, this weekend, or whatever, it's that kind of... you're kind of... you're balancing the pros and the cons, so that makes it something that you're like well do I or do you not... so that's often I think why... you know... you've had half a bottle of wine and you're probably a little bit more relaxed... ah fuck it I'll... try it and see what happens type of thing' (P-03)

However, at the other end of the spectrum some participants did not find the decision difficult at all as exemplified in the following quote:

'it is simply a logical decision, like the decision to put on reading glasses when trying to read small print'... (P-04)

Beliefs about capabilities (TDF)

There were a total of 14 quotes across 8 interviews, all of which were characterised by one belief statement relating to a man's confidence in his ability to successfully use his treatment for ED.

In relation to PDE5Is, one participant said the following:

'I don't think it's really a confidence thing it's a level of enthusiasm to take it... but I'm... I'm confident that I can'.... (P-03)

In relation to other treatments such as VEDs some men expressed less confidence with regards to using it:

'Not yet no... certainly the Cialis was easy to take but it didn't really have erm.... Sort of you know... the desired effect... so I'm not confident with the pump as yet... at all... erm... because I am still in the training phase with that and the errr... the injection is relatively easy to do... I can do that... and it's not difficult... it's just an injection basically' (P-05)

Emotion (TDF)

A total of 13 quotes across 6 interviews related to this domain. In turn, 5 belief statements were generated, the majority of which were single quotes made by individual participants. As a result the only belief statement that was rated as relevant was; 'My ED medication makes me feel more confident' (n participants = 4, n quotes = 8). This is exemplified in the following quote:

'I think you feel better psychologically if you know you can perform in that way and it's a natural instinct you are attracted naturally to a woman... erm... and erm... if you are heterosexual... erm and... it's a natural thing to do so I think it is a really good psychological erm... boost erm... and I think that's important erm... so hopefully err... it will continue and... that's what I get out of it because you know obviously you want companionship as well but the key is... it's a romantic companionship as well, I think knowing that you can actually carry on normally is a very important motivator'... (P-09)

Skills (TDF)

A small number of participants and subsequently a low frequency of quotes related to skills and treatment utilisation. When this was coupled with a lack of evidence from the systematic review for this domain, it was decided that none of the belief statements were salient.

Reinforcement (TDF)

This domain only elicited a small number of belief statements and when considered in the light of no supporting evidence from the systematic review, the belief statements were considered less salient than those indicated by other TDF domains.

5.7.4 Relevant SRM Illness Representations

In addition to beliefs relating to the treatment of ED, the interviews suggested that perceptions and beliefs about the condition itself could influence treatment utilisation. Therefore, beliefs men held about their experience of suffering with ED were coded according to the cognitive representations of illness presented in the SRM (Leventhal et al, 1984) i.e.; identity, timeline, perceived control, consequence, cause and emotional representations (See 4.3.5 for a full description). A total of 113 quotes across all 6 illness representation of the SRM were identified

resulting in 24 specific belief statements. The SRM domains are presented in Table 20 and are ordered in relation to the frequency of quotes in each domain.

Table 20: SRM Illness Representations and relevant quotes

Domains & Salient belief statements	N° of Participants	N° of Quotes
Consequences (SRM)	8	36
<i>ED has led to a change in the shape or size of my penis</i>	1	5
<i>ED makes my partner feel frustrated</i>	3	4
<i>ED means I am unable to have penetrative sex</i>	2	3
<i>ED reduces my level of intimacy with my partner</i>	2	3
<i>I avoid sexual encounters because of my ED</i>	2	2
<i>I lack confidence because of my erectile dysfunction</i>	4	5
<i>I masturbate less as a result of my ED</i>	1	1
<i>My ED has had a negative effect on my relationship with my partner</i>	3	7
Cause (SRM)	7	34
<i>Aging has caused my ED</i>	5	8
<i>I do not know the cause of my ED</i>	3	3
<i>My ED is caused by alcohol consumption</i>	2	2
<i>My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)</i>	5	19
<i>My ED is caused by poor lifestyle choices (e.g. related to diet and exercise)</i>	2	3
<i>My ED is caused by psychological problems</i>	4	10
<i>My ED is caused by too much oestrogen and not enough testosterone</i>	3	3
Identity (SRM)	6	14
<i>As a result of my ED I find that my erections are less powerful</i>	3	3
<i>I am completely unable to achieve an erection</i>	2	3
<i>I don't experience morning or nocturnal erections</i>	2	4
<i>It takes longer for me to achieve an erection</i>	2	2
<i>My inability to urinate effectively relates to my ED</i>	1	2
Cure/Control (SRM)	1	3
<i>Being able to have an erection should be an automatic process</i>	1	3
Timeline (SRM)	4	13
<i>ED is a long term condition</i>	2	5
<i>I do not always experience ED, it is intermittent</i>	2	7
Emotion (SRM)	4	6
<i>Suffering with ED is stressful and traumatic</i>	4	6

Consequences (SRM)

SRM consequences embodied 30 quotes across 8 interviews generating 8 belief statements. All of the belief statements relating to this illness representation related to changes in men's intimate relationships as a consequence of ED, specifically consequences on sexual function and

men's sex lives including their respective partners. The first belief statement; 'ED makes my partner feel frustrated' (n participants = 3, n quotes = 4) was typified by the following quote:

'You've got a wife who loves you and then... she feels hurt by it as well... you know... she feels hurt by it as well, it doesn't just affect me it affects her as well... you know... she gets frustrated, she gets upset and she tries to hold it down but you know, sometimes it just gets the better of her and she gets really angry.... You know'... (P-06)

It was evident that the treatment as well as the condition itself affected men's partners:

'No the condition you know... I mean the treatment you know, for her she doesn't get upset about the fact that I'm taking treatment... right... but you know, just the fact the condition and the fact, but not always does it work brilliantly, that can cause frustration sometimes... a lot of the time it does... but I mean the thing is the Peyronie's is causing a problem in that it's very difficult for us to have intercourse because of the Peyronie's you know'... (P-06)

There were a number of quotes relating to not being able to have penetrative sex and its effects on one's intimate relationship (n participants = 2, quotes = 3):

'Yea, yea I mean I've been with my partner for 3 years... and we never have had full sex because of my... because of my problem' (P-06)

Similarly, the belief statement 'ED reduces my level of intimacy with my partner' (n participants = 2, n quotes = 3) was also important and was typified by the following quote:

'I mean mostly any sexual contact that I have with my wife it's.... it is sort of like mutual masturbation really, that's what it would be and, and, in one sense we... that's our intimacy and that's our level of intimacy err... and anything that I can do to assist above that is a bonus really'... (P-05)

Lacking confidence and avoiding sexual encounters were encapsulated in the following belief statements; 'I avoid sexual encounters because of my ED' (n participants = 2, n quotes = 2) an example of which is demonstrated in the following quote:

'Yes I think to be honest you hold back a lot because you are conscious that you are not able to... you know have normal sexual intercourse'... (P-09)

And a lack of confidence as; 'I lack confidence because of my erectile dysfunction' ED' (n participants = 4, n quotes = 5). The following quote demonstrates the notion that the condition can cause a sense of low confidence; however, this can be bolstered to some degree through the use of ED treatment:

'Yea, yea, it definitely does knock your confidence; definitely, I'd say it knocked mine... I would definitely say that... that's 100%... if you... feel like that and it's happened to you on more than one occasion then you're confidence is going to be low, confidence is going to be low... and I don't know... and... in a sense of taking the medication... maybe for that day or that night of taking it then you're confidence is high because you know you can

actively participate in sexual activity that you wanted to do... so it does knock your confidence if it is happening... it does knock your confidence' (P-02)

Cause (SRM)

In terms of frequency, the domain incorporated 48 quotes across 7 interviews, generating 7 belief statements. The most frequent statements related to the belief that ED was either physiological; a result of surgery, nerve damage, circulation issues (n participants = 5, n quotes = 19), psychological or a combination of both (n participants = 4, n quotes = 10).

'the drugs are addressing the physical aspects to having an erection but it's the... it's mentally getting into the right... area'... (P-10)

'Yea that was... that was... arriving out of the original one... well the original two as they were sort of back to back... and then subsequently jump forward a few years... erm... about 2014... so 2008 was the original; 2014 was the equina syndrome and I was taken into hospital, you know, catheterised erm... they didn't have to operate after about 5 days it all calmed down but at that point I thought I've got two issues... one is the urinary issue and the other one is the erectile dysfunction and erm... I'm basically losing... erm... quality function of urinating and anything else'... (P-05)

'so I guess sometimes... maybe with ED... it can be... psychological thing as well but at the same time... if you think there is a physical problem, physical and psychological can overlap.. So if you are worrying about... you can end up having ED and if there is a medical problem then there is a psychological problem because you feel that it's going to happen... you can't trust yourself when you get into a situation and performing'... (P-02)

Three men were unsure of what the cause of their ED was exemplified by the following:

'...what I would like to see, personally, is trying to get to the root cause err... you know is it.. is it a circulation issue? If it is what do we need to do? Or is it, I don't think it is a psychological issue, it might be because, the death of my wife, but it was happening before then when she was ill, but I think it's one of those things... I suspect' (P-09)

Identity (SRM)

There were 6 participants, from which 14 beliefs statements were generated, relating to men's experiences of ED symptoms and subsequent diagnosis of the condition. In relation to first experiencing symptoms it was indicated:

'Well the fact that I couldn't get a... a full erection' (P-01)

Some participants indicated circumstances that symptoms changed depending on the surrounding circumstances:

'I think I can still probably still get an erection but it is a lot weaker and less vigorous but errr... in my experience it is still capable of penetration, having said that if I had had a large meal and was very drunk... it didn't work and I am sure that that would be the same today...' (P-04)

Cure/control (SRM)

There were 3 quotes from 1 participant, generating only one belief statement and due to the absence of this belief across the other interviews it was decided that this belief was not salient.

Timeline (SRM)

There were 12 quotes across 4 interviews from which 2 distinct belief statements were generated, centred on ED being a long-term condition (n participants = 2, n quotes = 5) and the intermittent nature of its symptoms (n participants = 2, n quotes = 7). For example:

‘...kind of plodded on, it was intermittent, happens don’t happen, happens don’t happen, then it happened quite frequently again’... (P-02)

‘when you consider I sort of haven’t been able to get an erection for the last... well nearly 5 years... I’ve lost a marriage through it’... (P-05)

Emotion (SRM)

There were four participants and a total of 6 quotes, which resulted in 1 belief statement relating to the negative psychological consequences of suffering with ED. Participants reported that suffering with ED is traumatic:

‘when you are young you think you are invincible... and you can just carry on as I am and its gunna be... always be the same and when it suddenly starts failing on you I mean it is... it is traumatic...’ (P-06)

Summary

There were many belief statements that emerged from the qualitative interviews. The salient issues which emerged from both the TDF and the SRM which were indicated as having an influence on ED treatment utilisation included: side-effects, treatment ineffectiveness, the cost of treatment, the necessity of treatment for intimacy, feeling encouraged to use treatment by one’s partner and the negative impact of treatment on men’s sense of masculinity. The aim of this thesis is to lay the foundation for future behaviour interventions to support men with ED

treatment utilisation. The MRCs guidelines suggest that prior to intervention design it is important to carry out an exploratory study in order to gain a greater perspective and understanding of the potential theories as well as the surrounding issues which would influence an intervention of this nature (Campbell et al, 2007). Further, it is suggested that a mixture of qualitative and quantitative methods is necessary in order to understand aspects such as barriers to a given behaviour. Therefore, a series of studies are required to progressively refine intervention design prior to embarking on a full-scale evaluation (Craig et al, 2013). In line with MRC guidelines, the current study i.e. the qualitative interviews constitutes an explorative study. Subsequently, the thesis will build on the findings of this study by exploring them with a larger study sample and in a quantitative manor, therefore, utilising mixed methods research design, refining the findings at each stage. The following section, therefore, will describe how the findings of the qualitative interviews were used to design a questionnaire for use in a subsequent cross-sectional, quantitative study (Study 3).

5.7.5 Statement of Reflexivity

For generations, my family lived in London in the UK until my Grandparents moved out of King's Cross to a London suburb; Hayes, where they purchased their first home. I grew up in the London suburb of Watford, North West of London and therefore am influenced by suburban UK culture as well as city life i.e. the London culture of my extended family. As a result, my formative years involved being surrounded by individuals from a variety of different social as well as economic backgrounds. This has provided insight into how differently individuals can interpret health related phenomena which has been an advantage when considering the field of health psychology and interacting with individuals in the health care system.

Professionally, I am trained as a Research Scientist and have a background in psychology. I have worked as a Research Assistant at various London based Universities. An incident as a youth brought about a psychological trauma which has been integral in my pursuit of studying and working in positions related to both psychology and health care. I have previously worked for the NHS Increasing Access to Psychological Therapies (IAPT) service, as well as for the Samaritans, where I was responsible for supporting individuals experiencing difficult and traumatic life events.

The strengths I bring to this research, with particular reference to qualitative interviews, involves a personal philosophical outlook which focusses on creating a collaborative space within which it is possible to explore one's behaviour in a safe and non-judgmental capacity. This is derived from my personal background, work with the Samaritans and from my experience of working with individuals in health care settings. My limitations for this work involve having predominantly an academic understanding of the problems this patient group are faced with. My knowledge of ED predominantly comes from a research background, rather than a clinical one. Therefore, my view of the challenges men and their partners face with regards to ED and its treatment are from an inherently outsider's perspective. Additionally, I am a relatively young, white, married, heterosexual male and am a native English speaker. Therefore, I acknowledge the limitations that my background may bring. For example, I am aware that I will have a particular cultural lens through which I view ED and its treatment. In addition, practical difficulties also exist, such as the existence of potential language barriers when interacting with individuals where English is not their first language. However, prior to starting this PhD thesis, I worked across a variety of London based cardiac rehabilitation clinics, which involved speaking to a wide variety of patients from various social-cultural and economic backgrounds about their experience of ED. As a result, I have a good idea of some of the difficulties and challenges such

interviews entail. For example, the private nature of the subject at hand, the different ways ED can be interpreted depending on one's cultural background as well as the different interpretations partners may have in relation to both the condition and how ED and its treatment is perceived.

An important constraint to consider is the nature of the interview i.e. the fact that it is a one-off event, lasting approximately 1 hour. Participants are asked a variety of questions which can be considered of a private and sensitive nature. My background involves experience of communicating and building rapport with individuals under emotive circumstances, a good background knowledge of the subject area and prior experience of speaking with patients suffering with ED. However, the nature of the interview necessitates that rapport is developed between both parties in a short period of time and that the participant feels comfortable enough to divulge honest, unbiased answers to questions of a sensitive nature. Although I was well placed to achieve this and every effort was made to provide an environment which encouraged and facilitated a sense of trust, an important aspect of trust exists in the consistency of a relationship over time i.e. in order to 'build trust'. This is important to consider alongside the limitations I bring as an interviewer.

5.7.6 Questionnaire Development: Barriers and Enablers to Erectile Dysfunction Treatment Questionnaire (BEED-TQ)

To examine the potential influence of barriers and enablers to treatment utilisation identified by the qualitative interviews, a quantitative cross-sectional questionnaire study was proposed. The barriers and enablers to ED treatment questionnaire (BEED-TQ) was developed using a synthesis of the evidence from both Studies 1 and 2 as well as discussion between the author and supervisory team.

Data derived from study 1 and the current study (Study 2) were compared and the strength of the data contrasted by synthesising relevant data (Table 22) brings together the results of the qualitative analyses in study 2 and the systematic review in study 1. This allows visual inspection of the consistencies and inconsistencies between the two studies, categorised by domain and belief statement. In relation to the systematic review (Study 1), the number of studies as well as the strength of the evidence i.e. whether descriptive or inferential statistics were used to explore the relationship between a particular variable and treatment utilisation was considered. In relation to the qualitative interviews, the impact of a belief statement on ED treatment utilisation was considered, as well as the frequency and number of belief statements that were generated in relation to a particular TDF or SRM domain. Both these methods were used to decide what belief statements would be used as a basis to create items for the questionnaire. This process was carried out by two researchers (PW, HM). In the event that there was any disagreement with regards to the inclusion or exclusion of a given item or wording a third researcher (KM) was consulted until consensus was reached.

Based on this synthesis, the TDF domains *reinforcement* and *skills* were found to be related to a very small number of interviews and subsequent belief statements. This in conjunction with a lack of evidence from the systematic review resulted in a decision not to include these in the questionnaire. In relation to SRM, *personal control* and *identity* were also not included in questionnaire development. The domain personal control involved belief statements from one participant and there was no evidence from the systematic review to suggest the domain is one which could be considered salient. The domain identity included three belief statements, however, they were considered as overlapping with questions from the IIEF-5 measure of ED

severity (Table 21), which subsequently would be used in the quantitative study (Study 3). Therefore the domain was not included in questionnaire development.

Table 21: IIEF and IPQ Consequences

IIEF Questions	Belief Statements
How do you rate your confidence that you could get and keep an erection?	<i>'It takes longer for me to achieve an erection'</i>
When you had erections with sexual stimulation. How often were your erections hard enough for penetration?	<i>'Because of my ED I find that my erections are less powerful'</i>
During sexual intercourse. How often were you able to maintain your erection after you had penetrated (entered) your partner?	<i>'I am completely unable to achieve an erection'</i>
During sexual intercourse, how difficult is it to maintain your erection to completion of intercourse?	
When you attempted sexual intercourse, how often was it satisfactory for you?	

The final questionnaire, the BEED-TQ, consisted of 38 items (See Appendix 13) which covered a total of 12 TDF domains: *Behavioural Regulation* (questions n=1), *Beliefs about Capabilities* (questions n=1), *Beliefs about Consequences* (questions n=7), *Emotion* (questions n=1), *Environmental Context and Resources* (questions n=2), *Goals* (questions n=3), *Intention* (questions n=2), *Knowledge* (questions n=1), *Memory Attention and Decision Processes* (questions n=1), *Optimism* (questions n=1), *Social Influences* (questions n=4) and *Social/Professional Role and Identity* (questions n=1). The questionnaire also included 4 SRM illness representations: *Cause* (questions n=1), *Consequences* (questions n=6), *Emotion*

(questions n=1) and *Timeline* (questions n=2). Each item was scored on a Likert scale ranging from 1 to 5, where a score of 1 indicated 'strongly disagree' and a score of 5 indicated 'strongly agree'. The BEED-TQ was subsequently used in study 3; a quantitative cross-sectional exploration of the barriers and enablers to ED treatment utilisation which will be the focus of the following chapter (Chapter 6).

Table 22: Mapping of salient beliefs on to the TDF and SRM domains

TDF Illness Representations	Domains/SRM Representations	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
TDF	Behavioural	9	39			
	regulation					
I ensure I have access to my ED medication in case I need it		2	5	-	-	☒
I ensure that I take my ED medication as prescribed (e.g. on an empty stomach)		2	2	-	-	☒
I have a plan or pattern with regards to taking my ED medication		9	25	-	-	☒
I take my ED medication as part of my daily routine		2	8	-	-	☒
I take my ED medication before every sexual encounter		2	2	-	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
TDF Beliefs about capabilities		8	14			
I feel confident that I am able to take my ED medication		8	14	PDE5Is: Buvat (2013); Buvat (2014)	-	☒
TDF Beliefs about consequences		10	170			
A small daily dose of ED medication is more effective than a larger dose		1	1	-	-	☒
ED medication can cause pain due to not having used my penis for a long period		1	4	-	-	☒
I do not always need to take my ED medication to achieve an erection adequate for sexual		4	9	-	-	☒

TDF Illness Representations	Domains/SRM Representations	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
intercourse						
I experience medication side-effects (e.g. headaches, facial flushing, pain, Peyronie’s disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of taking my ED medication		9	47	PDE5Is: Buvat (2013); Buvat (2014); Carvalheira (2012); Carvalheira (2014); Cimen (2009); El-Galley (2001); Fagelman (2001); Incrocci (2003); Jiann (2006); Kim (2014); Klotz (2005); Lee (2010); Ljunggren (2008); McMurray (2007); Ricardi (2010); Roumeguere (2008) ICI: Armstrong (1994); Gerber (1991); Irwin (1994); Kunelius (1999); Perimenis (2001); Polito (2012); Raina (2003a); Sexton (1998); Sung (2014) US; Raina (2007) Raina (2005) PP; Sexton (1998)	ICI: Rowland (1999)	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
I use a pump to grow my penis to a normal size and use injection therapy to maintain my erection		1	1	-	-	☒
My ED medication does not live up to my expectations		1	1	-	-	☒
My ED treatment enables me to have a sexual relationship with my partner		9	26	-	PDE5I; Carvalho (2014)	☒
My ED medication improves my ability to get an erection		9	22	-	-	☒
My ED treatment is quick to work upon taking it		4	5	PDE5Is; Buvat (2013); Buvat (2014)	-	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included
						☐ No ☒ Yes
My ED treatment works every time I take it.		9	39	PDE5Is; Buvat (2013); Buvat (2014); Carvalheira (2012); Carvalheira (2014); Conaglen (2012); El-Galley (2001); Fagelman (2001); Green (1999); Incrocci (2003); Jiann (2006); Lee (2010); Ljunggren (2008); McMurray (2007); Montorsi (2004); Raina (2003b); Roumeguere (2008); Rubio-Aurioles (2013); Salonia (2008) ICI; Alvarez (1998); Armstrong (1994); Gerber (1991); Kunelius (1999); Perimenis (2001); Polito (2012); Raina (2003a); Rowland (1999); Sung (2014); Sexton (1998) US; Mulhall (2001); Raina (2005); Raina (2007)	PDE5Is; Buvat (2013) ICI; Rowland (1999)	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
PP: Sexton (1998)						
My partner becomes frustrated when my ED medication does not work		1	1	-	-	☒
My partner does not like using ED treatment for the intimate aspects of our relationship		1	1	PDE5Is: Buvat (2013); Buvat (2014); Carvalheira (2014); Roumeguere (2008) ICI: Kunelius (1999)	PDE5Is: Buvat (2013) ICI: Lehmann (1999)	☒
Taking ED medication makes my sex life less spontaneous		6	16	PDE5Is: Carvalheira (2012); Kim (2014); Son (2004). ICI: Sexton (1998); Sung (2014) US: Mulhall (2001)	-	☒
Taking medication for my ED is a necessity rather than a choice		5	8	-	-	☒
The effect of my ED medication (i.e.		5	13	PDE5Is: Buvat (2013)	PDE5Is: Buvat (2013)	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included
						☒ No ☒ Yes
duration of erection) does not last long enough						
TDF Emotion		6	13			
Having my sex life depend on ED medication is depressing.		1	2	PDE5Is: Buvat (2013); Buvat (2014); Kim et al (2014); Son et al (2004)	PDE5Is: Buvat (2013)	☒
I am anxious about whether my ED medication will be effective		1	1	-	-	☒
I feel embarrassed about having to use medication for ED		1	1	PDE5Is: Carvalheira (2012); Jiann (2006)	-	☒
My ED medication makes me feel more confident		4	8	PDE5Is: Carvalheira (2014); Roumeguere (2008)	ICI: Lehmann (1999)	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included
						☒ No ☒ Yes
My mood dictates whether I take my ED medication		1	1	-	-	☒
TDF Environmental context and resources		9	43			
A lack of privacy makes it difficult to take my ED medication		1	2	-	-	☒
I am able to obtain more ED tablets if I need them		2	6	-	-	☒
I can easily get hold of a prescription for ED medication		4	7	-	-	☒
I find it difficult to pay for my ED medication.		9	21	PDE5i; Buvat (2014); Carvalheira (2012); Carvalheira (2014); Cimen (2009); Conaglen (2012);	-	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
				Fagelman (2001); Green (1999); Incrocci (2003); Jiann (2006); Kim (2014); Klotz (2005); Lee (2010); Ljunggren (2008); Roumeguere (2008); Rubio-Aurioles (2013); Son (2004) ICI ; Sung (2014); Gerber (1991); Sexton (1998): 4 (4.6) US ; Mulhall (2001)		
I have sought alternative treatments for my ED outside of the NHS		2	5	-	-	☒
Work makes it difficult for me to take my ED medication		2	2	PDE5Is : Armstrong (1994)	-	☒
TDF Goal		10	59			
I aim to have a sex life that does not rely on		7	23	-	-	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
medication.						
I would like to maintain or regain an intimate sexual relationship with my partner		6	8	-	-	☒
My aim is to find a more natural/holistic solution to my ED		2	14	-	-	☒
My aim is to use my treatment for ED as a rehabilitative measure		2	5	-	-	☒
My partner and I are trying for a baby		1	1	-	-	☒
Taking my ED medication as prescribed is high on my list of priorities		9	10	-	-	☒
TDF Intention		9	42			
I would like to take my		7	19	PDE5Is: Carvalheira (2012)	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
medication in the future						
If I think sex is likely then I take my ED medication in preparation		7	20	-	-	☒
If I want to be sure that I will be able to perform I will take my ED medication		2	3	-	-	☒
TDF Knowledge		10	37			
I know how my treatment for ED works		1	3	-	-	☒
I know how to take my ED medication, as prescribed, in order for it to work		10	33	-	-	☒
I know the possible side effects of my ED		2	2	-	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
medication						
If I needed to change the way I take my ED treatment I would know how to go about doing this		1	1	-	-	☒
TDF Memory, attention and decision process		9	15			
Decisions about whether to take my ED medication are difficult to make		6	7	-	-	☒
I can't remember my ED medication dosage		1	3	-	-	☒
I never forget to take my ED medication		6	6	-	-	☒
TDF Optimism		7	19			
I am hopeful that new ED medication will		1	1	-	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
become available to me						
I am optimistic about being able to take my ED medication		4	6	-	-	☐
I am optimistic that my ED medication will make my ED better		4	13	-	-	☒
TDF Reinforcement		4	5			
Being able to have an enjoyable sex life encourages me to take my ED medication		2	3	-	-	☐
The more my ED medication works the more I want to use it		2	2	-	-	☐
TDF Skills		3	8			
I have learnt when and how to take my ED medication from		1	1	-	-	☐

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
experience (e.g. in relation to food and alcohol consumption)						
I have not been able to use my pump effectively		1	4	-	-	☐
The more I practise using my pump the easier it is to use		1	2	-	-	☐
TDF Social Influence		10	95			
I feel encouraged by my doctor/nurse to take my ED medication		9	18	-	-	☒
I feel encouraged by my partner to take my ED medication		10	44	-	-	☒
I feel that there is a taboo around ED medication		2	2	-	-	☐

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
I have informed my partner that I use ED medication		4	8	-	PDE5Is: Carvalheira (2012)	☒
I know other men who take medication for ED		5	7	-	-	☒
I know who to contact if I had any issues with my ED medication		4	4	-	-	☒
If I wanted to change my ED medication or alter my dose I would speak to a doctor or nurse first		2	2	-	-	☒
My doctor or nurse has provided me with adequate instructions about how to take my ED medication correctly		6	15	-	-	☒
TDF Social, professional		9	20			

TDF Illness Representations	Domains/SRM Representations	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
role and identity						
Having ED affects the way I feel about myself		3	3	-	-	☒
I am too young to be relying on treatment to achieve an erection		1	2	-	-	☒
Sexual intimacy is important to me		2	2	-	-	☒
Taking medication for ED has a negative impact on my masculinity		6	11	-	-	☒
SRM Personal control						
Being able to have an erection should be an automatic process		1	3	-	-	☒
SRM Cause						
Aging has caused my ED		7	34	-	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
I do not know the cause of my ED		3	3	-	-	☒
My ED is caused by alcohol consumption		2	2	-	-	☒
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)		5	19	-	-	☒
My ED is caused by poor lifestyle choices (e.g. related to diet and exercise)		2	3	-	-	☒
My ED is caused by psychological problems		4	10	-	-	☒
My ED is caused by too much oestrogen and not enough testosterone		3	3	-	-	☒

TDF Illness Representations	Domains/SRM	No. Participants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☐ No ☒ Yes
SRM Consequences		8	36			
ED has led to a change in the shape or size of my penis		1	5	-	-	☐
ED makes my partner feel frustrated		3	4	-	-	☒
ED means I am unable to have penetrative sex		2	3	-	-	☒
ED reduces my level of intimacy with my partner		2	3	-	-	☒
I avoid sexual encounters because of my ED		2	2	-	-	☒
I lack confidence because of my erectile dysfunction		4	5	-	-	☒
I masturbate less because of my ED		1	1	-	-	☐

TDF Illness Representations	Domains/SRM Representations	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
My ED has had a negative effect on my relationship with my partner		3	7	-	-	☒
SRM Emotion		4	6			
Suffering with ED is stressful and traumatic		4	6	-	-	☒
SRM Identity		6	14			
Because of my ED I find that my erections are less powerful		3	3	-	-	☒
I am completely unable to achieve an erection		2	3	-	-	☒
I don't experience morning or nocturnal erections		2	4	-	-	☒
It takes longer for me to achieve an erection		2	2	-	-	☒

TDF Illness Representations	Domains/SRM	No. Particip ants	No. Quotes	Systematic Review (Study 1) descriptive statistics	Systematic Review (Study 1) Inferential statistics	Included ☒ No ☒ Yes
My inability to urinate effectively relates to my ED		1	2	-	-	☒
SRM Timeline		4	13			
ED is a long-term condition		2	5	-	-	☒
I do not always experience ED, it is intermittent		2	7	-	-	☒

5.8 Discussion

The aim of this study was to identify barriers and enablers that men experience to utilising their ED treatment. Successful utilisation of ED treatment is associated with a number of psychological and social aspects of individuals lives such as improvements in quality of life, psychological status, social functioning, self-esteem, social and familial roles, perceived relationship quality and both satisfaction and perception of one's own sex life (Turner et al, 1992; Costa et al, 2013; McCabe et al, 2011; Rosen et al, 2004b; Shabsigh et al, 2001; Williams et al, 1998 and Fugl-Meyer et al, 1997). Therefore, the objectives of this study were to carry out in-depth exploration of barriers and enablers to ED treatment utilisation. Through the use of the TDF and the SRM it was possible to systematically identify the most relevant barriers and enablers to ED treatment utilisation. Finally, the findings of which were used to develop the BEED-TQ which will be used in Study 3 (Chapter 6) to explore barriers and enablers to ED treatment utilisation in a larger study sample using a quantitative cross-sectional study. The following sections will consider the findings based on the analysis using the TDF and SRM.

5.8.1 ED Treatment Effectiveness and Side-Effects

The most frequently reported factor men reported as influencing their ED treatment utilisation was the experience of treatment side-effects. The role of side-effects and its impact on utilisation has been well documented in the research literature (Hackett, 2005). This was evident in the systematic review (Chapter 3), which indicated a wide variation in the extent to which side-effects were considered to be the reason for discontinuation. In relation to PDE5Is, between 4 and 36% (median 16.6%) of men reported discontinuing for this reason. The systematic review also indicated that discontinuation was not only related to side-effects, however, it was also related to the fear of side-effects (Carvalho et al, 2014; Son et al, 2004; 251

Carvalho et al, 2012). Further, it was also indicated that where side-effects were reported, men were less likely to discontinue their treatment (Carvalho, 2012). The mechanism of how this led to less likelihood of discontinuing is not discussed. However, the evidence points towards both the clinical aspects of side-effects as well as the psychological aspects e.g. where fear of side-effects can also impact on utilisation.

Results of the current study therefore compliment previous research. We can consider the experience of side-effects as a crucial subject for health care practitioners, in which to explore with patients and to ensure that individuals are aware of the potential to experience side-effects when using ED treatment and what these could be. This would enable the possibility to, for example, switch medications or alter doses. This is of particular importance when we consider the research which is highlighted above and which indicates that when side-effects are reported, men are less likely to discontinue their ED treatment (Carvalho, 2012).

The second most frequently reported barrier to ED treatment utilisation related to experiencing ED treatment as being ineffective, in terms of whether the treatment was conducive to a sufficient erection or indeed a sufficient erection for the desired amount of time. The systematic review (chapter 3) found that men's experiences of treatment ineffectiveness were the most predominant clinical factor associated with discontinuation across all treatment modalities. Research indicated that when treatment was reported as being effective by men, increased treatment persistence was reported. This is of particular importance given that men prescribed PDE5Is report significantly higher rates of persistence when they have the opportunity to try dose titration (Giann et al, 2006) or doses greater than 50mg (Giann et al, 2006; Roumeguere et al, 2008). Therefore, for health care professionals, encouraging patients to monitor not only side-effects but the effectiveness of treatment and ensuring men are aware of the possibility of

dose titration in the event of side-effects or ineffectiveness could potentially help to ensure that treatment utilisation is successful.

5.8.2 Knowledge and Confidence in Relation to Treatment

In relation to the TDF domain *knowledge*, men talked about their knowledge of how to use their ED treatment in order for it to work. However, the extent to which men's knowledge and understanding of ED treatments compared to the official prescribing instructions is not known and was not assessed as part of this study.

Men were likely to use their treatment based on a variety of information sources including following advice from HCPs, reading medication instructions and from others with real world experience of ED treatments. In some cases, knowledge in this respect was potentially linked to the effectiveness of the treatment where some participants reported finding out retrospectively, for instance, that certain PDE5Is should be taken on an empty stomach or without alcohol. There was some indication from the interviews that a number of men perhaps did not know how to use their treatment, which could have had implications in regards to their experience of treatment effectiveness. Previous research has shown that dosing instructions can impact on whether or not to continue with ED medication (Hackett, 2005). For example, participants who were prescribed either Tadalafil with Sildenafil or Tadalafil dosing instructions; the majority (67%) preferred Tadalafil dosing instructions, which was reported as improving treatment continuation (von Keitz et al, 2004).

It was evident from the *social influence* domain that HCPs had an influence on the extent to which men felt encouraged to use their treatment, where most reported positive affirmations.

However, not feeling supported by ones HCP were reported as being a reason for not being able to use their VED which was due to receiving insufficient instruction from a HCP. This is important considering research into diabetes treatment which has indicated that medication self-efficacy (belief in one's ability to use medication without difficulty) has a positive influence on treatment utilisation (Huang et al, 2018). Surprisingly, the domain *skills* related to a very small number of belief statements. This was also the case with regards to the systematic review (Study 1), which did not indicate that skills influenced treatment utilisation. This perhaps relates to the vast majority of men being prescribed oral medication which potentially most patients find they are capable of using.

The dialogue between participant and HCP provides an important opportunity for HCPs to ensure that patients understand how to administer their ED treatment as well as offering the patient an opportunity to ask any questions they may have regarding this aspect of treatment. This could potentially eradicate any effects of not knowing how to correctly use treatment which has the potential to improve ED treatment utilisation.

5.8.3 The Cost of ED Treatment

The most salient belief statement to emerge from the domain *environmental context and resources* related to the cost of medication and being able to pay for it. This was also a salient finding of the systematic review (Study 1) in which cost was a reason for discontinuation for those prescribed PDE5Is, ICI and US. It is important to note that the systematic review included studies which involved participants from a wide variety of countries throughout the world. The participants involved in the current study were all recruited via the NHS and therefore all participants were reflecting on the procurement methods set out by one health care service.

The interviews took place prior to March 2018, when Viagra became available without prescription from pharmacies in the UK (MHRA, 2017). Participants were of differing ages and varied with regards to personal wealth. This equated to very different experiences with regards to paying for treatment. Some participants qualified for free prescriptions whilst others paid for treatment. It was important to note that participants who reported that the financial cost was high (in combination with other important factors such as perceived side-effects) did a type of cost-benefit analysis with regards to whether treatment would be used or not. One participant reported that due to the cost of treatment, combined with the side-effects, that this ultimately led the participant to discontinue treatment. This can be considered in relation to the Necessity-Concerns Framework (NCF; Horne et al, 1999) which has previously been described (see section 4.3.6). In essence, the NCF posits that when faced with using treatment people undertake a cost-benefit analysis where their beliefs about the necessity of their medication for improving or maintaining their health are weighed against their concerns about possible adverse effects (Horne & Weinman, 1999) and ultimately impacts their adherence behaviour. This was an important finding and one which was not evident in the findings of the systematic review (Study 1) making this a novel finding from the qualitative interviews.

5.8.4 Men's Perceptions of ED and its Treatment

The SRM illness representation *consequences*, indicated that men experienced difficulties with sexual penetration, the avoidance of sexual encounters and a reduction in levels of intimacy due to ED. In addition, there was a wide variety of perceptions around the cause of ED which related to both psychological and physiological factors. Further, men reported that ED treatment lead to a negative view of themselves and their sense of masculinity which was evident from the domain *social, professional role and identity*. All participants shared the view that they would rather not rely on medication for their sex life and some men reported a desire for alternative

natural and holistic approaches to treat ED, but at the same time acknowledging the importance of intimacy with their partner. The negative impact of ED treatment on men's sense of masculinity, was a unique finding which emerged from the qualitative interviews, a finding that was not evident in the results of the systematic review (Study 1).

5.8.5 Using ED Treatment within the Sexual Relationship

The most frequently reported belief statement with regards to the domain *behavioural regulation*, related to having a plan or pattern with regards to using treatment. A number of participants did not necessarily have a plan with regards to using ED treatment and instead judged circumstances spontaneously i.e. if there was the likelihood of sexual intimacy whilst others described the importance and necessity of having a plan about how and when they would use their treatment. This highlights the unique aspects of using treatment for ED, making it different from treatment for other conditions. The domain *Reinforcement*, defined as any behaviour that is considered a habit, routine, automatic or a direct experience or past behaviour (Atkins et al, 2017) did not result in any belief statements. This could relate to ED treatment utilisation generally relating to behaviour that involves two people and subsequently a complex interaction of environmental, social, behavioural and clinical factors. Therefore, it is possible that forming a habit in relation to treatment utilisation may be unlikely.

The majority of treatment is considered PRN and therefore it is only used when there is a demand for it. In addition, it is taken in the context of a man and his partner and therefore whether the utilisation of treatment involves planning or whether it is used spontaneously will relate to two people and their relationship. It was evident from the interviews that whether the participant had a plan or not, the decision to either use treatment or not was significantly influenced by men's partners. Men indicated experiencing a variety of both acceptance and

encouragement, or a lack thereof, by respective partners, reported as impacting on ED treatment utilisation. A frequently reported belief statement under the domain *social influence*, related to the potential influence men's partners may have with regards to ED treatment utilisation. In the systematic review (Chapter 3), research carried out by Carvalheira (2012) indicated that where one's partner is aware of and involved in the use of treatment (PDE5Is), men were significantly less likely to discontinue. The current study complements these findings as interviews revealed that the following factors may impact treatment utilisation: receiving encouragement to use treatment by one's partner; decision not to be sexually active since receiving treatment, and men not disclosing their ED treatment use to their partner. Disclosure has been explored in relation to men with prostate cancer. In a qualitative study it was indicated that most men avoided disclosure about their illness. This was related to placing importance on sustaining a normal life, men's low perceived need for support, fear of stigmatization and the need to minimize the threat of illness to aid coping, as well as the desire to avoid burdening others (Gray, 2000). To the authors' knowledge this has not been explored in relation to ED treatment, however, this further emphasises the unique nature of using treatment for ED compared to other treatments.

Althoff (2002a) suggested that a couple's physical and emotional readiness to resume sexual activity, the period of time in which the couple have not been sexually active prior to seeking treatment, the man's approach to resuming a sex life with his partner and the partner's physical and emotional readiness to resume lovemaking, are important influential components influencing treatment utilisation. This is important to the potential success of treating ED., ED can often lead to a cessation of sexual activity and subsequently the withdrawal of affection may further lead to diminished sexual desire for both the man and his partner (Dunn, 2004). Under such circumstances, even when treatment for ED results in rectifying successful erectile function, relationship issues can prevent a successful outcome (Althoff, 2002a). Therefore, it is

suggested that HCPs take into account the complexity of the couple's relationship when developing a treatment plan (Dunn, 2004).

5.8.6 *Strengths and Limitations*

Through the use of both the TDF and the SRM, the findings of this study provide insight into the factors which have the potential to influence ED treatment utilisation. Utilising these frameworks has not previously been carried out before making this study a unique contribution to the wider literature. MRC guidelines aim to ensure that an evidence-base exists for interventions of high quality and effectiveness (Campbell et al, 2000; Campbell et al, 2007). It is suggested that carrying out an exploratory study in order to gain a greater perspective and understanding of what would influence an intervention in the desired field, is important for its development (Campbell et al, 2007). Therefore, the current study involved a systematic in-depth exploration of the barriers and enablers men experience in relation to ED treatment utilisation. A mixture of qualitative and quantitative methods is considered necessary to understand what barriers exist in relation to a given behaviour (Craig et al, 2013). Therefore, study 3 will involve exploring the findings of the current study in relation to a larger study population, in a cross-sectional quantitative study (Chapter 6).

The outcome of this exploration was the creation of the BEED-TQ, developed in conjunction with experienced clinicians, psychologists as well as 'expert' patients. Data was analysed by two independent researchers, with a third researcher available to consult with regards to any discrepancies. However, interviews were carried out by one researcher, where a limitation of qualitative research relates to it being heavily dependent on the individual skills of the researcher and more easily influenced by the researcher's personal biases and idiosyncrasies.

Additionally, self-report methods rely on the participant to be truthful with regards to their

responses, but also to be accurate with regard to their recall of events (Paulhus, 2002). This is potentially an important issue when discussing participants' erectile function, treatment for erectile function and aspects of their sexual intimacy with their partner i.e. topics which can be considered very sensitive in nature. This is also influenced by the researcher's presence during data gathering, which is often unavoidable in qualitative research. The researcher was male, in his late 30's and had a good level of previous experience of qualitative interviews. However, this does present the possibility of response bias i.e. participants' being motivated to present themselves in a positive light. Therefore, there could be a discrepancy with respect to the extent to which the interview data reflects the true nature of the participants' ED and the circumstances that surround it. However, participants were aware that the interview was confidential and anonymous and that if they felt uncomfortable at any point then they could cease the interview. As a result response bias was minimised as much as possible.

There were some differences between the two researchers with respect to the coding of interview transcripts, with low interrater agreement specifically for the TDF domains *goals*, *intention* and *environmental context and resources* (36.6- 53.5%). According to Atkins (2012), reliability between two coders is acceptable if 60% agreement is achieved. However, for other domains interrater agreement was high. It is important to note that the number of interviews that were analysed were limited (n=10). Therefore, considering the novelty of the research it is possible that over a larger number of interviews and more discussion across the research team accuracy could have improved. As mentioned, the research relates to a small number of participants in a context specific environment i.e. drawn from just two urology clinics in the United Kingdom. However, through the sampling method employed, participant variety was maximised and data from the interviews carried out, were considered to reach saturation where no new themes over and above what has been presented in this chapter emerged.

The problem of interrater agreement mentioned above needs to be considered in conjunction with a potential limitation of the TDF. The TDF domains, although descriptions are provided for its use, they are not explicit with regards to what beliefs they encompass, therefore creating ambiguity in relation to how domains are operationalised. Phillips et al (2015) carried out a mixed methods exploration of professionals from multiple disciplines to explore their experiences of using the TDF. It is indicated that one of the issues of using the TDF relates to its operationalization, which is described as challenging. The authors report that there are considerable variations in the reported understanding of the framework and its domains, and recommend that more work is required with regards to the provision of accurate descriptions of the TDF domains and its constructs. The ambiguity in the operations definitions may relate to the low level of interrater agreement, mentioned previously, for example, it was evident from our synthesis and interpretation that overlap may exist between the TDF domains knowledge and beliefs about capabilities.

A strength of using the TDF is that analysis is not prematurely confined to a particular psychological theory (Michie et al, 2005). As a result, through the methodology employed, the identification of a wide range of beliefs and experiences that influence treatment utilisation in this population were reported. This was the first step to potentially developing a psychological intervention and was carried out in line with MRC guidelines for intervention development as mentioned above. The TDF aims to reduce theory variability by offering an integrated systematised approach (Ogden, 2012) which was been discussed previously in Chapter 4. Ogden (2012) suggests that although this aim is admirable, the approach may indeed be limited in its effectiveness given that, in practise, variability in patient behaviour denotes the need for tailored interventions and patient centeredness. It is advised that in order to use the TDF for

qualitative research, the first step is to select the target behaviour (Atkins et al, 2017), however, although the broad domains of the TDF were utilised to explore the target behaviour i.e. treatment utilisation, this was at the expense of the condition itself which necessitated the inclusion of the SRM illness representations. Therefore, this questions the suitability of the broad approach of the TDF with respect to the unique aspects of ED treatment utilisation.

It was not possible to determine the extent to which domains and belief statement were likely to be the most important drivers of behaviour. With regards to ascertaining the most influential factors relating to ED treatment utilisation, frequency and the ubiquitous nature of factors is an important rule of thumb as it helps to determine the salience of factors. However, it is much more difficult to assign the strength of meaning for individuals. For example, side effects are potentially easier to report to a researcher than questions about intimate sexual relationships. Therefore, side-effects may have been more widely reported and considered as a more important factor with regards to ED treatment and its utilisation. This necessitates the exploration of the findings using quantitative methodology (see Chapter 6).

5.8.7 Conclusion

The most prevalent barriers to treatment utilisation, were participants' experiences of treatment, side-effects, and treatment ineffectiveness. Other factors influencing decisions around the use of treatment included the cost of treatment, the ability to use treatment effectively as well as the importance of feeling encouraged to use treatment by one's partner. However, there were aspects of using treatment for ED that emerged from the qualitative interviews that were not indicated in the systematic review (Study 1), and therefore were unique to this study. This involved factors relating to the necessity of treatment as well as perceiving treatment as having a negative impact on a man's sense of masculinity.

Through the reporting of these factors, it is possible to see that the utilisation of ED treatment relies on both the man and his partner, i.e., both the man and his partner will influence the extent to which treatment is used. Therefore, treatment utilisation is unique to the characteristics of a couple's relationship. In addition, ED treatment utilisation is likely to be impacted by the intermittent nature of ED as well as the use of ED treatments as a rehabilitative measure. Therefore, using treatment for ED is not synonymous with sexual intimacy. These characteristics have important implications with regards to measuring treatment utilisation i.e., treatment may not be used for every sexual encounter, however conversely, treatment may be used in the absence of sexual intercourse. The findings from this study were used to design a questionnaire aimed at exploring ED treatment utilisation quantitatively, in a larger sample, in order to establish the relationship between beliefs and treatment utilisation. This will constitute the content of the following chapter (Chapter 6).

6 Study 3. Barriers and Enablers to Erectile Dysfunction Treatment Utilisation

6.1 Chapter Overview

Study 2 (Chapter 5) used an established theoretical approach and qualitative interviews to systematically identify the barriers and enablers to ED treatment utilisation. The findings from study 2 were used as a basis to build a questionnaire aimed at exploring factors that may influence ED treatment utilisation, to be used in the current study. Study 2 was broad in its approach making it possible to carry out an in-depth exploration of the barriers and enablers men experience when using treatment for ED. This study will involve using the questionnaire, along with other measures to ascertain the extent to which the barriers and enablers that emerged from Study 2 influence ED treatment utilisation across a study sample of n=116 participants.

6.2 Aims

To identify the factors most strongly associated with ED treatment utilisation, using a theoretically informed approach.

6.3 Research questions

The dependent variable(s) for this study are measures of treatment utilisation. Based on the results of the qualitative study (Chapter 5), the aim of study 3 is to ascertain the extent to which the following independent variables impact treatment utilisation;

- Demographic and treatment characteristics
- Beliefs about ED and/or its treatment
- Perceptions of ED and the treatment prescribed to treat the condition
- The influence of men's partners

6.4 Methodology

6.4.1 Study Design

A cross-sectional questionnaire study.

6.4.2 Participants

Inclusion criteria

Men meeting the following criteria were invited to take part in the study:

- Aged ≥ 18 years
- Diagnosed with ED by an HCP (for online participants this was self-reported)
- Prescribed either phosphodiesterase 5 inhibitors (PDE5I), Intracavernosal Injection (ICI), urethral suppositories (US), vacuum erection devices (VED) or have had a penile prosthesis (PP) and had used treatment for a minimum of 4 weeks.
- Able to read English

Exclusion criteria

Men who had participated in the qualitative study (Study 2).

Sample size

An adequate sample size for a hierarchical regression is considered to be $104 + k$, where 'k' is the number of independent variables (Green, 1991). An adequate sample size for logistic regression analysis is considered to be $100 + 50i$ where 'i' is number of independent variables (Bujang et al, 2018). The total number of independent variables included in this study was 76 (see section 6.7), therefore, the study aimed to recruit a total of 180 participants.

Patient and public involvement (PPI)

INVOLVE, the UK's national advisory group to support active public involvement in the National Health Service, defines PPI in research as; research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them (National Institute for Health Research [NIHR], 2021). The utility of PPI for this study aimed to enhance the research quality and relevance of the research, by actively involving men with ED in deciding important aspects of how the study should be carried out. The design and development of the current study involved consultation with three men receiving treatment for ED. These men provided first-hand experience and insight into living with and being treated for ED. The PPI group were presented with the research background in lay language and were provided with the opportunity to ask any questions about the proposed research. The group reviewed the questionnaire components and recruitment materials, including the consent form to ensure the language was clear and the appropriate information was included. Aspects of how the study should be carried out were also discussed with the group, such as questionnaire format (i.e., for both those completed in clinic as well as the on-line version of the questionnaire) as well as the questionnaire duration and how to deal with patients who may be under potential time pressures (i.e., providing the opportunity to complete the questionnaire at home and return it by post). Amendments were subsequently made based on the group's recommendations.

6.4.3 Ethics

Ethical approval was gained from the North East - Newcastle & North Tyneside 1 Research Ethics Committee (HRA; REF: 16/NE/0333) and approval was also gained from Research & Development (R&D) departments at each of the study sites.

6.4.4 Procedures

Recruitment was carried out across four sites. This included three NHS urology clinics; University College London Hospitals (UCLH), Luton and Dunstable University Hospital and Watford General

Hospital. The fourth site was an online platform called the Men's Health Forum (MHF), a UK based website dedicated to men's health.

For the three urology clinics; on the day of the patient's outpatients' appointment, a specialist nurse from one of the urology clinics identified eligible men from the clinic's list of patients. Eligible men were asked by their healthcare provider (doctor, urologist, or urology nurse) if they would be interested in taking part in the study. If men had used their treatment for less than 4 weeks and were willing to participate, they were asked to complete the questionnaire 4 weeks after starting their ED treatment. Information regarding the study was provided and an opportunity for potential participants to ask questions. If the patient wished to proceed, they were given a patient information sheet (PIS) and consent form to sign (Appendix 11 and Appendix 12), as well as the study questionnaire (Appendix 13) to complete. If for any reason participants were not able to complete the questionnaire on the day of their appointment, they were given the option of completing the questionnaire over the phone or at home. If this was the case, participants were provided with a questionnaire pack including a PIS consent form and a pre-paid return envelope.

With respect to the MHF, an invitation was posted on the MHF website (Appendix 14), which provided a link to an online version of the questionnaire; developed using Qualtrics^{xm} and made available via a hyperlink on-line at the MHF. Men who visited the MHF website who were interested in completing the questionnaire were first directed to an online version of the PIS and an inclusion criteria questionnaire. If they confirmed that they were eligible, men were then asked a further set of questions with respect to the consent form. If all responses were positive with respect to both eligibility and consent, then they were able to proceed to the questionnaire.

6.4.5 Measures

Primary outcome measure

The primary outcome in this study was level of treatment utilisation. Due to the nature of ED treatment, i.e., most treatments being prescribed 'on demand', a search for an existing measure of treatment utilisation suitable for this population was carried out. The search indicated that the most common measures of treatment utilisation were not suitable for use in a population where treatment is on-demand. This involved an extensive review of the literature including systematic reviews of self-report adherence measures (Garfield et al, 2011 & Nguyen et al, 2014). Due to the nature of ED treatment, utilisation was defined according to adherence, persistence, and discontinuation. The terms have previously been defined (see section 2.3.1), and are summarised below. A suitable measure of treatment adherence, for use in the target patient population, was considered as needing to include measures of treatment utilisation (adherence, persistence, and discontinuation). This was due to each taking into account different aspects of medication utilisation and also in order that any results were comparable to the wider literature, which have used such measures, i.e. the studies included in the systematic review (Study 1). Therefore, a suitable measure was considered as capable of measuring the following:

- Capable of capturing rates of ED utilisation i.e., measuring adherence i.e., “the extent to which a person’s behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider” (WHO, 2003).
- Capable of measuring persistence i.e., “the extent to which a patient continues to follow treatment advice without a break and without stopping” (Cramer, 2008)

- Capable of measuring discontinuation i.e.” the failure to enter a treatment programme, premature termination of therapy and incomplete implementation of instructions (including prescriptions)” (Blackwell, 1976 p.153)
- Capture what was prescribed, when it was prescribed and how much was prescribed

The process included reviewing a total of 57 measures (Appendix 15). Many of the measures were condition specific and therefore were not suitable. Other reasons for measures not being suitable included having a specific time frame within which utilisation was measured. For example, some measures captured treatment utilisation over the previous 24 hours. The current study aimed at measuring treatment utilisation over a 4-week period, to indicate the extent to which prescription treatment is used which is prescribed on a 4 week basis (Waltham Forest Clinical Commissioning Group, 2018), and therefore measures were excluded on this basis. In addition, measures were not suitable for use with ED treatment, given that they were designed specifically for use with treatments for other conditions such as HIV/AIDS.

Based on the criteria above, the most suitable measure of ED treatment utilisation, was the Persistence and Adherence Questionnaire (PAQ), originally designed for men prescribed PDE5Is (El-Meliegy et al, 2013). However, to the author’s knowledge the PAQ has not been validated. The PAQ, was considered as having content validity, as it was originally generated by experts in a relevant field (El-Meliegy et al, 2013) and published in peer reviewed journals. The PAQ was also considered by the research team as having face validity and was designed specifically for use with ED treatment, containing questions relating to what treatment had been prescribed, the dose of treatment prescribed, e.g. the number of tablets used in the last 4 weeks as well as questions relating to the number of sexual attempts in the last 4 weeks and whether the individual had a

desire to be sexually active. The PAQ is a 19-item measure, but for the purposes of this research items 1-7 and 9 were included from the PAQ (Table 23).

Table 23: PAQ questionnaire items

Questionnaire Items	
1.	Have you wanted to be sexually active since your [physician consultation/last interview]? Y/N
2.	How many sexual attempts have you had during the last 4 weeks? _____ Attempts
3.	Have you used your <i>initially prescribed</i> ED treatment in the past 4 weeks? Y/N
4.	If yes, how many tablets in total have you used during the last 4 weeks _____ Tablets
5.	Please state the dose you have used most frequently _____ mg
6.	When was the last time you used your initially prescribed ED medication? _____ Month/Year
7.	Have you used any other medications for erectile dysfunction since your [physician consultation/last interview]? Y/N
9.	Which of the following erectile dysfunction treatments did you use? _____ Tadalafil (Cialis® or Snafi®) _____ Vardenafil (Levitra®) _____ Sildenafil (Viagra® or Sildenafil generic brand) _____ Injection therapy _____ Other

Study 2 (Chapter 5) indicated that participants potentially did not use treatment for every sexual encounter, which could be due to the intermittent nature of the condition for some participants as well as some participants using treatment as a rehabilitative measure. Importantly, the PAQ includes a question relating to the number of sexual attempts in the last 4 weeks which was considered important considering findings from study 2 (Chapter 5). Therefore, using treatment is not necessarily synonymous with sexual activity which may have different drivers.

Adaptations were made to the original PAQ, including adapting the wording of question 4 to ask about the amount of ‘doses’ rather ‘tablets’ in order to include ICI and US, question 9 was extended to include ICI, US, VEDs and PP (Appendix 13). These 8 items were used to calculate the following dependent measures:

Demographic characteristics

Age, ethnicity, sexual orientation, occupation, relationship status and level of education (Appendix 13) were collected as part of the questionnaire.

Clinical characteristics

The severity of ED was assessed using the abridged version of the International Index of Erectile Function (IIEF-5) (Rosen et al, 1999). This is an easily administered, validated, self-report diagnostic tool (Rosen et al, 1999) containing 5 items. Each item of the IIEF-5 is scored on a 5-point Likert scale from 1 to 5. A total score is calculated, which can be categorised into five grades of severity: no ED (IIEF-5 total score, 22 – 25), mild ED (17 – 21), mild to moderate (12 – 16), moderate (8 – 11), and severe ED (5 – 7) (Rosen et al, 2002).

Other self-reported clinical data such as ED duration and previous ED treatments were all collected using categorical responses. In relation to comorbidities a list was developed to include common comorbidities along with a free text response option.

Psychosocial measures

The Hospital Anxiety and Depression Scale (HADS)

Results from the qualitative study (Study 2) indicated that suffering with ED and the necessity to utilise treatment were associated with negative psychological outcomes for some participants. Comorbid anxiety disorders and depression, are commonly seen in men with sexual disorders such as ED (Mourikis et al, 2015). Research also indicates that depressed patients are three times more likely not to comply with their treatment than those not depressed (DiMatteo et al, 2000), it was therefore essential that anxiety and depression were captured in the current study. The Hospital Anxiety and Depression Scale (HADS; See Appendix 13), is considered a validated measure of psychological distress and research has confirmed its two-factor structure and internal

consistency (Djukanovic et al, 2017). The HADS is a 14-item questionnaire with two 7-item subscales, each question scoring 0-3, aimed at determining levels of both anxiety and depression (Zigmond & Snaith, 1983). A score of 7 or less represents non-cases, 8–10 possible clinical cases, and 11 or more probable clinical cases of either depression or anxiety (Zigmond & Snaith, 1983).

The Brief illness perception questionnaire (IPQ)

The Illness Perception Questionnaire (IPQ) was developed to measure SRM illness representations (Weinman et al, 1996). The IPQ (Appendix 13) was used in conjunction with questions which emerged from the qualitative interviews (Study 2) which were considered aspects of the SRM domains (see section 4.3.5), and incorporated into the BEED-TQ. This enabled ED specific illness representations to be included. For example, in relation to the illness representation *timeline* the BEED-TQ has a specific question about the intermittent nature of ED and under the SRM illness representation *consequences*, men are asked about the negative impact of ED on men's relationships with their partner for example. Therefore, this enabled both specific ED and broader IPQ questions to be included.

The Brief IPQ (Broadbent et al, 2006), which is a revised version of the Illness Perception Questionnaire–Revised (IPQ-R) (Moss-Morris et al, 2002) is quick to administer and less taxing for elderly participants as well as being more acceptable for those with limited reading and writing ability. It has good test–retest reliability, and there are moderate to good associations between the Brief IPQ and the IPQ-R on all equivalent dimensions (Broadbent et al, 2006). The measure has nine items overall, 8 are scored on a Likert scale which ranges from 0 – 10, where higher scores indicate stronger perceptions along that dimension (Broadbent et al, 2015). Five of the items assess cognitive illness representations: consequences (Item 1), timeline (Item 2), personal control (Item 3), treatment control (Item 4), and identity (Item 5). Two of the items assess

emotional representations: concern (Item 6), and emotions (Item 8). One item assesses illness comprehensibility (Item 7), (See section 4.3.5). The ninth item has a free text response, asking the respondent to indicate the 3 most prominent beliefs relating to the cause of their illness. Each item is scored individually, with higher scores reflecting a more threatening view of illness (Cordingley et al, 2014). The Brief IPQ has not previously been used in relation to ED, therefore, wording of the items were adjusted to refer to the condition and its treatment as recommended by the questionnaire developers (Appendix 13).

The Beliefs about Medicines Questionnaire (BMQ)

Data derived from study 2, indicated that men's beliefs about their ED treatment were important considerations with regards to treatment utilisation. The BMQ (Horne et al, 1999; Appendix 13), was developed for the purpose of investigating the role of medication beliefs in medication adherence and has been described as a useful tool across chronic conditions, where long-term medication is needed and also has high reliability (Tsianou et al, 2017) and validity (Horne, 1999). It is comprised of two components, (i) *specific*; which consists of two factors assessing beliefs about the necessity and concerns in relation to a prescribed medication, and (ii) *general*; which consists of two factors; the general-overuse subscale, which addresses views about the way in which medicines are used by doctors, and the general-harm scale, which assesses beliefs about the degree to which an individual perceives their medicine as harmful.

The current research used the BMQ specific subscales only questionnaire (See Appendix 13), as this study was interested in beliefs specific to ED treatment. The BMQ specific domain contains a total of 10 items; participants indicate their degree of agreement with each individual statement on a 5-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. A higher score on the specific section of the questionnaire indicates stronger beliefs in the concepts of the scale.

For example, a high score on the necessity subscale suggests an individual has strong beliefs in the necessity of their medicine, and a high score on the concerns subscale, suggests the individual has strong concerns about the negative effects of taking medicines (Horne, 1999; Horne et al, 1999).

Self-Esteem and Relationship (SEAR)

Based on study 2, the quality of one's sexual relationship emerged as important with regards to its impact on ED treatment utilisation. The Self-Esteem and Relationship questionnaire (SEAR; See Appendix 13) (Cappelleri et al, 2004), was therefore selected for inclusion in this study. The 14-item SEAR questionnaire possesses strong psychometric properties that support its validity and reliability for measuring two domains; sexual relationship and confidence, where the confidence domain has two sub-scales; self-esteem and overall relationship (Cappelleri et al, 2004). All items are scored on a 5-point Likert scale which ranges from; 1 almost always/always; to 5 almost never/never. A score is calculated for each domain and sub-domain as well as a total overall score. Each domain score, subscale score, and overall score are transformed onto a 0–100 scale. Higher scores indicate a more favourable response e.g., a higher score on the subscale self-esteem relates to a higher self-reported level of self-esteem (Althof et al, 2003).

The Brief COPE

Research has shown that illness identity can affect the way in which patients cope with a given condition (Hagger & Orbell, 2003), which in turn has the potential to influence treatment utilisation. Leventhal et al, (1984) proposed that these perceptions guide how a person manages their illness, as well as their strategy for coping. An individual's coping style was therefore measured using the Brief COPE (Carver, 1997; See Appendix 13). The scale is a validated, multidimensional questionnaire focussed on individuals' coping styles. The Brief COPE is a short-form version of the COPE, with a total of 28 items; 2 items for each of the 14 conceptually different subscales aimed at ascertaining both adaptive and maladaptive coping strategies. Each

item is assessed on a Likert scale ranging from 0 (I have not been doing this at all) to 3 (I have been doing this a lot). Higher scores indicate more frequent use of a particular coping strategy (Table 24).

Table 24: Brief COPE domain descriptions

Domain	Description
Acceptance	Accepting the reality that has happened/learning to live with it.
Emotional support	Obtaining emotional support/comfort and understanding.
Humour	Making jokes about it/ making fun of the situation.
Positive reframing	Trying to see the situation from a different light, make it seem more positive/look for something good in it.
Religion	Finding comfort in religious or spiritual beliefs/praying or meditating.
Active coping	Concentrating the efforts on doing something about the situation/taking action to try to make it better.
Instrumental support is	Getting help and advice from other people/trying to get advice or help from others about what to do.
Planning	Trying to come up with a strategy about what to do/thinking hard about what steps to take.
Behavioural disengagement	Giving up trying to deal with it/the attempt to cope.
Denial	Saying to myself, "this is not real"/refusing to believe that it has happened.
Self-distraction	Turning to work or other activities to take my mind off things/doing something to think about it less.
Self-blaming	Criticizing myself/blaming myself for things that happened.
Substance use	Using alcohol or other drugs to feel better/to help me get through it.
Venting	Saying things to let unpleasant feelings escape/expressing negative feelings.

The 14 domains of the Brief COPE have been grouped in different ways (Carver (1997; Cooper et al, 2008; Snell et al 2011; Wang et al, 2016). A principal components analysis (PCA) was therefore carried out on the data from the current study to inform the structure used in the analysis (Appendix 16). The PCA found support for a 3-factor solution (Table 25), which explained 40.98%

of the variance. There was significant overlap between the 3-factor solution found in this study to that proposed by Wang et al (2016), Cooper et al (2008) and Snell et al (2011).

Table 25: Brief COPE, 3-factor solution

Factors	Included domains
Self-sufficient coping	Active Coping / Planning / Positive reframing / Acceptance/Humour. The scale had good internal reliability with a Cronbach alpha of .703. Overall scores ranging from 10 – 40).
Socially supported coping	Accessing emotional support; Religion/Accessing instrumental support/Venting. The Brief COPE scale socially supported coping has good internal reliability with a Cronbach alpha of .712. Overall scores ranging from 8 – 32).
Avoidant coping	Denial/Behavioural disengagement/Self-blame/Distraction/Substance use. The Brief COPE scale avoidant coping had good internal reliability with a Cronbach alpha of .780. Overall scores ranging from 10 – 40.

Barriers and Enablers to Erectile Dysfunction Treatment utilisation Questionnaire (BEED-TQ)

The barriers and enablers to erectile dysfunction treatment questionnaire (BEED-TQ) was developed in Study 2 as described in Chapter 5. The questionnaire consisted of 38 items, each scored on a Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) (Appendix 13). A number of questions were framed negatively i.e., ‘using treatment for ED has a negative impact

on my masculinity' as a result the following items were reverse scored: 8, 9, 12, 20, 26, 28, 29-35, therefore a high score on the Likert scale would reflect a positive response and therefore would fit in line with other BEED-TQ items. Table 26 shows the TDF and SRM domains included in the BEED-TQ, the number of items as well as the final questionnaire items. The items were scored individually, so that it was possible to understand how specific beliefs impacted on adherence. Therefore, items were treated individually rather than by domains.

Table 26: TDF and SRM domains and relevant Items Included in the BEED-TQ

TDF Domains	No of items	Questionnaire Items
Behavioural regulation	1	I have a plan or pattern with regards to using my ED treatment
Beliefs about capabilities	1	I feel confident that I am able to use my ED treatment
Beliefs about consequences	7	I experience treatment side-effects (e.g. headaches, facial flushing, pain, Peyronie's disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of my ED treatment My ED treatment enables me to have a sexual relationship with my partner My ED treatment improves my ability to get an erection My ED treatment is quick to work upon using it My ED treatment works effectively every time I take it Taking ED treatment makes my sex life less spontaneous The effect of my ED treatment (i.e. duration of erection) does not last long enough
Emotion	1	My ED treatment makes me feel more confident
Environmental context and resources	2	I find it difficult to pay for my ED treatment I have sought alternative treatments for my ED outside of the NHS

TDF Domains	No of items	Questionnaire Items
Goal	4	I aim to have a sex life that does not rely on treatment My aim is to find a more natural/holistic solution to my ED My aim is to use my treatment for ED as a rehabilitative measure Taking my ED treatment as prescribed is high on my list of priorities
Intention	2	I intend to take my treatment in the future If I think sex is likely then I will use my ED treatment
Knowledge	1	I know how to use my ED treatment, as prescribed, in order for it to work effectively
Memory, attention and decision processes	1	Decisions about whether to use my ED treatment are difficult to make
Optimism	1	I am optimistic that my ED treatment will make my ED better
Social Influence	4	I feel encouraged by my doctor/nurse to use my ED treatment I feel encouraged by my partner to use my ED treatment I have informed my partner that I use ED treatment My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly
Social professional role and identity	1	Using treatment for ED has a negative impact on my masculinity
SRM Domains		
Cause	3	I know the cause of my ED My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues) My ED is caused by psychological problems
Consequence	6	ED makes my partner feel frustrated

TDF Domains	No of items	Questionnaire Items
		ED means I am unable to have penetrative sex
		ED reduces my level of intimacy with my partner
		I avoid sexual encounters because of my ED
		I lack confidence because of my ED
		My ED has had a negative effect on my relationship with my partner
Emotion	1	Suffering from ED is stressful and traumatic
Timeline	2	ED is a long-term condition
		I do not always experience ED, it is intermittent

6.4.6 Analysis

Statistical analysis was carried out using IBM SPSS statistics version 25. Data derived from the online questionnaire was downloaded to MS Excel and then imported into SPSS. Four main stages of data checking were carried out to ensure the information contained within the database was correctly prepared for analysis.

Data Integrity and Item Scoring

The accuracy of the entered data was checked twice by the author by comparing raw questionnaire scores with inputted SPSS data. In addition, 10% of the data were checked for accuracy by an independent assessor. The SPSS function 'recode' was used to reverse score relevant items. Recoded variables were then manually checked to ensure that scores were reversed to the figures intended. Prior to calculating mean scores, items data ranges were checked to ensure that they fell within the expected limits. After calculating scale scores in SPSS, a test sample of ten participants were calculated manually and checked against the SPSS database. In addition, a member of the research team manually calculated each scale score for ten different participants.

Missing Data

An analysis of missing data at item level was carried out and indicated that a total of 3.7% of data was absent. There were no participants who had more than 50% missing data. Appendix 17 provides details of missing data levels for each variable. The variable with the most missing data (n=19, 15.6%) asked participants when they last used their ED treatment.

Prior to dealing with missing data and therefore prior to being able to subject the data to any statistical tests, it was essential to establish whether the data was missing in a random or non-random fashion. To ascertain whether any data was Missing Completely At Random (MCAR) (Scheffer, 2002), Little's MCAR test was carried out (Little, 1988). The analysis was carried out at item level resulting in a non-significant result ($p=0.54$) and at scale level, which was also non-significant ($p=1.00$), therefore data was considered MCAR. These indicate that the missing values in the current data set do not relate to any other data collected.

Imputation

As the data were MCAR they were therefore suitable for multiple imputation (MI). The MI procedure replaces missing values with plausible estimates based on the data characteristics. This is achieved by using other variables in the data set to predict the missing value. To handle the missing data in the dataset imputation was carried out at the item level. The number of imputations is dependent upon the amount of missing data (White et al, 2011). Bodner (2008) recommends having as many imputations as the percentage of missing data. For example, when 10% of the cases are missing, 10 imputed datasets must be generated. The overall missing data was calculated as 3.7%, using SPSS version 25, the closest number of data imputations available was five.

Outliers and Normality

Data were screened for outliers and assessed for normality. Distributions of responses were examined using histograms and by performing the Shapiro-Wilk test ($p \leq 0.01$) (Appendix 18). According to tests of normal data distribution and accompanying histograms, the continuous dependent variables i.e., adherence (the percent of medication used in the last 4 weeks) and persistence (the number of days since last using treatment for ED) as well as the number of sexual attempts in the last 4 weeks were positively skewed. Similarly, all the continuous dependent variables produced a significant result according to the Shapiro-Wilk test ($p < .05$), meaning that the data was not normally distributed, which was highlighted by the Q-Q plots where the data plot for each variable strayed from the Q-Q normal-plot line (Appendix 18).

For each dependent variable, outliers were defined as exceeding an inter-quartile range (IQR) of 3. Research indicates that using an IQR of 1.5 to identify outliers is inaccurate where approximately 50% of the time data is identified as an outlier when it is not (Hoaglin & Iglewicz, 1987). The IQR for persistence was >3 and therefore this variable was winsorized. This involved replacing any outlier values with the nearest values of an observation not considered an outlier (Dixon, 1980).

Prior to conducting linear regressions correlations were carried out for all relevant variables and assessed for homoscedasticity using scatterplots and multicollinearity which indicated that variables were not correlated to a sufficient magnitude to adversely affect regression estimates. In relation to the dependent variable persistence, the use of winsorizing, in this instance, improved all the parameters of normality (Appendix 19).

Univariate analyses

A series of analyses were carried out to investigate the associations between the dependent and independent variables (Appendix 20). The dependent and independent variables varied with regards to their nature. For example, where dependent variables were binary (i.e., discontinued/did not discontinue treatment) and the independent variables were continuous; T-tests were used to see if there were significant differences between the variable means. Where both dependent and independent variables were binary in nature; chi-squared cross-tabulations were used to explore associations. Finally, where both independent and dependent variables were continuous in nature; bivariate correlations were used to explore associations. Due to continuous dependent variables being non-normal in terms of data distribution; Spearman's correlations were used.

Multivariate Analyses

Multiple linear regressions (Appendix 21) using the enter method were carried out to examine which of the independent variables explained most variance in continuous outcomes (adherence and persistence). To enter all of the 76 independent variables into the regressions would have required a sample size of 180. Based on the rule of thumb (described in the 'Sample size' section), the study recruited a total of 116 participants, therefore it was possible to enter a maximum number of 11 variables ($104 + 11 = 116$) into a regression (Green, 1991). The measure of discontinuation (i.e. have you used your ED treatment in the last 4 weeks?) is a binary dependent variable, therefore, a logistic regression was carried out (Appendix 22). The sample size for this was carried out using the rule of thumb for logistic regression analysis (See section 6.4.2). The sample size for logistic regression is calculated as follows; $100 + 50i$ where 'i' is number of independent variables (Bujang et al, 2018). The study recruited a total of 116 participants; therefore, it was possible to enter a maximum number of 16 variables ($100 + 16 = 116$) into the logistic regression. It has been indicated that for inclusion in regressions models, setting the p value to 0.05 is

recommended; however, it may subsequently fail to identify variables which are potentially important (Hosmer et al, 2013). Therefore, to reduce the number of independent variables entered, an entry criterion of $p \leq 0.1$ in the univariate analysis was used (Hosmer et al, 2013).

6.4.7 Recruitment

Recruitment was carried out across 4 sites over a period of 22 months, between September 2017 and July 2019. A total of 565 clinic patients were screened for eligibility in the NHS urology clinics, of which 373 (66%) were not eligible to take part in the study. Reasons for ineligibility included attending clinic for an issue not related to ED, e.g., for fertility problems (40%), not currently or previously used ED treatment (6%), had Peyronies disease and were not able to use treatment for ED (7%), were female (10%) or could not speak English (3%). It was not possible to record the number of individuals who saw the advert on the MHF and decided not to take part, or who met the eligibility criteria, but 34 met the inclusion criteria and completed the questionnaire. A total of 116 men took part in the study (Figure 13).

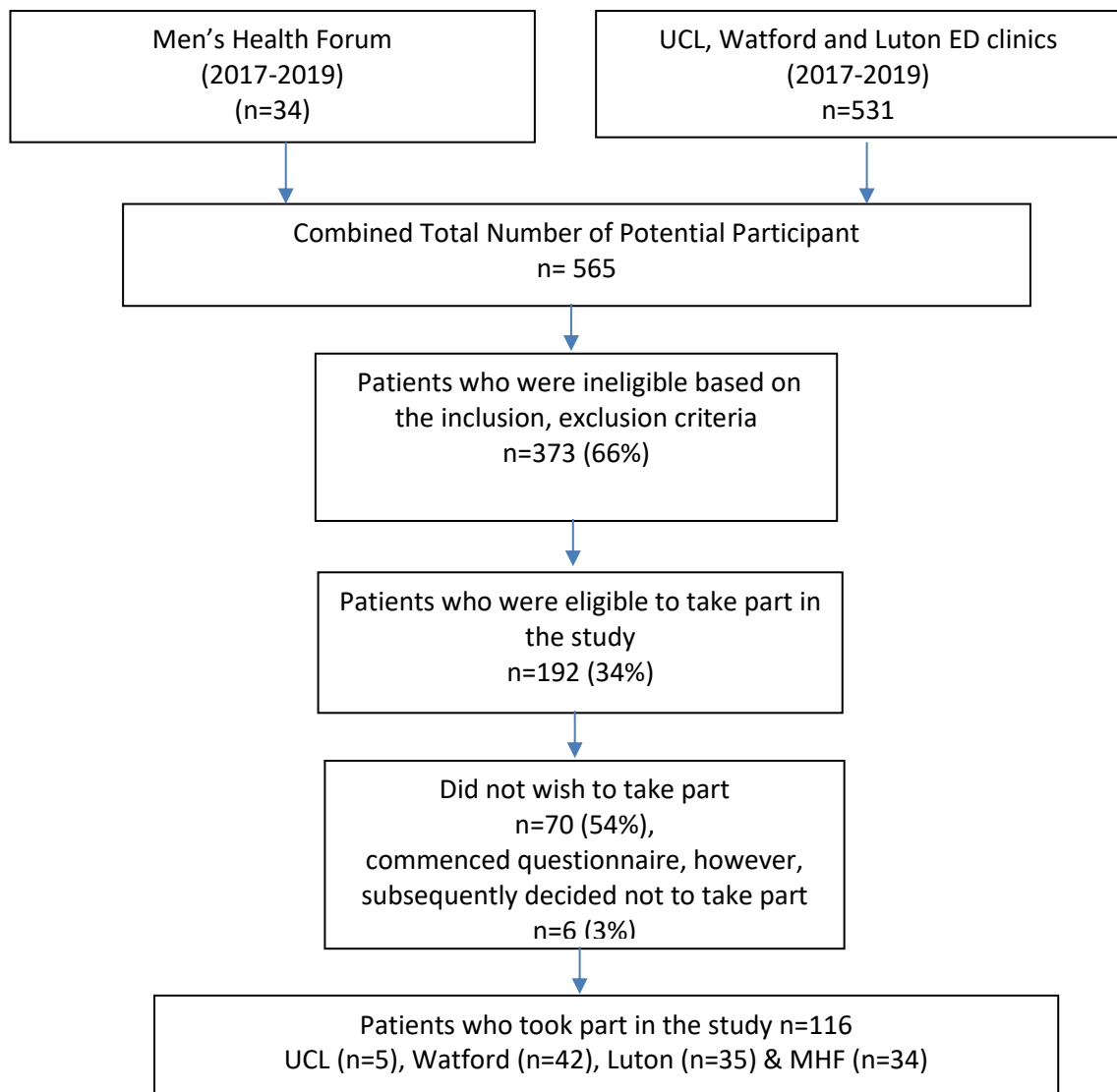


Figure 13: Recruitment flowchart

6.5 Results

6.5.1 Participants

Demographic data

Of the 166 men, a majority were between 55–64 years of age (35.3%), most were Caucasian (77.6%), heterosexual (84.5%), employed (52.6%), married or in a relationship (77.6%) and had GCSE or O-level qualifications (25.9%) (Table 27).

Table 27: Participant's demographics

	n	%
Participant Age		
18 - 24	6	5.2
25 - 34	4	3.4
35 - 44	5	4.3
45 - 54	16	13.8
55 - 64	41	35.3
65 - 74	30	25.9
75 - 84	10	8.6
Ethnic Background		
White British	79	68.1
Black or Black British	12	10.3
Asian or Asian British	9	7.8
Other White British	4	3.4
White USA	4	3.4
New Zealand	3	2.6
White European	3	2.6
Other	2	1.7
Sexual Orientation		
Heterosexual	98	84.5
Homosexual	8	6.9
Bisexual	6	5.2
Prefer not to answer	2	1.7
Occupation		
Employed full-time	49	42.2
Retired	41	35.3
Employed part-time	9	7.8
Unemployed	8	6.9
Other	5	4.3
Self-employed	3	2.6
Relationship Status		
Married	64	55.2
Living with partner	21	18.1
Single	14	12.1
In a relationship	5	4.3
Divorced	4	3.4
Widower	3	2.6
Other	1	0.9
Level of Education		
GCSE/O Level	30	25.9
No Qualifications	18	15.5
Graduate	18	15.5
Post graduate	16	13.8
Other	13	11.2
A-Level	12	10.3
City and Guilds	4	3.4

	n	%
Under graduate	2	1.7

6.5.2 Comorbidities

71.6% of participants (n=83) living reported at least one comorbidity, of which hypertension was the most common (42.2%), followed by high cholesterol (31.9%) and Type 1 or 2 diabetes (28.4%) (Table 28). Nineteen (16.4%) participants had undergone prostatectomy.

Table 28: Participant Comorbidities

Comorbidity	n	%
High blood pressure/Hypertension	49	42.2
High cholesterol	37	31.9
Diabetes	33	28.4
Prostatectomy	19	16.4
Heart failure	6	5.2
Arterial fibrillation	3	2.6
Transient ischemic attack	2	1.7
Chronic obstructive pulmonary Disease	2	1.7
Other	20	17.2
Number of comorbidities:		
0	33	28.4
1	39	33.6
2	22	19.0
3	19	16.4

6.5.3 Clinical Characteristics

Erectile Dysfunction

Symptom duration

ED duration ranged from 0–30 years (Table 29), where the average (Median) duration was 60 months (IQR: 24–160).

ED severity

Most men had moderate ED (41 participants; 35.3%) according to the IIEF-5 (Rosen et al, 1999) (Table 29), supported by a median ED severity of 9 (IQR: 6-14.75). No ED symptoms were reported by 3.4% of men, potentially indicative of effective ED treatment.

Table 29: ED Clinical Data

	n	%
Duration		
0 – 6 months	5	4.3
6 – 12 months	11	9.5
1 – 2 Years	17	14.7
2 – 3 Years	14	26.7
3 – 5 Years	19	16.4
5 – 10 Years	28	24.1
10+ Years	15	12.9
ED severity		

	n	%
Severe (5 – 7)	34	29.3
Moderate (8 – 11)	41	35.3
Mild- moderate (12 – 16)	26	22.4
Mild (17 – 21)	11	9.5
No ED (22 – 25)	4	3.4

Treatment for ED

Current Treatment

At the time of completing the questionnaire, the most common ED treatment being used was PDE5Is (97.4%). Sildenafil was the most commonly used PDE5I (62.1%). All participants in the study were prescribed PRN treatment, as opposed to OaD treatments. There were no participants included in the study who had undergone PP (

Table 30).

Previous Treatment

Participants were asked about what, if any, previous ED treatments they had used other than their current prescribed treatment, 23.8% had previously used PDEI5s, 9.8% VEDs and 2.4% ICI treatment (

Table 30).

Table 30: ED treatment

ED Treatment	n	%	Dose Prescribed (no. of prescribed tablets/pellets for a 4-week period)		
Current ED Treatment			Median	IQR	Range
Sildenafil	72	62.1	8	1	2 - 28
Tadalafil	36	31.0	8	1	2 - 48
Vardenafil	5	4.3	6	0	4 - 7
ICI	13	11.2	4	0	4 - 8
US	2	1.7	4	0	4
VED	11	9.5	N/A	N/A	N/A
Overall No of treatments used over the last 4 weeks			8	8.9	2 - 48
Previously tried ED treatments					
Previously used PDE5Is	29	23.8			
Previously used ICI	3	2.4			
Previously used VED	12	9.8			

6.6 Treatment utilisation and sexual attempts

Men reported utilisation rates for their predominant treatment. A total of 41 (35.3%) men had discontinued treatment (Table 31) and this percentage was similar across treatments. The mean (SD) rate of adherence (i.e., the percentage of prescribed medication used in the last 4 weeks) across the study sample was 41.8% (52.1). Only two participants were using US, where it was reported that 125% of treatment had been used. This is due to using more medication than prescribed for a 4-week period. In relation to persistence, the median (IQR) amount of time since using their last treatment for ED was 24.5 days (83.9). Since their last appointment with their HCP, the majority of men had wanted to be sexually active and the median number of sexual attempts in the last 4 weeks was 3.6 (SD 5.0). Over a quarter (27.6%) of participants had not had any sexual attempts over the same period (Table 32).

Table 31: PAQ Questionnaire items and Rates of treatment utilisation

			Total	PDE5Is (n=94, 80.2%)	(n=94, 80.2%)	ICI (n=13, 11.2%)	US (n=2, 1.7%)	VED (n=11, 9.5%)			
			n	%	n	%	n	%	n	%	
Discontinuation (last 4 weeks)											
	NO	41	35.3	29	30.9	4	30.8	1	50	4	36.4
	YES	75	64.7	65	69.1	9	69.2	1	50	7	63.6
Adherence (% used in the last 4 weeks)											
	0%	35	30.2	28	29.8	3	23.1	1	50	n/a	n/a
	1 - 25%	24	20.7	21	22.3	6	38.5	0	0	n/a	n/a
	26 - 50%	20	17.2	18	19.2	2	15.4	0	0	n/a	n/a
	51% - 75%	11	9.5	7	7.5	3	23.1	0	0	n/a	n/a
	76% - 100%	16	13.8	16	17	0	0	0	0	n/a	n/a
	>100%	5	4.3	4	4.2	0	0	1	50	n/a	n/a
Mean			41.8		41.6		31.2		125.0		n/a
St. Deviation			52.1		49.9		27.6		176.8		n/a
Persistence (N° of days)											
	</= 1 day	15	12.9	11	11.7	1	7.7	1	50	2	18
	≥ 1 – 7 days	27	23.3	23.0	24.5	2	15.4	0	0	4	36
	> 8 – 14 days	11	9.5	9.0	9.6	1	7.7	0	0	1	9
	> 15 – 21 days	4	3.4	3.0	3.2	2	15.4	0	0	1	9
	> 22 – 28 days	4	3.4	3	3.2	1	7.7	0	0	0	0
	> 4 weeks (28 days)	55	47.4	45	47.9	6	46.2	1	50	3	27
Mean			24.5		25.5		25		28.5		7
St. Deviation			753.4		346		289		38.9		392.7

Table 32: Sexual Activity

Sexual Activity		n	%
Wanted to be sexually active (Since last physician appointment)	No	9	7.8
	Yes	106	91.4
Sexual Attempts (last 4 weeks)	0	32	27.6
	1 -10	76	65.5
	11 - 20	7	6
	21 - 30	0	0
	31 - 40	1	0.9
Mean			3.6 (SD 5.0)

6.7 Psychosocial measures

Men's scores on the psychosocial measures are reported in Table 33 and are summarised below.

6.7.1 The Hospital Anxiety and Depression Scale (HADS)

There were 49 (42.2%) men who scored 7 or less on the HADS anxiety subscale, and were therefore considered 'non-cases' (Table 33). There were 18 men (15.5%) scored between 7 and 10 and were considered 'possible' clinical cases and 49 (42.2%) scored over 11 and were therefore considered 'probable' clinical cases of anxiety.

There were 74 men (63.8%) who scored 7 or less on the HADS depression subscale and were and therefore considered 'non-cases'. 23 (19.8%) scored between 7 and 10, considered 'possible' clinical cases and 19 (16.4%) scored 11 or more and were considered 'probable' clinical cases.

6.7.2 The Brief Illness Perception Questionnaire (IPQ)

The Brief IPQ, indicated that men had some concern about the consequences of their condition, believed that their ED would last a long time and that they did not have much control over the condition. Participants reported being substantially affected emotionally in relation to their condition, along with having a low level of understanding with regards to their ED (Table 33).

6.7.3 The Beliefs about Medicines Questionnaire (BMQ)

The BMQ indicated a similar level of perceived treatment necessity as well as concerns with regards to treatment (Table 33). The scores exist on a scale of between 5 and 25. Overall the median (IPQ) necessity score was 14 (7) and the median (IQR) concerns score was 15 (7) indicating a moderate perception of necessity and concerns about ED treatment.

6.7.4 The Self-Esteem and Relationship Questionnaire (SEAR)

In relation to the SEAR, Men scored most poorly in response to the sexual relationship domain, suggesting that men in the sample had lower levels of sexual well-being and functioning. Confidence in relation to their overall disposition and relationship was less favourable for self-esteem (Table 33).

6.7.5 The Brief COPE

In relation to the Brief COPE, self-sufficient coping, was the most frequently used coping strategy and avoidant coping the least utilised by this study population (Table 33).

Table 33: Psychosocial measures

HADS (possible score 0-21)	Median	Range	IQR
Anxiety	9	0-21	8
Depression	6	0-19	7
BMQ (possible score 5-25)			
Necessity	14	5-25	7
Concerns	15	5-25	7
Brief COPE			
Self-sufficient coping (score 10 – 40)	24	13-39	8
Socially supported coping (Score 8 – 32)	15	8-31	7
Avoidant coping (Score 10 – 40)	20	10-37	10
SEAR (possible score 0-100)			
Sexual relationship	32	0-77.5	29.5
Confidence	42	0-80	30
Self-esteem	38.5	0-80	34
Overall relationship	50	0-80	40
Total Score	36	0-78.6	28
Brief IPQ (possible score 0-10)			
Consequences	7	0-10	4
Timeline	8	0-10	5
Personal control	8	0-10	5
Treatment control	4	0-10	3
Identity	6	0-10	4
Illness concern	9	0-10	3
Coherence	3	0-10	5
Emotional representation	8	0-10	4

6.7.6 Barriers and enablers to erectile dysfunction treatment questionnaire (BEED-TQ)

Table 34 provides the median (IQR) scores for each item within each domain of the BEED-TQ. The percentage of overall participants responses for each item of the BEED-TQ on the 5 point Likert scale is presented in Figure 14. The TDF domains; goal (item 16), intention (items 17 and 18), knowledge (item 19), memory, attention, and decision processes (item 20) and social influence (items 21-25), had a median score of 4 on a Likert scale of 1-5 scale. This suggests that participants collectively had a positive perception of their ED treatment. Men therefore showed intent to use their ED treatment, knowledge of how to use it effectively and felt encouraged to use their treatment (Table 34). In relation to the domain Goal (items 13-16) men reported a desire to explore alternative treatments for ED, outside of the NHS and aimed to have a sex life that was not reliant on treatment.

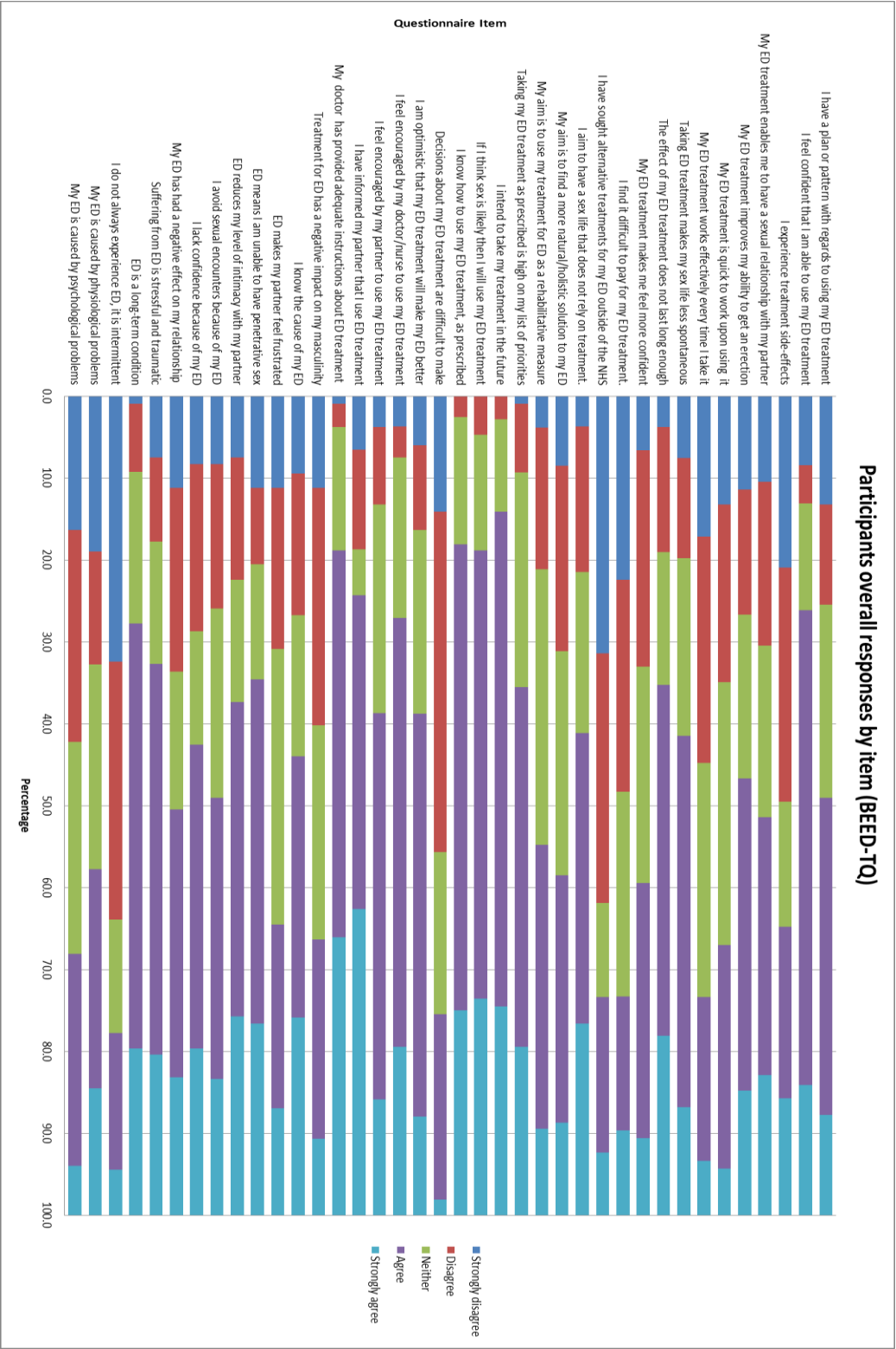


Figure 14: Responses to BEED-TQ

In relation to the SRM domains, scores indicated that on average participants were aware of the cause of their ED, that it was long-term, that due to ED they were unable to have penetrative sex, experienced a reduced level of intimacy, avoided sexual encounters; lacked confidence and believed that their ED had a negative effect on their relationship with their partner. Further, men agreed that having ED was stressful and traumatic.

Table 34: Descriptive data for the BEED-TQ

Model	Domains	Questionnaire Items	Median Score	IQR
TDF	Behavioural regulation Beliefs about capabilities Beliefs about consequences	1) I have a plan or pattern with regards to using my ED treatment	3	2
		2) I feel confident that I am able to use my ED treatment	4	1
		3) I experience treatment side-effects (e.g. headaches, facial flushing, pain, Peyronie's disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of my ED treatment	2.9	2
		4) My ED treatment enables me to have a sexual relationship with my partner	3.2	2
		5) My ED treatment improves my ability to get an erection	3.9	1.9
		6) My ED treatment is quick to work upon using it	3	2
		7) My ED treatment works effectively every time I take it	3	1.7
		8) Taking ED treatment makes my sex life less spontaneous (R)	2	1
		9) The effect of my ED treatment (i.e. duration of erection) does not last long enough (R)	2	1
	Emotion	10) My ED treatment makes me feel more confident	3	2
	Environmental context and resources	11) I find it difficult to pay for my ED treatment	2.9	1.9
		12) I have sought alternative treatments for my ED outside of the NHS (R)	4	3
	Goal	13) I aim to have a sex life that does not rely on treatment	4	1
		14) My aim is to find a more natural/holistic solution to my ED	3	2
		15) My aim is to use my treatment for ED as a rehabilitative measure	3	1.1
		16) Taking my ED treatment as prescribed is high on my list of priorities	4	1
	Intention	17) I intend to take my treatment in the future	4	0.2
		18) If I think sex is likely then I will use my ED treatment	4	0.6
	Knowledge	19) I know how to use my ED treatment, as prescribed, in order for it to work effectively	4	0.3

Model	Domains	Questionnaire Items	Median Score	IQR
SRM	Memory, attention and decision processes	20) Decisions about whether to use my ED treatment are difficult to make (R)	4	1.4
		Optimism	4	1
	Social Influence	21) I am optimistic that my ED treatment will make my ED better	4	1
		22) I feel encouraged by my doctor/nurse to use my ED treatment	4	1
		23) I feel encouraged by my partner to use my ED treatment	4	1
		24) I have informed my partner that I use ED treatment	4	1.9
		25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	4	1
	Social professional role and identity	26) Using treatment for ED has a negative impact on my masculinity (R)	3	2
		27) I know the cause of my ED	4	1.9
		37) My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	3	2
		38) My ED is caused by psychological problems	3	2
	Cause	28) ED makes my partner feel frustrated (R)	3	2
		29) ED means I am unable to have penetrative sex (R)	2	1
		30) ED reduces my level of intimacy with my partner (R)	2	1.4
		31) I avoid sexual encounters because of my ED (R)	2.5	1.7
		32) I lack confidence because of my ED (R)	2	2
		33) My ED has had a negative effect on my relationship with my partner (R)	2.6	2
		34) Suffering from ED is stressful and traumatic (R)	2	1
		35) ED is a long-term condition (R)	2	1
	Consequence	36) I do not always experience ED, it is intermittent	2	2
	Emotion			
	Timeline			

**R = Reverse scored*

6.8 What factors are associated with treatment utilisation?

The following sections report the results of the analyses that examined the relationship between the potential barriers and enablers of ED treatment utilisation and the three measures of treatment utilisation i.e., adherence, persistence, and discontinuation. The findings of the univariate analyses, followed by the regression analysis are reported within each outcome. Only independent variables that met the entry criterion of $p \leq 0.1$ in the univariate analyses were entered into the regressions. All of the following regressions have 6 or fewer IVs which were deemed suitable according to the rule of thumb for regressions mentioned previously (See section 6.4.6).

6.8.1 Discontinuation

Univariate Analysis

Univariate analysis was used to explore the relationship between discontinuation and the independent variables. Chi-Squared tests were carried out to explore discontinuation and the categorical independent variables, none of which were statistically significant (Appendix 23). T-tests were carried out for dichotomous independent variables where those that met the criteria for entry into the regression ($p < 0.1$) can be seen below (Table 35; for a complete table of results see Appendix 24).

Table 35: T-test for discontinuation and Independent variables

Independent Variables	Used treatment in the last 4 weeks (Y/N)	N	M(SD)	t	df	p
Comorbidities						
Total number of comorbidities	NO	41	1.02(0.99)	-2.15	95.30	0.03
	YES	75	1.47(1.18)			
IPQ Items						
IPQ: identity	NO	41	5.00(3.15)	-1.84	114.00	0.07
	YES	75	6.10(3.03)			
BEED-TQ Items						
9) The effect of my ED treatment (i.e. duration erection does not last long enough (R)	NO	41	2.70(1.12)	2.31	114.00	0.02
	YES	75	2.22(1.07)			
26) Using treatment for ED had a negative impact on my masculinity (R)	NO	41	3.45(1.13)	2.95	114.00	0.00
	YES	75	2.79(1.17)			
37) My ED is caused by physiological problems	NO	41	2.77(1.33)	-1.81	114.00	0.07
	YES	75	3.24(1.33)			

Multivariate Analysis

Five variables were associated with adherence at $p \leq 0.1$ and therefore met the criterion for entry into the regression analysis. The variables that were associated with the outcome of treatment discontinuation and therefore met the criterion were: fewer comorbidities, perceived fewer ED symptoms according to the IPQ *Identity* domain, were less likely to believe that ED treatment did not last long according the TDF domain *beliefs about consequences*, had a stronger belief that ED treatment had an impact on masculinity according to the TDF domain *Social, professional role and identity* and were less likely to think that ED was caused by physiological problems according to the SRM *cause* domain (Table 36).

These independent variables were entered into a logistic regression to ascertain if they were associated with treatment discontinuation. Overall, the independent variables accounted for 21.28% of the variance according to Nagelkerke R Square. The model was a good fit for the data [Chi-Square=5.74, df=8 and $p=0.671$ (>0.05)]. One significant independent predictor of whether participants had used their ED treatment in the last 4 weeks at the 5% level was item 26, from the TDF domain *social professional role and identity* i.e., 'Using treatment for ED has a negative impact on my masculinity' [*TDF26*; Wald=4.511, $p=0.047$ (<0.05)]. The odds ratio (R) for *item 26* is 0.660 (95% CI 0.437 - 0.995). Therefore, those who had discontinued treatment disagreed more strongly with the statement. The model correctly predicted 44.42% of cases where men were not using ED treatment and 86.04% of those that were using their treatment, giving an overall percentage correct prediction rate of 71.24%.

The negative impact on ED treatment on participant's masculinity, as mentioned, was a significant predictor of whether ED treatment had been used in the last 4 weeks with an OR of 0.660 (95% CI 0.437 - 0.995). Therefore, as the extent to which participants increasingly perceive

their ED treatment as having a negative impact on their masculinity by one point on the scale, the odds of discontinuing treatment for ED is 0.660 times higher if all other variables stay the same.

Table 36: Variables in the equation

Variable	B	S.E.	Wald	df	Sig.	OR	95% C.I. for EXP(B)	Fracti on Missi ng Info.	Relative Increase Variance	Relative Efficiency
Total N°		0.21								
Comorbidities	0.372	5	3.399	1	0.085	1.451	0.950	2.215	0.116	0.124
How much do you experience symptoms from your ED?	0.087	0.07 0	1.583	1	0.213	1.091	0.952	1.250	0.014	0.014
The effect of my ED treatment (i.e. duration of erection) does not last long enough	-0.395	0.20 8	3.781	1	0.058	0.674	0.448	1.013	0.044	0.045
Using treatment for ED has a negative impact on my masculinity	-0.416	0.20 9	4.511	1	0.047	0.660	0.437	0.995	0.113	0.121
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	0.324	0.17 8	3.586	1	0.069	1.382	0.974	1.961	0.072	0.075
Constant	0.943	1.22 0	0.689	1	0.440	2.568	0.234	28.18 3	0.072	0.075

6.8.2 Adherence

Univariate Analysis

Univariate analysis i.e., t- tests (in the case of categorical independent variables) were carried out and statistically significant results are reported below (Table 37); for a complete table of results see Appendix 25). Bivariate Spearman's correlations (in the case of continuous independent variables) were used to explore the relationship between adherence and the independent variables where those that met the criteria for entry into the regression ($p < 0.1$) can be seen below (Table 38; for a complete table of results see Appendix 26).

Table 37: Comparison of Means - Binary and categorical demographic independent variables and adherence to ED treatment (t-tests)

				t	df	p
Sexuality						
	Heterosexual	96	34.22(37.78)	-1.83	108	0.07
	Other	14	54.23(40.74)			

Table 38: Bivariate Spearman's correlations for adherence and continuous independent variables

			r_s	p
BMQ Items				
	BMQ Necessity		0.16	0.09
BEED-TQ Items				
Optimism	21) I am optimistic that my ED treatment will make my ED better		-0.20	0.04
Social Influence	25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly		-0.18	0.06
Social professional role and identity	26) Using treatment for ED has a negative impact on my masculinity (R)		-0.18	0.08
SRM Domains				
Cause	37) My ED is caused by physiological problems		0.18	0.08

R = Reverse Scored

Multivariate Analysis

Six variables were associated with adherence at $p \leq 0.1$ and therefore met the criterion for entry into the regression analysis. These were reporting 'other' with regards to sexuality, a higher level of necessity according to the BMQ necessity domain, being less optimistic about the effects of treatment according to the BEED-TQ optimism domain, not feeling as if ones doctor or nurse has provided adequate instructions about how to use my ED treatment correctly according to the BEED-TQ social influence domain, agreeing that ED treatment has a negative impact on one's masculinity according to the BEED-TQ Social, professional role and identity domain and believing that ED is caused by physiological problems according to the BEED-TQ cause domain.

On entry of these variables into a multilevel linear regression, there were slight deviations from the line of normality according to the P-P plot, however, there was an absence of multicollinearity (Appendix 18). The regression analysis indicated that the independent variables accounted for only 1.8% of the variance. The independent variables did not significantly predict the dependent variable; adjusted $R^2 = .017$ $F(6, 96) = 1.212$, $p = .38$. None of the variables independently predicted the DV (Table 39).

Table 39: Adherence - Linear regression Coefficients (Pooled data)

Model	Unstandardized Coefficients		Standardized Coefficients	Collinearity Statistics			
1	B	Std. Error	Beta	t	Sig.	Tolerance	VIF
(Constant)	49.056	59.641	0.050	0.823	0.429		
Sexual orientation	6.283	18.835	0.115	0.334	0.741	0.834	1.200
BMQ Necessity Score	1.148	1.077	-0.050	1.065	0.288	0.896	1.117
I am optimistic that my ED treatment will make my ED better (TDF Optimism)	-2.493	5.815	-0.043	-0.429	0.670	0.766	1.305
My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly (TDF Social Influence)	-2.517	7.104	-0.143	-0.354	0.724	0.742	1.349
Using treatment for ED has a negative impact on my masculinity (TDF Social professional role and identity)	-5.594	4.763	0.037	-1.174	0.245	0.843	1.187
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues) (SRM Cause)	1.071	4.366	0.050	0.245	0.808	0.929	1.077

6.8.3 Persistence

Univariate Analysis

Univariate analysis and bivariate Spearman's correlations were used to explore the relationship between adherence and the independent variables. The comparison of means between both binary and categorical independent variables and persistence indicated that no variables met the criteria for entry into the regression ($p < 0.1$) (Appendix 27). However, bivariate correlations of continuous variables and persistence indicated several significant results (Table 40; for a complete table of results see Appendix 28).

Table 40: Bivariate correlations between persistence and continuous independent variables

		r	p
BMQ Items			
	BMQ Necessity	-0.18	0.05
	BMQ Concerns	-0.23	0.01
BEED-TQ			
Goal	13) I aim to have a sex life that does not rely on treatment.	-0.18	0.06
Social professional role and identity	26) Using treatment for ED has a negative impact on my masculinity (R)	0.22	0.02
SRM Domains			
Cause	37) My ED is caused by physiological problems	-0.22	0.02

Multivariate Analysis

Five variables were associated with persistence i.e., more recent treatment utilisation, at $p \leq 0.1$ and therefore met the criterion for entry into the regression analysis. These were a higher level of necessity as well as concerns in relation to ED treatment according to the BMQ *necessity* and *concerns* domains, aiming to have a sex life that did not rely on treatment according to the TDF domain *goal*, agreeing that ED treatment had a negative impact on masculinity according to the TDF domain *Social, professional role and identity*, and believing that ED is caused by physiological problems according to the SRM illness representation *cause*.

The dependent variable, persistence, was subjected to a process of winsorizing, which improved the line of normality according to the P-P plot and there was an absence of multicollinearity (Appendix 18). The regression analysis indicated that the independent variables account for 9% of the variance. These variables statistically predicted the number of days since last using treatment; $F(6, 105) = 3.059$, $p = 0.025$, adjusted $R^2 = 0.09$. Agreeing that ED is caused by physiological problems was the only statistically significant independent predictor, $p < 0.05$ (

Table 41).

Table 41: Persistence - Linear regression Coefficients

Model	Unstandardized		Standardized		Collinearity		
	Coefficients		Coefficients		Statistics		
	B	Std. Error	Beta	t	Sig.	Tolerance	VIF
1							
(Constant)	112.808	44.900		2.512	0.013		
Total BMQ Necessity Score	0.166	1.815	0.011	0.092	0.927	0.578	1.729
Total BMQ Concerns Score	-1.441	2.124	-0.081	-0.679	0.499	0.548	1.825
I aim to have a sex life that does not rely on treatment.	-6.776	6.157	-0.102	-1.101	0.274	0.914	1.094
Using treatment for ED has a negative impact on my masculinity	11.208	5.928	0.176	1.891	0.061	0.899	1.113
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.457	5.354	-0.256	-2.700	0.008	0.865	1.156

6.8.4 Sexual Attempts, Adherence and Persistence

Across the study sample 91.4% of men had a desire to be sexually active (Table 32). Further, most participants (n=66, 56.9%) had been sexually active and had used treatment in the past 4 weeks (Table 42). Several men (n=9, 7.8%) had not been sexually active, however, had used treatment (participants n=18, 15.5%) and also there were also a number of men who were sexually active but had not used treatment in the past 4 weeks (Table 42).

Table 42: Treatment utilisation and sexual attempts

Status	n(%)
Not sexually active & Not used medication in the last 4 weeks	23 (19.8)
Sexually Active & Not used medication in the last 4 weeks	18 (15.5)
Not sexually active & Has used medication in the last 4 weeks	9 (7.8)
Sexually Active & Has used Medication in the last 4 weeks	66 (56.9)
Total	116 (100)

Univariate analysis using Spearman's correlations was carried out to explore the relationship between adherence, persistence, and the number of sexual attempts (Table 43). The correlation between adherence and the number of sexual attempts was significant and considered moderate, therefore a higher number of sexual attempts was significantly related to higher rates of adherence. The relationship with persistence was also significant, although negative (i.e., a lower number of days indicated treatment being used more recently) therefore a higher number of sexual attempts was significantly associated with higher persistence.

Table 43: Bivariate correlations between adherence, persistence and sexual attempts

Utilisation Measure	r	p
Adherence	0.49	0.00
Persistence	-0.27	0.00

6.8.5 Sexual Attempts

Univariate Analysis

Bivariate spearman's correlations were used to explore the relationship between the number of sexual attempts in the last 4 weeks and continuous independent variables. There were no variables that met the criteria for entry into the regression ($p < 0.1$) (see Appendix 29). However, bivariate correlations involving continuous independent variables indicated several significant correlations with the number of sexual attempts in the last 4 weeks (Table 44; for a complete table of results see Appendix 30).

Table 44: Bivariate correlations for sexual attempts in the last 4 weeks and continuous independent variables

		r	p
Clinical Characteristics			
ED severity (IIEF-5)		0.18	0.05
BMQ Items			
BMQ Necessity		.298	0.00
SEAR Items			
SEAR Sexual relationship		.226	0.01
BEED-TQ Items			
Beliefs about consequences	4) My ED treatment enables me to have a sexual relationship with my partner	0.19	0.06
Social professional role and identity	26) Using treatment for ED has a negative impact on my masculinity (R)	-0.23	0.03
SRM Domains			
Timeline	36) I do not always experience ED, it is intermittent	0.18	0.07

Multivariate Analysis

There were 6 variables that met the criterion of $p \leq 0.1$ for entry into the regression analysis. A higher number of sexual attempts in the prior 4 weeks was associated with a lower severity of ED, higher perceived need for ED treatment according to the BMQ *necessity* domain, a positive outlook with regards to one's sexual relationship according to the SEAR *sexual relationship domain*, the belief that treatment enables the ability to have a sexual relationship according to the TDF domain *beliefs about consequences*, believing that ED treatment has a negative impact on one's sense of masculinity according to the TDF domain *social, professional role and identity* and experiencing ED as intermittent according to the SRM illness representation *timeline*.

Using P-P plots it was established that there was some deviation from the line of normality, however, there was an absence of multicollinearity (Appendix 18). The regression analysis indicated that the independent variables accounted for 11.5% of the variance. The independent variables statistically predicted the number of sexual attempts in the last 4 weeks, $F(5, 104) = 3.619$, $p \leq .000$, adjusted $R^2 = .115$. The BMQ Necessity Score independently significantly predicted the number of sexual attempts in the last 4 weeks ($p < .05$) (Table 45).

Table 45: Number of sexual attempts in the last 4 weeks - Linear regression Coefficients (Pooled data)

Model	Unstandardized Coefficients		Standardized Coefficients			Collinearity Statistics	
1	B	Std. Error	Beta	t	Sig.	Tolerance	VIF
(Constant)	-0.034	2.595		-0.013	0.990		
IIEF-5 Total Score	0.150	0.106	0.155	1.410	0.161	0.690	1.450
Total BMQ Necessity Score - total of reversed items	0.302	0.107	0.276	2.829	0.006	0.877	1.141
Final SEAR sexual relationship score	-0.031	0.030	-0.118	-1.012	0.314	0.614	1.629
My ED treatment enables me to have a sexual relationship with my partner	0.289	0.448	0.068	0.645	0.520	0.745	1.342
Using treatment for ED has a negative impact on my masculinity	-0.045	0.399	-0.011	-0.113	0.910	0.958	1.044
I do not always experience ED, it is intermittent	0.578	0.429	0.139	1.347	0.181	0.784	1.276

6.9 Discussion

6.9.1 Treatment Utilisation

Across all treatments for ED, 35.3% (n=41) of men had discontinued ED treatment in the previous 4 weeks. The median number of sexual attempts in the last 4 weeks was 3.6 and over the same period, one quarter (27.6%) of participants had not had any sexual attempts. On average, the last time treatment was used was 24.5 days prior to completing the questionnaire and those who were using treatment had used under half of their prescribed treatment, however, this varied substantially between treatments (PDE5Is 41.6%, ICI 31.2%, US 125%).

We can consider this in the context of treatment utilisation in general, where broadly speaking, it is reported that approximately 50% of individuals do not adhere to their medication regimen (Haynes et al, 2002). As well as considering the results of this study against rates of adherence to treatment in general, we can consider the results against research focussed specifically on ED treatment utilisation. The systematic review reported in Study 1, indicated that across 45 studies, 40% of participants had discontinued PDE5Is, 46% had discontinued ICI and 52% had discontinued US. In relation to the current study, reported discontinuation was less in comparison i.e., the discontinuation rate of PDE5Is was 30.9%, for ICI treatment it was 30.8% and for US it was 50%. The systematic review did not find any previous research offering discontinuation rates for VEDs, however, the current research indicated that the rate of discontinuation was 36.4%.

6.9.2 Representativeness of the sample

It was reported by the International Consultation Committee for Sexual Medicine that the prevalence of ED increases with age (Lewis et al, 2010). It was evident in the current study that the proportion of participants with ED increased with age; where 12.9% were between 18 and 316

44 years of age and 83.6% were between the ages of 45 and 84 years of age. In relation to the systematic review (Study 1), across included studies, participants were between 40.4 and 69.1 years (Green & Martin, 2000; Ricardi et al, 2010) and were therefore of a similar age to the majority of participants in the current study, however, the cohort of participants in the current study covered a border age range.

In relation to erectile function, participants in the current research differed with respect to those across included studies in the systematic review (Study 1). According to the IIEF-5, on average, participants were suffering with moderate ED (35.3%), where the systematic review (Study 1) indicated that across studies a higher proportion of men were suffering with moderate ED i.e., between 45 - 61.7%. In relation to ED duration on average men had been suffering with ED for approximately 60 months, 26.7% of men in this study reported suffering with ED for between 2 and 3 years, 16.4% between 3 and 5 years and 24.1% between 5 and 10 years. The systematic review (Study 1) indicated that across studies, men had suffered with ED for between 1 and 5 years. Therefore, participants included in the current review, on average had suffered with ED for a longer period of time.

There were 42.2% of participants who reported that they were suffering with hypertension. This is comparable to previous studies, for example, the systematic review indicated eighteen studies which provided data on patient comorbidities where the most prevalent were hypertension and diabetes. Hypertension was reported as being present in 9.4 to 51.9% of study participants. This is not surprising in this patient population where previous research has indicated a high prevalence of ED in conjunction with vascular conditions such as coronary artery disease (Solomon et al, 2003) and hypertension (Burchardt et al, 2001). The arterial size hypothesis posits that both cardiovascular disease and ED can be caused by plaque build-up. Due to their

size, penile arteries (1 – 2mm) are likely to become blocked before larger coronary arteries (3 – 4mm) (Jackson, 2013). Therefore, a large portion of participants recruited were likely to be suffering with some coronary artery disease caused by arterial degradation.

Men with ED have been found to suffer with significantly lower QoL than men without ED (Jonler et al, 1995). According to the HADS, the median anxiety score was 9 and the median depression score was 6. A study carried out in the UK involving over six thousand participants indicated that in the general population, the median anxiety score in men was 5 and the median depression score was 3 (Breeman et al, 2015). Therefore, the cohort of men who took part in this study indicated an increased level of anxiety and depression compared to men in the general population. However, the coexistence of ED and depression is complex. It has been suggested that psychosocial distress which can accompany ED may cause depression or ED may be a symptom of a major depressive disorder associated with decreased libido, sexual activity, and erectile function (Rosen et al, 2004a).

Due to the nature of the busy urological clinics the current research was carried out in, some men completed the questionnaire immediately before their medical consultation, whereas others completed the questionnaires after. This may have influenced questionnaire responses. For example, if a patient were told during their medical consultation that instead of oral PDE5Is, perhaps a second line treatment would be more appropriate, this could alter the perception of their medication. Many participants were recruited from ED clinics (60.6%) and a smaller number from an online forum (39.4%). It is possible that participants coming through the clinics were returning potentially to have doses increased or to change ED treatment to e.g., second line treatments where first line treatment had failed. With this in mind, it is possible that treatment ineffectiveness played a part in treatment utilisation rates for men who were coming through the clinic. It is also important to consider that the characteristics of men coming through the clinics are potentially different to those who completed the on-line survey. For example, men who attend clinic indicate to some degree that they are seeking help for their condition. However, this may not be the case for participants who completed the questionnaire on-line. Research has indicated, for example, that up to 70% of men with ED are not treated (Kubin, 2003) and that e.g., 45.2% of men do not seek any help for ED, whether from a partner, friend, the internet or from an HCP (Laumann et al, 2009). Therefore, samples were not homogeneous in this respect and it is possible that men encounter different barriers and enablers to ED treatment utilisation on this premise. Future studies could consider using a prospective study design where participants who are newly prescribed treatment are followed longitudinally, which could reduce the potential heterogeneity that may have existed in the current study sample.

6.9.3 Barriers and enablers to ED Treatment Utilisation and Sexual Attempts

Across all the dependent variables, discontinuation was the only measure in which the independent variables could be seen to account for a small proportion of the variance (24.04%). Adherence, persistence, and the number of sexual attempts accounted for 1.8%, 9% and 11.5% of the variance, respectively. Previous research has indicated that psychological frameworks predict modest levels of the variance in health-related behaviour. For example, a recent systematic review showed that at best, the SRM predicted 24% of the variance in adherence to medication, and the review concluded that a combination of theoretical frameworks to promote treatment adherence is advisable, until more is known about the predictors (Holmes et al, 2014).

The most salient factors associated with treatment utilisation according to the results of the current study, were the negative impact of ED treatment on men's perception of masculinity, which was significantly related to increased discontinuation of treatment. Perceiving ED as being caused by physiological problems, which was significantly associated with medication persistence i.e. using treatment more recently. In addition, participants who had a higher number of sexual attempts over the previous 4 weeks had a significantly higher perceived need for treatment.

The significant association between discontinuation and the negative impact of treatment was evident across other measures of utilisation, although regression analysis did not show a significant relationship; it was evident in relation to adherence, persistence, sexual attempts at the $p \leq 0.1$, the criterion for entry into the regression analysis. Therefore, higher rates of adherence as well as increased persistence and sexual attempts were associated with believing that ED treatment has a negative impact on masculinity. This is an important finding and one

which, to the authors' knowledge, has not been reported in previous research investigating barriers and enablers to ED treatment utilisation, being absent from the systematic review (Study 1). However, the interpretation of the term 'masculinity', may differ between participants who took part in the study or indeed between individuals more generally. Sand et al (2008), carried out an exploration of the attitudes of men, both with and without self-reported ED to assess the impact of ED on masculine identity and quality of life. The research indicated that men's perceptions of masculinity differ substantially from stereotypes. Men reported that important determinants of self-perceived masculinity included being honourable, self-reliant, and respected by friends, and that factors stereotypically associated with masculinity i.e., being physically attractive, sexually active and successful with women, were less important (Sand et al, 2008). Therefore, although the negative impact of treatment on men's perception and its impact on treatment utilisation is an important finding, caution is important when drawing inferences from this finding as further investigation is needed to ascertain what the term masculinity means to the individual. With this complexity in mind, further investigation is needed.

Perceiving ED as being caused by physiological problems was significantly associated with persistence and therefore, participants who had used treatment more recently, were more likely to perceive their ED as being caused by physiological problems. It is important to note that, although not significant in regression analysis, perceiving ED as being caused by physiological problems was associated with both other measures of treatment utilisation i.e., adherence, and discontinuation at $p \leq 0.1$, the criterion for entry into the regression analysis. The IPQ domain *cause* is described as personal ideas about aetiology, which may include simple single causes, or more complex multiple causal models. This could indicate that having a mental model which involves the cause of ED including a physiological component is likely to be advantageous with

regards to treatment utilisation. However, this could also relate to the arterial size hypothesis mentioned above i.e., many participants indicated comorbid conditions which stem from atherosclerosis and therefore successful treatment may relate to rectifying ED which is physiological in nature. Those with ED considered more psychological in origin, potentially face a different set of barriers. For example, in relation to utilising hypertensive medication, research has shown that patients with mild anxiety and depression are at increased risk of becoming non-adherent to antihypertensive medication (Bautista et al, 2012). This study did not indicate that depression and anxiety were related to treatment utilisation, however, this study was cross-sectional in design and therefore it would be advantageous to ascertain if anxiety and depression potentially influence treatment utilisation over time, by exploring the impact of anxiety and depression using prospective research methodology.

The current study indicated that an increased perception of need for treatment, according to the BMQ *necessity* domain, was associated with an increased number of sexual attempts. However, it is important to note that the BMQ *necessity* domain was significantly related to increased adherence and persistence in univariate analysis at the $p \leq 0.1$, the criterion for entry into the regression analysis. Necessity beliefs are thought to promote adherence (Horne & Weinman, 1999) and it is suggested that treatment utilisation occurs when the benefit of medication outweighs the risks (Horne, 2000). Perceived necessity and concerns have been found to predict treatment adherence across a range of conditions (Foot, 2015). A meta-analysis carried out by Horne et al (2013) indicated that across studies, higher adherence was significantly associated with stronger perceptions of necessity of treatment and fewer concerns about treatment. It was interesting to note, however, that treatment necessity was most strongly associated with sexual attempts and less so with measures of treatment utilisation. Although not significant, according to the regressions analysis, two other variables which

indicated significant correlations at the $p \leq 0.1$ level for entry into the regression. The first was the SEAR *sexual relationship* domain which is indicated that increased sexual attempts were related to a positive perception of one's intimate relationship. The second was the TDF *beliefs about consequences* domain which indicated that a higher number of sexual attempts were related to perceiving ED treatment as enabling participants to have a sexual relationship with their partner. Therefore, the perceived necessity for treatment could relate to (1) having a more positive perception of one's intimate relationship with their partner and (2) perceiving treatment as enabling participation in an intimate relationship. This finding indicates the potential importance of exploring men's perceptions of necessity and concern in relation to ED treatment, which would enable the exploration of important aspects which relate to the complexity of using ED treatment, i.e. where treatment utilisation occurs on the basis of the perceptions and behaviour of both the man and his partner.

There were a number of variables that were expected to play a role, yet did not emerge as a central theme in the findings of the current study. The systematic review (Study 1), indicated that across the 45 included studies, the experience of treatment side-effects and treatment ineffectiveness, were the most frequently reported factors associated with treatment discontinuation, which was subsequently evident in study 2 (Chapter 5). However, the BMQ concerns domain, indicated that higher levels of concern with regards to treatment was associated with increased persistence according to univariate analysis. The BMQ concerns domain includes questions such as 'having to use treatment for ED worries me', 'I sometimes worry about long-term effects of my ED treatment' and 'I sometimes worry about becoming too dependent on my ED treatment'. Therefore, it is possible that the physical manifestation of side-effects was less of a problem than perceptions related to concerns, such as, e.g. the potential long-term effects of using treatment. It was interesting to note, that in the systematic review,

where participants reported side-effects, they were less likely to discontinue (Carvalho, 2012). Concerns about treatment can be considered a psychological factor which is potentially amenable to change, and therefore, HCPs could indeed help to reduce concern and enhance treatment utilisation by exploring patient's perceptions around treatment concerns. The cost of treatment was also a widely reported factor associated with increased treatment discontinuation according to the wider literature. This was explored in the systematic review (Study 1) and was evident in study 2 (Chapter 5) as likely to be associated with treatment discontinuation. However, this was not indicated as a barrier in the current study. This could relate to 62.1% of participants in the current study cohort being prescribed Sildenafil, which can be provided to all patients at the expense of the NHS (McKernan et al, 2015), therefore, reducing the impact of cost on treatment utilisation.

6.9.4 Strengths and Limitations

The study was retrospective, with men being asked to recall how many doses or times they had used their ED treatment over the last 4 weeks. Research has indicated that self-report measures can produce an overestimation of adherence (Ziller et al, 2011), due to the notion that they are subject to social desirability, recall bias, and response bias (Shi et al, 2010). Although the study was cross-sectional and therefore the direction of the relationship between variables cannot be determined, several advantages to this methodology exists, including being relatively inexpensive, quick and easy to administer, useful for generating and clarifying hypotheses, piloting new measures and laying the groundwork for decisions about future follow-up studies (Kraemer, 1994).

Use of the PAQ, as a primary measure treatment utilisation brings with it limitations. Based on a literature review of adherence measures, the PAQ was the only measure that was designed

specifically for use with an ED population and in relation to ED treatment and it was deemed to have both content and face validity. However, there is no 'gold standard' when it comes to measuring treatment utilisation. Each method of measuring adherence has its own strengths and weaknesses (Wagner et al, 2001). Self-report measures are considered the most convenient and commonly used method of measurement, yet criticism relates to their validity (Baumeister, 2007). People may be motivated to present themselves as adherent, rather than accurately reporting their medication-taking behaviour. Research has indicated that self-report measures tend to produce estimates of adherence that are 10–20% higher than those from electronic drug monitoring methods, such as medication events monitoring system (MEMS) caps (Arnsten et al, 2001; Wagner & Miller, 2004). Therefore, their weaknesses in terms of their validity must be considered when interpreting the utilisation rates found in this study. However, The PAQ is a self-report measure and in relation to self-report measures, research has indicated that they have reasonable predictive power (Lam & Fresco, 2015). When considering the environment under which the questionnaire would be administered and the resources available for this research, a self-report measure was considered the most appropriate method, as they have been described as, being useful in a busy, resource-limited clinical settings (Lam & Fresco, 2015).

The study also developed and subsequently administered the BEED-TQ to participants that took part in the quantitative cross-sectional study (Study 3). Cronbach's alpha was used to explore the internal consistency of the BEED-TQ and ascertain if the questionnaire items of each TDF domain reliably measure the same construct. It has been indicated that a Cronbach's alpha of 0.7 and over is considered adequate for a survey instrument (Bland and Altman, 1997). However, each of the TDF domains scored below 0.7 and therefore were below this cut off point. Subsequently, the questionnaire items (n=36) were treated separately when entering them into subsequent univariate and multivariate analysis. However, the questionnaire was considered to

have face validity which was established through the PPI group as well as relevant clinical specialists involved in the research. Therefore, the evaluation of the appearance of the questionnaire in terms of feasibility, readability, clarity, language, consistency of style and formatting was assessed (Taherdoost, 2016).

This research raises a question around the use of the terms; adherence, persistence, and discontinuation, perhaps not being suitable with regards to exploring treatment utilisation in the ED population. This is problematic for several reasons. Firstly, due to both the idiosyncrasies of the condition itself, the current research indicates that men do not necessarily always use treatment for sexual intercourse, demonstrated by 15.5% of participants who were sexually active and had not used medication in the last 4 weeks which could relate to the intermittent nature of ED for some participants. Also, there were 7.8% of participants who were not sexually active, however, had used treatment in the last 4 weeks, which could relate to those participants who are using treatment for rehabilitative purposes. Therefore, a measure of; adherence or persistence or discontinuation, relates only to medication use, and not to sexual activity. Secondly, participants' sexual relationship with their partner determines whether ED treatment is used or not, and therefore treatment utilisation does not relate to an individual, i.e. the man, but rather relates to both the man and his partner who influence whether it is utilised. The central tenant of this problem relates to the unique nature of a couple's approach to the sexual relationship as well as the idiosyncrasies associated with the condition itself. Measuring treatment utilisation in this population contains unique challenges which the results of this study have highlighted. This, to the authors' knowledge, has not been explored in previous research and therefore is a novel finding from the current study.

The current study used the TDF as a basis for exploration of the barriers and enablers to ED treatment utilisation. The strength of the TDF exists in its theoretical lens, which enables the identification of barriers and enablers whilst being grounded in accepted psychological behavioural theories (Cane, 2012). The TDF by its nature is comprehensive, covering a wide range of domains. This was further broadened by the addition of SRM illness beliefs, the importance of which was highlighted by study 2 (Chapter 5). The TDF enabled the development of the BEED-TQ, which was designed specifically for use in this study, the findings of which align with the 'development' phase of the MRCs guidelines for the design and evaluation of complex interventions. Using the TDF, enabled the possibility of potentially laying of foundations for developing a behaviour change intervention, that is likely to be more effective than those developed without use of theory (Craig et al, 2008).

6.9.5 Conclusion

To the author's knowledge, this study was the first to use both the TDF and SRM in a theoretically informed approach to exploring the barriers and enablers to ED treatment utilisation. The study found that participants that took part in the study reported treatment utilisation rates that are comparable to other ED research.

Results indicated that the amount of variance explained in each instance was low. However, there were a number of novel findings that emerged from the study. This included the potential negative impact of treatment on men's sense of masculinity, as well as the perception that ED is caused by physiological problems. It was established that treatment use is not necessarily synonymous with sexual attempts and that an increased number of sexual attempts is associated with an increased perception of ED treatment necessity.

Using terms such as adherence, persistence, and discontinuation in relation to ED treatment utilisation is potentially problematic for a medication which is used on demand and in conjunction with men's partners. Future research needs to incorporate a method of assessing a couples goals with respect to sexual intimacy. This is considered important, in order to make measurement of treatment utilisation meaningful in this population.

7 General Discussion

7.1 Chapter Overview

The overall aim of the research presented in this thesis was to explore what barriers and enablers exist and the extent to which they have the potential to influence men's decisions about utilising treatment for ED. This final chapter will consider the overall findings of the three phases in this mixed methods research study, involving a systematic review (Study 1), semi-structured qualitative interviews (Study 2) and a cross-sectional quantitative study (Study 3). All of these studies were designed to increase our understanding of the barriers and enablers men experience in relation to using treatment for ED. This chapter will consider the findings of the three studies and their contribution, with respect to existing literature and research, as well as consider the implications of these findings for future research and clinical practice. The limitations of each study will be considered and finally, the chapter will be drawn to a close with overall conclusions.

7.2 Contribution to Knowledge about ED Treatment Utilisation

7.2.1 Rates of ED Treatment Utilisation

To date, research has indicated, that regardless of advances in ED treatment, adherence is considered sub-optimal, typically involving a pattern of uptake followed by abandonment (Conaglen & Conaglen, 2012). It was evident from the systematic review (Study 1), that discontinuation rates, although they varied widely from study to study, was a problem regardless of treatment. The median rates of discontinuation across studies included in the systemic review (Study 1), was higher than median rates reported in the quantitative study (Study 3). It is likely that methodological differences, operational definitions, type of adherence measure, treatment regimens, the variety of comorbidities and patient characteristics, are potential reasons for the variety of reported rates (Dimatteo, 2004). However, it is important to

note that overall, across both Study 1 and Study 3, PDE5Is were the most frequently prescribed treatment, and had the lowest levels of discontinuation. With regards to second-line treatments, ICI therapy was most frequently prescribed and had the lowest discontinuation rate compared to other second line treatments such as US and VEDs. It must be noted that in relation to the systematic review (Study 1), most studies (n=29) focussed on PDE5Is and similarly, in relation to the quantitative study (Study 3) most participants were prescribed PDE5Is (97.4%). As a result, there was less data related to other treatments and therefore caution is necessary when generalising these results.

7.2.2 Barriers and Enablers to ED Treatment Utilisation

Side-effects, Ineffectiveness and the cost of ED treatment

The importance of the impact of treatment side-effects, treatment ineffectiveness and the cost of treatment, was established in the systematic review (Study 1) as well as the qualitative interviews (Study 2). In relation to side-effects, the systematic review (Study 1), indicated that three studies used inferential statistics to examine the relationship between side-effects and treatment utilisation. Of these, one study indicated a non-significant relationship, one indicated higher rates of persistence as being associated with increased incidence of adverse events and one study reported that men who reported side effects to their HCP were less likely to discontinue treatment. The qualitative interviews (Study 2) indicated that some men considered the impact of side-effects as a reason for not using treatment. The quantitative study (Study 3), however, did not indicate that side-effects related to measures of treatment utilisation, using univariate analysis or indeed regression analysis. However, it is important to consider that approximately 35% of participants in study 3 either agreed, or strongly agreed, that they had experienced side-effects. It is also important to consider the BMQ *concerns* domain, which when using univariate analysis indicated that higher levels of concern with regards to treatment, was associated with increased persistence. The BMQ *concerns* domain includes items such as 'having

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to use treatment for ED worries me', 'I sometimes worry about long-term effects of my ED treatment' and 'I sometimes worry about becoming too dependent on my ED treatment'. Therefore, in addition to physical side-effects, concerns with regards to treatment are also considered important. It is evident from the studies involved in this thesis, that side-effects as well as concerns in relation to treatment, have the potential to influence treatment utilisation. We know that psychological and cognitive factors are amenable to change (Horne et al, 2005), therefore this is potentially an important subject which can be explored by HCPs with patients when prescribing treatment. It is noteworthy that one of the studies included in the systematic review reported that where participants reported side-effects, they were less likely to discontinue (Carvalho, 2012).

In addition to side-effects, the systematic review (Study 1) also indicated that treatment ineffectiveness was widely reported by studies as a reason for discontinuation. In addition, the review included two studies which utilised inferential statistics to examine the relationship between treatment ineffectiveness and utilisation. One study indicated that ineffectiveness was significantly related to discontinuation of ICI treatment and the other study indicated that Tadalafil (OaD and PRN) were related to significantly higher rates of persistence compared to Sildenafil (PRN). The qualitative interviews (Study 2) also indicated that treatment ineffectiveness was widely reported by men with the potential to negatively impact ED treatment utilisation. However, similar to side-effects, the quantitative cross-sectional study (Study 3) did not indicate ineffectiveness as being associated with treatment utilisation according to univariate analysis, however, approximately 40% of participants disagreed, or strongly disagreed, that their treatment worked effectively every time. Ineffectiveness has wider connotations than the treatment simply not working and brings into question the knowledge patients have, with regards to how to use their treatment successfully. The qualitative

interviews indicated that in some instances participants indicated that not knowing how to use treatment was related to inadequate instructions from their HCP, which impacted the extent to which treatment was used. It has been indicated that potentially, there are two common misunderstandings in relation to PDE5Is; firstly, that they work without sexual stimulation and secondly, that they work first time (Steggall et al, 2021). Therefore, similar to side-effects, there is an opportunity for HCPs to explore both the extent to which patients know how to use their treatment successfully, as well as the extent to which treatment is truly ineffective. Research has indicated that 8–12% of treatment failures respond to a second or third PDE5I (NICE, 2019). Therefore, under such circumstances, swapping to an alternative PDE5I could be beneficial (Steggall et al, 2021).

In relation to cost, the studies included in the systematic review (Study 1) reported that cost was widely reported as a reason for treatment discontinuation. However, none of the studies examined cost using inferential statistics. The qualitative interviews (Study 2), indicated that cost is potentially an important barrier to treatment utilisation and was a reason some men gave as to why they had discontinued treatment. The quantitative cross-sectional study (Study 3) did not indicate cost as being related to measures of treatment utilisation when using univariate analysis. However, approximately 25% agreed, or strongly agreed, that they found it difficult to pay for their ED treatment. It is therefore evident that cost has the potential to play a role in ED treatment utilisation and it has previously been highlighted that there is a need to explore the impact of cost in more depth (see section 3.6.3) particularly considering the recent changes to the availability of ED treatment over-the counter (PMAP, 2019).

Impact of Treatment on Masculinity

The qualitative interviews (Study 2) indicated that having to use treatment for ED can have a negative impact on the way men see themselves, impacting on their sense of masculinity. Based

on the systematic review, this finding was novel and was a unique finding of the interviews (Study 2), which was confirmed in Study 3, where it was indicated that the negative impact of using ED treatment on men's sense of masculinity was significantly related to increased treatment discontinuation. Research has indicated that men's perceptions of masculinity differ substantially from stereotypes. Sand et al (2008), reported that important determinants of self-perceived masculinity include being honourable, self-reliant, and respected by friends, and that factors stereotypically associated with masculinity i.e., being physically attractive, sexually active and successful with women, were less important (Sand et al, 2008). The concept of masculinity has been considered in relation to how men respond to prostate cancer treatment and ED, however, it is suggested that the exact nature of this link is unclear (Chambers et al, 2017). However, in a review carried out by Chambers et al (2017), it was found that men's perceptions with regards to their masculinity, is negatively impacted by their experience of both prostate cancer treatment, as well as ED.

The review included both qualitative and quantitative studies. The qualitative studies indicated that men with ED consistently reported that they felt less like a man or they no longer felt like a man and that this was subsequently linked to depression, embarrassment, decreased self-worth as well as fear of being stigmatised. The relationship between ED and masculinity was also supported by quantitative studies, where masculinity was indicated as a moderator of poorer QoL, as well as poorer mental health outcomes for those patients with prostate cancer and ED. A systematic review which aimed at examining the impact of physical exercise on masculinity indicated that exercise interventions could improve perceptions of masculinity through the creation of: a safe community, the refocusing on valued male traits, the provision of a source of distraction, as well as being a means of establishing control over one's illness. The review

indicated that both aerobic and resistance training exerted positive effects on perceived feelings of masculinity, body image, and personal identity (Langelier et al, 2019).

Perceptions of the Physiological cause of ED

Another novel finding from the qualitative interviews (Study 2) was the importance of causal beliefs about ED, where men reported beliefs relating to ED being caused by psychological, physiological or a mixture of the two. This was confirmed in the quantitative cross-sectional study (study 3), which indicated that perceiving ED as being caused by physiological problems was significantly associated with increased persistence and therefore, participants who had used treatment more recently were more likely to perceive their ED as being caused by physiological problems. The illness representation *cause*, is described as personal ideas about aetiology, which may include simple single causes, or more complex multiple causal models. Therefore, ascertaining the extent to which this perception maps accurately onto the clinical diagnosis of ED, is important to understand. This would determine whether patients who have ED, do so due to conditions related to e.g., the arterial size hypothesis, and therefore whether it is the diagnosis of ED, or the perception itself, that is important in this respect, or indeed a mixture of the two. This needs to be explored by further research in order to establish how individuals form their mental model of ED, which in turn could potentially indicate ways in which illness representations, which are amenable to change, could be addressed to improve treatment utilisation.

The Sexual Relationship and ED treatment Utilisation

A prevalent factor that emerged from the systematic review (Study 1) was the negative impact resulting from loss of libido and its impact on treatment utilisation. Libido was not a finding to explicitly emerge from the qualitative interviews (Study 2), however, there were several factors

which related to the impact of the men's partners on treatment utilisation, and also the negative impact of the condition itself, on men's partners and subsequent treatment utilisation. The quantitative study (Study 3) included the SEAR sexual relationship score, which is an indication of the perceived quality of men's intimate relationship with their partner. Participants, who reported a higher score, or a more positive perception, indicated a significant correlation with increased frequency of sexual attempts when using univariate analysis. However, this did not indicate a significant relationship when entered into regression analysis. It has previously been highlighted that there was ambiguity around the term libido, across the studies included in the systematic review (see section 3.5.14) and as a result there is difficulty with regards to interpreting these results. The term could relate to many aspects of men's intimate relationships, such as a lack of emotional readiness for restoration of sexual activity or conflict within one's relationship; where low libido can also be the result of testosterone deficiency (Wu et al, 2010).

The importance of men's relationships with their partners, as a factor related to treatment utilisation, highlights the problematic nature of considering treatment utilisation from a unidimensional perspective i.e. only from the perspective of the man instead of; the man, his partner and their subsequent relationship. It is evident, that the perceived quality of men's intimate relationships, were significantly related to sexual attempts but not measures of treatment utilisation. Therefore, ED treatment utilisation must be considered as different from using treatments for other conditions, where only individuals determine whether treatment is used. Treatment utilisation exists on the foundations of both the man and his partner. Therefore, it is important for HCPs to consider both the man and his partner when prescribing treatment for ED. Steggall (2021) suggests that for HCPs to provide the best chance for

treatment to work, communication with the person the man is going to have sexual activity with, and consideration of the context in which any sexual activity will take place is essential.

ED Treatment: Necessity and Concerns

Horne, (2000) suggests that treatment utilisation occurs when the benefit of medication outweighs the risks, i.e., concerns such as side effects becoming dependent on medication, overuse of medication prescriptions, ingestion of harmful chemicals, for example (Horne, 1997). This is described as a cost benefit analysis involving both an individual's perception of cost (concerns), which is weighed against their perceptions of benefit (necessity), and is referred to as the necessity-concern differential. It was evident from the qualitative interviews (Study 2), that such a cost-benefit analysis is involved in men's decisions with regards to ED treatment utilisation, for example:

'If I take it of my own accord to try and maintain the spontaneity... a) I've got the side effect b) I've burnt £15 for no good reason because I'm getting headaches for 24 hours and burnt £15 for the pleasure of it...' (P-03).

There was a thread from the systematic review (study 1), through to the quantitative cross-sectional study (Study 3), which related to not wanting to have to rely on ED treatment for intimacy. The systematic review (Study 1) indicated that not being willing to have a sex life dependent on medication, or the perception that medication controls one's sex life, was a factor related to significantly higher rates of discontinuation. In relation to the qualitative interviews (Study 2), the domain *Goals* indicated that all participants shared the view that they would rather not rely on medication for their sex life, and some men reported a desire for alternative natural and holistic approaches to treat ED. However, although participants did not necessarily want to rely on treatment, the qualitative interviews (Study 2) indicated that there was an

overwhelming need for ED treatment. Men reported being able to enjoy their sex life as important and something which encouraged the use of treatment for the condition. There was a high prevalence of belief statements across interviews which related to the intention to use treatment if sex was thought to be likely. The importance of the necessity for ED treatment was underlined in study 3, where according to regression analysis the BMQ *necessity* domain, independently, significantly predicted the number of sexual attempts in the last 4 weeks. It is important to highlight that in addition, the BMQ *necessity* domain was significantly associated with both adherence and persistence and the BMQ *concerns* domain was significantly associated with persistence using univariate analysis. A higher level of concern with regards to treatment was associated with increased persistence, according to the univariate analysis (see section 6.8.3). Therefore, the BMQ domains were consistently indicated as having a relationship with persistence, adherence and most strongly with respect to the frequency of sexual activity. Therefore, ED treatment like other treatments involves a cost–benefit analysis which relates to beliefs about the necessity of treatment for improving or maintaining health, weighed against concerns about possible adverse effects which ultimately impacts adherence behaviour (Horne & Weinman, 1999).

Summary

This PhD thesis employed a mixed-methods approach, specifically an exploratory sequential design (Creswell et al, 2011) which is considered appropriate for exploring a given phenomenon (i.e. barriers and enablers to ED treatment utilisation) qualitatively and then subsequently expanding on the findings using quantitative methods (Creswell & Creswell, 2017). The research as a whole, drew on the MRC's framework for the design and evaluation of complex interventions and includes: a systematic review of the literature (Study 1), a qualitative interview study to explore patients' experience of using treatment for ED and finally, a quantitative study

(Study 3), in which men's beliefs about both their treatment and their condition were explored in a cross-sectional questionnaire study.

The results of each of the three studies incorporated into this PhD thesis indicated a different emphasis with respect to the barriers and enablers they indicated as being salient with regard to ED treatment utilisation. However, there were also similarities which emerged from each component of this thesis.

There were a number of factors that were evident in the systematic review (Study 1) and the qualitative interviews (Study 2) which were considered important factors and were expected to emerge from the quantitative study (Study 3) and did not. The systematic review (Study 1) indicated that the two most frequently reported factors associated with the discontinuation of ED treatment across the 45 included studies, were treatment side-effects and treatment ineffectiveness. For example, treatment ineffectiveness was the most predominant clinical factor associated with discontinuation across all treatment modalities. The pervasiveness of both side-effects and treatment ineffectiveness was also evident in men's experiences of treatment as indicated by the qualitative interviews carried out in Study 2. However, when this was explored in the quantitative cross-sectional study (Study 3), neither side-effects or treatment ineffectiveness were significantly related to any measure of treatment utilisation. In a similar vein, the cost of treatment was widely reported as being associated with increased treatment discontinuation according to the systematic review (Study 1) which was also evident in the qualitative interviews carried out in Study 2. However, the cost of treatment, when explored quantitatively (Study 3), was not indicated as being significantly associated with measures of treatment utilisation.

However, there were several factors that were not evident in previous research i.e. research included in the systematic review (Study 1). There were several factors to emerge from both the qualitative interviews (Study 2) and the quantitative cross-sectional study (Study 3) which were considered novel findings of this PhD thesis. These include, men's perceptions of treatment necessity and treatment concerns, the negative impact of ED treatment on men's perception of masculinity as well as men's perceptions with regards to the underlying cause of their ED. All of these factors emerged from the qualitative interviews (Study 2) and were subsequently explored in the quantitative cross-sectional study (Study 3), in which it was indicated that perceiving ED treatment as necessary was associated with a significantly higher number of sexual attempts. Study 3 also indicated that where men perceived ED treatment as having a negative impact on their sense of masculinity, a significantly higher rate of treatment discontinuation was indicated. In addition, men who perceived the cause of their ED to be physiological in origin, reported significantly higher rates of persistence. Therefore, these factors were considered novel findings and constitute potentially important factors to be explored in subsequent future research. The use of a mixed methods approach i.e. the use of both qualitative and quantitative methods may in part be responsible for the differing emphases each component of the study put on the barriers and enablers to ED treatment. This will be explored in more detail in the following section.

7.3 Conceptual, Methodological and Theoretical Implications

7.3.1 Mixed Methods Approach

Mixed-methods design is described as combining the strengths of both qualitative and quantitative research for addressing a given research question (Creswell et al, 2011). Specifically, this research utilised exploratory sequential design (Creswell et al, 2011), which was considered the most suitable mixed-methods approach to address the research questions posed in this PhD thesis. This was for several reasons which are considered below.

Althof (2002a) suggests that getting men to make use of ED treatment regularly in sexual intercourse is complex. In addition, prior to this PhD thesis, there had been no synthesis of existing research focused on barriers and enablers to ED treatment utilisation. The Systematic Review (Study 1) constitutes the first study to synthesise such research. As a result, prior to the research which constitutes this PhD, there was a lack of clarity with regards to what is known about this particular complex behaviour i.e. what barriers and enablers influence ED treatment utilisation. In addition, the systematic review (Study 1), indicated that none of the included studies utilised theory to underpin their research.

MRC guidelines, aim to ensure that an evidence-base exists for interventions of high quality and effectiveness (Campbell et al, 2000; Campbell et al, 2007). Therefore, prior to intervention design, an important step involves carrying out an exploratory study to gain a greater perspective and understanding of the potential theories, as well as the surrounding issues influencing an intervention of this nature (Campbell et al, 2007). Therefore, a qualitative study, underpinned by theory (Study 2) was deemed necessary and enabled an in-depth exploration of the research area and subsequently the identification of factors that have the potential to influence the target behaviour i.e. ED treatment utilisation, including those previously unknown (Creswell et al, 2011).

It was evident from the Systematic Review (Study 1) and exploration of the wider literature that there was no available suitable measure of barriers and enablers to ED treatment utilisation. Exploratory sequential design, a mixed methods approach, is often considered the methodology of choice when there is a need to develop a measure in the absence of any pre-existing ones. This was achieved in line with Creswell & Clark's (2017) three-phase approach, which led to the

development of the BEED-TQ. The three phases involve qualitative data being gathered and analysed (Phase 1). Using the qualitative analysis to develop an adequate measure (Phase 2) and finally, the measure being administered to a relevant sample of a population (Phase 3).

The final phase of the research contained in this PhD thesis was a quantitative cross-sectional study (Study 3). Exploratory sequential design is described as being beneficial for exploring a given phenomenon qualitatively and then subsequently expanding on the findings using quantitative methods (Creswell & Creswell, 2017). As previously mentioned, the findings of the qualitative study (Study 2) were used to design a questionnaire (BEED-TQ) which then enabled further exploration of the findings in the quantitative study (Study 3). This process enabled the measurement of the pervasiveness (Pasick et al., 2009) of barriers and enablers to ED treatment utilisation identified in the qualitative study (Study 2). For example, the results of the qualitative study (Study 2) indicated a novel finding that was not evident in the systematic review (Study 1). This novel finding was that ED treatment has a potential negative impact on men's sense of masculinity. Subsequently, this finding was then explored quantitatively in Study 3, where it was indicated that the negative impact of ED treatment on men's sense of masculinity was associated with a significant increase in treatment discontinuation.

A potential limitation of exploratory sequential design, is referred to as the process of 'quantitizing', defined as 'the process of assigning numerical values (nominal or ordinal) to data conceived as not numerical' (Sandelowski et al., 2009) or 'transforming qualitative data into numerical format' (Collingridge, 2013). This relates to the subsequent development of the BEED-TQ which was based on the qualitative study (Study 2) and subsequently used to explore the barriers and enablers to ED treatment utilisation in the quantitative study (Study 3). Therefore, the BEED-TQ was developed as part of this process which involved capturing the various

qualitative nuances from Study 2 on a subsequent questionnaire scale i.e. the BEED-TQ. However, it has been highlighted that quantitizing comes at a cost. For example, it has been criticised for trying to count the uncountable (Nzabonimpa, 2018) and potentially reducing the multidimensionality of qualitative data (Driscoll et al., 2007). In addition, it has been highlighted that the process undermines the rationale for conducting qualitative research by underrepresenting contextual and cultural meaning (Kerrigan, 2014). However, both quantitative and qualitative methods have been described as entailing each other (Sandelowski et al, 2009), for example it is suggested that, based on existing evidence, there is no way in which quantitizing can be carried out in a way that does not involve a qualitative thumbprint (Chang et al., 2009). Nzabonimpa (2018) states that in mixed methods research, both qualitative and quantitative research are necessarily brought together to understand what is expressed qualitatively and whether it converges with what is expressed quantitatively. Therefore, a mixed methods approach is necessary in order to establish a full picture of a given phenomenon, in this case, the barriers and enablers to ED treatment utilisation.

7.3.2 The Inclusion of Theory

One of the important contributions of study 1, was the finding that none of the studies included in the systematic review had used any psychological theory to underpin their research, as well as the finding that none of the studies had utilised a validated measures of treatment utilisation or indeed barriers to ED treatment utilisation. This brings into the question the overall quality of the studies which were assessed in a systematic way, through the use of a measure of study quality; the QualSyst assessment tool (Kmet et al, 2004). Total percentage scores for each study were classified using the following cut off points; studies that scored <50% were considered limited in terms of quality, those that scored 50–70% were considered adequate; 71–80% were considered good and a score of >80% was considered strong (Greenwood & Smith, 2015; Johnson et al, 2016). In terms of the n=45 studies which were included in the systematic review

(Study 1), 9% were considered good, 31% strong, however 60% were classified as either having only limited or adequate quality, which needs to be considered when interpreting the findings from the review. The systematic review also indicated that none of the studies had used a validated measure of treatment utilisation or barriers to treatment utilisation. As a result, this thesis included an extensive review of the literature, to establish a suitable measure of treatment utilisation. However, on the basis of this search it was evident that a suitable, validated measure of treatment utilisation or barriers and enablers of ED treatment utilisation did not exist. The PAQ, although not a validated measure of treatment utilisation, was designed specifically for use with patients using treatment for ED. The use of the PAQ will be considered below.

7.3.3 Questionnaire Development

The first step in ascertaining a suitable measure of treatment utilisation was the consideration of the wider literature. When selecting an appropriate measure of ED treatment utilisation, it was essential that the measure be capable of measuring not only, adherence, persistence and discontinuation, in order that utilisation rates can be compared to the wider literature, but also be capable of measuring treatment utilisation to PRN treatments. It is generally accepted that a measure of adherence needs to be, valid, reliable, and sensitive to change (Vermeire et al, 2001; Vitolins et al, 2000). Although, there were numerous measures available and many validated measures, none had the individual attributes suitable for the goals of the study i.e. a measure that can cope with on demand medications, capable of measuring, adherence, persistence and discontinuation, as well as prescribed ED treatments. These were considered essential in order that findings could be compared to that of previous research, i.e. the studies included in the systematic review (Study 1). Although valid measures are advised, it is also considered important that when selecting a measure it is suitable with regards to its intended use (Lam & Fresco, 2015). The literature search involved an extensive review of a total of 57 measures, including

two systematic reviews of self-report adherence measures (Garfield et al, 2011 & Nguyen et al, 2014). Based on a broad literature review of measures, it was evident that the most suitable measure for the purposes of the research was the PAQ.

As previously mentioned, the systematic review (Study 1) also indicated that none of the included studies used a validated measure of barriers and enablers of ED treatment utilisation. Both the systematic review (study 1) and the qualitative interviews (Study 2), which were based on the TDF, were used as a basis for the development of the BEED-TQ. Therefore, the development of the BEED-TQ followed a systematic process, being developed on the back of a series of qualitative interviews where analysis was carried out using a process of coding, generating specific beliefs and then identifying key domains, a process which has been utilised by other research utilising the TDF (Atkins et al, 2017). Previous studies have found good construct validity when developing questionnaires based on the TDF (e.g. Huijg et al, 2014), which confirm the viability of using the framework for the construction of theory-based questionnaires. The BEED-TQ, although based on psychological theory, has not been statistically validated and therefore this exists as a weakness of the questionnaire and its use in this study. However, the questionnaire was considered to have face validity and through the use of PPI, the evaluation of the appearance of the questionnaire in terms of feasibility, readability, clarity, language, consistency of style and formatting was assessed (Taherdoost, 2016).

7.3.4 The Integration of Theory

One of the most important findings of the systematic review (Study 1), was that none of the included studies employed psychological theory to guide their investigations. This was surprising given the work of e.g. Althof (2002a) who highlights the importance of psychological factors and their potential to contribute to sub-optimal ED treatment utilisation. Therefore, the potential to improve upon previous research was the driving force behind the research contained in this

thesis. Research promotes the use of theory and this notion is supported by research which indicates that, on average, interventions in general have a statistically small but significant effect on health-related behaviour ($d+ = 0.16$, 95% CI 0.09 to 0.23), however, interventions which utilise more extensive use of theory are reported as being associated with increased effect size ($P = .049$) (Webb, 2010). The MRCs guidelines suggested that the precursor to designing an intervention of high quality and effectiveness, involves the selection of a theory upon which to base the intervention (Campbell et al, 2000; Craig et al, 2008). The TDF was selected as an appropriate framework to investigate the ED treatment utilisation which will be discussed below.

7.3.5 The TDF and the SRM

Campbell et al, (2007) suggest that it is necessary to carry out an exploratory study in order to gain a greater perspective and understanding of what relevant theories exist and are relevant to a given research study. To the authors' knowledge, the qualitative research (Study 2), was the first study focussed on ED treatment utilisation to use a theoretical underpinning to explore what barriers and enablers to ED treatment exist in relation to using treatment for ED. Building on the findings of the systematic review (Study 1), the interview schedule used a combination of the original (Michie et al, 2005) and the refined version of the TDF (Cane et al, 2012). In addition, it was clear from the analysis of the semi-structured interviews that important themes existed outside of the TDF domains, which were strongly associated with illness perceptions and subsequently the SRM (Leventhal et al, 1992).

The advantage of selecting the TDF as the framework to underpin this research was firstly that, based on the systematic review (Study 1), no prior research had employed a theoretical framework for exploring ED treatment utilisation. Secondly, individual theories or models are potentially limited to the contexts in which they were developed (Ashing-Giwa, 1999). Instead,

the current study took the approach that there is an evidential need for theoretical integration (Stewart & Klein, 2016) which has previously been highlighted in chapter 4 (see section 4.5). Therefore, it was decided that in line with the suggestion of Francis et al (2009), the TDF would be the most appropriate framework to underpin the study, given that the TDF offers a more inclusive approach involving a comprehensive set of theoretical construct domains.

As mentioned above, there were certain belief statements that emerged from the qualitative interviews (Study 2), which were considered as relating to domains of the SRM and therefore related to illness representations with respect to ED. Although one of the advantages that the TDF offers, is a broad set of relevant domains which were utilised to explore barriers and enablers to ED treatment utilisation, it was limited in this instance by omitting other potentially important factors. Additionally, in relation to the 15 TDF domains included for exploring ED treatment barriers and enablers in the qualitative interviews (Study 2), only 12 contained relevant beliefs statements. There were no belief statements which were elicited from the domain *nature of the behaviour*, defined as any behaviour, that is considered a habit, routine, automatic or a direct experience or past behaviour (Atkins et al, 2017). This suggests that perhaps due to ED treatment utilisation being related to a behaviour that involves two people i.e. a complex interaction of, for example; environmental, social, behavioural and clinical factors. Therefore, forming a habit in relation to treatment utilisation may be unlikely.

In addition, *reinforcement*, defined as factors which increase the probability of a particular response via a dependent relationship, and the domain *skills*, considered an ability or proficiency acquired through practice, both did not consist of any belief statements that were salient with regards to barriers and enablers to ED treatment utilisation. Removing TDF domains which are considered less relevant to a target behaviour, is common place in studies utilising the TDF

(Amemori et al, 2011; Taylor et al, 2013) and is recommended in guidance on the use of the TDF (Michie et al, 2005; Atkins et al, 2017). However, the TDF has been criticized for being overly deductive when adhering rigidly to TDF utilisation guidance, which can result in potentially overlooking important factors (McGowan et al, 2020). In a systematic review of TDF-based qualitative studies it was indicated that the rigid application of the existing guidance provided by Michie et al (2005) and Atkins et al (2017) has the potential to be restrictive, particularly with reference to studies which are explorative in nature (McGowen, 2020), which was the approach this thesis adopted. McGowen et al (2020) suggest that this could be improved, for example, by using TDF questions to influence the topic guide, rather than as a rigid structure. The authors also suggest this would potentially give participants the freedom to offer their perspectives in a less constrained way and subsequently enable a broader, deeper understanding of participants' perspectives with respect to the topic being explored.

7.3.6 Adherence, Persistence and Discontinuation; Measuring ED Treatment Utilisation

The research that constitutes this thesis, makes a significant contribution to Health Psychology theory in a number of ways. Althof (2002a) suggested that;

'...to be effective in enabling patients to achieve their goal of making love, clinicians' need a means of assessing what the man or couple requires to attain their goal. Success can no longer be defined as a rapid, sustained genital response...'

The essence of what Althof was calling for, was for clinicians to place more of an emphasis on the biopsychosocial aspects involved in ED treatment utilisation. The research carried out as part of this thesis aimed at exploring ED treatment utilisation from a Health Psychology perspective,

whereby it was possible to focus a biopsychosocial lens on the problem of ED treatment adherence.

This research has significant implications for the conceptualisation of adherence behaviour with respect to ED treatment utilisation. An important finding of the systematic review related to the wide range of operational definitions employed by studies to describe both adherence and persistence as well as discontinuation. There are a number of reasons why standard terminology in adherence research is not suitable with respect to ED treatment utilisation. We can consider the following definitions which were referred to in Chapter 2 (See section 2.3.1);

Adherence is referred to as: *‘the extent to which a person’s behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider’* (WHO, 2003).

Persistence is referred to as: *‘the extent to which a patient continues to follow treatment advice without a break and without stopping’* (Cramer, 2008).

Discontinuation is referred to as: *“the failure to enter a treatment programme, premature termination of therapy and incomplete implementation of instructions (including prescriptions)”* (Blackwell, 1976)

All of the above terms either explicitly refer to ‘a patient’ or ‘a person’ or imply that it is an individual that is responsible for treatment utilisation. A key finding of this thesis is the notion that treatment utilisation with respect to ED rests on complex foundations. Referring to an individual, in this case the man, or the ‘patient’ (as outlined above) in abstract, is too limited in

scope to be useful when considering utilisation of treatment in this population. Based on the analyses of studies 1, 2 and 3 there is important evidence which establishes that decisions around treatment use, relates to men as well as their partner. A recommendation which is based on the above premise is a call for the use of more inclusive terminology, which has the capacity to encompass the joint decision making of both the man and his partner that is likely to be involved in the utilisation of ED treatment. This has the potential to position conversations as well as consultations between men, their partner and the health care service in a more accurate and inclusive manor. The importance of including a man's partner in the process from the offset, with regards to improving the utilisation of ED treatment, is highlighted by the systematic review, which included research that indicated where partners were aware of and involved in the use of treatment, significantly higher rates of treatment utilisation were reported (Carvalho et al, 2014).

It is evident from this research that treatment adherence or persistence is not synonymous with using treatment for sexual intimacy. For example, it was found that some participants were sexually active but were not using treatment, conversely there were participants who reported that they were not sexually active, however, they were using treatment. In addition, the extent to which treatment use, maps onto frequency of sexual attempts, brings into question the capacity for measures of treatment utilisation to provide a picture of the more complex nature of treatment use which involves the man, his partner and their relationship, as well as aspects of the condition itself. This phenomenon can be considered in relation to what has been termed the 'intention-behaviour gap' i.e. whether or not intentions are translated into action. The intention-behaviour gap is suggested as reflecting the black-box nature of the underlying psychological process that leads from intention to action (Sniedhotta et al, 2005). Therefore, it is

conceivable that a man may well have the intention to use ED treatment for sexual intercourse, however, it follows that the man's partner would also need to share a similar intention if treatment is to be used. Therefore, any objective measurement of treatment utilisation is limited if it omits an understanding of the unique aspects of a couple's sexual relationship as well as the impact of the condition itself. Althof (2002b) suggest that in order for ED to be treated successfully, clinicians need a way of assessing what the couple requires to attain their goal. Therefore, a recommendation based on the results of this thesis is that any measure of ED treatment utilisation needs to consider the goals of the couple using treatment. Objective measures of treatment utilisation are potentially limited in this respect. It is important for a measure to be more subjective with a consideration of a couple's goals in relation to their sexual relationship. Therefore, successful treatment utilisation can be considered the extent to which treatment supports a couple to attain the goals with respect to their intimate relationship.

7.4 Strengths and Limitations

The research studies which constitute this thesis, i.e. study 1, 2 and 3, have a number of limitations. These have been discussed at the end of each relevant chapter, however, the following section will bring together the main limitations of the research contained within this thesis.

As previously mentioned, the systematic review employed the QualSyst assessment tool (Kmet et al, 2004) which determined that the majority of studies i.e. 60%, were classified as either having adequate or limited quality. This was reflective of the overall lack of validated measures of treatment utilisation, as well as barriers and enablers to treatment utilisation. This is important given that the systematic review (Study 1), was the foundation for the subsequent studies (Study2 and 3). The results to the systematic review, in conjunction with the TDF, guided

the subsequent development of the semi-structured interview guide which was used for the qualitative interviews (Study 2). Therefore, a limitation runs through the research which relates to the limitations in the overall study quality included in the initial systematic review. However, it must be highlighted that all studies included in the systematic review met the inclusion criteria and contributed to findings of the review. The absence of theory to guide previous research was a guiding principle with respect to the aims of the research contained in this thesis.

The qualitative interviews (Study 2) offered, to the authors' knowledge, the first exploration of barriers and enablers to ED treatment utilisation using a theoretically informed approach. Qualitative interviews were carried out face-to-face and over the telephone. As a result there may have been differences with regards to the extent to which participants felt comfortable talking about such a sensitive subject. Interviews via telephone have been criticised in relation to potential distractive elements in a participant's environment (McCoyd & Kerson, 2006; Opdenakker, 2006), the absence of visual cues (Garbett & McCormack, 2001) which may lead to other problems such as a reduction in disclosure of sensitive information and the communication of emotions (Groves, 1990; Henson et al, 1978; Moum, 1998). In addition, it is suggested they may increase social distance (Aquilino, 1994; Groves, 1990) and a reduction of "feedback cues" (Henson et al, 1978, p. 128). However, the literature is not consistent and indicates both increases and decreases in socially desirable responses (Groves, 1990; Henson et al, 1978; Moum, 1998) as well as rapport (Smith, 2005). In addition, research has shown that in the absence of being in the interviewer's presence, participants may feel more relaxed and able to disclose sensitive information (Chapple, 1999; Kavanaugh & Ayres, 1998; Opdenakker, 2006) and therefore telephone interviews contain several features that render it particularly suitable for qualitative research (Hopper, 1992). It is possible that both face-to-face and telephone interviews may be preferable based on individual preference. Participants were offered both

formats and the interviewer was happy to accommodate participants regardless of which medium they used. Therefore, based on the resources available, participants were able to choose when and where the interview took place and importantly, they were made aware that participation was not obligatory and that they could rescind their participation at any point should they wish.

The qualitative interviews involved in study 2 depend heavily on the individual skills of the researcher and are potentially influenced by the researcher's personal biases and idiosyncrasies. Interviews can pose many challenges for researchers including issues related to maintaining boundaries (Dickson-Swift et al, 2006), developing rapport (Liamputtong & Ezzy, 2005), reflexivity (Ellingson, 1998; Kiesinger, 1998) and managing emotions (Payne & Westwell, 1994; Rager, 2005). In order to ensure that personal biases and idiosyncrasies are accounted for, firstly, the interview schedule was developed using the TDF (Michie et al, 2005; Cane et al, 2012), which has been successfully used to explore a variety of chronic conditions. In addition, the interview schedule was developed in conjunction with experienced clinicians, psychologists as well as expert patients. Secondly, qualitative interviews were analysed using a process previously used to analyse qualitative data derived from the TDF (Patey et al, 2012; Islam et al, 2012). This involved a multidisciplinary approach where the research team worked collaboratively on the analysis of the interviews which established reflexivity within the study and reduced bias.

It was important that the measure of treatment utilisation employed for the quantitative study (Study 3) was appropriate for use within an ED population and suitable for measuring treatment that is predominantly taken on demand. As a result, the pursuit of a validated measure of ED treatment utilisation had to be weighed against the suitability of the measure for the task at

hand. Although it was not validated, the PAQ was selected as the measure for ED treatment utilisation. The PAQ is a self-report measure, and self-report measures are regarded as having reasonable predictive power (Lam & Fresco, 2015). However, they are limited in some respects. For example, self-report measures are reported as likely to produce an overestimation of adherence (Ziller et al, 2011), due to the notion that they are subject to measurement bias such as social desirability, recall bias, and response bias (Shi et al, 2010). Other potential methods include, for example, patient interviews which are preferred for low literacy populations, pill count such as MEMS, an objective measure requiring both staff and time to administer and pharmacy refill measures which are more favourable for large research populations. Lam & Fresco, (2015) suggest that despite more than four decades of research, focussed on how to properly measure and quantify medication adherence, no one method has been considered the gold standard. Therefore, with the patient population in mind, the environment under which the questionnaire was administered and the resources available for this research, it was most advantageous to employ a self-report measure, which are considered as being particularly useful in a busy, resource-limited clinical setting (Lam & Fresco, 2015).

7.5 Implications for Research and Practice

It emerged from this research that the lens through which ED is viewed could be improved in terms of the terminology describing ED treatment utilisation. The use of terms such as adherence and persistence are reductive when considering ED treatment utilisation, which involves a complex relationship between the man and his partner, their relationship as well as the nature of the condition itself. The importance of the terminology used is essential, as it can determine the focus of a given conversation relating to ED and its treatment. Therefore, as a result of this research it is advised that in both research and in clinical practice, the implications of the use of terminology is considered and that it is a goal of future research, to craft

terminology suitable for describing the use of treatment, that is dependent on both the man and his partner. This in turn, would begin to incorporate men's partners into the conversation about ED treatment which may potentially increase treatment utilisation, as demonstrated in previous research (Carvalho et al, 2014). The expansion of terminology that incorporates both the man and his partner, rather than only the individual could potentially have important implication with regards to how we measure the phenomenon of ED treatment utilisation.

It is a recommendation of this research that for any measure of ED treatment to be meaningful, it must include the goals of the couple using treatment, as successful treatment utilisation will involve parameters that are governed by the complex relationship between a man and his partner. Therefore, incorporating a couple's aims with regards to the frequency of sexual activity as a baseline against which treatment utilisation could be compared would be a more accurate way of measuring successful utilisation. As a result the future development of a meaningful measure of ED treatment utilisation should include this subjective element to be considered meaningful.

The design of the quantitative study was cross-sectional. The advantages of this design have been described as relatively inexpensive, quick and easy to administer, useful for generating and clarifying hypotheses as well as piloting new measures and laying the groundwork for decisions about future follow-up studies (Kraemer, 1994). However, cross-sectional designs have been criticised for a variety of reasons. For example, the use of a survey at one point in time is not sufficient to establish a cause and effect relationship (Price & Murnan, 2004). By their nature they are not capable of answering questions about the stability of a characteristic or process over time (Schmidt & Teti, 2005, Miller, 1998). Therefore, the interaction of the variables measured in study 3 is not known with regards to their impact on treatment utilisation over

time. Therefore, it is a suggestion for future research to investigate the problem of ED treatment utilisation using longitudinal study design. Such a design is able to consider both inter and intra-individual change as well as consider e.g. developmental sequences, and co-occurring social and environmental change which in turn can enable the development of theoretical and explanatory accounts of evidenced change (McCall, 1977).

There are several implications for clinical practice with respect to the findings of the research contained within this thesis. The research has highlighted a number of important factors related to ED treatment utilisation that can be considered as both psychological and cognitive, both of which are considered amenable to change (Horne et al, 2005). Participants involved in the qualitative interviews (Study 2) indicated the importance of receiving adequate instructions from their HCP in relation to how to use ED treatment correctly. Therefore, consultations provide a potentially important opportunity to explore certain issues with patients. The importance of including both the man and his partner in consultations is recommended in order to ensure that there is communication not only with the man but also with the person the man is going to engage in sexual activity with. This would ensure that there is an understanding and consideration of the context in which sexual activity takes place and subsequently the nature of a couple's intimate relationship as well as what their goals are with respect to their sexual activity, which would then enable consideration of which treatment would be beneficial on the basis of these insights.

Research which has used the TDF to explore barriers and enablers to adherence has resulted in the development of behaviour change interventions to improve treatment adherence to, for example, bronchiectasis treatment (McCullough et al, 2015). Therefore, the research contained within this thesis has the potential to lay the groundwork for future behaviour change

interventions aimed at supporting men to achieve successful ED treatment utilisation. The purpose of using the MRC's framework for the design and evaluation of complex interventions, is that the framework enables research to build on each stage of intervention development, the result of which increases the evidence regarding effectiveness (Campbell, 2007).

7.6 Overall Conclusions

The research contained in this thesis indicated that approximately one third of men, regardless of treatment modality, discontinue ED treatment. Both PDE5Is and ICIs indicated the lowest level of treatment discontinuation. In terms of adherence, overall, men had used under half of the treatment they had been prescribed, but more PDE5Is than other treatments. Although men, on average, had not used treatment for around 3.5 weeks, approximately 2 sexual attempts had been made in the same period.

There were several important factors associated with ED treatment utilisation. Most prominently, the negative impact treatment has on men's sense of masculinity, which was significantly related to increased treatment discontinuation, as well as perceiving the condition as being caused by physiological problems, which was significantly associated with increased persistence. In addition, the perception of increased treatment necessity related to a significantly higher frequency of sexual attempts. It is suggested that such beliefs may be amenable to change, which if addressed may contain the possibility of improving ED treatment utilisation.

Future research would be advised to craft appropriate terminology to describe and discuss treatment utilisation which involves both a man and his partner, as well as the development of a measure of ED treatment utilisation which involves the goals of the couple, against which successful treatment for ED can be assessed. Finally, it would be advantageous for future

research to employ a longitudinal study design to ascertain the relationship between barriers and enablers to ED treatment utilisation over time. This thesis represents the first step in the use of psychological theory in the investigation of ED treatment utilisation and hence the first step to developing a psychological intervention to support ED treatment utilisation.

8 References

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9 Appendices

Appendix 1: PRISMA 27 item check list

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Adapted from Moher et al (2009)

Appendix 2. A measurement tool to assess systematic reviews (AMSTAR)

1. Was a <i>a priori</i> design provided? The research question and inclusion criteria should be established before the conduct of the review.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
7. Was the scientific quality of the included studies assessed and documented? A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I ²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
11. Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable

Appendix 3: Detailed Search Terms

General Terms		
Erectile Dysfunction	Adherence	Treatment for ED
Erectile Dysfunction*	Medication AND (adher* OR -use OR taking)	PDE5 Inhibitor*
Impoten*	(complan* OR non-complan*)	Phosphodiesterase type 5 inhibitor*
penis erection*	(adhere* OR non-adhere*)	Sildenafil Citrate (Viagra)
male erectile disorder*	(persistence OR non-persistence)	Tadalafil (Cialis)
Sexual dysfunction*	Patient complian*	Vardenafil (Levitra)
Male reproductive disorder*	Non-fulfilment	PDE5I
Sex disorder*	Drug-use	Uprima
Penile Erection*	Mean possession ratio	Intracavernosal injection*
Erection*	Medication possession ratio	Alprostadil pellet
	Treatment refusal	Vacuum device
	Uptake	Viagra
	adheren*	Cialis
	non?adheren*	Levitra
	persist* or non?persist*	penile prosthesis
	complia*	Psychosexual counselling
	non?complan*	Apomorphine hydrochloride
	Drug utilization	Medicated urethral system for erections (MUSE)
	Health rationing	Viridal duo
		Caverject
		Caverject dual chamber
		urethral suppositories

MeSH Terms		
Embase 1974 to 2015 July		
Erectile Dysfunction	Adherence	Treatment for ED
Erectile dysfunction	Medication compliance	Phosphodiesterase V inhibitor
Impotence	Patient compliance	Sildenafil
Penis erection	Compliance	Vardenafil
Sexual dysfunction	Drug utilization	Apomorphine
	Drug use	intracavernous drug administration
	Treatment refusal	prostaglandin E1
		Tadalafil
		penis prosthesis
		prostaglandin E1
Ovid MEDLINE(R) 1946 to 2015 July		
Sexual dysfunction, Physiological	Medication Adherence	Alprostadil
Sexual dysfunction, Psychological	Patient Compliance	penile prosthesis
Sexual dysfunctions, Psychological	Compliance	Apomorphine
Penis	Treatment Refusal	
Penile Erection	Drug Utilisation	
AMED (Allied and Complementary Medicine) 1985 to July 2015		
Sex disorders male	Patient compliance	Enzyme inhibitors
Impotence	Treatment refusal	Sex Counselling
Sexual dysfunctions	Patient acceptance of health care	Phosphodiesterase 5 Inhibitors
Penis		Penile prosthesis
Genital diseases, male		Apomorphine
		Alprostadil
HMIC Health Management Information Consortium 1979 to July 2015		
Male reproductive disorders	Drug compliance	
Impotence	Patient compliance	
Penis	Drug Consumption	
Sex disorders	Drug administration	
	Patient non-compliance	
	Patient participation	
	Patient response to treatment	
	Decision making	
	Health rationing	

	Patient consent to treatment	
	Cochrane Central Register of Controlled Trials	
Erectile dysfunction	Medication adherence	Phosphodiesterase 5 Inhibitors
Sexual dysfunction, Psychological	Compliance	Penile prosthesis
Sexual dysfunction, Physiological	Patient compliance	Apomorphine
Penis	Treatment refusal	Alprostadil
	Health Technology Assessment 2nd Quarter 2015	
Impotence	Patient compliance	Phosphodiesterase Inhibitors
Sexual dysfunction, physiological	Treatment Outcome	Penile prosthesis
Penile Erection	Drug utilization	Alprostadil
	Decision making	
	Health care rationing	
	CINAHL plus with full text®	
Impotence	Medication compliance	Phosphodiesterase Inhibitors
Sexual dysfunction, Male	Patient compliance	Sildenafil
Penile erection	Treatment refusal	Tadalafil
Penile prosthesis	Drug utilization	Vardenafil Hydrochloride
	Decision making, patient	penile prosthesis
		Couple counselling
		Sexual counselling
	PsychARTICLES®	
Erectile Dysfunction	Treatment compliance	Phosphodiesterase
Erection (penis)	Treatment refusal	Sildenafil
Male genital disorders	Decision making	Apomorphine
	PsychINFO®	
Erectile dysfunction	Treatment compliance	Phosphodiesterase
Erection (penis)	Treatment refusal	Apomorphine
Male genital disorder	Decision making	Sildenafil

Appendix 4: Data extraction sheet

General Information	Researcher:
	Date of extraction:
Citation:	Record Number:
	Author:
	Year:
	Article Title:
	Country of origin:
	Journal:
Methods	Aim/objectives of the study:
	Study design: ☐ Randomized controlled trial (RCT) (including cluster and cross-over trials) ☐ Cross-sectional study ☐ Prospective cohort study ☐ Retrospective cohort study ☐ Observational study ☐ Qualitative study ☐ Other.....
	Inclusion/exclusion criteria:
	Power calculation: ☐ Yes ☐ No Sample size:
	Recruitment procedures:
	ED treatment ☐ PDE5I's ☐ intracavernosal vasoactive drug injection therapy (ICI) ☐ intraurethral suppository e.g. URETHERAL SUPPOSITORY ☐ vacuum devices ☐ pelvic floor retraining ☐ penile implant

	Recommended dose/regimen:
	Materials/measures: Adherence/persistence measure (e.g. self-report): Validated measure: • Yes • No Barriers: Measure? Validated?
	Length of follow-up (if applicable):
Results	
Participants	Number of participants:
	Age: mean (SD)
	Ethnicity:
	SES (occupation/income/education):
	Relationship status:
	Comorbidities: ☐ Coronary heart disease ☐ Hypotension ☐ Other CVD..... ☐ Hypercholesterolemia ☐ Diabetes ☐ Anxiety/depression ☐ Other.....
	ED diagnosis (severity): ☐ Normal ☐ Mild ☐ Mild/moderate ☐ Moderate ☐ Severe ☐ Not specified
Attrition	
Rates of adherence/persistence	

Barriers to treatment adherence/persistence	Reported barriers: ☐ Clinical/treatment related (e.g. side effects) ☐ Demographic (e.g. education) ☐ Psychosocial (e.g. relationship) ☐ Other..... Specify barrier:
Relationship between adherence/persistence and barrier:	
Statistical analyses:	
Reviewers comments:	

Appendix 5: QualSyst - quality assessment tool

Checklist for assessing the quality of quantitative studies

Criteria	Yes (2)	Partial (1)	No (0)	N/A
1 Question/objective sufficiently described?				Cannot answer N/A
2 Study design evident and appropriate?				Cannot answer N/A
3 Method of subject/comparison group selection or source of information/input variables described and appropriate?				
4 Subject (and comparison group, if applicable) characteristics sufficiently described?				Cannot answer N/A
5 If interventional and random allocation was possible, was it described?				
6 If interventional and blinding of investigators was possible, was it reported?				
7 If interventional and blinding of subjects was possible, was it reported?				
8 Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias - Means of assessment reported?				
9 Sample size appropriate?				
10 Analytic methods described/justified and appropriate?				
11 Some estimate of variance is reported for the main results?				
12 Controlled for confounding?				
13 Results reported in sufficient detail?				Cannot answer N/A
14 Conclusions supported by results?				Cannot answer N/A

Check list for assessing the quality of qualitative studies

Criteria	Yes (2)	Partial (1)	No (0)
1 Question/objective sufficiently described?			
2 Study design evident and appropriate?			
3 Context for the study clear?			
4 Connection to a theoretical framework/wider body of knowledge?			

Criteria	Yes (2)	Partial (1)	No (0)
5 Sampling strategy described, relevant and justified?			
6 Data collection methods clearly described and systematic?			
7 Data analysis clearly described and systematic?			
8 Use of verification procedure(s) to establish credibility?		Cannot answer N/A	
9 Conclusions supported by the results?			
10 Reflexivity of the account?			

Note: Qualsyst Quality Assessment Tool (Kmet et al, 2004)



Men's beliefs about treatment for erectile dysfunction—what influences treatment use? A systematic review

Paul Williams¹ · Hayley McBain¹ · Aliya Amirova¹ · Stanton Newman¹ · Kathleen Mulligan^{1,2}

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Abstract

Successful treatment of erectile dysfunction (ED) is associated with improvements in quality of life; however, treatment utilisation is sub-optimal. The aim of this systematic review was to identify the rates of ED treatment utilisation and the barriers and enablers men experience when using treatment. We searched: MEDLINE[®], Embase, the Cochrane library; AMED; HMC; HTA; CINAHL; PsychARTICLES; PsychINFO up to August 2018. Data on rates of treatment utilisation and barriers and enablers of utilisation were extracted and summarised. Fifty studies were included. Discontinuation rates ranged from 4.4 to 76% for phosphodiesterase type 5 inhibitors, 18.6 to 79.9% for intracavernosal injections, and 32 to 69.2% for urethral suppositories. In relation to those with a penile prosthesis, 30% discontinued having sex due to, e.g. device complications, lack of partner or a loss of sexual interest. Most research included in the current review examined barriers to treatment utilisation and therefore focussed on reasons for discontinuing treatment. However, a small number explored factors that men found helpful with regards to treatment utilisation. The most prevalent barriers to utilisation were treatment ineffectiveness, side effects, the quality of men's intimate relationships and treatment costs. With regards to treatment enablers, the most salient finding was that men who reported side effects to a healthcare professionals (HCPs) were significantly less likely to discontinue treatment. There were limitations in methodology in that the studies did not use validated measures of treatment utilisation or barriers and enablers and no study used psychological theory to inform the examination of factors that influenced treatment utilisation. This review identifies a number of influential factors relating to ED treatment utilisation and highlights the importance of men's beliefs with regards to ED and its treatment. Beliefs are potentially modifiable and therefore the findings of this review highlight important considerations for HCPs with regards to supporting men to make better use of treatment.

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and/or maintain a penile erection adequate for sexual performance [1]. Prevalence increases with age affecting ~1–10% of men up to the age of 40 years, 2–9% of

men aged between 40 and 49 years, increasing to 20–40% in those aged 60–69 years and 50–100% in those aged over 70 years [2]. ED can have a negative impact on self-confidence, mood and quality of life [3–9]. Improvements in psychological status, self-esteem and perceived relationship quality can be achieved by improving sexual function through the use of treatment [10–15].

Phosphodiesterase type 5 inhibitors (PDE5Is) are the first-line treatment for ED [16]. Where PDE5Is are ineffective or contraindicated, alternatives such as intracavernous injections (ICI), urethral suppositories (US), vacuum erection devices (VEDs) and penile prosthesis (PP) remain available [17].

PDE5Is are considered safe, effective and tolerable for men with ED [18]. Despite this, adherence to PDE5Is has been described as sub-optimal due to factors such as, side effects, not wanting a sexual schedule dependent on a medication regimen, the delayed response between taking

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SPRINGER NATURE

An exploration of men's experience and use of treatments for erectile dysfunction (ED).

Introduction: Thank you for agreeing to take part in this interview. We are conducting this study to help us understand your experience of treatment for ED and what factors you have found helpful or unhelpful. Some of the questions may appear to be quite similar or obvious to answer but we are trying to understand the topic from different perspectives so bear with me, take your time and answer as frankly as possible. Are you happy to get started?

General Questions

I'd like to start by asking you to tell me about when you first realised that you were experiencing erectile dysfunction (ED).

- When did you first seek treatment?
 - **Prompt: first prescription / main reason for seeking medical help/treatment**
- Are you currently using treatment for ED? If so, what treatment are you currently using?
 - **Prompt: choice in relation to treatment / heard of treatment before**
- Have you previously tried treatment for ED? If yes, were there any problems with your previous prescription?
- What were your expectations in relation to your current treatment?
 - **Prompt: likes and/or dislikes about treatment**

1. NATURE OF THE BEHAVIOUR

How do you currently use your ED treatment?

- **Prompt: usage patterns, needed for every sexual encounter, used exclusively with a partner**

Do you plan your sexual encounters around the treatment?

- **Prompt: daily schedule, time interval for treatment effectiveness, foreplay**

Is there anything that could be done differently by yourself or your partner that could improve the likelihood of using your ED treatment?

- **Prompt: discussion about the treatment, plan time for intimacy**

2. KNOWLEDGE

Do you know how to successfully take your treatment?

- **Prompt: advice from HCPs, take on an empty stomach (PDE5Is), use with stimulation, recommended dosage instructions**

Do you know if there are any side effects/risks of taking your treatment and what to do if you experience them?

- **Prompt: Who to contact in the event of side effects/issues with treatment**

3. SKILLS

Have you worked out any strategies or techniques to help you take your ED treatment?

- **Prompt: Food, delay in treatment onset, stimulation**

4. SOCIAL ROLE AND IDENTITY

Who is it that manages the way you take your treatment?

- **Prompt: partner, HCP**

Do you feel encouraged to take you treatment?

How does your partner feel about you taking treatment for ED?

Does taking treatment for ED affect how you see yourself?

5. BELIEFS ABOUT CAPABILITIES

How confident do you feel about taking treatment for your ED?

- **Prompt: dealing with any potential unwanted side effects, able to follow prescription?**

Have you had any problems with taking your prescribed treatment for ED and of so can you tell me about the problems?

- **Prompt: forgetting, external factors such as influence of partner**

Are there ever any factors that dissuade you from taking your treatment?

6. OPTIMISM

How optimistic are you about continuing to use treatment for your ED?

Is there anything you believe will hinder you taking your treatment in the future?

7. BELIEFS ABOUT CONSEQUENCES

What do you think would happen if you didn't take treatment for your ED?

To what extent does your treatment make your condition better?

Do you have concerns about taking your treatment?

- **Prompt: side effects, reliance, partners concerns**

8. REINFORCEMENT

What encourages you to take your treatment?

- **Prompt: benefits to taking treatment**

Have you ever stopped taking your ED treatment? If so, why did you stop taking it?

- **Prompt: embarrassment/partner**

9. INTENTIONS

Do you think you will take your treatment in the future?

10. GOALS

To what extent is taking your treatment for ED a priority?

11. MEMORY, ATTENTION AND DECISION PROCESSES

Do you ever forget to take your ED treatment?

Have you ever deliberately missed a dose of your treatment?

Are decisions about whether you take your treatment easy or difficult to make and if so in what way?

12. ENVIRONMENTAL CONTEXT AND RESOURCES

Are there any aspects of your daily life that may interrupt or alternatively help when it comes to using your ED treatment?

Are there times or situations in the past when you have had problems and not been able to take your ED treatment?

- **Prompts: time constraints, getting to pharmacy**

Do you pay for your treatment? Does the cost of the treatment play a part in whether you take your treatment?

13. SOCIAL INFLUENCES

Apart from yourself are there any people that influence whether you take your treatment or not?

- **Prompt: partner acceptance of treatment, partner libido**

Do you know anyone else who takes treatment for ED?

14. EMOTION

How do you feel about taking treatment for ED?

Do you sometimes not feel like taking your treatment?

15. BEHAVIOURAL REGULATION

Did you make a plan (do you have a plan) for how you take your treatment?

If you wanted to change the way you take your ED treatment, how would you do this?

- **Prompt: Other medications/treatments**

Close: That's all the questions I have for you, has anything occurred to you about this topic during the interview that we haven't discussed?

Thank you for taking part.



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REC reference: 16/NE/0333

PARTICIPANT INFORMATION SHEET

**Study Title: An exploration of men's experience and use of treatments
for erectile dysfunction (ED).**

We would like to invite you to take part in a research study. Before you decide whether you would like to take part it is important that you understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and

discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Current research suggests that when treatment of erectile dysfunction (ED) is successful then both the man and his partner experience improvements in their quality of life. However, it has also been indicated that levels of adherence to treatment (such as Viagra) for ED are low, potentially reducing beneficial aspects of the medication. Therefore this research study aims to explore aspects that you find helpful or unhelpful when it comes to using treatment for ED.

Why have I been invited?

You have been invited to take part in the study because you have been prescribed treatment for ED. We are seeking a total of 12 people to take part in this study.

Do I have to take part?

No, taking part in the research is voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. Nobody will be upset if you do decide not to take part. Please be assured that deciding to withdraw at any time or choosing not to take part at all will not affect the standard of care you receive at any time, either now or in the future. Taking part in the study will not affect your current or future treatment.

What will happen if I take part?

If you decide to take part in the study, you will be asked to take part in an interview which will ask about your experience of taking medication for erectile dysfunction. The interview will last

approximately 45 minutes and can take place at the clinic, at City University London, in your home or over the telephone, whichever you prefer. The interview will be audio-recorded so that it is recorded accurately and will then be typed up for analysis.

What are the possible disadvantages and risks of taking part?

Erectile dysfunction can be a sensitive subject and questions in relation to it can be of a personal nature. However, you can refuse to answer any question that you feel is too sensitive or if at any point in the interview you feel that you no longer wish to participate please inform the researcher who will then terminate the interview.

What are the possible benefits of taking part?

We do not expect there to be any direct benefits for you in taking part, but by taking part you will potentially be helping to inform improvements to treatment for future patients.

Will my taking part in the study be kept confidential?

All information that is collected from you during the course of the research will be kept strictly confidential. Study researchers will need access to your medical records to carry out this research. Only the research investigators who are running the study will have access to the study data.

The data that we collect will be stored anonymously on a password protected computer system and in locked filing cabinets at City University London and will only be available to the research team. The recording of the interview will be sent to an external company to be typed up and this company will provide assurance of confidentiality.

When the study is complete, data will be kept for a further 10 years and will be archived at City University London secure storage facility.

What will happen to results of the research study?

The research study is part of a PhD thesis and therefore will be written up for this purpose. In addition the research will be written up for publication in a relevant academic journal. We may use your quotations from the interview to illustrate what participants have said, however, you will remain anonymous and anything that could identify you will be removed.

If at any point during the study you lose capacity to take part, the data you have provided up until that point will remain within the study.

What will happen if I don't want to carry on with the study?

If you decide at any point during your participation in the study that you wish to withdraw, you can contact any of the research team to discuss this. It would be useful for us to use the information you have given us up until that point in the study; however, if you wish for us to destroy the data, this can also be arranged.

What if there is a problem?

If you have any problems, concerns or questions about this study, you should ask to speak to a member of the research team (please see contact details at the end of this form). If you remain unhappy and wish to complain formally, you can do this through the University complaints procedure. To complain about the study, you need to phone 020 7040 3040. You can then ask to speak to the Secretary to Senate Research Ethics Committee and inform them that the name

of the project is: An exploration of men's experience and use of treatments for erectile dysfunction (ED).

You could also write to the Secretary at:

[REDACTED]

Secretary to Senate Research Ethics Committee

Research Office, E214

City University London

Northampton Square

London

EC1V 0HB

[REDACTED]

City University London holds insurance policies which apply to this study. If you feel you have been harmed or injured by taking part in this study you may be eligible to claim compensation. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for legal action.

Who is organizing the research?

The research study is being organised by researchers at City University London along with urologists at Barts Health NHS Trust, King's College Hospital NHS Foundation trust, University College Hospitals NHS Foundation trust.

Who has reviewed the study?

This study has been approved by NHS ethics committee (Reference number XXXX)

Further information and contact details

If you want some general information about taking part in research please contact the Patient Advice Liaison Service (PALS) at PALS@uclh.nhs.uk

Should you require any further details please contact the lead researcher or a supervisor at the following:

Lead researcher: Paul Williams, [REDACTED]

Supervisor: Dr Kathleen Mulligan, [REDACTED]

Supervisor: Dr Hayley McBain, email: [REDACTED]



Study Title: An exploration of men's experience and use of treatments for erectile dysfunction (ED).

REC reference: 207576

Please initial box

1.	I confirm that I have read and understood the participant information sheet dated 30.11.2016 (version 1.1) for the above study and have had the opportunity to ask questions.	
2.	I understand that taking part in the study will involve: • The research team having access to my medical records • being interviewed by the researcher • allowing the interview to be audiotaped • transcription of recorded interviews by a third party	
3.	I understand that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published. The identifiable data will not be shared with any other organisation.	
4.	I understand that my participation is voluntary, that I can choose not to participate in part or all of the project, and that I can withdraw at	

	any stage of the project without being penalized or disadvantaged in any way.	
5.	I give my permission for the researcher to use direct quotes in the final project report and/or subsequent publications and presentations arising from this work. I understand that if used, any quotes will be anonymised in order that I may not be identified.	
6.	I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from City University London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
7.	I would like to receive feedback about the findings of the study.	
8.	I agree to City University London recording and processing this information about me. I understand that this information will be used only for the purpose(s) set out in this statement and my consent is conditional on the University complying with its duties and obligations under the Data Protection Act 1998.	
9.	I agree to take part in the above study.	

Name of Participant

Signature

Date

Name of Researcher

Signature

Date

When completed, 1 copy for participant; 1 copy for medical notes, 1 copy for researcher file.

Appendix 10: Barriers and Enablers to Erectile Dysfunction Treatment Questionnaire

Factors Influencing ED Medication Use

The following questions ask about your condition, your sexual life with your partner as well as your expectations and attitude towards oral treatment you are using to help with your erectile dysfunction (ED) **(please circle only one box for each statement)**

1) I have a plan or pattern with regards to using my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
2) I feel confident that I am able to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
3) I experience treatment side-effects (e.g. headaches, facial flushing, pain, Peyronie's disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
4) My ED treatment enables me to have a sexual relationship with my partner				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
5) My ED treatment improves my ability to get an erection				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
6) My ED treatment is quick to work upon using it				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
7) My ED treatment works effectively every time I take it.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
8) Taking ED treatment makes my sex life less spontaneous				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
9) The effect of my ED treatment (i.e. duration of erection) does not last long enough				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
10) My ED treatment makes me feel more confident				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
11) I find it difficult to pay for my ED treatment.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
12) I have sought alternative treatments for my ED outside of the NHS				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
13) I aim to have a sex life that does not rely on treatment.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree

Disagree		nor disagree		
14) My aim is to find a more natural/holistic solution to my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
15) My aim is to use my treatment for ED as a rehabilitative measure				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
16) Taking my ED treatment as prescribed is high on my list of priorities				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
17) I intend to take my treatment in the future				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
18) If I think sex is likely then I will use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
19) I know how to use my ED treatment, as prescribed, in order for it to work effectively				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
20) Decisions about whether to use my ED treatment are difficult to make				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
21) I am optimistic that my ED treatment will make my ED better				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
22) I feel encouraged by my doctor/nurse to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
23) I feel encouraged by my partner to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
24) I have informed my partner that I use ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
26) Using treatment for ED has a negative impact on my masculinity				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
27) I know the cause of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
28) ED makes my partner feel frustrated				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
29) ED means I am unable to have penetrative sex				
Strongly	Disagree	Neither agree	Agree	Strongly agree

Disagree		nor disagree		
30) ED reduces my level of intimacy with my partner				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
31) I avoid sexual encounters because of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
32) I lack confidence because of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
33) My ED has had a negative effect on my relationship with my partner				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
34) Suffering from ED is stressful and traumatic				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
35) ED is a long-term condition				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
36) I do not always experience ED, it is intermittent				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
37) My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
38) My ED is caused by psychological problems				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree

Project ID number: XXXX

Version: Thesis v0.11_PaulWilliams v0.13

Date: 14.08.2018

REC reference: 207576

PARTICIPANT INFORMATION SHEET

Study title: An exploration of men's experience and use of treatments for erectile dysfunction (ED).

We would like to invite you to take part in a research study. Before you decide whether you would like to take part it is important that you understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Current research suggests that when treatment of erectile dysfunction (ED) is successful then both the man and his partner experience improvements in their quality of life. However, it has also been indicated that levels of adherence to treatment (such as Viagra) for ED are low, potentially reducing beneficial aspects of the medication. Therefore this research study aims to explore aspects that you find helpful or unhelpful when it comes to using treatment for ED. As a result the study asks about information which is of a personal nature including your racial and ethnic background as well as data concerning your health and sex life.

Why have I been invited?

You have been invited to take part in the study because you have been prescribed treatment for ED. We are seeking approximately 209 people to take part in this study.

Do I have to take part?

No, taking part in the research is voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. Nobody will be upset if you do decide not to take part. Please be assured that deciding to withdraw at any time or choosing not to take part at all will not affect the standard of care you receive at any time, either now or in the future. Taking part in the study will not affect your current or future treatment.

What will happen if I take part?

If you decide to take part in the study you will be asked to complete a questionnaire pack that asks about your wellbeing and your views about ED and the treatment you have been prescribed. The questionnaire will take approximately 20 minutes to complete. Questionnaires can be completed now or alternatively you can take it home with you and return it in the Freepost envelope that we will give you. Additionally, you can complete it over the telephone or alternatively you can complete the questionnaire on-line at [insert link].

What are the possible disadvantages and risks of taking part?

Erectile dysfunction can be a sensitive subject and questions in relation to it can be of a personal nature. However, you can refuse to answer any question that you feel is too sensitive or if at any point you feel that you no longer wish to participate, you can decide to withdraw from the study.

What are the possible benefits of taking part?

We do not expect there to be any direct benefits for you in taking part, but by taking part you will potentially be helping to inform improvements to treatment for future patients.

Will my taking part in the study be kept confidential?

All information that is collected from you during the course of the research will be kept strictly confidential. Study researchers will need access to your medical records to carry out this research. Only the research investigators who are running the study will have access to the study data.

We will not report your responses on the questionnaire to your clinical team. If you would like help with any of the issues that you have reported in the questionnaire, please tell your doctor or nurse who will be able to refer you to appropriate support services.

The data that we collect will be stored anonymously on a password protected computer system and in locked filing cabinets at City, University of London and will only be available to the research team.

When the study is complete, data will be kept for a further 10 years and will be archived at City University London secure storage facility.

What will happen to results of the research study?

The research study is part of a PhD thesis and therefore will be written up for this purpose. In addition the research will be written up for publication in a relevant academic journal. For all written reports and relevant publications the anonymity of all participants will be maintained.

If at any point during the study you lose capacity to take part, the data you have provided up until that point will remain within the study.

What will happen if I don't want to carry on with the study?

If you decide at any point during your participation in the study that you wish to withdraw, you can contact any of the research team to discuss this. It would be useful for us to use the information you have given us up until that point in the study; however, if you wish for us to destroy the data, this can also be arranged.

What if there is a problem?

If you have any problems, concerns or questions about this study, you should ask to speak to a member of the research team (please see contact details at the end of this form). If you remain unhappy and wish to complain formally, you can do this through the University complaints procedure. To complain about the study, you need to phone 020 7040 3040. You can then ask to speak to the Secretary to Senate Research Ethics Committee and inform them that the name of the project is: An exploration of men's experience and use of treatments for erectile dysfunction (ED).

You could also write to the Secretary at:

[REDACTED]

Secretary to Senate Research Ethics Committee

Research Office, E214

City University London

Northampton Square

London

EC1V 0HB

[REDACTED]

City University London holds insurance policies which apply to this study. If you feel you have been harmed or injured by taking part in this study you may be eligible to claim compensation. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for legal action.

Who is organizing the research?

The research study is being organised by researchers at City University London along with urologists at Barts Health NHS Trust, King's College Hospital NHS Foundation trust, University College Hospitals NHS Foundation trust.

Who has reviewed the study?

This study has been approved by the Newcastle and North Tyneside 1 Research Ethics Committee (Reference number 207576)

Further information and contact details

If you want some general information about taking part in research please contact the Patient Advice Liaison Service (PALS) at PALS@uclh.nhs.uk

Should you require any further details please contact the lead researcher or a supervisor at the following:

Lead researcher: Paul Williams, [REDACTED]

Supervisor: Dr Kathleen Mulligan, [REDACTED]

Supervisor: Dr Hayley McBain, email: [REDACTED]

Data Protection Privacy Notice: What are my rights under the data protection legislation?

City, University of London is the data controller for the personal data collected for this research project. Your personal data will be processed for the purposes outlined in this notice. The legal basis for processing your personal data will be that this research is a task in the public interest, that is City, University of London considers the lawful basis for processing personal

data to fall under Article 6(1)(e) of GDPR (public task) as the processing of research participant data is necessary for learning and teaching purposes and all research with human participants by staff and students has to be scrutinised and approved by one of City's Research Ethics Committees.

Further, City considers the processing of special category personal data will fall under Article 9(2)(g) of the GDPR as the processing of special category data has to be for the public interest in order to receive research ethics approval and occurs on the basis of law that is, inter alia, proportionate to the aim pursued and protects the rights of data subjects.

The rights you have under the data protection legislation are listed below, but not all of the rights will apply to the personal data collected in each research project.

*right to be informed *right of access *right to rectification *right to erasure *right to restrict processing *right to object to data processing *right to data portability *right to object *rights in relation to automated decision making and profiling

For more information, please visit www.city.ac.uk/about/city-information/legal

What if I have concerns about how my personal data will be used after I have participated in the research?

In the first instance you should raise any concerns with the research team, but if you are dissatisfied with the response, you may contact the Information Compliance Team at dataprotection@city.ac.uk or phone 0207 040 4000, who will liaise with City's Data Protection Officer [REDACTED] to answer your query.

If you are dissatisfied with City's response you may also complain to the Information Commissioner's Office at www.ico.org.uk

Thank you for taking the time to read this information sheet.

**Study title: An exploration of men's experience and use of treatments
for erectile dysfunction (ED).**

REC reference: 207576

Please initial box

1.	I confirm that I have read and understood the participant information sheet dated 14.08.2018 (version v5.0) for the above study and have had the opportunity to ask questions. I understand that taking part in the study will involve: • Completing a questionnaire which will take approximately 20 minutes.	
2.	I understand that data being collected relates to part of a research study looking at men's experience of using treatment for erectile dysfunction. As a result City, University of London is responsible for my personal information which will include data relating to my health, racial or ethnic origin, sex life and sexual orientation. This research is necessary for learning and teaching purposes and therefore processing of personal data is covered under the General Data Protection Regulation (GDPR).	
3.	I understand that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published. The identifiable data will not be shared with any other organisation.	
4.	I understand that my participation is voluntary, that I can choose not to participate in part or all of the project, and that I can withdraw at any stage of the project without being penalized or disadvantaged in any way.	
5.	I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from City University London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
6.	I agree to City recording and processing this information about me. I understand that this information will be used only for the purpose(s) set out in this statement and my consent is conditional on City complying with its duties and obligations under the General Data Protection Regulation (GDPR).	
7.	I agree to the arrangements for data storage and archiving.	
8.	I agree to take part in the above study.	

Name of Participant

Signature

Date

Name of Researcher

Signature

Date

When completed, 1 copy for participant; 1 copy for medical notes; 1 copy for researcher file.

Strictly Confidential

**An exploration of men's experience and use of
treatments for erectile dysfunction (ED).**

Questionnaire Pack

Study ID:

Date of completion:

Introduction

This questionnaire contains questions which will ask about your health and well-being. Please remember that we are interested in your personal views and therefore there are no right or wrong answers. Some of the questions are very similar to each other but we would be very grateful if you would answer all questions. Finally, on behalf of the research team I would like to thank you very much for taking part in this study.

Demographic and Clinical Data

Under 18 ☐

18-24 ☐

25-34 ☐

35-44 ☐

45-54 ☐

55-64 ☐

65-74 ☐

75-84 ☐

85 or over ☐

Ethnicity:

White British ☐

White Irish ☐

Other white British ☐

Asian or Asian British ☐

Black or Black British ☐

Other (please specify):

Sexual orientation:

Heterosexual ☐

Bisexual ☐

Homosexual ☐

Prefer not to answer ☐

Other (please specify):

Occupation

Employed full-time ☐

Employed part-time ☐

Unemployed ☐

Retired ☐

Other (please specify):

Relationship status:

Married ☐

Living with partner ☐

Divorced ☐

Single ☐

Other (please specify):

Level of education

No qualifications ☐

GCSE / O Level ☐

A Level ☐

Undergraduate ☐

A Level ☐

Graduate ☐

Post graduate ☐

Other (please specify):

.....

Have you been diagnosed with any of the following? Please tick all that apply:

Diabetes ☐

Hypertension ☐

High Cholesterol ☐

High blood pressure ☐

Arterial fibrillation ☐

Heart Failure ☐

Transient Ischemic attack ☐

Chronic obstructive pulmonary disease ☐

Other (please specify):

.....

.....

Duration of ED (time since first symptom):

.....

Medication Usage

When you visited the doctor, you were prescribed treatment for your erectile dysfunction. That treatment may have been oral medication, injection therapy, pellets or prosthesis. The following questions pertain to the treatment you have been prescribed most recently.

10. What ED treatment/s are you currently prescribed by your GP/relevant health care professional?	☐ Tadalafil (Cialis® or Snafi®) ☐ Vardenafil (Levitra®) ☐ Sildenafil (Viagra® or sildenafil generic brand) ☐ Penile injections (ICI) ☐ Penile Pellets (MUSE) ☐ Penile implant ☐ Vacuum erection device (VED) ☐ Other, please specify:
11. If you are prescribed medication for your ED, how many doses have you been prescribed?	_____ per month/week
12. Have you wanted to be sexually active since your last visit to your HCP in relation to your ED?	☐ Yes ☐ No
13. How many sexual attempts have you had in the last 4 weeks of using your ED treatment	_____ Attempts
14. Have you used your prescribed ED treatment in the past 4 weeks?	☐ Yes ☐ No
15. <u>If yes</u> , how many times in the last 4 weeks have you used your treatment?	_____ Tablets
16. When was the last time you used your prescribed ED treatment?	Day/Month/Year: _____
17. Have you used any other treatment for ED since your last visit to your HCP in relation to your ED?	☐ Yes ☐ No If yes, please provide details _____ _____ _____

Previous Treatments for Erectile Dysfunction

18. If you have tried any other treatment/s for erectile dysfunction other than your current treatment, please list them in order starting with the first one you tried and how long you tried the treatment for?	Name of treatment: 1. _____ 2. _____ 3. _____ 4. _____	Length of time using the treatment _____ _____ _____ _____

International Index of Erectile Function (IIEF-5)

Each question has several responses from which you are asked to choose the one that best describes your own situation. Please be sure that you select at least one but only one response by circling the number that best fits your answer.

Over the past six months:

How do you rate your confidence that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
When you had erections with sexual stimulation. How often were your erections hard enough for penetration?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ Always 5
During sexual intercourse, how often were you able to maintain your erection	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/ Always

after you had penetrated (entered) your partner?	1	2	3	4	5
During sexual intercourse, how difficult is it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ Always 5

The Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views about erectile dysfunction (ED):

How much does your ED affect your life?										
0 no affect at all	1	2	3	4	5	6	7	8	9	10 severely affects my life
How long do you think your ED will continue?										
0 a very short time	1	2	3	4	5	6	7	8	9	10 forever
How much control do you feel you have over your ED?										
0 Absolutely no control	1	2	3	4	5	6	7	8	9	10 extreme amount of control
How much do you think your treatment can help your ED?										
0 not at all	1	2	3	4	5	6	7	8	9	10 extremely helpful
How much do you experience symptoms from your ED?										
0 no symptoms at all	1	2	3	4	5	6	7	8	9	10 many severe symptoms
How concerned are you about your ED?										
0 not at all concerned	1	2	3	4	5	6	7	8	9	10 extremely concerned
How well do you feel you understand your ED?										

0 don't understand at all	1	2	3	4	5	6	7	8	9	10 understand very clearly
How much does your ED affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)										
0 not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 extremely affected emotionally
Please list in rank-order the three most important factors that you believe caused your ED. The most important causes for me: 1. _____ 2. _____ 3. _____										

Hospital Anxiety and Depression Scale (HADS)

Read each item below and indicate which comes closest to how you have been feeling in the **past week**. Ignore the numbers printed at the side. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long, thought-out response.

I feel tense or 'wound up':	A	I feel as if I am slowed down:	D
Most of the time	3	Nearly all of the time	3
A lot of the time	2	Very often	2
Time to time, occasionally	1	Sometimes	1
Not at all	0	Not at all	0
I still enjoy the things I used to enjoy:	D	I get a sort of frightened feeling like 'butterflies in the stomach':	A
Definitely as much	0	Not at all	0
Not quite so much	1	Occasionally	1
Only a little	2	Quite often	2
Not at all	3	Very often	3
I get a sort of frightened feeling like something awful is about to happen:	A	I have lost interest in my appearance:	D
Very definitely and quite badly	3	Definitely	3
Yes, but not too badly	2	I don't take as much care as I should	2
A little, but it doesn't worry me	1	I may not take quite as much care	1
Not at all	0	I take just as much care as ever	0
I can laugh and see the funny side of things:	D	I feel restless as if I have to be on the move:	A
As much as I always could	0	Very much indeed	3
Not quite so much now	1	Quite a lot	2
Definitely not so much now	2	Not very much	1
Not at all	3	Not at all	0
Worrying thoughts go through my mind:	A	I look forward with enjoyment to things:	D
A great deal of the time	3	As much as I ever did	0
A lot of the time	2	Rather less than I used to	1
From time to time but not too often	1	Definitely less than I used to	3
Only occasionally	0	Hardly at all	2
I feel cheerful:	D	I get sudden feelings of panic:	A
Not at all	3	Very often indeed	3
Not often	2	Quite often	2
Sometimes	1	Not very often	1
Most of the time	0	Not at all	0
I can sit at ease and feel relaxed:	A	I can enjoy a good book or radio or TV programme:	D
Definitely	0	Often	0
Usually	1	Sometimes	1
Not often	2	Not often	2
Not at all	3	Very seldom	3

Beliefs about Medicines Questionnaire (BMQ)

We would like to ask you about your personal views about medicines prescribed for you. These are statements other people have made about their medicines. Please indicate the extent to which you agree or disagree with them by ticking the relevant box. There are no right or wrong answers. We are interested in your personal views.

	<i>strongly agree</i>	<i>agree</i>	<i>uncertain</i>	<i>disagree</i>	<i>strongly disagree</i>
My health, at present, depends on my treatment for ED					
Having to use treatment for ED worries me					
My life would be impossible without my ED treatment					
Without my ED treatment I would be very ill					
I sometimes worry about long-term effects of my ED treatment					
My ED treatment is a mystery to me					
My health in the future will depend on my ED treatment					
My ED treatment disrupts my life					
I sometimes worry about becoming too dependent on my ED treatment					
My ED treatment protects me from becoming worse					

Self-Esteem and Relationship Questionnaire (SEAR)

Please think about **the past 4 weeks** when responding to the following statements (**please circle only one box for each statement**).

1. I felt relaxed about initiating sex with my partner				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
2. I felt confident that during sex my erection would last long enough.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
3. I was satisfied with my sexual performance.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
4. I felt that sex could be spontaneous.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
5. I was likely to initiate sex.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
6. I felt confident about performing sexually.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
7. I was satisfied with our sexual relationship.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
8. My partner was unhappy with the quality of our sex life.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
9. I had high self-esteem.				

Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
10. I felt complete as a man.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
11. I was inclined to feel that I was a failure.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
12. I had confidence in myself.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
13. My partner was satisfied with our relationship as a whole.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never
14. I was satisfied with our relationship as a whole.				
Almost always/always	Most of the time (much more than half of the time)	Sometimes (about half of the time)	A few times (much less than half of the time)	Almost never/never

The Brief COPE

These items deal with ways you've been coping with the stress in your life since you found out about your erectile dysfunction. We are interested in how you've tried to deal with it and what you've been doing to cope. Each item says something about a particular way of coping. Please make your answers as true **FOR YOU** as you can. Use these response choices:

1 = I haven't been doing this at all

2 = I've been doing this a little bit

3 = I've been doing this a medium amount

4 = I've been doing this a lot

1. I've been turning to work or other activities to take my mind off things	1	2	3	4
2. I've been concentrating my efforts on doing something about the situation I'm in.	1	2	3	4
3. I've been saying to myself "this isn't real."	1	2	3	4
4. I've been using alcohol or other drugs to make myself feel better.	1	2	3	4
5. I've been getting emotional support from others.	1	2	3	4
6. I've been giving up trying to deal with it.	1	2	3	4
7. I've been taking action to try to make the situation better.	1	2	3	4
8. I've been refusing to believe that it has happened.	1	2	3	4
9. I've been saying things to let my unpleasant feelings escape.	1	2	3	4
10. I've been getting help and advice from other people.	1	2	3	4
11. I've been using alcohol or other drugs to help me get through it.	1	2	3	4

12. I've been trying to see it in a different light, to make it seem more positive.	1	2	3	4
13. I've been criticizing myself.	1	2	3	4
14. I've been trying to come up with a strategy about what to do.	1	2	3	4
15. I've been getting comfort and understanding from someone.	1	2	3	4
16. I've been giving up the attempt to cope.	1	2	3	4
17. I've been looking for something good in what is happening.	1	2	3	4
18. I've been making jokes about it.	1	2	3	4
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	1	2	3	4
20. I've been accepting the reality of the fact that it has happened.	1	2	3	4
21. I've been expressing my negative feelings.	1	2	3	4
22. I've been trying to find comfort in my religion or spiritual beliefs.	1	2	3	4
23. I've been trying to get advice or help from other people about what to do.	1	2	3	4
24. I've been learning to live with it.	1	2	3	4
25. I've been thinking hard about what steps to take.	1	2	3	4
26. I've been blaming myself for things that happened.	1	2	3	4
27. I've been praying or meditating.	1	2	3	4
28. I've been making fun of the situation.	1	2	3	4

Factors Influencing ED Medication Use

The following questions ask about your condition, your sexual life with your partner as well as your expectations and attitude towards oral treatment you are using to help with your erectile dysfunction (ED) **(please circle only one box for each statement)**

39) I have a plan or pattern with regards to using my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
40) I feel confident that I am able to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
41) I experience treatment side-effects (e.g. headaches, facial flushing, pain, Peyronie's disease, heartburn, heart racing, scarring, dry mouth, heart palpitations) as a consequence of my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
42) My ED treatment enables me to have a sexual relationship with my partner				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
43) My ED treatment improves my ability to get an erection				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
44) My ED treatment is quick to work upon using it				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
45) My ED treatment works effectively every time I take it.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
46) Taking ED treatment makes my sex life less spontaneous				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
47) The effect of my ED treatment (i.e. duration of erection) does not last long enough				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
48) My ED treatment makes me feel more confident				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
49) I find it difficult to pay for my ED treatment.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
50) I have sought alternative treatments for my ED outside of the NHS				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
51) I aim to have a sex life that does not rely on treatment.				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
52) My aim is to find a more natural/holistic solution to my ED				

Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
53) My aim is to use my treatment for ED as a rehabilitative measure				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
54) Taking my ED treatment as prescribed is high on my list of priorities				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
55) I intend to take my treatment in the future				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
56) If I think sex is likely then I will use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
57) I know how to use my ED treatment, as prescribed, in order for it to work effectively				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
58) Decisions about whether to use my ED treatment are difficult to make				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
59) I am optimistic that my ED treatment will make my ED better				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
60) I feel encouraged by my doctor/nurse to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
61) I feel encouraged by my partner to use my ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
62) I have informed my partner that I use ED treatment				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
63) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
64) Using treatment for ED has a negative impact on my masculinity				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
65) I know the cause of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
66) ED makes my partner feel frustrated				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
67) ED means I am unable to have penetrative sex				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
68) ED reduces my level of intimacy with my partner				

Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
69) I avoid sexual encounters because of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
70) I lack confidence because of my ED				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
71) My ED has had a negative effect on my relationship with my partner				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
72) Suffering from ED is stressful and traumatic				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
73) ED is a long-term condition				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
74) I do not always experience ED, it is intermittent				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
75) My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
76) My ED is caused by psychological problems				
Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree

Thank you for taking the time to complete this questionnaire.

INVITATION TO TAKE PART IN RESEARCH

THE EXPERIENCE OF USING TREATMENT FOR ERECTILE DYSFUNCTION

Dear Member,

We would like to invite you to take part in a research study which has been developed by researchers at City University London. The purpose of the research is to ask people who have erectile dysfunction (ED) about their experience of using ED treatments. We are inviting members of Men's Health Forum to complete a survey and hope this is a welcome opportunity for you to express your views on this topic.

To be eligible to take part, you will need to be over 18, been diagnosed with erectile dysfunction, been prescribed treatment for erectile dysfunction and been using it for a minimum of 4 weeks.

If you decide to take part, you will be asked to fill in a survey questionnaire which will take approximately 20 minutes. There are no right or wrong answers; every view is valuable and important.

The survey is anonymous and your participation is entirely voluntary. You can withdraw at any stage by exiting the survey and do not have to tell us your reasons for doing so.

For more details about the study and to complete the study survey, please follow this link [insert link]. If you have any questions about the research or would like to receive a paper copy of the survey or to complete the survey over the telephone, please contact Paul Williams on [REDACTED]

Kind regards

Paul Williams

Appendix 15: Adherence measure selection

Adherence Measure Selection

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Adult AIDS Clinical Trials Group (AACTG) 4 day version	HIV	4	Continuous	Previous 4 days	No: HIV based and only over 4 days	N/A	N/A	N/A
AACTG 3 day version	HIV	3	Continuous	Previous 3 days	No: HIV based and only over 3 days	N/A	N/A	N/A
AACTG last 2 day + Saturday version	HIV	3	Continuous	Previous 2 days and previous Saturday	No: HIV based and only over 2 days	N/A	N/A	N/A
AACTG 7 day version	HIV	1	Continuous	Previous 7 days	No: HIV based and only over 7 days	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
AACTG one month version	HIV	3	Continuous	Previous month	No: HIV based and only over 4 weeks	N/A	N/A	N/A
Adherence Self Report Questionnaire (ASRQ)	Hypertension diabetes dyslipidaemia	1	Likert	None Specified	No: Condition specific	N/A	N/A	N/A
Adherence to Refills and Medication Scale (ARMS)	Coronary heart disease Hypertension	12	Likert	None specified	No, closed set of reasons for non- adherence and no measure of utilisaiton.	N/A	N/A	N/A
Ask 12 behaviour subscale	asthma, diabetes or congestive heart failure	5	Dichotomo us	Previous month	No: specific to the last month	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Barroso	HIV	1	Likert	Previous 7 days	No: only captures the last 7 days	N/A	N/A	N/A
Byerly MJ (2008)	schizophrenia and schizoaffective disorder	3	Continuous (visual analogue) Likert	Past month	No: only captures the last month	N/A	N/A	N/A
Bell	HIV	1 (4 parts)	Dichotomous	Previous day, week, month and ever	No: HIV specific	N/A	N/A	N/A
Brooks Medication Adherence Scale	Asthma	4	Dichotomous	Previous 3 months	No: Based on prior 3 months and tailored to reasons for non- adherence to asthma treatment	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Choo	Hypertension	5	3 continuous items, 1 dichotomo us item and 1 likert scale item	3 items previous week 2 items none specified	No: concerned with reasons for non- adherence only	N/A	N/A	N/A
Cohn	HIV	8	Dichotomo us	Previous 24 hours, 48 hours and 2 weeks	No: 24/48/2 weeks adherence specific	N/A	N/A	N/A
Composite self report measure	Home Care clients	5	Likert	None Specified	No: participants were asked whether they had “taken their study medications in the	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
					past week” and during “the week prior to last week.” “Nonadherence to MAC prophylactic study medication” was defined as missing ≥ 1 dose during the preceding 2 weeks			
CPCRA antiretroviral medication self- report 3 day adherence	HIV	3	Likert and dichotomo us items	Previous 3 days	No: HIV specific and limited to the past 3 days	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
CPRCA antiretroviral self-report 7 day adherence	HIV	3	Likert and dichotomous items	Previous 7 days	No: HIV / over 3 and 7 day scales	N/A	N/A	N/A
El-Meliegy (Persistence and Adherence questionnaire, PAQ)	Erectile dysfunction	19	Likert, dichotomous, tick box, data driven answers	No limitations	YES: many items relevant to the desired measure.	YES	YES	NO
Erickson	Asthma	4	Likert	Previous 3 months	No: Developed for asthma, not appropriate see below.	N/A	N/A	N/A
Fodor	Blue collar workers with hypertension	3	Likert	None specified	No: concentrates on reasons for non-	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
					adherence to hypertension			
Gehi		1	Likert	Previous month	No: not detailed enough	N/A	N/A	N/A
Grymonpre	Patients over 65	2	Continuous	None specified	YES	YES	YES	Not reported
Hill Briggs	type 2 diabetes	5	Dichotomous	None specified	No: Not suitable four questions which focus on reasons for non-adherence	N/A	N/A	N/A
Immunosuppressant Therapy Adherence Scale (ITAS)	Transplant recipients	5	Likert	Previous 3 months	No: focusses on forgetfulness, carelessness, cessation as a result of feeling worse and neglect	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Inui	hypertension	1	Dichotomous	Previous 2 months	No: items are not suitable	N/A	N/A	N/A
Kerr	Injection drug users	1	Dichotomous	Previous 2 months	No, measures adherence over 2 months only	N/A	N/A	N/A
Leopold		21	Likert	Previous month	No: concerned with reasons for nonadherence only	N/A	N/A	N/A
Liu		1	Continuous	Previous 7 days	No: specific to the last 3 – 7 days	N/A	N/A	N/A
Lu 1 month rating response scale	Patients taking protease inhibitors or non- nucleoside	1	Likert	Previous month	No, measures adherence over the last month only	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
	reverse transcriptase							
Multicentre AIDS cohort study (MACS) adherence form	HIV positive men	5	Continuous and dichotomous items	Previous 4 days	No: limited to the last 4 days utilisation	N/A	N/A	N/A
MARS	Renal transplant patients, Patients with schizophrenia and bipolar disorder	5	Likert	None specified	No: not appropriate as it centres on reasons for non- adherence.	N/A	N/A	N/A
MATI	HIV positive adults	1	Continuous	None specified	No: specific to HIV medication	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Melbourne	HIV patients	1	Likert	None Specified	No: designed for HIV patients	N/A	N/A	N/A
Mooney	Patients between 18 and 55 with cocaine dependence	1	Dichotomo us	Since last clinic visit	No: Condition specific	N/A	N/A	N/A
Morisky 4	Outpatients with high blood pressure, HIV infected persons over 18 attending hospital	4	Dichotomo us	None specified	No: focusses on reasons for non- adherence	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
	outpatient clinics, Patients over 18 infected with HIV, Patients over 18 with a confirmed diagnosis of Crohns disease or ulcerative colitis							
Morisky 4 likert	Home Care clients over 65	4	Likert	None specified	No: closed set of reasons	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Morisky 8	Patients with hypertension	8	Dichotomous and one likert scale item	One item- previous day, one item previous 2 weeks Remainder none specified	No: closed set of reasons	N/A	N/A	N/A
Murphy 1	HIV positive adolescents aged between 13-18.	2	Likert	Previous month	HIV specific	N/A	N/A	N/A
Murphy 2	Mothers with HIV with well children	2	Likert	Previous month	HIV specific	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Prado	Patients with high blood pressure	1	Dichotomous	Previous month	No	N/A	N/A	N/A
Pratt	Patients over 50 with serious mental illness other than dementia	1	Continuous (visual analogue)	None Specified	No: One question on medication using a visual analogue scale; therefore percentage of use is not possible.	N/A	N/A	N/A
Reported adherence to medication (RAM)	HIV infected persons, Patients with asthma or diabetes, psychiatric patients,	4	Likert	Previous 4 days	No: limited to the last 4 days	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
	cardiac, general medical and renal in- patients.							
Regimen screen of Brief Medication Questionnaire (BMQ)	Patients over 18 with hypertension, diabetes mellitus, hypercholest erolemia, hypothyroidis m or condition requiring HRT	5	Continuous	Previous week	No, previous week of medication use only	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Remington	Patients with schizophrenia aged between 18-65	1	Likert	None specified	No questions relating to duration of adherence/non-adherence	N/A	N/A	N/A
Schneider	Patients with HIV	4	Likert	Previous 4 weeks	No: concentrated on side effects only	N/A	N/A	N/A
Schuman	HIV seropositive women	1	Likert	Previous 7 days	No: only over 7 days	N/A	N/A	N/A
Self-reported adherence (SERAD)	HIV outpatients over 18 taking HAART	15	Continuous	Previous week, month and 3 months	No: only measures adherence over a maximum of the last 3 months.	N/A	N/A	N/A
Simplified Medication Adherence	Patients with HIV taking nelfinavir in	6	Dichotomous and	Previous week and previous 3	No: only measures adherence over a	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Questionnaire (SMAQ)	combination with other antiretroviral drugs		continuous items	months and ever	maximum of the last 3 months.			
7SR Recall	HIV infected persons over 18	11	Continuous	Previous 7 days	No: only covers last 7 days	N/A	N/A	N/A
Stages of change (SOC)	Persons over 18 living with HIV	2	Likert	Over a year	No; types of medication, amounts taken etc not included	N/A	N/A	N/A
Stewart	Primary care patients other than those aged between 8 and 18	11	Continuous	Previous 7 days	No: only covers last 7 days	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Tool for Adherence Behaviour screening (TABS)	Patients with chronic lung conditions	8	Likert	None specified	No: condition specific.	N/A	N/A	N/A
The patterns of asthma medication use questionnai-re	Patients with asthma aged 20-60	5	Dichotomous and likert items	None specified	No: condition specific.	N/A	N/A	N/A
Visual Analogue Scale (VAS) 1 week version	Patients with schizophrenia and bipolar disorder	1	Continuous (visual analogue)	Previous week	No: only covers the last week	N/A	N/A	N/A
Visual Analogue Scale (VAS) one month version	Persons over 18 living with HIV	1	Continuous (visual analogue)	Previous month	No: tailored to HIV medication.	N/A	N/A	N/A

Scale Name	Condition	Number of items / scale type		Time period	Suitability	Measure of adherence as a percentage?	Measure of persistence ?	Validity
Visual Analogue Scale (VAS) six month version	Patients over 18 with diabetes	1	Continuous (visual analogue)	Previous 6 months	No; previous 6 months only	N/A	N/A	N/A
Visual Analogue Scale (VAS) carers' version	Carers of patients with HIV	1	Continuous (visual analogue)		No: Visual analogue scale.	N/A	N/A	N/A

Appendix 16: Brief COPE factor analysis (Study 3)

The component correlation matrix indicated a 3-factor solution explained 40.98% of the variance.

Item	Sub-scale	Component		
		1	2	3
7) I've been taking action to try to make the situation better.	Active coping	.675	.416	
2) I've been concentrating my efforts on doing something about the situation I'm in.	Active coping	.648	.379	
25) I've been thinking hard about what steps to take.	Planning coping	.587		
3) I've been saying to myself "this isn't real."	Denial coping	.561		-.309
27) I've been praying or meditating.	Religious coping	.541		
1) I've been turning to work or other activities to take my mind off things	Self-distraction	.526		
22) I've been trying to find comfort in my religion or spiritual beliefs.	Religious coping	.502		
14) I've been trying to come up with a strategy about what to do.	Planning coping	.501		
9) I've been saying things to let my unpleasant feelings escape.	Venting	.493	-.433	
8) I've been refusing to believe that it has happened.	Denial coping	.474	-.420	
12) I've been trying to see it in a different light, to make it seem more positive.	Positive Reframing	.435		
19) I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	Self-distraction			
20) I've been accepting the reality of the fact that it has happened.	Acceptance coping			
16) I've been giving up the attempt to cope.	Behavioural disengagement		-.774	
11) I've been using alcohol or other drugs to help me get through it.	Substance Use		-.716	
13) I've been criticizing myself.	Self-blame coping		-.694	
4) I've been using alcohol or other drugs to make myself feel better.	Substance Use		-.655	
26) I've been blaming myself for things that happened.	Self-blame coping		-.580	
6) I've been giving up trying to deal with it.	Behavioural disengagement		-.556	
21) I've been expressing my negative feelings.	Venting		-.545	.319
24) I've been learning to live with it.	Acceptance coping		.319	
10) I've been getting help and advice from other people.	Use of Instrumental Support			.725
18) I've been making jokes about it.	Humour coping			.672
28) I've been making fun of the situation.	Humour coping	-.321		.646
15) I've been getting comfort and understanding from someone.	Emotional support			.606
23) I've been trying to get advice or help from other people about what to do	Use of Instrumental Support			.555
5) I've been getting emotional support from others.	Emotional Support			.477

17) I've been looking for something good in what is happening.	Positive reframing	.400		.415

Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.
a. Rotation converged in 16 iterations.

Appendix 17: Missing data analysis

Variable	% of missing data	Variable	% of missing data
TOTAL_COMMORB	.0	Q4_SEAR_SR	5.7
ED_Mths	5.7	Q5_SEAR_SR	6.6
SILD_No	11.5	Q6_SEAR_SR	6.6
TAD_No	9.8	Q7_SEAR_SR	5.7
VARD_No	7.4	Q8_SEAR_SR_REV	5.7
MUSE_No	7.4	Q9_SEAR_C_SEffic	5.7
ICI_No	8.2	Q10_SEAR_C_SEffic	4.9
No_Prescribed	12.3	Q11_SEAR_C_SEffic_REV	4.9
No_Used_4WKS	7.4	Q12_SEAR_C_SEffic	4.9
Utilisation	14.8	Q13_SEAR_C_OR	4.9
S_Attempts	7.4	Q14_SEAR_C_OR	4.9
Last_used_DAYS	15.6	Q1_COPE_Dist_Avoid_Cope	7.4
TOTAL_IIEF	4.1	Q2_COPE_ActiveC_SelfSuff_Cope	7.4
TOTAL_IPQ	9.0	Q3_COPE_Deni_Avoid_Cope	7.4
TOTAL_HADS_A	9.0	Q4_COPE_SubM_Avoid_Cope	7.4
TOTAL_HADS_D	7.4	Q5_COPE_Emo_SocSupp_Cope	6.6
TOTAL_BMQ_N	9.8	Q6_COPE_Be_Dis_Avoid_Cope	8.2
TOTAL_BMQ_C	6.6	Q7_COPE_ActiveC_SelfSuff_Cope	8.2
TOTAL_SEAR_SR	8.2	Q8_COPE_Deni_Avoid_Cope	7.4
FINAL_SEAR_SR	8.2	Q9_COPE_Vent_SocSupp_Cope	9.8
TOTAL_SEAR_SEffic	5.7	Q10_COPE_Inst_SocSupp_Cope	8.2
FINAL_SEAR_C_SE	5.7	Q11_COPE_SubM_Avoid_Cope	8.2
TOTAL_SEAR_OR	4.9	Q12_COPE_Pos_Ref_SelfSuff_Cope	8.2
FINAL_SEAR_C_OR	4.9	Q13_COPE_SeflBI_Dist_Avoid_Cope	7.4
TOTAL_SEAR_C	5.7	Q14_COPE_Plan_SelfSuff_Cope	7.4
FINAL_SEAR_C	5.7	Q15_COPE_Emo_SocSupp_Cope	7.4
TOTAL_SEAR	8.2	Q16_COPE_Be_Dis_Avoid_Cope	9.0
FINAL_SEAR_OVERALL	8.2	Q17_COPE_Pos_Ref_SelfSuff_Cope	7.4
TOTAL_SelfSuff_Cope	12.3	Q18_COPE_Hum_SelfSuff_Cope	9.0
TOTAL_SocSupp_Cope	10.7	Q19_COPE_Dist_Avoid_Cope	6.6
TOTAL_Avoid_Cope	11.5	Q20_COPE_Acc_SelfSuff_Cope	8.2
TOTAL_TDF_BACON	13.1	Q21_COPE_Vent_SocSupp_Cope	7.4
TOTAL_TDF_EC_AND_R	13.9	Q22_COPE_Relg_SocSupp_Cope	8.2
TOTAL_TDF_GOAL	12.3	Q23_COPE_Inst_SocSupp_Cope	7.4
TOTAL_TDF_INTEN	12.3	Q24_COPE_Acc_SelfSuff_Cope	7.4
TOTAL_TDF_SOCINF	12.3	Q25_COPE_Plan_SelfSuff_Cope	7.4
TOTAL_IPQ_CONSEQ	11.5	Q26_COPE_SeflBI_Dist_Avoid_Cope	7.4
TOTAL_IPQ_TIME	11.5	Q27_COPE_Relg_SocSupp_Cope	7.4
TOTAL_IPQ_CAUSE	11.5	Q28_COPE_Hum_SelfSuff_Cope	8.2
Age	3.3	Q1_TDF_BR	13.1
Ethn_RECD_2	.0	Q2_TDF_BACAP	12.3

Variable	% of missing data	Variable	% of missing data
S_Orien_RECD	1.6	Q3_TDF_BACON	13.9
Job_RECD	.8	Q4_TDF_BACON	13.9
Rela_RECD	3.3	Q5_TDF_BACON	13.9
Educ_RECD	2.5	Q6_TDF_BACON	13.1
SILD	6.6	Q7_TDF_BACON	13.9
TAD	6.6	Q8_TDF_REV_BACON	13.1
VARD	6.6	Q9_TDF_REV_BACON	13.9
MUSE	6.6	Q10_TDF_EMO	13.1
ICI	6.6	Q11_TDF_EC_AND_R	13.9
VED	6.6	Q12_TDF_REV_EC_AND_R	13.9
S_Active	4.9	Q13_TDF_GOAL	12.3
Used_4WKS_YorN	4.9	Q14_TDF_GOAL	13.1
PDE5Is_B4	4.1	Q15_TDF_GOAL	14.8
VED_B4	4.1	Q16_TDF_GOAL	12.3
ICI_B4	4.1	Q17_TDF_INTEN	13.1
Other_B4	4.1	Q18_TDF_INTEN	13.1
Q1_IIEF	4.1	Q19_TDF_KNOW	13.9
Q2_IIEF	4.1	Q20_TDF_REV_MA_AND_D	13.1
Q3_IIEF	4.1	Q21_TDF_OPTI	13.1
Q4_IIEF	4.1	Q22_TDF_SOCINF	12.3
Q5_IIEF	4.1	Q23_TDF_SOCINF	13.1
Q1_IPQ	4.1	Q24_TDF_SOCINF	12.3
Q2_IPQ	6.6	Q25_TDF_SOCINF	13.1
Q3_IPQ_REV	4.1	Q26_TDF_REV_SPR_AND_ID	12.3
Q4_IPQ_REV	4.9	Q27_TDF_IPQ_CAU	13.1
Q5_IPQ	5.7	Q28_TDF_REV_IPQ_CON	12.3
Q6_IPQ	4.1	Q29_TDF_REV_IPQ_CON	12.3
Q7_IPQ_REV	4.1	Q30_TDF_REV_IPQ_CON	12.3
Q8_IPQ	4.1	Q31_TDF_REV_IPQ_CON	11.5
Q1_HADS_A	5.7	Q32_TDF_REV_IPQ_CON	11.5
Q2_HADS_D	6.6	Q33_TDF_REV_IPQ_CON	12.3
Q3_HADS_D	5.7	Q34_TDF_REV_IPQ_EMO	12.3
Q4_HADS_A	7.4	Q35_TDF_REV_IPQ_TIME	11.5
Q5_HADS_A	6.6	Q36_TDF_IPQ_TIME	11.5
Q6_HADS_D	6.6	Q37_TDF_IPQ_CAU	12.3
Q7_HADS_D	5.7	Q38_TDF_IPQ_CAU	11.5
Q8_HADS_A	5.7		
Q9_HADS_A	6.6		
Q10_HADS_D	6.6		
Q11_HADS_D	5.7		
Q12_HADS_A	6.6		
Q13_HADS_A	5.7		
Q14_HADS_D	5.7		
Q1_BMQ_N	4.9		
Q2_BMQ_C	5.7		

Variable	% of missing data	Variable	% of missing data
Q3_BMQ_N	5.7		
Q4_BMQ_N	7.4		
Q5_BMQ_C	4.9		
Q6_BMQ_C	5.7		
Q7_BMQ_N	6.6		
Q8_BMQ_C	5.7		
Q9_BMQ_C	4.9		
Q10_BMQ_N	4.9		
Q1_SEAR_SR	7.4		
Q2_SEAR_SR	5.7		
Q3_SEAR_SR	5.7		

Appendix 18: Normality and Outliers

DV: Percent (%) of Medication used in the last 4 Weeks

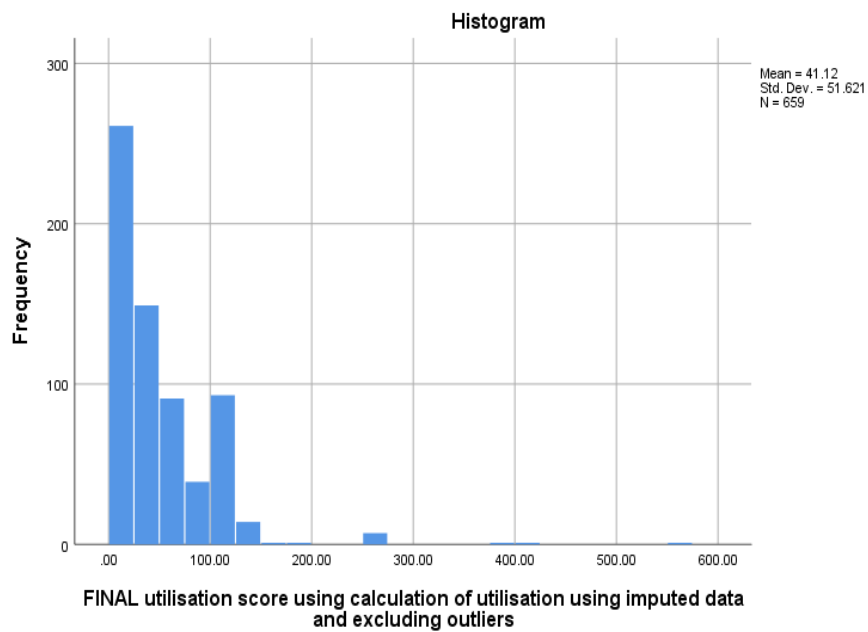


Figure 15: Histogram of data distribution for % of treatment used in the last 4 weeks

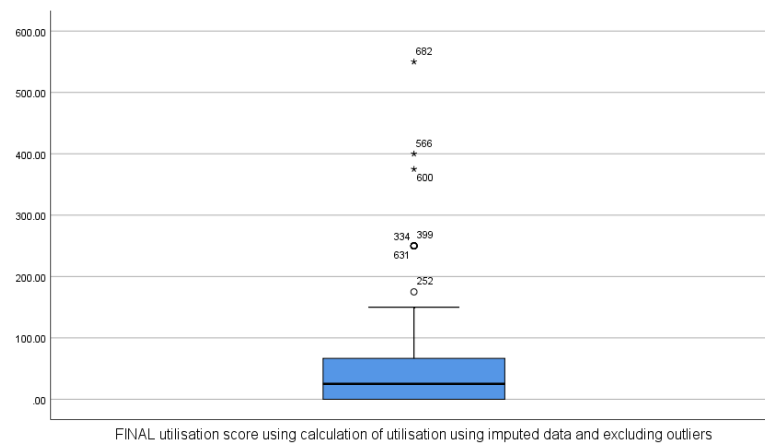


Figure 16: Outliers-Box plot of data distribution for % of treatment used in the last 4 weeks

DV: Number of treatment used in the last 4 weeks

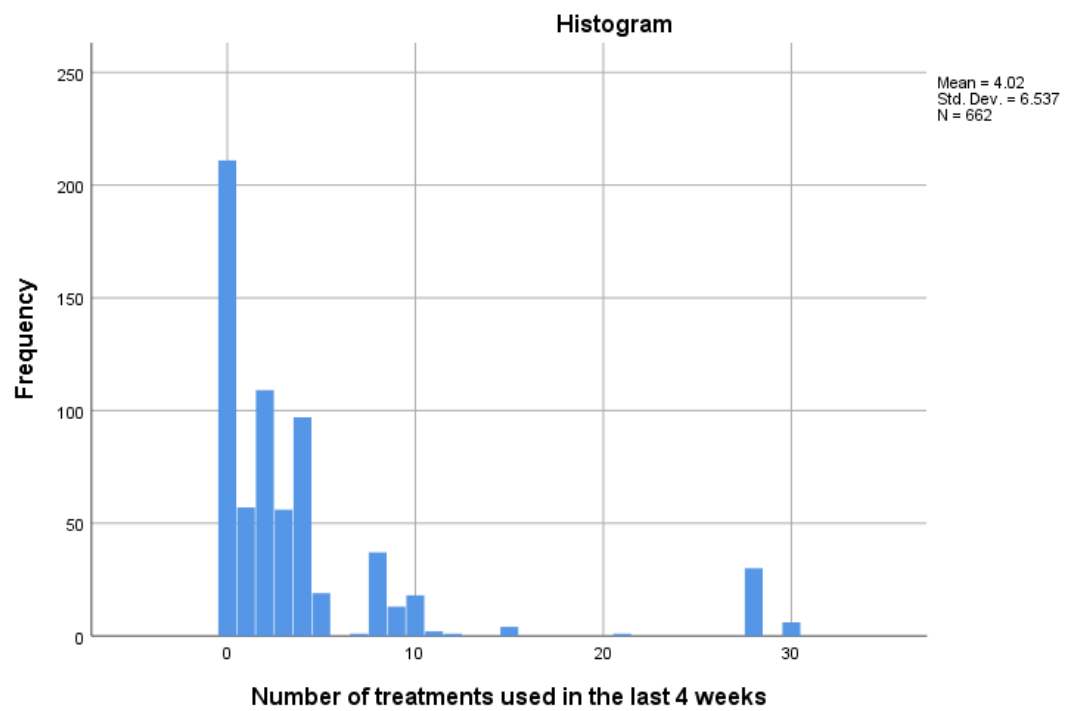


Figure 17: Histogram of data distribution for number of treatments used in the last 4 weeks

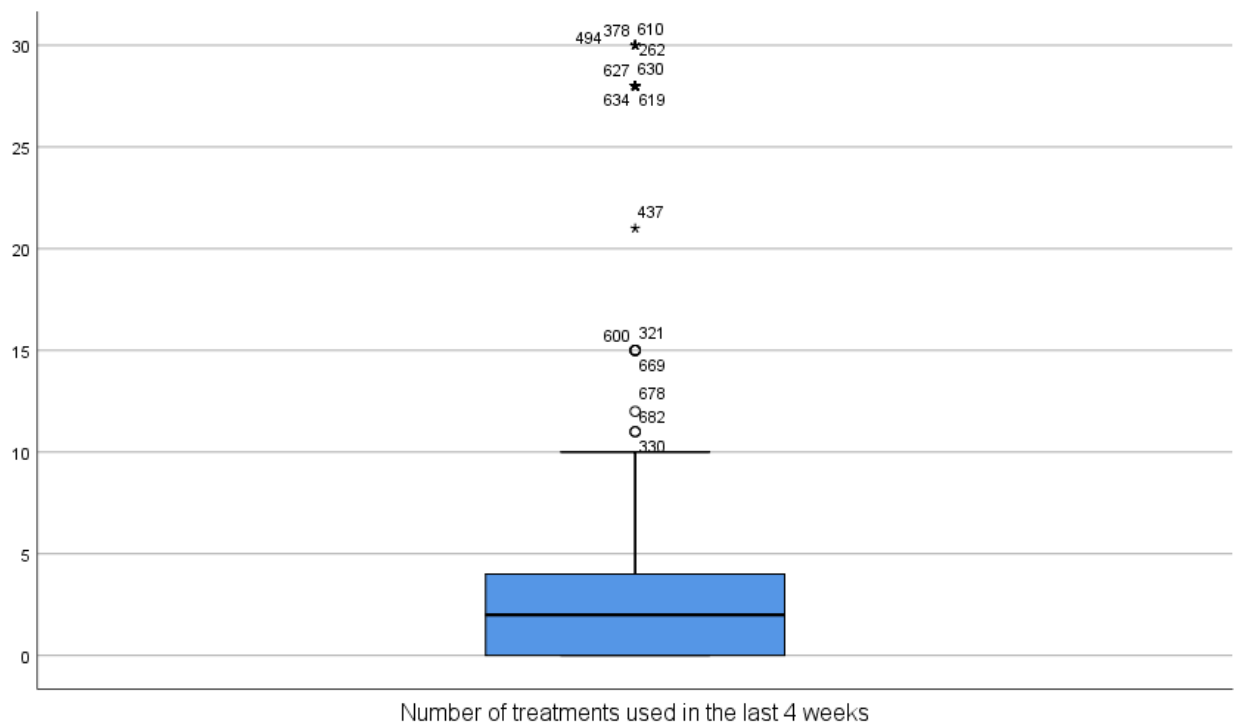


Figure 18: Outliers-Box plot of data distribution for number of treatments used in the last 4 weeks

Test of normal distribution

Table 46: Descriptive data for number of treatments used in the last 4 weeks

Descriptives		Statistic	Std. Error
Number of treatments used in the last 4 weeks	Mean	4.02	.254
	95% Confidence Interval for Lower Bound	3.52	
	Mean Upper Bound	4.52	
	5% Trimmed Mean	2.89	
	Median	2.00	
	Variance	42.730	
	Std. Deviation	6.537	
	Minimum	0	
	Maximum	30	
	Range	30	
	Interquartile Range	4	
	Skewness	2.835	.095
	Kurtosis	7.778	.190

Table 47: Test of normality for number of treatments used in the last 4 weeks

	Tests of Normality					
	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Number of treatments used in the last 4 weeks	.302	662	.000	.591	662	.000

a. Lilliefors Significance Correction

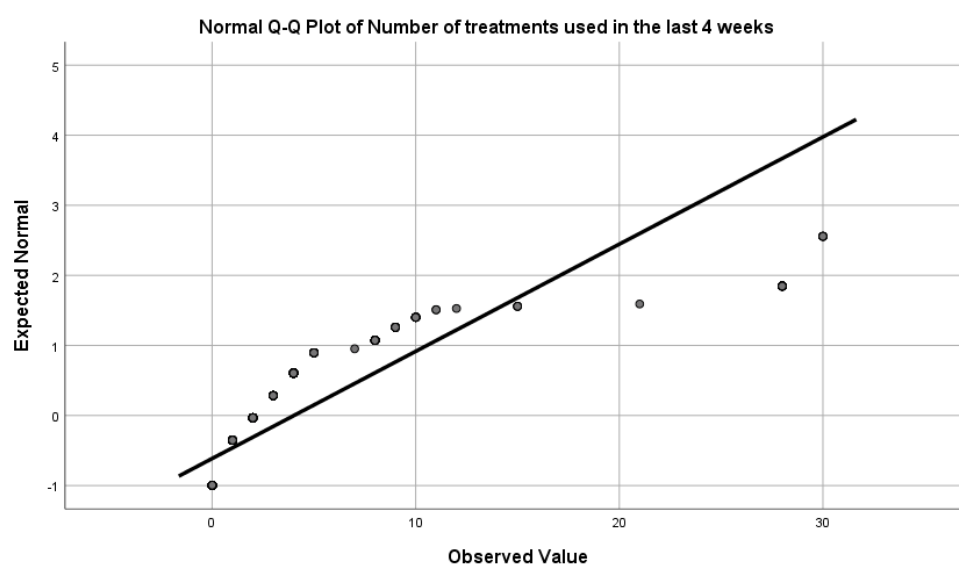


Figure 19: Q-Q plot for number of treatments used in the last 4 weeks

DV: Last time treatment was used (days)

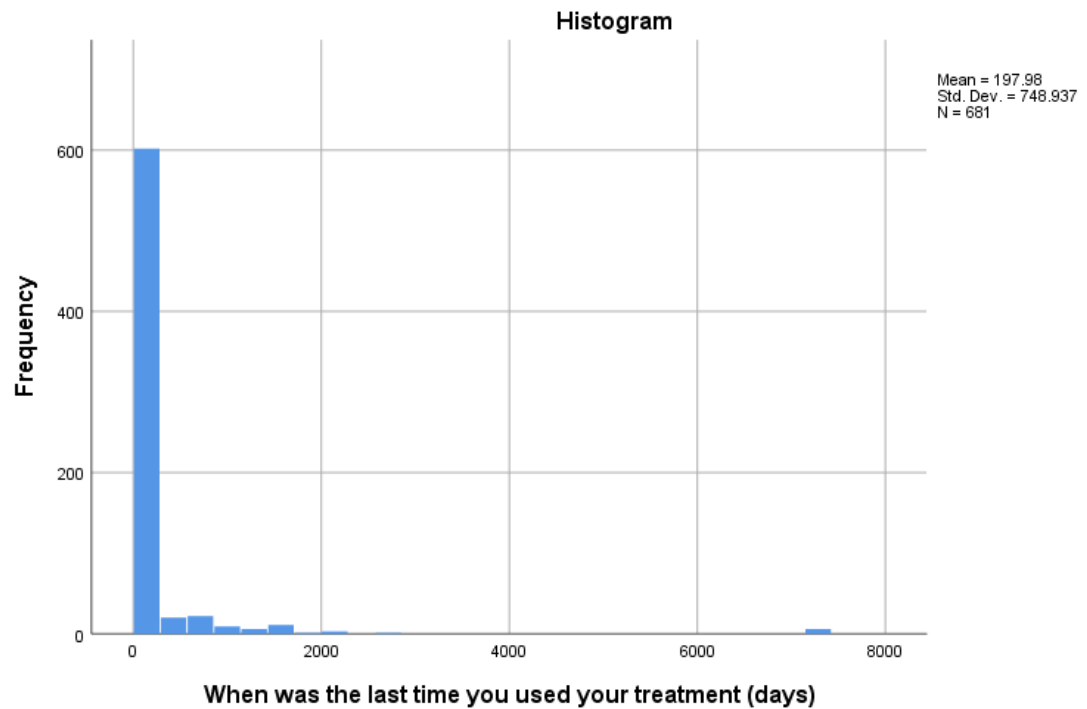


Figure 20: Histogram of data distribution for number of Last time treatment was used (days)

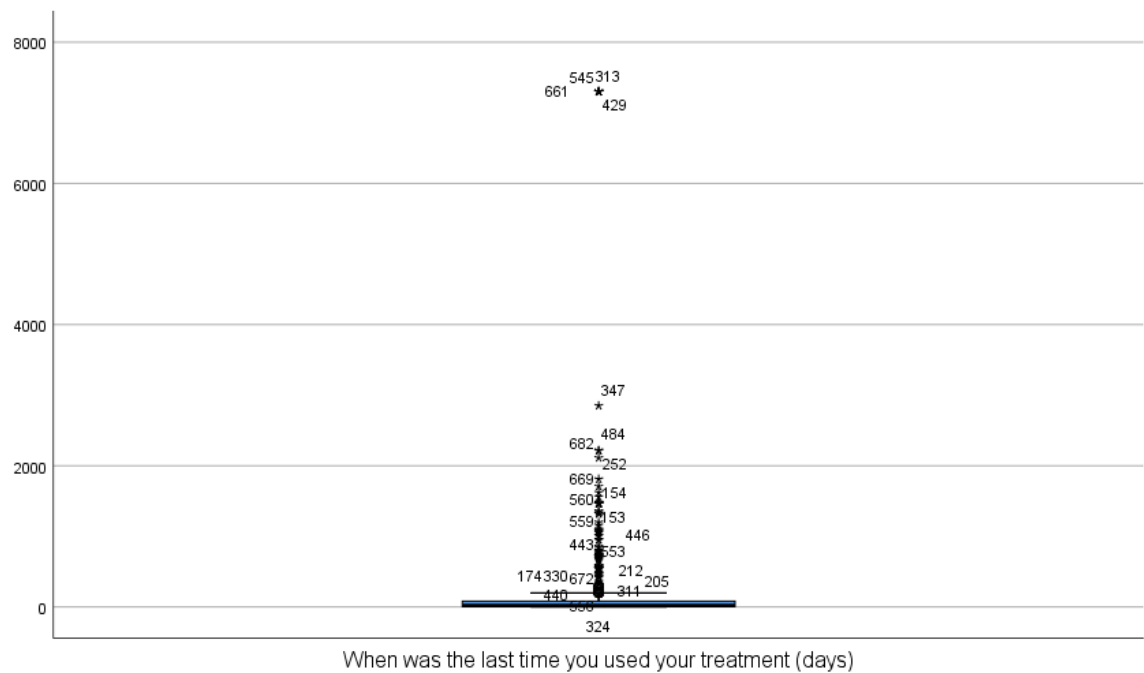


Figure 21: Outliers-Box plot of data distribution for number of Last time treatment was used (days)

Test of normal distribution

Table 48: Descriptive data for number of Last time treatment was used (days)

Descriptives		Statistic	Std. Error
When was the last time you used your treatment (days)	Mean	197.98	28.699
	95% Confidence Interval for Lower Bound	141.63	
	Mean Upper Bound	254.33	
	5% Trimmed Mean	79.98	
	Median	20.00	
	Variance	560906.411	
	Std. Deviation	748.937	
	Minimum	0	
	Maximum	7300	
	Range	7300	
	Interquartile Range	78	
	Skewness	7.845	.094
	Kurtosis	69.685	.187

Table 49: Test of normality for number of Last time treatment was used (days)

Tests of Normality						
	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
When was the last time you used your treatment (days)	.396	681	.000	.251	681	.000

a. Lilliefors Significance Correction

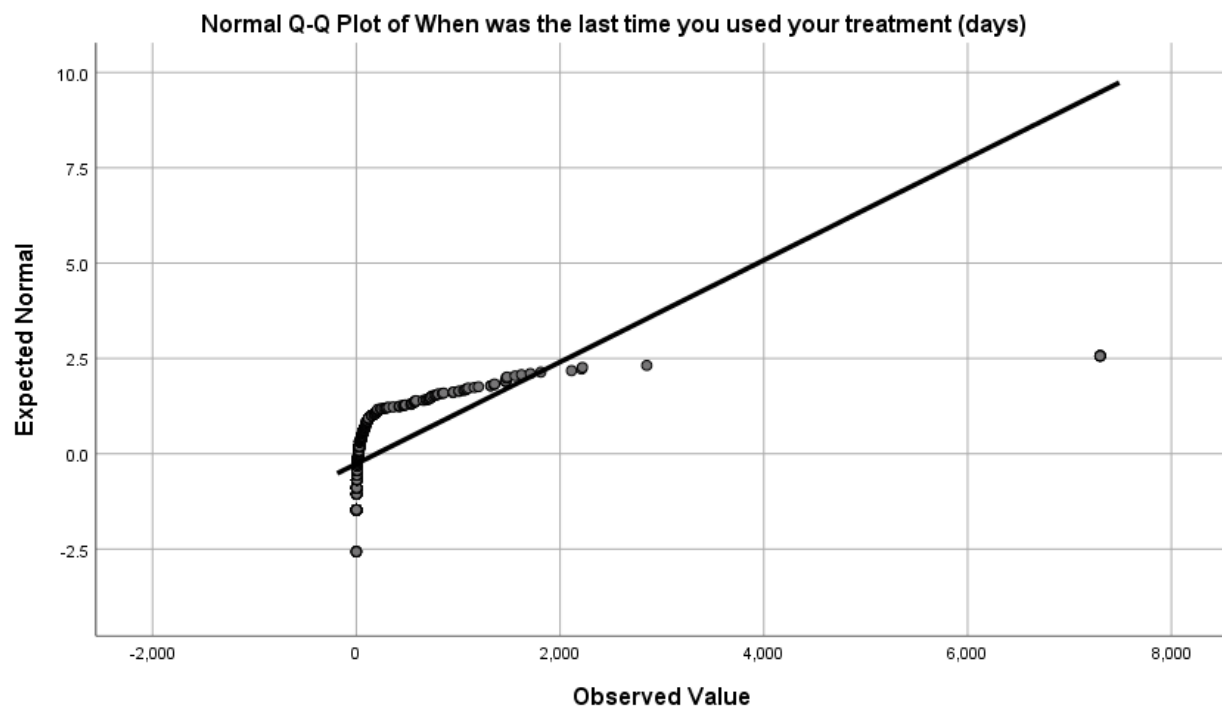


Figure 22: Q-Q plot for number of Last time treatment was used (days)

DV: Number of Sexual Attempts in the last 4 Weeks

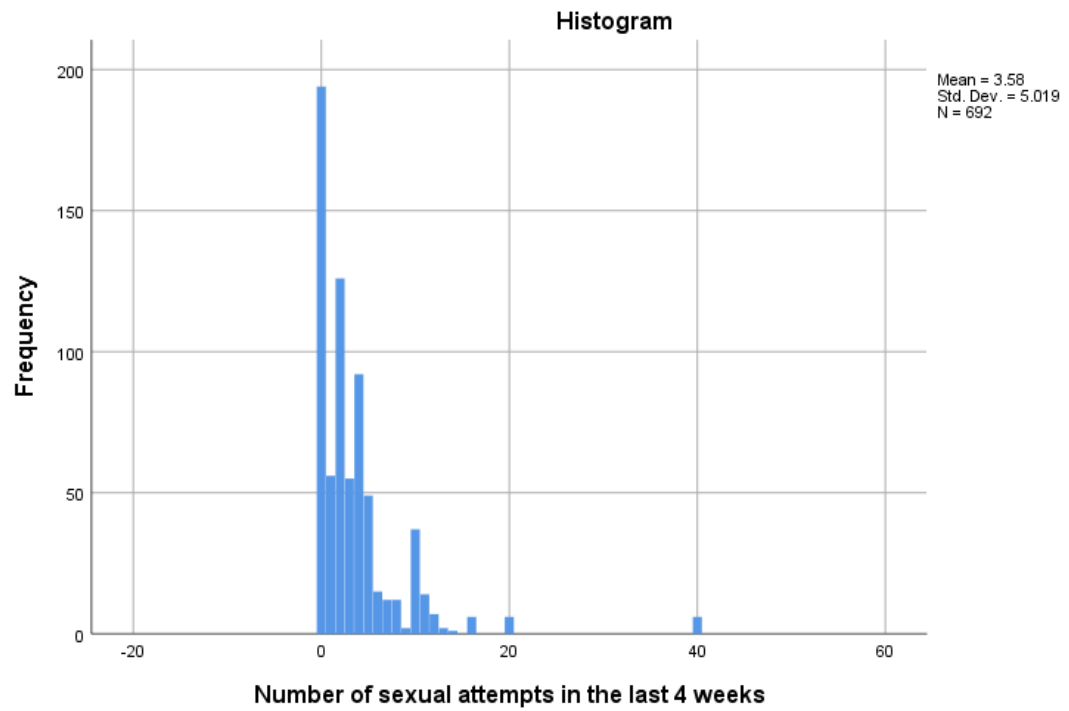


Figure 23: Histogram of data distribution for number of sexual attempts in the last 4 weeks

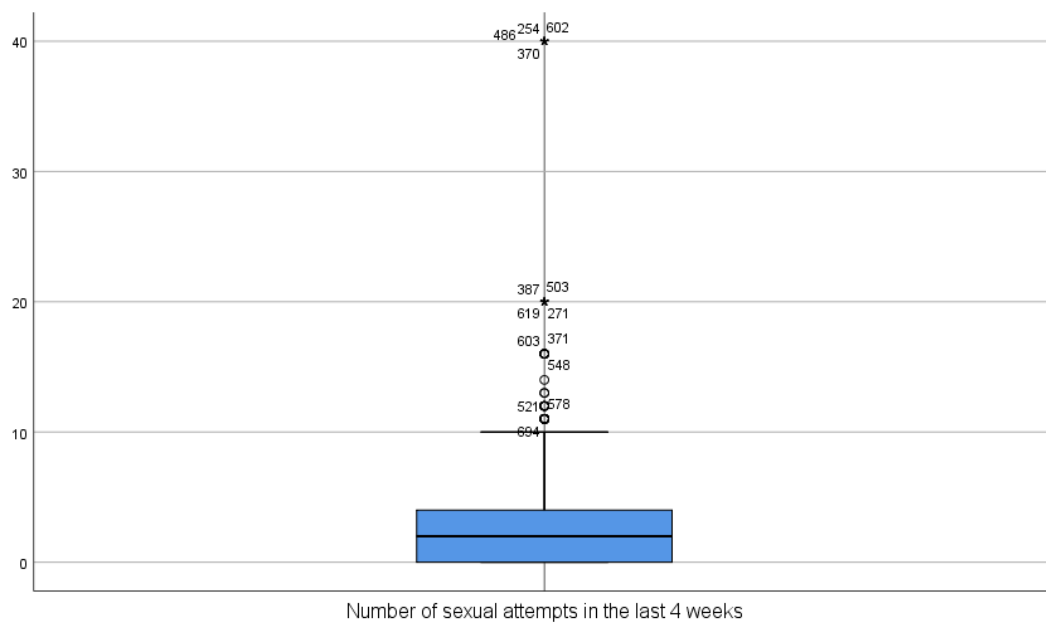


Figure 24: Outliers-Box plot of data distribution for number of sexual attempts in the last 4 weeks

Test of normal distribution

Table 50: Descriptive data for number of sexual attempts in the last 4 weeks

Descriptives		Statistic	Std. Error
Number of sexual attempts in the last 4 weeks	Mean	3.58	.191
	95% Confidence Interval for Lower Bound	3.21	
	Mean Upper Bound	3.96	
	5% Trimmed Mean	2.93	
	Median	2.00	
	Variance	25.193	
	Std. Deviation	5.019	
	Minimum	0	
	Maximum	40	
	Range	40	
	Interquartile Range	4	
	Skewness	3.927	.093
	Kurtosis	23.082	.186

Table 51: Test of normality for number of sexual attempts in the last 4 weeks

Tests of Normality						
	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Number of sexual attempts in the last 4 weeks	.238	692	.000	.637	692	.000

a. Lilliefors Significance Correction

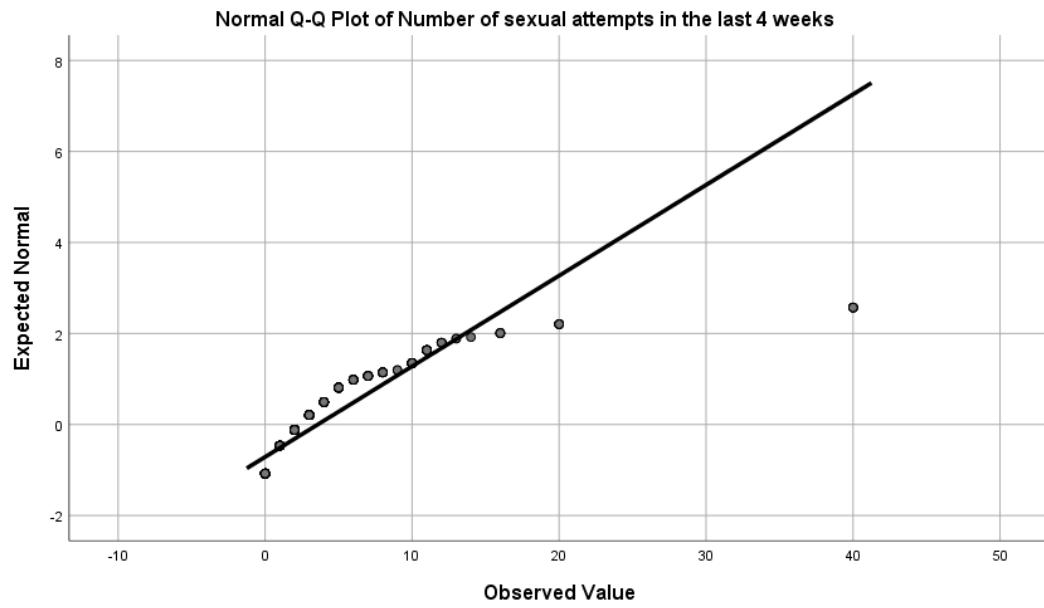


Figure 25: Q-Q plot for number of sexual attempts in the last 4 weeks

IV: Total number of comorbidities

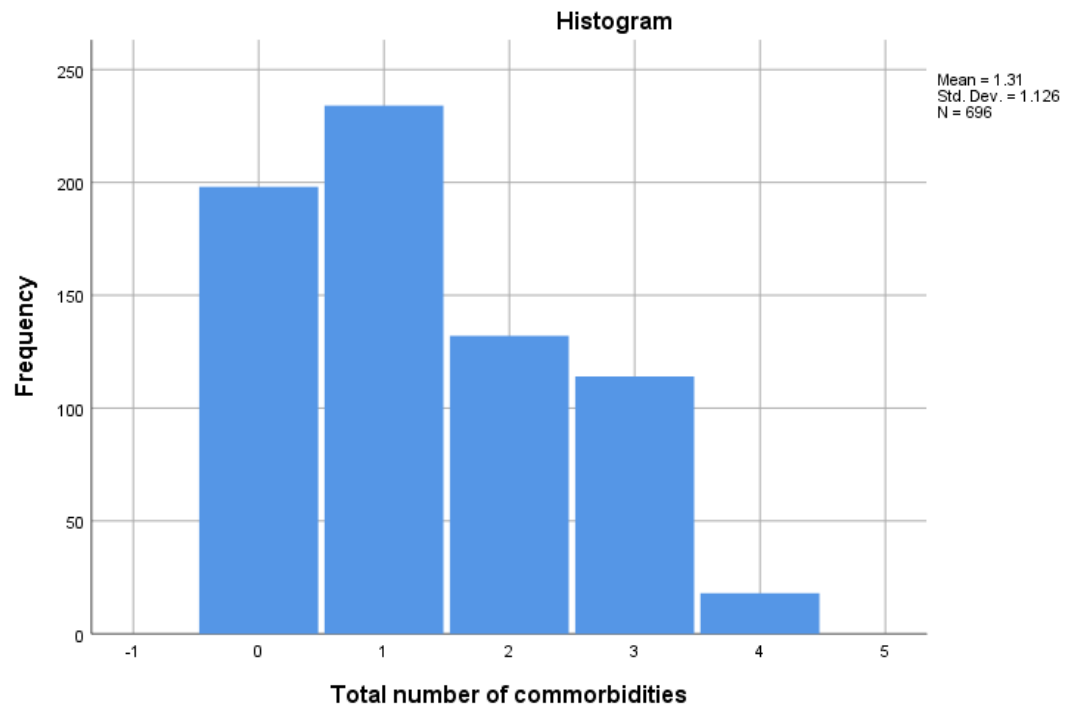


Figure 26: Histogram of data distribution for total number of comorbidities

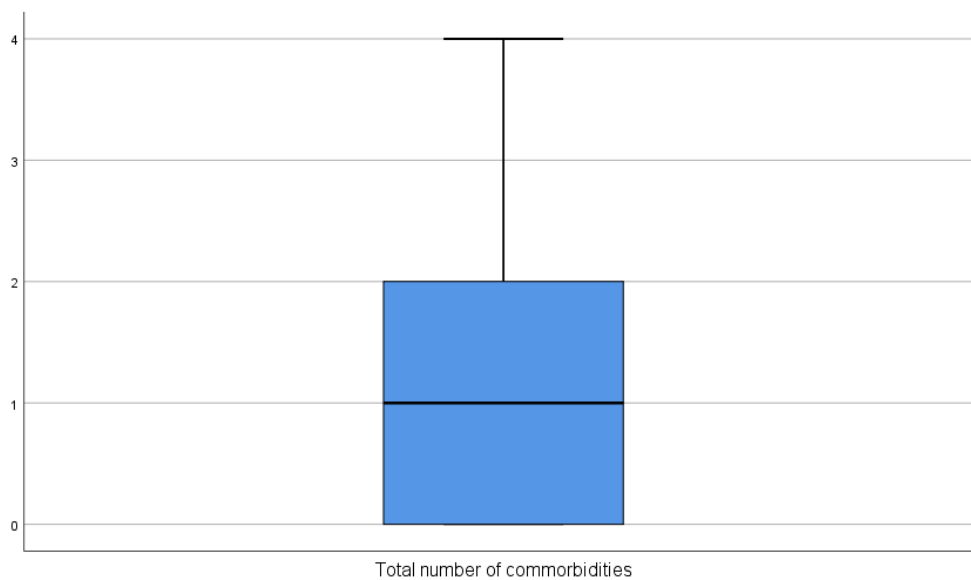


Figure 27: Outliers-Box plot of data distribution for total number of comorbidities

Test of normal distribution

Table 52: Descriptive data for total number of comorbidities

Descriptives				Statistic	Std. Error
Total number of comorbidities	Mean			1.31	.043
	95% Confidence Interval for Lower Bound			1.23	
	Mean Upper Bound			1.39	
	5% Trimmed Mean			1.26	
	Median			1.00	
	Variance			1.268	
	Std. Deviation			1.126	
	Minimum			0	
	Maximum			4	
	Range			4	
	Interquartile Range			2	
	Skewness			.496	.093
	Kurtosis			-.767	.185

Table 53: Test of normality for total number of comorbidities

Tests of Normality							
			Kolmogorov-Smirnov ^a			Shapiro-Wilk	
			Statistic	df	Sig.	Statistic	Sig.
Total number of comorbidities			.229	696	.000	.872	.000

a. Lilliefors Significance Correction

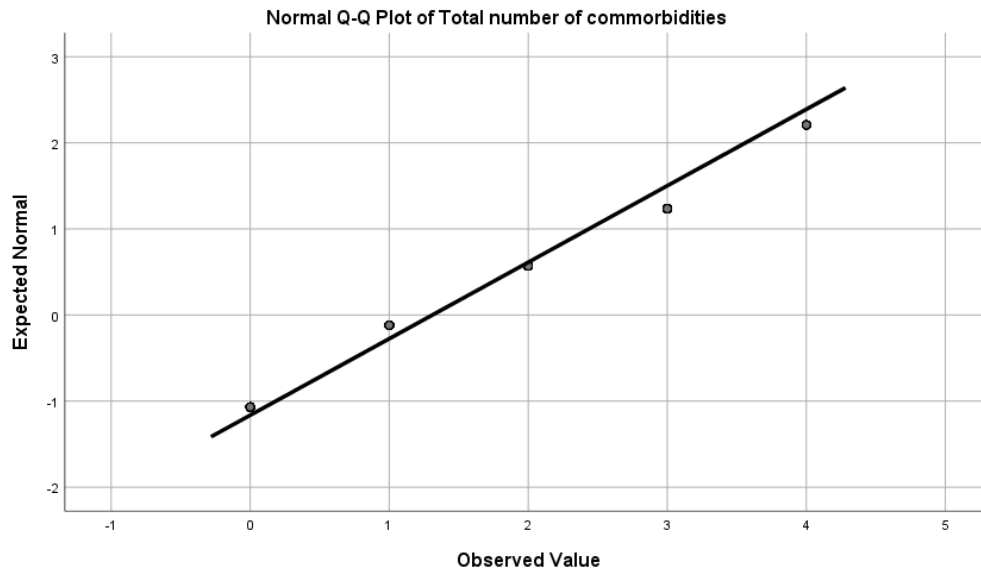


Figure 28: Q-Q plot for total number of comorbidities

IV: ED Duration

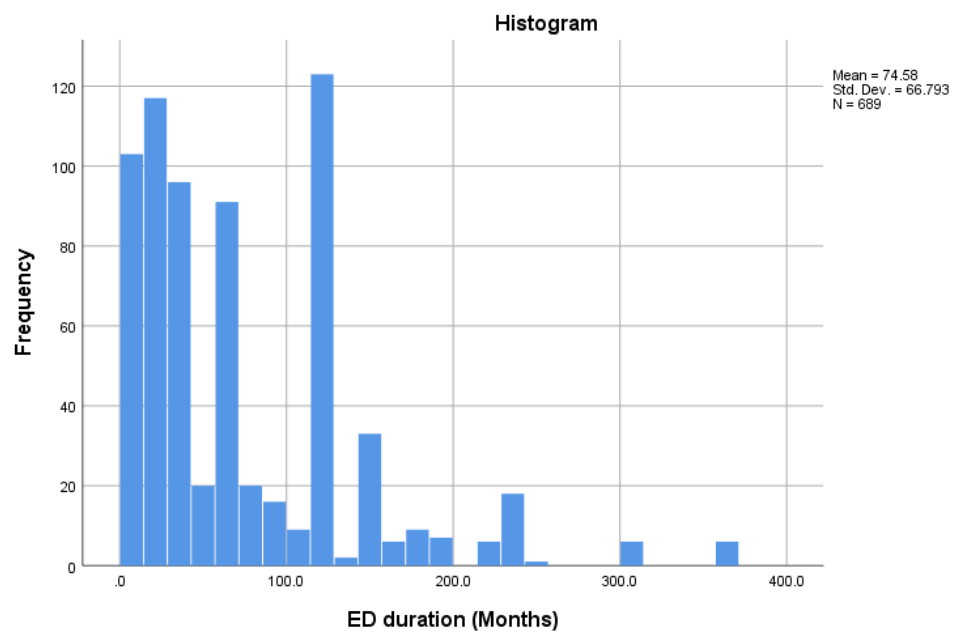


Figure 29: Histogram of data distribution for ED Duration

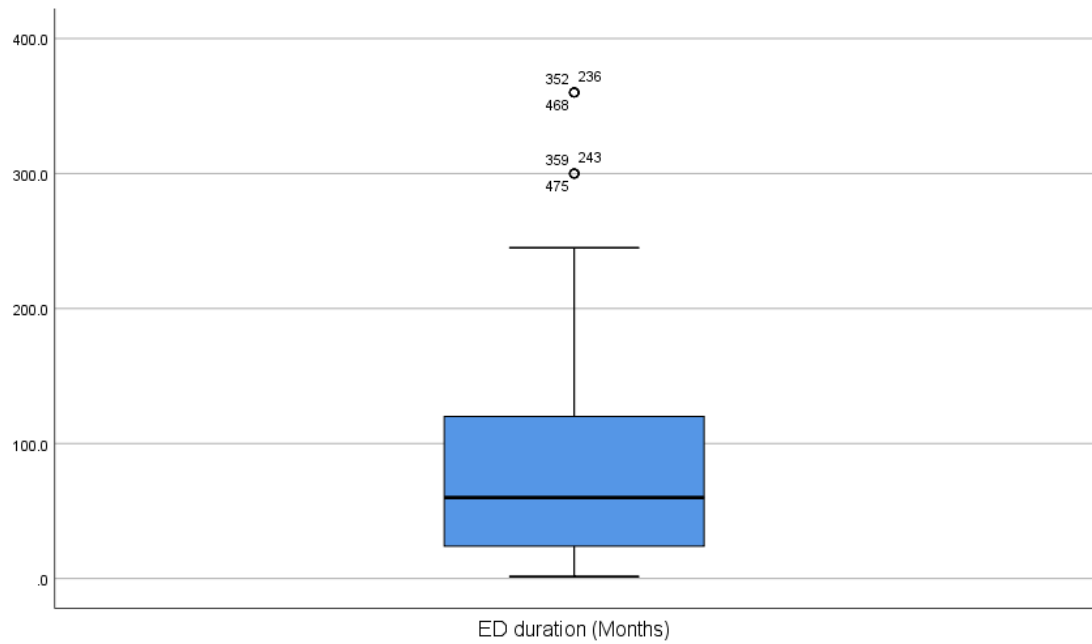


Figure 30: Outliers-Box plot of data distribution for ED Duration

Test of normal distribution

Table 54: Descriptive data for ED Duration

Descriptives		Statistic	Std. Error
ED duration (Months)	Mean	74.576	2.5446
	95% Confidence Interval for Lower Bound	69.580	
	Mean Upper Bound	79.572	
	5% Trimmed Mean	67.652	
	Median	60.000	
	Variance	4461.357	
	Std. Deviation	66.7934	
	Minimum	1.5	
	Maximum	360.0	
	Range	358.5	
	Interquartile Range	96.0	
	Skewness	1.524	.093
	Kurtosis	2.831	.186

Table 55: Test of normality for ED Duration

Tests of Normality						
	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
ED duration (Months)	.179	689	.000	.844	689	.000

a. Lilliefors Significance Correction

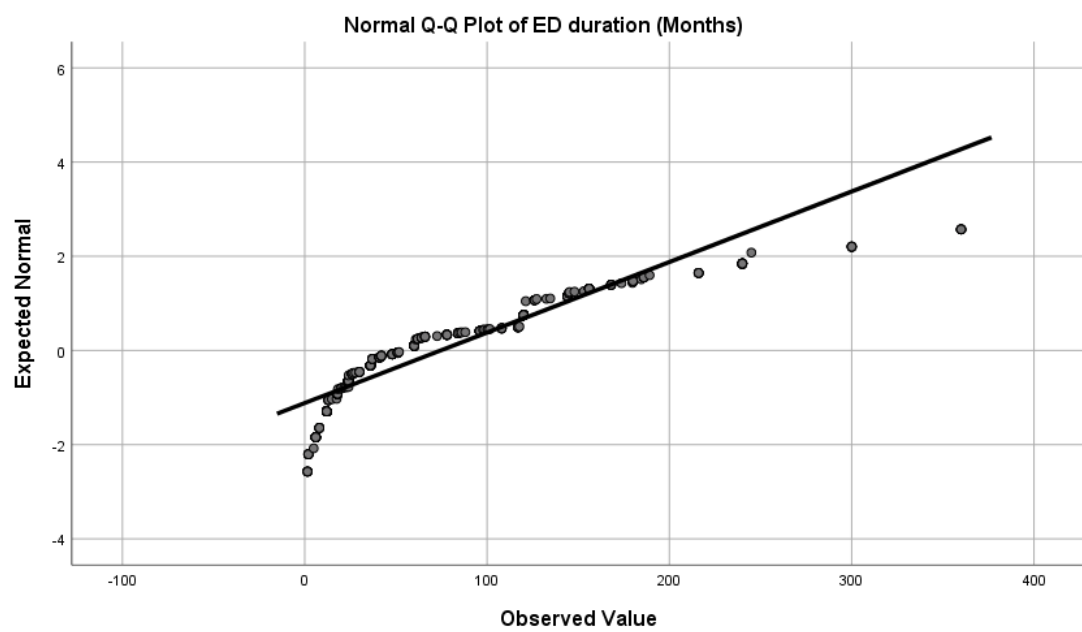


Figure 31: Q-Q plot for ED Duration

IV: Number of Treatments Prescribed for the last 4 weeks

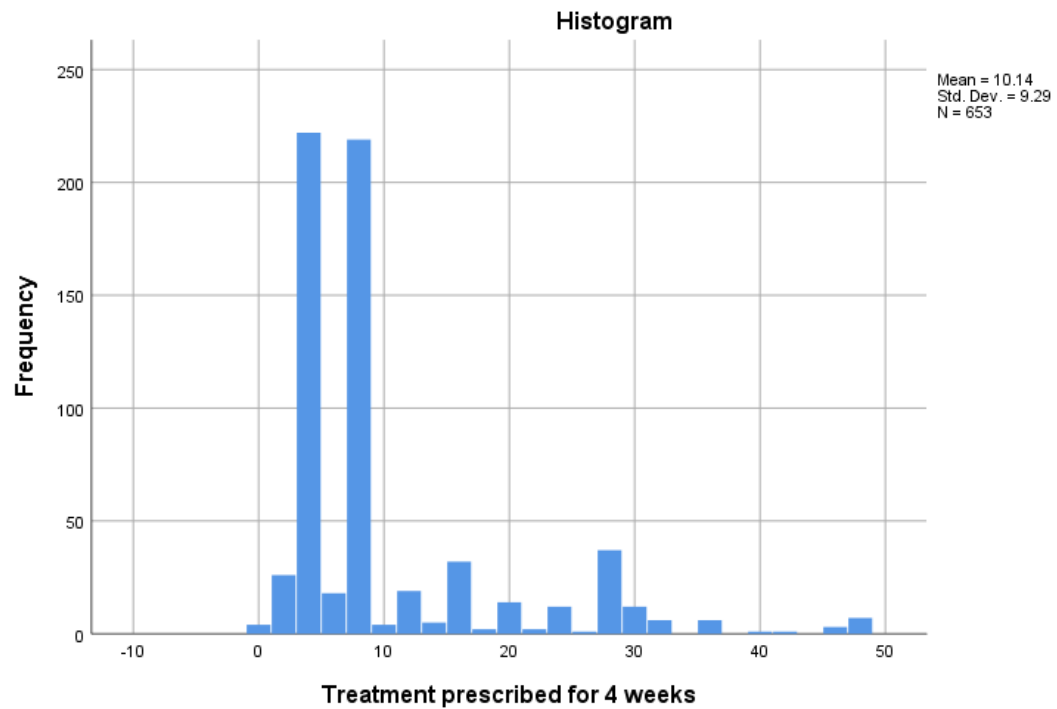


Figure 32: Histogram of data distribution for number of treatments prescribed for the last 4 weeks

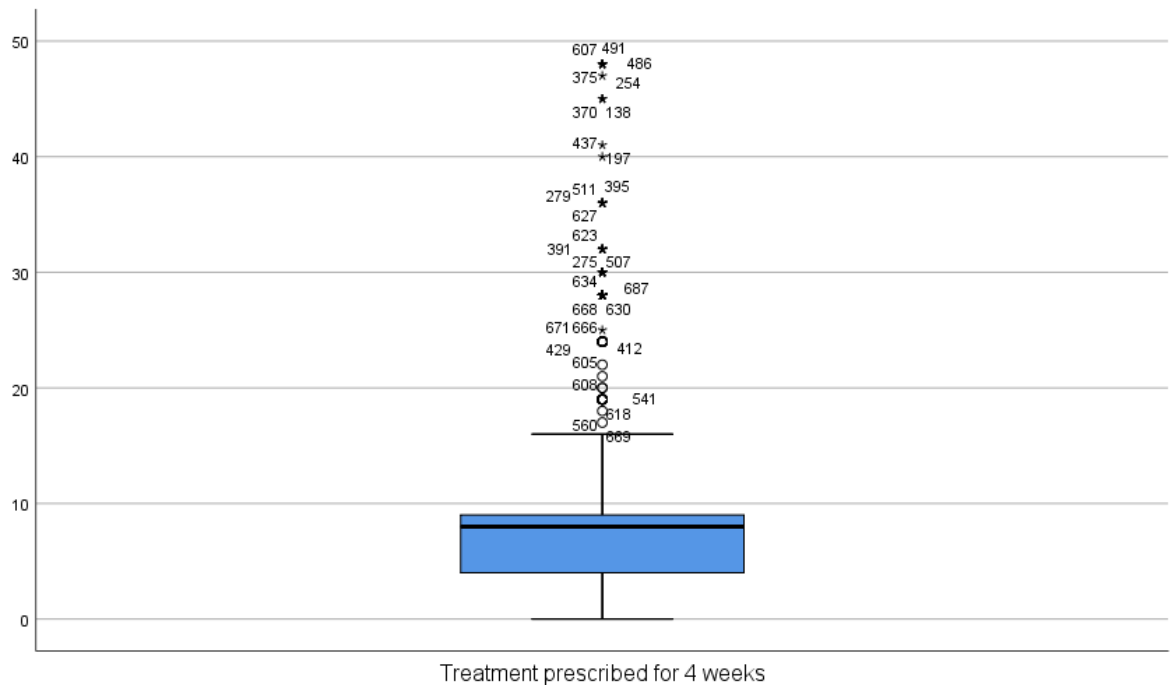


Figure 33: Outliers-Box plot of data distribution for number of treatments prescribed for the last 4 weeks

Test of normal distribution

Table 56: Descriptive data for number of treatments prescribed for the last 4 weeks

Descriptives		Statistic	Std. Error
Treatment prescribed for 4 weeks	Mean	10.14	.364
	95% Confidence Interval for Lower Bound	9.43	
	Mean Upper Bound	10.85	
	5% Trimmed Mean	9.10	
	Median	8.00	
	Variance	86.308	
	Std. Deviation	9.290	
	Minimum	0	
	Maximum	48	
	Range	48	
	Interquartile Range	5	
	Skewness	1.937	.096
	Kurtosis	3.461	.191

Table 57: Test of normality for number of treatments prescribed for the last 4 weeks

Tests of Normality						
	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Treatment prescribed for 4 weeks	.340	653	.000	.724	653	.000

a. Lilliefors Significance Correction

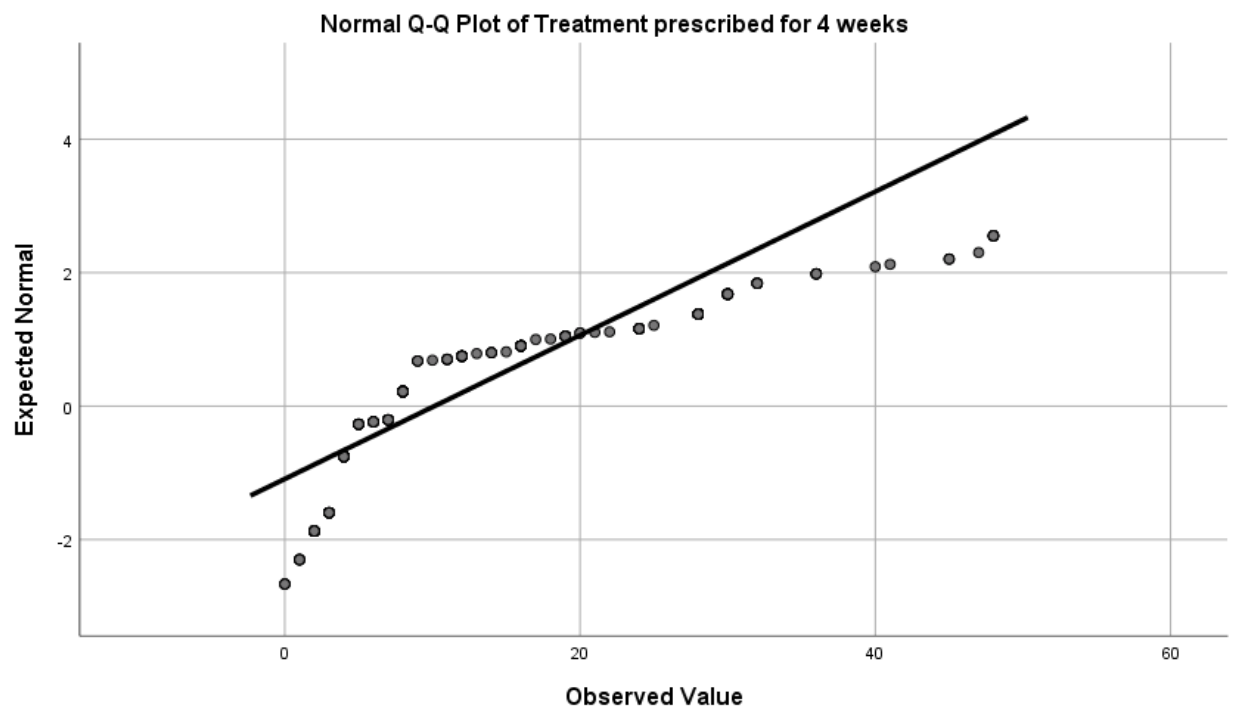


Figure 34: Q-Q plot for number of treatments prescribed for the last 4 weeks

Appendix 19: Winsorized Linear Regression: Number of days since last using treatment

Normality

Based on the P-P plot there is a deviation from the line of normality, however, the Winsorized data improves the line of normality (See Figure 36).

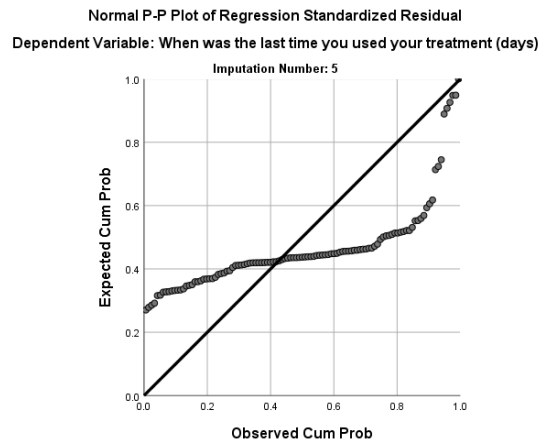


Figure 35: P-P plot for DV: No of days since last using treatment (pre-winsorized)

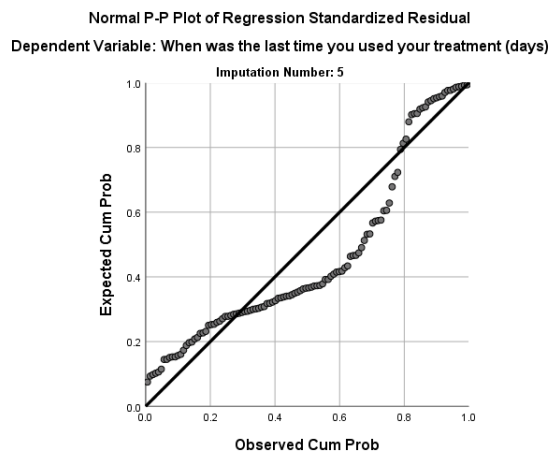


Figure 36: P-P plot for DV: No of days since last using treatment (winsorized)

Homoscedasticity

In relation to whether the data is homoscedastic, there is a very tight distribution at the bottom, centre of the plot, and a very wide distribution to the right, left and top of the plot, again the winsorizing process improves the homoscedacity of the data (Figure 37 and Figure 38)

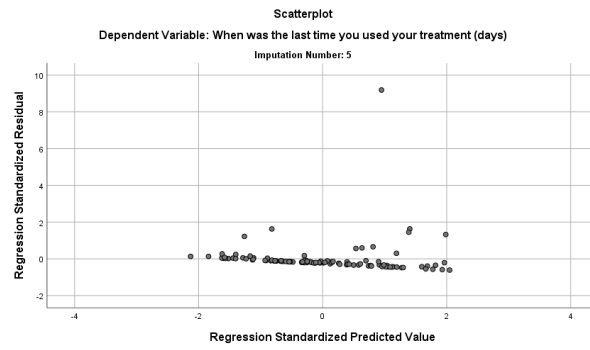


Figure 37: homoscedasticity of number of days since last using treatment of treatment (pre-winsorized)

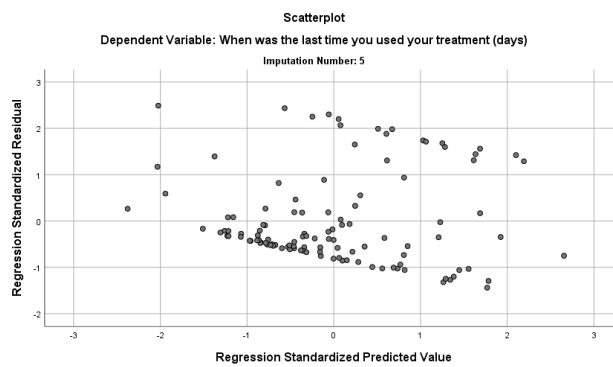


Figure 38: homoscedasticity of number of days since last using treatment of treatment (post-winsorized)

Multicollinearity

According to the data presented in Table 58 , each VIF value is below 10 in both instances, indicating that the assumption is met and therefore there is an absence of multicollinearity.

Table 58: Linear regression Coefficients

a) Pre-winsorized data

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Collinearity Statistics	
	B	Std. Error	Beta			Tolerance	VIF
1							
(Constant)	-260.881	482.447		-0.541	0.590		
Total BMQ Necessity Score - total of reversed items	6.764	21.290	0.042	0.318	0.751	0.530	1.887
Total BMQ Concerns Score - total of reversed items	-6.349	24.104	-0.036	-0.263	0.793	0.505	1.981
I aim to have a sex life that does not rely on treatment.	32.380	68.077	0.048	0.476	0.635	0.912	1.097
Using treatment for ED has a negative impact on my masculinity	109.266	63.874	0.174	1.711	0.090	0.905	1.105
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	2.258	57.675	0.004	0.039	0.969	0.863	1.159

b) Post-winsorized data

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Collinearity Statistics	
	B	Std. Error	Beta			Tolerance	VIF
1							
(Constant)	112.808	44.900		2.512	0.013		
Total BMQ Necessity Score - total of reversed items	0.166	1.815	0.011	0.092	0.927	0.578	1.729
Total BMQ Concerns Score - total of reversed items	-1.441	2.124	-0.081	-0.679	0.499	0.548	1.825
I aim to have a sex life that does not rely on treatment.	-6.776	6.157	-0.102	-1.101	0.274	0.914	1.094
Using treatment for ED has a negative impact on my masculinity	11.208	5.928	0.176	1.891	0.061	0.899	1.113

My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.457	5.354	-0.256	-2.700	0.008	0.865	1.156

Interpretation of the Multi-linear Regression

The following output indicates that the independent variables account for between 1.4 (imputation number 4) and 3.3 % (imputation number 3) of the variance in relation to the pre-winsorized data. However, using the winsorized data, the model accounted for between 10.2% (original data) and 14.4% of the data (See Table 59).

Table 59: Model Summary

a) Pre-winsorized data

Model Summary ^b					
Imputation Number	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
Original data	1	.167 ^a	.028	-.031	798.968
1	1	.157 ^c	.025	-.023	769.107
2	1	.164 ^c	.027	-.021	812.831
3	1	.182 ^c	.033	-.014	766.783
4	1	.120 ^c	.014	-.033	782.707
5	1	.178 ^c	.032	-.015	759.308

a. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items

b. Dependent Variable: When was the last time you used your treatment (days)

c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

b) Post-winsorized data

Model Summary ^b					
Imputation Number	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
Original data	1	.319 ^a	.102	.048	45.489
1	1	.360 ^c	.129	.089	72.901
2	1	.350 ^c	.122	.082	72.965
3	1	.366 ^c	.134	.094	84.054
4	1	.350 ^c	.123	.083	79.745

5	1	.379 ^c	.144	.105	71.777

a. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items

b. Dependent Variable: When was the last time you used your treatment (days)

c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

Table 60: ANOVA

a) Pre-winsorized data

ANOVA ^a							
Imputation Number	Model		Sum of Squares	df	Mean Square	F	Sig.
Original data	1	Regression	1529026.292	5	305805.258	.479	.791 ^b
		Residual	52983082.989	83	638350.397		
		Total	54512109.281	88			
1	1	Regression	1533862.877	5	306772.575	.519	.762 ^c
		Residual	60335553.752	102	591525.037		
		Total	61869416.630	107			
2	1	Regression	1869954.178	5	373990.836	.566	.726 ^c
		Residual	68051525.143	103	660694.419		
		Total	69921479.321	108			
3	1	Regression	2072706.953	5	414541.391	.705	.621 ^c
		Residual	60559489.010	103	587956.204		
		Total	62632195.963	108			
4	1	Regression	927321.502	5	185464.300	.303	.910 ^c
		Residual	63100964.149	103	612630.720		
		Total	64028285.651	108			
5	1	Regression	1946958.681	5	389391.736	.675	.643 ^c
		Residual	59384492.309	103	576548.469		
		Total	61331450.991	108			

a. Dependent Variable: When was the last time you used your treatment (days)

- b. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items
- c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

b) Post-winsorized data

ANOVA ^a							
Imputation Number	Model		Sum of Squares	df	Mean Square	F	Sig.
Original data	1	Regression	19429.102	5	3885.820	1.878	.107 ^b
		Residual	171744.179	83	2069.207		
		Total	191173.281	88			
1	1	Regression	86065.219	5	17213.044	3.239	.009 ^c
		Residual	579284.225	109	5314.534		
		Total	665349.443	114			
2	1	Regression	81600.160	5	16320.032	3.065	.013 ^c
		Residual	585632.556	110	5323.932		
		Total	667232.716	115			
3	1	Regression	120041.146	5	24008.229	3.398	.007 ^c
		Residual	777162.095	110	7065.110		
		Total	897203.241	115			

4	1	Regression	97796.854	5	19559.371	3.076	.012 ^c
		Residual	699520.697	110	6359.279		
		Total	797317.552	115			
5	1	Regression	95239.766	5	19047.953	3.697	.004 ^c
		Residual	566708.682	110	5151.897		
		Total	661948.448	115			

a. Dependent Variable: When was the last time you used your treatment (days)

b. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items

c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

Table 61: Coefficients

a) Pre-winsorized data

		Coefficients ^a									
Imputation Number	Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Collinearity Statistics		Fraction Missing Info.	Relative Increase in Variance	Relative Efficiency
		B	Std. Error	Beta			Tolerance	VIF			
Original data	1 (Constant)	-574.204	560.203		-.976	.332					
	Total BMQ Necessity Score - total of reversed items	9.171	23.735	.055	.386	.700	.568	1.761			
	Total BMQ Concerns Score - total of reversed items	-4.393	26.566	-.024	-.165	.869	.536	1.867			

		I aim to have a sex life that does not rely on treatment.	47.688	79.737	.068	.598	.551	.904	1.106			
		Using treatment for ED has a negative impact on my masculinity	112.500	78.097	.164	1.441	.153	.903	1.108			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	39.101	66.348	.067	.589	.557	.906	1.104			
		(Constant)	- 299.786	479.875		-.625	.534					
1	1	Total BMQ Necessity Score - total of reversed items	8.576	21.343	.053	.402	.689	.543	1.842			

		Total BMQ Concerns Score - total of reversed items	-2.444	24.154	-.014	-.101	.920	.516	1.939			
		I aim to have a sex life that does not rely on treatment.	37.440	67.655	.056	.553	.581	.944	1.060			
		Using treatment for ED has a negative impact on my masculinity	94.832	66.088	.145	1.435	.154	.934	1.071			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-5.537	57.434	-.010	-.096	.923	.922	1.085			
2	1	(Constant)	-156.102	532.623		-.293	.770					

Total BMQ Necessity Score - total of reversed items	15.591	22.733	.091	.686	.494	.533	1.877			
Total BMQ Concerns Score - total of reversed items	-13.014	25.713	-.069	-.506	.614	.508	1.967			
I aim to have a sex life that does not rely on treatment.	36.378	70.160	.052	.518	.605	.926	1.080			
Using treatment for ED has a negative impact on my masculinity	88.768	70.892	.128	1.252	.213	.900	1.111			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	- 19.376	62.508	-.032	-.310	.757	.875	1.143			
3	1	(Constant)	- 128.684	482.079		-.267	.790					
		Total BMQ Necessity Score - total of reversed items	2.843	21.221	.018	.134	.894	.544	1.839			
		Total BMQ Concerns Score - total of reversed items	-7.018	24.305	-.039	-.289	.773	.506	1.975			
		I aim to have a sex life that does not rely on treatment.	27.710	67.579	.041	.410	.683	.924	1.083			

		Using treatment for ED has a negative impact on my masculinity	108.588	65.512	.170	1.658	.100	.897	1.115			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-7.712	56.978	-.014	-.135	.893	.902	1.109			
4	1	(Constant)	73.643	508.425		.145	.885					
		Total BMQ Necessity Score - total of reversed items	9.418	21.654	.058	.435	.665	.544	1.837			
		Total BMQ Concerns Score - total of reversed items	-11.802	24.635	-.065	-.479	.633	.513	1.948			

		I aim to have a sex life that does not rely on treatment.	8.082	71.637	.011	.113	.910	.927	1.079			
		Using treatment for ED has a negative impact on my masculinity	61.604	68.615	.093	.898	.371	.894	1.119			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	- 15.327	58.770	-.027	-.261	.795	.895	1.117			
5	1	(Constant)	- 260.881	482.447		-.541	.590					
		Total BMQ Necessity Score - total of reversed items	6.764	21.290	.042	.318	.751	.530	1.887			

	Total BMQ Concerns Score - total of reversed items	-6.349	24.104	-.036	-.263	.793	.505	1.981			
	I aim to have a sex life that does not rely on treatment.	32.380	68.077	.048	.476	.635	.912	1.097			
	Using treatment for ED has a negative impact on my masculinity	109.266	63.874	.174	1.711	.090	.905	1.105			
	My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	2.258	57.675	.004	.039	.969	.863	1.159			
Pooled	1 (Constant)	-154.362	522.558		-.295	.768			.097	.103	.981

Total BMQ Necessity Score - total of reversed items	8.638	22.244		.388	.698			.053	.055	.989
Total BMQ Concerns Score - total of reversed items	-8.125	25.037		-.325	.746			.036	.037	.993
I aim to have a sex life that does not rely on treatment.	28.398	70.278		.404	.686			.035	.036	.993
Using treatment for ED has a negative impact on my masculinity	92.612	70.347		1.316	.189			.096	.101	.981

My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-9.138	59.439		-.154	.878			.025	.025	.995

a. Dependent Variable: When was the last time you used your treatment (days)

b) Post Winsorized data

		Coefficients ^a									
		Unstandardized Coefficients		Standardized Coefficients			Collinearity Statistics		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
Imputation Number	Model	B	Std. Error	Beta	t	Sig.	Tolerance	VIF			
Original data	1 (Constant)	85.977	32.692		2.630	.010					

Total BMQ Necessity Score - total of reversed items	-0.062	1.351	-.006	-.046	.964	.568	1.761			
Total BMQ Concerns Score - total of reversed items	-1.109	1.513	-.104	-.734	.465	.536	1.867			
I aim to have a sex life that does not rely on treatment.	-7.470	4.540	-.180	-1.645	.104	.904	1.106			
Using treatment for ED has a negative impact on my masculinity	4.050	4.446	.100	.911	.365	.903	1.108			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-5.435	3.777	-.157	-1.439	.154	.906	1.104			
1	1	(Constant)	122.283	44.625		2.740	.007					
		Total BMQ Necessity Score - total of reversed items	.349	1.906	.022	.183	.855	.552	1.811			
		Total BMQ Concerns Score - total of reversed items	-2.035	2.217	-.113	-.918	.361	.525	1.905			
		I aim to have a sex life that does not rely on treatment.	-6.959	6.148	-.104	-1.132	.260	.943	1.061			

		Using treatment for ED has a negative impact on my masculinity	9.512	6.122	.144	1.554	.123	.934	1.071			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.123	5.370	-.246	-2.630	.010	.911	1.097			
2	1	(Constant)	134.685	46.681		2.885	.005					
		Total BMQ Necessity Score - total of reversed items	.844	1.975	.053	.428	.670	.528	1.893			
		Total BMQ Concerns Score - total of reversed items	-2.543	2.260	-.142	-1.125	.263	.503	1.987			

		I aim to have a sex life that does not rely on treatment.	-9.601	6.076	-.147	-1.580	.117	.919	1.088			
		Using treatment for ED has a negative impact on my masculinity	7.219	6.217	.109	1.161	.248	.901	1.110			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-12.989	5.504	-.225	-2.360	.020	.877	1.140			
3	1	(Constant)	104.955	51.563		2.035	.044					
		Total BMQ Necessity Score - total of reversed items	1.404	2.172	.076	.646	.519	.576	1.737			

		Total BMQ Concerns Score - total of reversed items	-2.985	2.504	-.146	-1.192	.236	.525	1.905			
		I aim to have a sex life that does not rely on treatment.	-4.221	7.093	-.055	-.595	.553	.926	1.079			
		Using treatment for ED has a negative impact on my masculinity	13.657	7.049	.182	1.937	.055	.891	1.123			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.889	6.145	-.212	-2.260	.026	.895	1.117			
4	1	(Constant)	144.480	50.287		2.873	.005					

Total BMQ Necessity Score - total of reversed items	.938	2.080	.054	.451	.653	.557	1.79 5			
Total BMQ Concerns Score - total of reversed items	-3.019	2.402	-.155	- 1.25 7	.211	.526	1.90 1			
I aim to have a sex life that does not rely on treatment.	-9.594	6.939	-.128	- 1.38 3	.170	.934	1.07 1			
Using treatment for ED has a negative impact on my masculinity	7.983	6.821	.110	1.17 0	.244	.896	1.11 6			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.666	5.909	-.220	-2.313	.023	.885	1.131			
5	1	(Constant)	112.808	44.900		2.512	.013					
		Total BMQ Necessity Score - total of reversed items	.166	1.815	.011	.092	.927	.578	1.729			
		Total BMQ Concerns Score - total of reversed items	-1.441	2.124	-.081	-.679	.499	.548	1.825			
		I aim to have a sex life that does not rely on treatment.	-6.776	6.157	-.102	-1.101	.274	.914	1.094			

		Using treatment for ED has a negative impact on my masculinity	11.208	5.928	.176	1.891	.061	.899	1.113			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.457	5.354	-.256	-2.700	.008	.865	1.156			
Pooled	1	(Constant)	123.842	50.815		2.437	.015			.125	.135	.976
		Total BMQ Necessity Score - total of reversed items	.740	2.066		.358	.720			.071	.073	.986
		Total BMQ Concerns Score - total of reversed items	-2.405	2.420		-.994	.321			.096	.102	.981

I aim to have a sex life that does not rely on treatment.	-7.430	6.951		-1.069	.286			.133	.145	.974
Using treatment for ED has a negative impact on my masculinity	9.916	7.039		1.409	.161			.173	.194	.966
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.825	5.697		-2.426	.015			.011	.011	.998

a. Dependent Variable: When was the last time you used your treatment (days)

Appendix 20: Univariate Correlations

Figure 39: Binary IV's and continuous DV's

Independent Variables	Dependent Variable	Results						
		Group	N	Mean	St. Deviation	t:	df:	Sig. (2-tailed)
Ethnicity (only 2 levels of data)*	Utilisation (% of treatment used in the last 4 weeks)	Caucasian	84	36.07	38.95	-0.34	108	0.73
		Other	26	39.02	37.91			
	Number of treatments used in the last 4 weeks	Caucasian	85	3.95	6.60	0.39	109	0.69
		Other	26	3.38	5.97			
	When was the last time you used your treatment? (Days)	Caucasian	89	221.94	817.12	0.63	113	0.53
		Other	26	117.12	363.83			
	Number of sexual attempts in the last 4 weeks	Caucasian	90	3.68	5.49	0.40	114	0.64
		Other	26	3.23	2.80			
Sexual Orientation	Utilisation (% of treatment used in the last 4 weeks)	Heterosexual	96	34.22	37.78	-1.83	108	0.07
		Other	14	54.23	40.74			

Independent Variables	Dependent Variable	Results						
		Group	N	Mean	St. Deviation	t:	df:	Sig. (2-tailed)
<i>(only 2 levels of data)*</i>	Number of treatments used in the last 4 weeks	Heterosexual	99	3.76	6.81	-0.24	109	0.81
		Other	14	4.21	2.89			
	When was the last time you used your treatment? (Days)	Heterosexual	99	215.41	785.51	0.62	113	0.54
		Other	16	92.00	327.50			
	Number of sexual attempts in the last 4 weeks	Heterosexual	100	3.37	5.06	-1.48	114	0.14
		Other	16	5.31	4.59			
<i>Occupation (only 2 levels of data)*</i>	Utilisation (% of treatment used in the last 4 weeks)	Employed	60	35.88	37.89	-0.26	108	0.79
		Retired, unemployed, other	50	37.83	39.69			
	Number of treatments used in the last 4 weeks	Employed	60	3.97	6.26	0.26	109	0.79
		Retired, unemployed, other	51	3.65	6.69			

Independent Variables	Dependent Variable	Results							
		Group	N	Mean	St. Deviation	t:	df:	Sig. (2-tailed)	
	When was the last time you used your treatment? (Days)	Employed	61	151.89	377.07	-0.71	113	0.48	
		Retired, unemployed, other	54	250.61	1004.49				
	Number of sexual attempts in the last 4 weeks	Employed	62	4.10	6.01	0.90	114	0.37	
		Retired, unemployed, other	54	3.11	3.39				
	Relationship status (<i>only 2 levels of data</i>)*	Utilisation (% of treatment used in the last 4 weeks)	Married or in a relationship	88	36.49	35.41	0.22	108.00	0.82
			Divorced, single or other	22	35.98	41.40			
Number of treatments used in the last 4 weeks		Married or in a relationship	89	3.94	6.53	0.29	114.00	0.77	

Independent Variables	Dependent Variable	Results						
		Group	N	Mean	St. Deviation	t:	df:	Sig. (2-tailed)
		Divorced, single or other	22	3.32	6.18			
		Married or in a relationship	93	145.01	308.78	-0.92	21.42	0.37
	When was the last time you used your treatment? (Days)	Divorced, single or other	23	499.78	1541.04			
	Number of sexual attempts in the last 4 weeks	Married or in a relationship	93	3.70	5.07	0.09	114.00	0.93
		Divorced, single or other	23	3.26	5.14			

DV: Percent of Medication Used

Normality

Normal P-P Plot of Regression Standardized Residual

Dependent Variable: FINAL utilisation score using calculation of utilisation using imputed data and excluding outliers

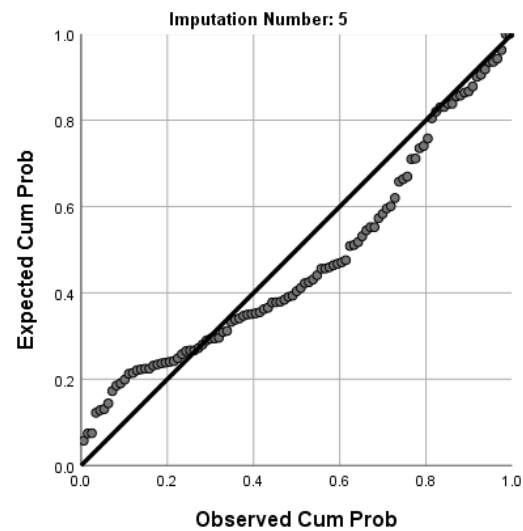


Figure 40: P-P plot for DV: % of medication used in the last 4 weeks

Homoscedasticity

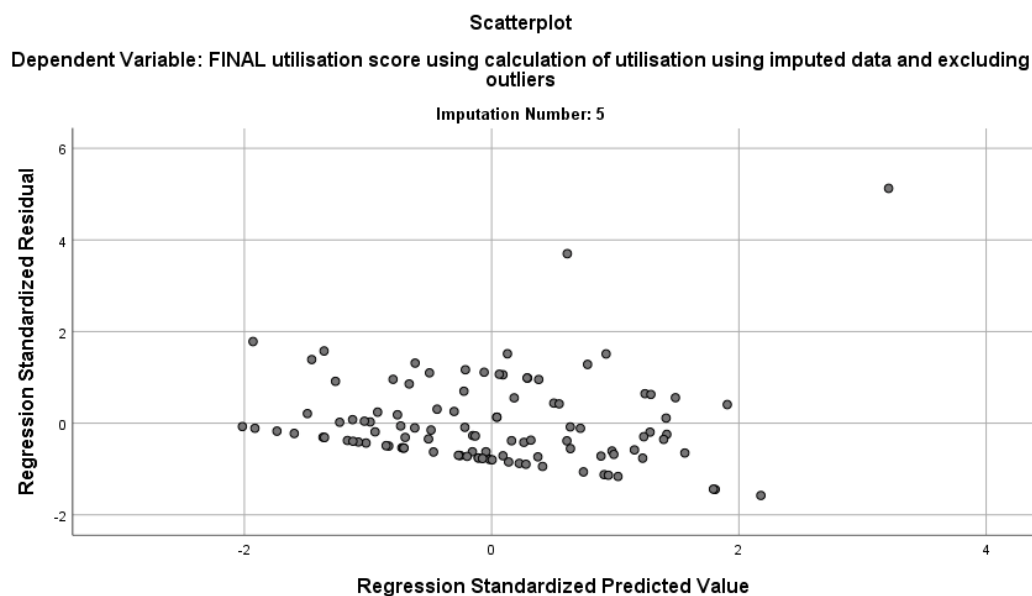


Figure 41: homoscedasticity of % of treatment used in the last 4 weeks

Multicollinearity

Table 62: Linear regression Coefficients (Pooled data)

Model	Unstandardized Coefficients		Standardized Coefficients			Collinearity Statistics	
	B	Std. Error	Beta	t	Sig.	Tolerance	VIF
1							
(Constant)	49.056	59.641	0.050	0.823	0.429		
Sexual orientation recoded	6.283	18.835	0.115	0.334	0.741	0.834	1.200
Total BMQ Necessity Score - total of reversed items	1.148	1.077	-0.050	1.065	0.288	0.896	1.117
I am optimistic that my ED treatment will make my ED better	-2.493	5.815	-0.043	-0.429	0.670	0.766	1.305
My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-2.517	7.104	-0.143	-0.354	0.724	0.742	1.349

Using treatment for ED has a negative impact on my masculinity	-5.594	4.763	0.037	-1.174	0.245	0.843	1.187
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	1.071	4.366	0.050	0.245	0.808	0.929	1.077

Interpretation of the Multi-linear Regression

Table 63: Model Summary (pooled data)

Model Summary ^b					
Imputation Number	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
Original data	1	.207 ^a	.043	-.025	44.01092
1	1	.237 ^c	.056	-.002	42.79842
2	1	.284 ^a	.080	.024	45.19237
3	1	.256 ^c	.065	.008	42.09788
4	1	.225 ^c	.051	-.007	42.89879
5	1	.347 ^a	.120	.066	53.00562

- a. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Sexual orientation recoded, I am optimistic that my ED treatment will make my ED better, Total BMQ Necessity Score - total of reversed items, Using treatment for ED has a negative impact on my masculinity, My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly
- b. Dependent Variable: FINAL utilisation score using calculation of utilisation using imputed data and excluding outliers
- c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly, Using treatment for ED has a negative impact on my masculinity, Sexual orientation recoded, I am optimistic that my ED treatment will make my ED better

Overall regression model and whether it is a good fit for the data

Table 64: ANOVA (pooled data)

ANOVA ^a							
Imputation Number	Model		Sum of Squares	df	Mean Square	F	Sig.
Original data	1	Regression	7314.116	6	1219.019	.629	.706 ^b
		Residual	162704.766	84	1936.961		
		Total	170018.881	90			
1	1	Regression	10678.497	6	1779.749	.972	.449 ^c
		Residual	179507.049	98	1831.705		
		Total	190185.545	104			
2	1	Regression	17495.788	6	2915.965	1.428	.212 ^b
		Residual	200150.312	98	2042.350		
		Total	217646.100	104			
3	1	Regression	12146.223	6	2024.370	1.142	.344 ^c
		Residual	173678.659	98	1772.231		
		Total	185824.882	104			

4	1	Regression	9627.237	6	1604.539	.872	.519 ^c
		Residual	180350.022	98	1840.306		
		Total	189977.259	104			
5	1	Regression	37604.480	6	6267.413	2.231	.046 ^b
		Residual	275340.424	98	2809.596		
		Total	312944.905	104			

a. Dependent Variable: FINAL utilisation score using calculation of utilisation using imputed data and excluding outliers

b. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Sexul orientation recoded, I am optimistic that my ED treatment will make my ED better, Total BMQ Necessity Score - total of reversed items, Using treatment for ED has a negative impact on my masculinity, My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly

c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly, Using treatment for ED has a negative impact on my masculinity, Sexul orientation recoded, I am optimistic that my ED treatment will make my ED better

Table 65: Coefficients

		Coefficients ^a										
Imputation		Unstandardized Coefficients			Standardized Coefficients			Collinearity Statistics		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
Number	Model	B	Std. Error		Beta	t	Sig.	Tolerance	VIF			
Original data	1	(Constant)	26.507	41.816		.634	.528					
		Sexual orientation recoded	8.913	17.693	.058	.504	.616	.848	1.179			
		Total BMQ Necessity Score - total of reversed items	.795	1.050	.085	.757	.451	.903	1.108			
		I am optimistic that my ED treatment will make my ED better	-1.829	5.414	-.041	-.338	.736	.780	1.283			
		My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	1.682	7.000	.030	.240	.811	.754	1.326			
		Using treatment for ED has a negative impact on my masculinity	-5.454	4.203	-.148	-1.298	.198	.881	1.135			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	1.270	3.570	.039	.356	.723	.928	1.078			
1	1	(Constant)	11.897	34.850		.341	.734					
		Sexual orientation recoded	9.273	14.377	.069	.645	.520	.834	1.199			

		Total BMQ Necessity Score - total of reversed items	1.094	.945	.119	1.158	.250	.909	1.100			
		I am optimistic that my ED treatment will make my ED better	-1.052	4.550	-.025	-.231	.818	.801	1.249			
		My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-.081	5.788	-.002	-.014	.989	.768	1.302			
		Using treatment for ED has a negative impact on my masculinity	-2.862	3.812	-.079	-.751	.455	.877	1.140			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	4.128	3.204	.130	1.288	.201	.946	1.057			
2	1	(Constant)	52.789	36.758		1.436	.154					
		Sexul orientation recoded	13.413	14.995	.094	.895	.373	.855	1.170			
		Total BMQ Necessity Score - total of reversed items	1.100	1.009	.112	1.090	.278	.888	1.126			
		I am optimistic that my ED treatment will make my ED better	-2.552	4.989	-.057	-.512	.610	.761	1.313			

3	1	My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-3.692	6.009	-.068	-.614	.540	.775	1.291			
		Using treatment for ED has a negative impact on my masculinity	-6.164	4.111	-.159	-1.499	.137	.839	1.192			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.241	3.431	.007	.070	.944	.926	1.080			
		(Constant)	40.557	34.387		1.179	.241					
		Sexual orientation recoded	7.126	14.115	.054	.505	.615	.837	1.195			
		Total BMQ Necessity Score - total of reversed items	.987	.934	.109	1.056	.293	.899	1.113			
		I am optimistic that my ED treatment will make my ED better	-.494	4.609	-.012	-.107	.915	.760	1.316			
		My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-3.163	5.655	-.064	-.559	.577	.722	1.386			
		Using treatment for ED has a negative impact on my masculinity	-5.115	3.742	-.145	-1.367	.175	.848	1.179			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	1.779	3.159	.057	.563	.575	.921	1.086			
4	1	(Constant)	20.543	35.990		.571	.569					
		Sexual orientation recoded	12.778	14.575	.096	.877	.383	.815	1.227			
		Total BMQ Necessity Score - total of reversed items	.828	.955	.090	.868	.388	.894	1.119			
		I am optimistic that my ED treatment will make my ED better	-1.157	4.803	-.028	-.241	.810	.741	1.350			
		My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	1.285	6.115	.025	.210	.834	.708	1.412			
		Using treatment for ED has a negative impact on my masculinity	-4.852	3.945	-.133	-1.230	.222	.831	1.203			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	1.849	3.221	.059	.574	.567	.924	1.083			
5	1	(Constant)	119.494	43.356		2.756	.007					
		Sexual orientation recoded	-11.173	17.873	-.065	-.625	.533	.827	1.208			

		Total BMQ Necessity Score - total of reversed items	1.729	1.183	.147	1.461	.147	.888	1.126			
		I am optimistic that my ED treatment will make my ED better	-7.211	5.827	-.134	-1.237	.219	.770	1.299			
		My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-6.935	7.125	-.107	-.973	.333	.736	1.358			
		Using treatment for ED has a negative impact on my masculinity	-8.978	4.735	-.199	-1.896	.061	.818	1.222			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-2.640	3.943	-.066	-.670	.505	.928	1.078			
Pooled	1	(Constant)	49.056	59.641		.823	.429			.667	1.569	.882
		Sexual orientation recoded	6.283	18.835		.334	.741			.380	.526	.929
		Total BMQ Necessity Score - total of reversed items	1.148	1.077		1.065	.288			.128	.139	.975
		I am optimistic that my ED treatment will make my ED better	-2.493	5.815		-.429	.670			.292	.365	.945

My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-2.517	7.104		-.354	.724			.270	.330	.949
Using treatment for ED has a negative impact on my masculinity	-5.594	4.763		-1.174	.245			.289	.360	.945
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	1.071	4.366		.245	.808			.434	.645	.920

a. Dependent Variable: FINAL utilisation score using calculation of utilisation using imputed data and excluding outliers

Linear Regression N° 2: Winsorized Linear Regression: Number of days since last using treatment

Normality

Post-winsorized data

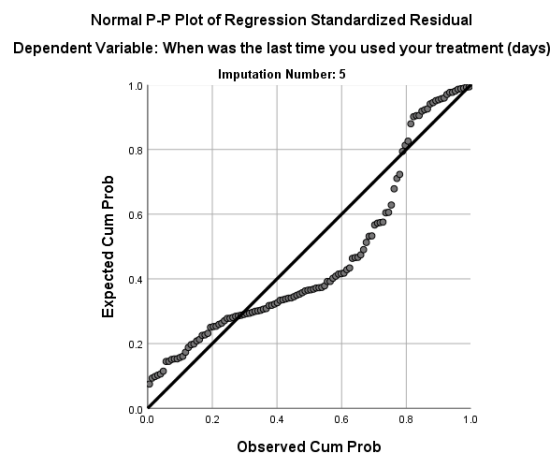


Figure 42: P-P plot for DV: No of days since last using treatment

Homoscedasticity

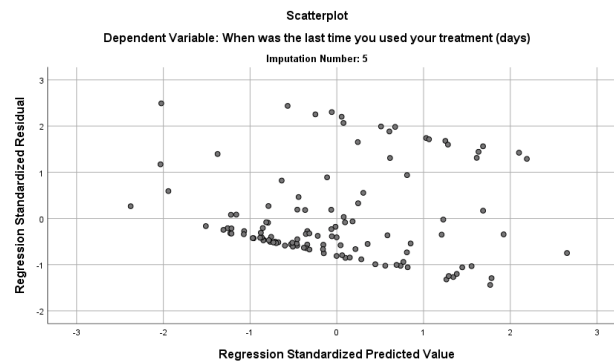


Figure 43: homoscedasticity of number of days since last using treatment of treatment

Table 66: Linear regression Coefficients

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Collinearity Statistics	
	B	Std. Error	Beta			Tolerance	VIF
1							
(Constant)	112.808	44.900		2.512	0.013		
Total BMQ Necessity Score - total of reversed items	0.166	1.815	0.011	0.092	0.927	0.578	1.729
Total BMQ Concerns Score - total of reversed items	-1.441	2.124	-0.081	-0.679	0.499	0.548	1.825
I aim to have a sex life that does not rely on treatment.	-6.776	6.157	-0.102	-1.101	0.274	0.914	1.094
Using treatment for ED has a negative impact on my masculinity	11.208	5.928	0.176	1.891	0.061	0.899	1.113
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.457	5.354	-0.256	-2.700	0.008	0.865	1.156

Interpretation of the Multi-linear Regression

Table 67: Model Summary (Pooled data)

Model Summary ^b					
Imputation Number	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
Original data	1	.319 ^a	.102	.048	45.489
1	1	.360 ^c	.129	.089	72.901
2	1	.350 ^c	.122	.082	72.965
3	1	.366 ^c	.134	.094	84.054
4	1	.350 ^c	.123	.083	79.745
5	1	.379 ^c	.144	.105	71.777

a. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items

b. Dependent Variable: When was the last time you used your treatment (days)

c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

Overall regression model and whether it is a good fit for the data

Table 68: Anova

ANOVA ^a							
Imputation Number	Model		Sum of Squares	df	Mean Square	F	Sig.
Original data	1	Regression	19429.102	5	3885.820	1.878	.107 ^b
		Residual	171744.179	83	2069.207		
		Total	191173.281	88			
1	1	Regression	86065.219	5	17213.044	3.239	.009 ^c
		Residual	579284.225	109	5314.534		
		Total	665349.443	114			
2	1	Regression	81600.160	5	16320.032	3.065	.013 ^c
		Residual	585632.556	110	5323.932		
		Total	667232.716	115			
3	1	Regression	120041.146	5	24008.229	3.398	.007 ^c
		Residual	777162.095	110	7065.110		
		Total	897203.241	115			
4	1	Regression	97796.854	5	19559.371	3.076	.012 ^c
		Residual	699520.697	110	6359.279		
		Total	797317.552	115			
5	1	Regression	95239.766	5	19047.953	3.697	.004 ^c
		Residual	566708.682	110	5151.897		
		Total	661948.448	115			

a. Dependent Variable: When was the last time you used your treatment (days)

- b. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Concerns Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Necessity Score - total of reversed items
- c. Predictors: (Constant), My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues), Total BMQ Necessity Score - total of reversed items, I aim to have a sex life that does not rely on treatment., Using treatment for ED has a negative impact on my masculinity, Total BMQ Concerns Score - total of reversed items

Table 69: Coefficients

		Coefficients ^a										
Imputation Number	Model	Unstandardized Coefficients			Standardized Coefficients			Collinearity Statistics		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
		B	Std. Error		Beta	t	Sig.	Tolerance	VIF			
Original data	1 (Constant)	85.977	32.692			2.630	.010					
	Total BMQ Necessity Score - total of reversed items	-.062	1.351		-.006	-.046	.964	.568	1.761			
	Total BMQ Concerns Score - total of reversed items	-1.109	1.513		-.104	-.734	.465	.536	1.867			
	I aim to have a sex life that does not rely on treatment.	-7.470	4.540		-.180	-1.645	.104	.904	1.106			

		Using treatment for ED has a negative impact on my masculinity	4.050	4.446	.100	.911	.365	.903	1.108			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-5.435	3.777	-.157	-1.439	.154	.906	1.104			
1	1	(Constant)	122.283	44.625		2.740	.007					
		Total BMQ Necessity Score - total of reversed items	.349	1.906	.022	.183	.855	.552	1.811			
		Total BMQ Concerns Score - total of reversed items	-2.035	2.217	-.113	-.918	.361	.525	1.905			

		I aim to have a sex life that does not rely on treatment.	-6.959	6.148	-.104	-1.132	.260	.943	1.061			
		Using treatment for ED has a negative impact on my masculinity	9.512	6.122	.144	1.554	.123	.934	1.071			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.123	5.370	-.246	-2.630	.010	.911	1.097			
2	1	(Constant)	134.685	46.681		2.885	.005					
		Total BMQ Necessity Score - total of reversed items	.844	1.975	.053	.428	.670	.528	1.893			

		Total BMQ Concerns Score - total of reversed items	-2.543	2.260	-.142	-1.125	.263	.503	1.987			
		I aim to have a sex life that does not rely on treatment.	-9.601	6.076	-.147	-1.580	.117	.919	1.088			
		Using treatment for ED has a negative impact on my masculinity	7.219	6.217	.109	1.161	.248	.901	1.110			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-12.989	5.504	-.225	-2.360	.020	.877	1.140			
3	1	(Constant)	104.955	51.563		2.035	.044					

Total BMQ Necessity Score - total of reversed items	1.404	2.172	.076	.646	.519	.576	1.737			
Total BMQ Concerns Score - total of reversed items	-2.985	2.504	-.146	-1.192	.236	.525	1.905			
I aim to have a sex life that does not rely on treatment.	-4.221	7.093	-.055	-.595	.553	.926	1.079			
Using treatment for ED has a negative impact on my masculinity	13.657	7.049	.182	1.937	.055	.891	1.123			
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.889	6.145	-.212	-2.260	.026	.895	1.117			

4	1	(Constant)	144.48 0	50.287		2.87 3	.005					
		Total BMQ Necessity Score - total of reversed items	.938	2.080	.054	.451	.653	.557	1.795			
		Total BMQ Concerns Score - total of reversed items	-3.019	2.402	-.155	- 1.25 7	.211	.526	1.901			
		I aim to have a sex life that does not rely on treatment.	-9.594	6.939	-.128	- 1.38 3	.170	.934	1.071			
		Using treatment for ED has a negative impact on my masculinity	7.983	6.821	.110	1.17 0	.244	.896	1.116			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.666	5.909	-.220	-2.313	.023	.885	1.131			
5	1	(Constant)	112.808	44.900		2.512	.013					
		Total BMQ Necessity Score - total of reversed items	.166	1.815	.011	.092	.927	.578	1.729			
		Total BMQ Concerns Score - total of reversed items	-1.441	2.124	-.081	-.679	.499	.548	1.825			
		I aim to have a sex life that does not rely on treatment.	-6.776	6.157	-.102	-1.101	.274	.914	1.094			

		Using treatment for ED has a negative impact on my masculinity	11.208	5.928	.176	1.891	.061	.899	1.113			
		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-14.457	5.354	-.256	-2.700	.008	.865	1.156			
Pooled	1	(Constant)	123.842	50.815		2.437	.015			.125	.135	.976
		Total BMQ Necessity Score - total of reversed items	.740	2.066		.358	.720			.071	.073	.986
		Total BMQ Concerns Score - total of reversed items	-2.405	2.420		-.994	.321			.096	.102	.981

I aim to have a sex life that does not rely on treatment.	-7.430	6.951		-1.069	.286			.133	.145	.974
Using treatment for ED has a negative impact on my masculinity	9.916	7.039		1.409	.161			.173	.194	.966
My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	-13.825	5.697		-2.426	.015			.011	.011	.998

a. Dependent Variable: When was the last time you used your treatment (days)

Appendix 22: Binomial Logistic Regression

Table 70: Omnibus Tests of Model Coefficients

Omnibus Tests of Model Coefficients					
Imputation Number			Chi-square	df	Sig.
Original data	Step 1	Step	16.598	5	.005
		Block	16.598	5	.005
		Model	16.598	5	.005
1	Step 1	Step	18.375	5	.003
		Block	18.375	5	.003
		Model	18.375	5	.003
2	Step 1	Step	18.001	5	.003
		Block	18.001	5	.003
		Model	18.001	5	.003
3	Step 1	Step	21.132	5	.001
		Block	21.132	5	.001
		Model	21.132	5	.001
4	Step 1	Step	16.996	5	.005
		Block	16.996	5	.005
		Model	16.996	5	.005
5	Step 1	Step	23.299	5	.000
		Block	23.299	5	.000
		Model	23.299	5	.000

Table 71: Table: Model Summary

Model Summary			Cox & Snell R	Nagelkerke R
Imputation Number	Step	-2 Log likelihood	Square	Square
Original data	1	120.061 ^a	.149	.203
1	1	132.322 ^b	.146	.201
2	1	133.866 ^c	.144	.197
3	1	129.564 ^d	.167	.229
4	1	134.871 ^e	.136	.187
5	1	127.397 ^f	.182	.250

a. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = Original data.

b. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = 1.

c. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = 2.

d. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = 3.

e. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = 4.

f. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001 for split file Imputation Number = 5.

Table 72: Hosmer and Lemeshow test

Hosmer and Lemeshow Test				
Imputation Number	Step	Chi-square	df	Sig.
Original data	1	6.499	8	.591
1	1	6.224	8	.622
2	1	3.655	8	.887
3	1	4.248	8	.834
4	1	7.234	8	.512
5	1	7.340	8	.500

Table 73: Classification Table

Classification Table^a

Imputation Number		Observed		Predicted		Percentage Correct
				Used treatment in the last 4 weeks NO	YES	
Original data	Step 1	Used treatment in the last 4 weeks	NO	19	20	48.7
			YES	12	52	81.3
			Overall Percentage			68.9
1	Step 1	Used treatment in the last 4 weeks	NO	16	25	39.0
			YES	11	64	85.3
			Overall Percentage			69.0
2	Step 1	Used treatment in the last 4 weeks	NO	19	23	45.2
			YES	11	63	85.1
			Overall Percentage			70.7
3	Step 1	Used treatment in the last 4 weeks	NO	17	24	41.5
			YES	9	66	88.0
			Overall Percentage			71.6
4	Step 1	Used treatment in the last 4 weeks	NO	19	23	45.2
			YES	10	64	86.5
			Overall Percentage			71.6
5	Step 1	Used treatment in the last 4 weeks	NO	21	20	51.2
			YES	11	64	85.3

Overall Percentage			73.3

a. The cut value is .500

Table 74: Variables in the equation

Variables in the Equation													
Imputation Number			B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
Original data	Step 1 ^a	Total number of comorbidities	.394	.220	3.211	1	.073	1.483	.964	2.281			
		How much do you experience symptoms from your ED?	.077	.070	1.192	1	.275	1.080	.941	1.239			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.419	.212	3.887	1	.049	.658	.434	.998			
		Using treatment for ED has a negative impact on my masculinity	-.414	.208	3.971	1	.046	.661	.440	.993			

1	Step 1 ^a	My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.276	.178	2.393	1	.122	1.317	.929	1.868			
		Constant	1.054	1.241	.721	1	.396	2.869					
		Total number of comorbidities	.384	.201	3.663	1	.056	1.468	.991	2.177			
		How much do you experience symptoms from your ED?	.096	.069	1.951	1	.163	1.101	.962	1.260			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.416	.208	4.006	1	.045	.660	.439	.991			
		Using treatment for ED has a negative impact on my masculinity	-.318	.196	2.639	1	.104	.727	.495	1.068			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.342	.172	3.969	1	.046	1.408	1.006	1.972			
		Constant	.578	1.159	.248	1	.618	1.782					
2	Step 1 ^a	Total number of comorbidities	.318	.197	2.608	1	.106	1.375	.934	2.024			
		How much do you experience symptoms from your ED?	.082	.069	1.439	1	.230	1.086	.949	1.243			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.339	.200	2.868	1	.090	.712	.481	1.055			
		Using treatment for ED has a negative impact on my masculinity	-.395	.196	4.039	1	.044	.674	.459	.990			

3	Step 1 ^a	My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.363	.173	4.433	1	.035	1.438	1.025	2.017			
		Constant	.693	1.172	.350	1	.554	2.000					
		Total number of comorbidities	.434	.210	4.274	1	.039	1.544	1.023	2.331			
		How much do you experience symptoms from your ED?	.091	.069	1.720	1	.190	1.095	.956	1.255			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.381	.202	3.548	1	.060	.683	.460	1.016			
		Using treatment for ED has a negative impact on my masculinity	-.468	.197	5.627	1	.018	.626	.425	.922			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.278	.172	2.628	1	.105	1.321	.943	1.849			
		Constant	1.130	1.180	.917	1	.338	3.096					
4	Step 1 ^a	Total number of comorbidities	.291	.195	2.221	1	.136	1.338	.912	1.962			
		How much do you experience symptoms from your ED?	.077	.068	1.267	1	.260	1.080	.945	1.234			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.395	.199	3.928	1	.047	.674	.456	.996			
		Using treatment for ED has a negative impact on my masculinity	-.429	.198	4.675	1	.031	.651	.441	.961			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.277	.168	2.732	1	.098	1.319	.950	1.832			
		Constant	1.262	1.164	1.177	1	.278	3.533					
5	Step 1 ^a	Total number of comorbidities	.432	.210	4.230	1	.040	1.540	1.021	2.325			
		How much do you experience symptoms from your ED?	.087	.070	1.539	1	.215	1.091	.951	1.252			
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.444	.208	4.556	1	.033	.642	.427	.964			
		Using treatment for ED has a negative impact on my masculinity	-.469	.199	5.576	1	.018	.625	.424	.923			

		My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.358	.176	4.167	1	.041	1.431	1.014	2.019			
		Constant	1.053	1.211	.755	1	.385	2.866					
Pooled	Step 1 ^a	Total number of comorbidities	.372	.215			.085	1.451	.950	2.215	.116	.124	.977
		How much do you experience symptoms from your ED?	.087	.070			.213	1.091	.952	1.250	.014	.014	.997
		The effect of my ED treatment (i.e. duration of erection) does not last long enough	-.395	.208			.058	.674	.448	1.013	.044	.045	.991
		Using treatment for ED has a negative impact on my masculinity	-.416	.209			.047	.660	.437	.995	.113	.121	.978

My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues)	.324	.178			.069	1.382	.974	1.961	.072	.075	.986
Constant	.943	1.220			.440	2.568	.234	28.183	.072	.075	.986

a. Variable(s) entered on step 1: Total number of comorbidities, How much do you experience symptoms from your ED?, The effect of my ED treatment (i.e. duration of erection) does not last long enough, Using treatment for ED has a negative impact on my masculinity, My ED is caused by physiological problems (e.g. surgery, nerve damage, circulation issues).

Appendix 23: Chi-Squared cross tabulations for discontinuation and categorical independent variables

Appendix 23: Chi-Squared cross tabulations for discontinuation and categorical independent variables

Independent Variables		Using Treatment n(%)	Discontinued n(%)	df	p
Age					
18-34		4	6		
	35 - 54	13	8		
	55 - 74	50	23		
	>75	3	6	3	0.20
Ethnicity					
	Caucasian	57(49.1)	33(28.4)	1	0.58
	Other	18(15.5)	8(6.9)		
Sexual Orientation					
	Heterosexual	62(53.4)	37(31.9)	1	0.27
	Other	13(11.2)	4(3.4)		
Occupation					
	Employed	40(34.5)	22(18.9)	1	0.97
	Other	35(30.2)	19(15.9)		
Relationship status					
	Married or in a relationship	62(53.4)	31(26.7)	1	0.36
	Divorced, single or Other	13(11.2)	10(8.6)		

Appendix 24: t-tests for independent variables

Independent Variables	Used treatment in the last 4 weeks (Y/N)	N	M(SD)	t	df	p
Comorbidities						
Total number of comorbidities	No	41	1.02(0.99)	-2.15	95.30	0.03
	Yes	75	1.47(1.18)			
Clinical Characteristics						
ED duration (Months)	No	41	62.04(55.40)	-1.43	114.00	0.15
	Yes	75	80.94(73.73)			
ED severity (IIEF-5)	No	41	10.63(5.27)	0.18	114.00	0.86
	Yes	75	10.45(5.21)			
IPQ Items						
IPQ: consequences	No	41	6.66(2.90)	0.19	114.00	0.85
	Yes	75	6.56(2.56)			
IPQ: timeline	No	41	6.78(2.64)	-0.87	114.00	0.38
	Yes	75	7.26(2.92)			
IPQ: personal control	No	41	6.85(3.05)	-0.71	114.00	0.48
	Yes	75	7.24(2.64)			
IPQ: treatment control	No	41	4.07(2.81)	-0.51	114.00	0.61
	Yes	75	4.33(2.63)			

IPQ: identity	No	41	5.00(3.15)	-1.84	114.00	0.07
	Yes	75	6.10(3.03)			
IPQ: Illness concern	No	41	8.46(2.40)	0.84	114.00	0.40
	Yes	75	8.09(2.20)			
IPQ: coherence	No	41	3.71(3.36)	0.72	114.00	0.47
	Yes	75	3.27(3.01)			
IPQ: emotional representation	No	41	7.32(2.64)	0.71	114.00	0.48
	Yes	75	6.96(2.57)			
HADS Items						
HADS Anxiety	No	41	8.88(5.34)	-0.14	114.00	0.89
	Yes	75	9.03(5.41)			
HADS Depression	No	41	6.39(4.48)	0.57	114.00	0.57
	Yes	75	5.89(4.48)			
BMQ Items						
BMQ Necessity	No	41	14.00(4.85)	-0.42	114.00	0.67
	Yes	75	14.40(4.88)			
BMQ Concerns	No	41	14.27(4.57)	-0.85	114.00	0.40
	Yes	75	14.97(4.09)			
SEAR Items						
SEAR Sexual relationship	No	41	30.61(20.12)	-0.75	114.00	0.46
	Yes	75	33.43(19.10)			
SEAR Self-efficacy	No	41	36.59(23.03)	-0.77	114.00	0.44

	Yes	75	39.87(21.24)			
SEAR Overall relationship	No	41	48.29(22.68)	-0.26	114.00	0.80
	Yes	75	49.47(24.04)			
SEAR Confidence and self-esteem	No	41	40.49(20.15)	-0.71	114.00	0.48
	Yes	75	43.20(19.47)			
SEAR Total	No	41	34.84(18.04)	-0.79	114.00	0.43
	Yes	75	37.62(17.99)			
Brief COPE Items						
Brief COPE Self-sufficient coping	No	41	25.12(5.31)	0.10	114.00	0.92
	Yes	75	25.01(6.07)			
Brief COPE Social support coping	No	41	14.24(4.45)	-1.26	114.00	0.21
	Yes	75	15.44(5.12)			
Brief COPE Avoidant coping	No	41	19.98(6.84)	-0.26	114.00	0.80
	Yes	75	20.29(6.14)			
BEED-TQ Items						
1) I have a plan or pattern with regards to using my ED treatment	NO	41	3.09(1.240)	-0.62	114.00	0.54
	YES	75	3.24(1.23)			
2) feel confident that I am able to use my ED treatment	NO	41	3.68(0.94)	0.29	114.00	0.77
	YES	75	3.62(1.15)			

3) I experience treatment side-effects as a consequence of my ED treatment	NO	41	2.64(1.32)	-1.15	114.00	0.25
	YES	75	2.94(1.38)			
4) My ED treatment enables me to have a sexual relationship with my partner	NO	41	3.27(1.12)	0.46	114.00	0.65
	YES	75	3.16(1.28)			
5) My ED treatment improves my ability to get an erection	NO	41	3.22(1.09)	-0.37	95.07	0.71
	YES	75	3.31(1.30)			
6) My ED treatment is quick to work upon using it	NO	41	2.93(0.99)	-0.19	95.09	0.85
	YES	75	2.97(1.18)			
7) My ED treatment works effectively every time I take it.	NO	41	2.67(0.99)	-0.42	97.66	0.68
	YES	75	2.75(1.22)			
8) Taking ED treatment makes my sex life less spontaneous (R)	NO	41	2.65(1.04)	0.41	114.00	0.68
	YES	75	2.56(1.14)			
9) The effect of my ED treatment (i.e. duration of erection	NO	41	2.70(1.12)	2.31	114.00	0.02
	YES	75	2.22(1.07)			

does not last long
enough (R)

10) My ED	NO	41	3.07(1.03)	-0.36	114.00	0.72
treatment makes	YES	75	3.15(1.10)			
me feel more						
confident						
11) I find it difficult	NO	41	2.79(1.35)	0.85	114.00	0.40
to pay for my ED	YES	75	2.58(1.24)			
treatment.						
12) I have sought	NO	41	3.66(1.34)	0.93	114.00	0.36
alternative	YES	75	3.43(1.30)			
treatments for my						
ED outside of the						
NHS (R)						
13) I aim to have a	NO	41	3.61(1.14)	0.50	114.00	0.62
sex life that does	YES	75	3.50(1.14)			
not rely on						
treatment.						
14) My aim is to	NO	41	3.26(1.06)	1.16	114.00	0.25
find a more	YES	75	3.00(1.19)			
natural/holistic						
solution to my ED						
15) My aim is to use	NO	41	3.31(0.98)	0.00	114.00	1.00
my treatment for	YES	75	3.31(0.98)			
ED as a						
rehabilitative						
measure						

16) Taking my ED treatment as prescribed is high on my list of priorities	NO	41	3.56(0.89)	-1.08	114.00	0.28
	YES	75	3.76(0.97)			
17) I intend to take my treatment in the future	NO	41	3.89(0.88)	-1.60	114.00	0.11
	YES	75	4.11(0.62)			
18) If I think sex is likely then I will use my ED treatment	NO	41	4.05(0.77)	0.80	114.00	0.43
	YES	75	3.93(0.80)			
19) I know how to use my ED treatment, as prescribed, in order for it to work effectively	NO	41	4.14(0.61)	1.08	114.00	0.28
	YES	75	4.00(0.71)			
20) Decisions about whether to use my ED treatment are difficult to make (R)	NO	41	3.48(1.01)	0.67	114.00	0.50
	YES	75	3.34(1.08)			
21) I am optimistic that my ED treatment will make my ED better	NO	41	3.76(0.95)	1.58	114.00	0.12
	YES	75	3.46(1.01)			
	NO	41	3.83(1.02)	0.26	114.00	0.79

22) I feel encouraged by my doctor/nurse to use my ED treatment	YES	75	3.78(0.88)			
23) I feel encouraged by my partner to use my ED treatment	NO	41	3.61(0.97)	0.85	114.00	0.40
	YES	75	3.44(1.04)			
24) I have informed my partner that I use ED treatment	NO	41	3.60(1.31)	-1.34	114.00	0.18
	YES	75	3.92(1.18)			
25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	NO	41	4.09(0.95)	0.60	114.00	0.55
	YES	75	3.98(0.85)			
26) Using treatment for ED has a negative impact on my masculinity (R)	NO	41	3.45(1.13)	2.95	114.00	0.00
	YES	75	2.79(1.17)			
27) I know the cause of my ED	NO	41	3.23(1.28)	-1.62	114.00	0.11
	YES	75	3.63(1.26)			
37) My ED is caused by physiological problems	NO	41	2.77(1.33)	-1.81	114.00	0.07

	YES	75	3.24(1.33)			
38) My ED is caused by psychological problems	NO	41	2.71(1.31)	-0.25	71.99	0.80
	YES	75	2.77(1.11)			
28) ED makes my partner feel frustrated (R)	NO	41	3.11(1.22)	1.22	114.00	0.23
	YES	75	2.83(1.14)			
29) ED means I am unable to have penetrative sex (R)	NO	41	2.39(1.16)	-0.66	114.00	0.51
	YES	75	2.55(1.31)			
30) ED reduces my level of intimacy with my partner (R)	NO	41	2.42(1.30)	-0.12	114.00	0.90
	YES	75	2.45(1.16)			
31) I avoid sexual encounters because of my ED (R)	NO	41	2.61(1.34)	-0.43	69.91	0.67
	YES	75	2.72(1.10)			
32) I lack confidence because of my ED (R)	NO	41	2.49(1.27)	-0.79	114.00	0.43
	YES	75	2.68(1.22)			
33) My ED has had a negative effect on my relationship with my partner (R)	NO	41	2.71(1.33)	-0.19	114.00	0.85
	YES	75	2.76(1.24)			
	NO	41	2.30(1.14)	-0.71	114.00	0.48

34) Suffering from ED is stressful and traumatic (R)	YES	75	2.46(1.13)			
35) ED is a long-term condition (R)	NO	41	2.24(0.90)	0.29	114.00	0.77
	YES	75	2.19(0.89)			
36) I do not always experience ED, it is intermittent	NO	41	2.49(1.38)	0.94	69.80	0.35
	YES	75	2.25(1.13)			

Appendix 25: Comparison of Means - Binary and categorical demographic independent variables and adherence to ED treatment (t-tests and ANOVA)

		n	M(SD)	F	df	p
Age						
	18 - 34	9	40.48(57.78)			
	35 - 54	21	31.94(36.42)			
	55 - 74	72	52.96(43.93)			
	>75	9	43.83(41.88)	4.92	3, 107	0.69
Education						
	No Qualifications	17	24.63(31.13)			
	Higher Education Qualification	31	33.21(33.62)			
	Secondary school and Further Education Qualification	42	44.11(52.33)			
	Other	12	45.96(41.41)	1.49	3, 107	0.22
				t	df	p
Ethnicity						
	Caucasian	85	36.07(38.95)			
	Other	26	39.02(37.91)	-0.34	108	0.73
Sexuality						
	Heterosexual	96	34.22(37.78)			
	Other	14	54.23(40.74)	-1.83	108	0.07
Employment status						
	Employed	60	35.88(37.89)			
	Retired, unemployed, other	50	37.83(39.69)	-0.26	108	0.79
Relationship status						
	Married or in a relationship	88	36.49(35.41)			
	Divorced, single or other	22	35.98(41.40)	0.22	108	0.82

Appendix 26: Bivariate Spearman's correlations for adherence and continuous independent variables

	r_s	p
Clinical Characteristics		
Comorbidities		
Total number of comorbidities	0.14	0.15
ED duration (Months)	-0.01	0.88
ED severity (IIEF-5)	0.03	0.79
IPQ Items		
IPQ: consequences	0.11	0.25
IPQ: timeline	0.15	0.15
IPQ: personal control	0.10	0.30
IPQ: treatment control	0.06	0.56
IPQ: identity	0.13	0.23
IPQ: Illness concern	-0.08	0.39
IPQ: coherence	-0.06	0.51
IPQ: emotional representation	-0.09	0.39
HADS Items		
HADS Anxiety	0.04	0.66
HADS Depression	0.04	0.68
BMQ Items		
BMQ Necessity	0.16	0.09
BMQ Concerns	0.06	0.52
SEAR Items		
SEAR Sexual relationship	0.07	0.47
SEAR Self-efficacy	0.02	0.86
SEAR Overall relationship	-0.03	0.75
SEAR Confidence and self-esteem	0.00	0.97
SEAR Total	0.05	0.61
Brief COPE Items		
Brief COPE Self-sufficient coping	0.01	0.94
Brief COPE Social support coping	0.10	0.32
Brief COPE Avoidant coping	0.10	0.30
BEED-TQ Items		
Behavioural regulation	1) I have a plan or pattern with regards to using my ED treatment	0.02 0.84
Beliefs about capabilities	2) I feel confident that I am able to use my ED treatment capabilities	-0.08 0.44
Beliefs about consequences	3) I experience treatment side-effects as a consequence of my ED treatment	0.01 0.90
	4) My ED treatment enables me to have a sexual relationship with my partner	0.07 0.48

		r_s	p
	5) My ED treatment improves my ability to get an erection	0.05	0.66
	6) My ED treatment is quick to work upon using it	0.08	0.44
	7) My ED treatment works effectively every time I take it.	0.11	0.39
	8) Taking ED treatment makes my sex life less spontaneous (R)	0.04	0.67
	9) The effect of my ED treatment (i.e. duration of erection does not last long enough (R)	-0.11	0.31
Emotion	10) My ED treatment makes me feel more confident	0.03	0.72
Environmental context and resources	11) I find it difficult to pay for my ED treatment.	0.00	0.99
	12) I have sought alternative treatments for my ED outside of the NHS (R)	-0.09	0.37
Goal	13) I aim to have a sex life that does not rely on treatment.	0.03	0.80
	14) My aim is to find a more natural/holistic solution to my ED	-0.08	0.42
	15) My aim is to use my treatment for ED as a rehabilitative measure	-0.04	0.66
	16) Taking my ED treatment as prescribed is high on my list of priorities	0.17	0.11
Intention	17) I intend to take my treatment in the future	0.02	0.81
	18) If I think sex is likely then I will use my ED treatment	-0.10	0.33
Knowledge	19) I know how to use my ED treatment, as prescribed, in order for it to work effectively	-0.13	0.20
Memory, attention and decision processes	20) Decisions about whether to use my ED treatment are difficult to make (R)	-0.02	0.85
Optimism	21) I am optimistic that my ED treatment will make my ED better	-0.20	0.04
Social Influence	22) I feel encouraged by my doctor/nurse to use my ED treatment	-0.10	0.36
	23) I feel encouraged by my partner to use my ED treatment	-0.10	0.37
	24) I have informed my partner that I use ED treatment	0.04	0.70
	25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	-0.18	0.06
Social professional role and identity	26) Using treatment for ED has a negative impact on my masculinity (R)	-0.18	0.08
SRM Domains			
Cause	27) I know the cause of my ED	0.10	0.31
	37) My ED is caused by physiological problems	0.18	0.08

		r_s	p
	38) My ED is caused by psychological problems	-0.02	0.84
Consequence	28) ED makes my partner feel frustrated (R)	0.00	0.96
	29) ED means I am unable to have penetrative sex (R)	-0.04	0.70
	30) ED reduces my level of intimacy with my partner (R)	0.00	0.97
	31) I avoid sexual encounters because of my ED (R)	0.00	0.99
	32) I lack confidence because of my ED (R)	0.01	0.90
	33) My ED has had a negative effect on my relationship with my partner (R)	-0.01	0.94
Emotion	34) Suffering from ED is stressful and traumatic (R)	0.03	0.80
Timeline	35) ED is a long-term condition (R)	-0.05	0.63
	36) I do not always experience ED, it is intermittent	-0.02	0.81

R = Reverse Scored

Appendix 27: Comparison of Means - Binary and categorical demographic independent variables and persistence to ED treatment (t-tests and ANOVA)

		n	M(SD)	F	df	p
Age						
	18 - 34	11	48.38(56.22)	1.16	3, 112	0.33
	35 - 54	21	42.25(49.25)			
	55 - 74	74	30.67(41.61)			
	>75	10	33.57(54.18)			
Education						
	No Qualifications	19	62.58(85.04)	1.09	3, 112	0.36
	Higher Education Qualification	36	46.83(68.96)			
	Secondary school and Further Education Qualification	47	67.11(75.54)			
	Other	14	61.79(85.07)			
		n	M(SD)	t	df	p
Ethnicity						
	Caucasian	90	221.94(817.12)	0.63	113	0.53
	Other	26	117.12(363.83)			
Sexuality						
	Heterosexual	100	215.41(785.51)	0.62	113	0.54
	Other	16	92.00(327.50)			
Employment status						
	Employed	61	151.89(377.07)	-0.71	113	0.48
	Retired, unemployed, other	54	250.61(1004.49)			
Relationship status						
	Married or in a relationship	93	145.01(308.78)	-0.92	21.42	0.37
	Divorced, single or other	23	499.78(1541.04)			

Appendix 28: Bivariate correlations for persistence and continuous independent variables

		r	p
Clinical Characteristics			
Comorbidities			
Total number of comorbidities		-0.08	0.42
ED duration (Months)		0.06	0.56
ED severity (IIEF-5)		-0.03	0.74
IPQ Items			
IPQ: consequences		0.00	0.99
IPQ: timeline		0.03	0.78
IPQ: personal control		0.04	0.69
IPQ: treatment control		0.00	0.96
IPQ: identity		-0.01	0.96
IPQ: Illness concern		0.05	0.59
IPQ: coherence		-0.05	0.57
IPQ: emotional representation		0.04	0.69
HADS Items			
HADS Anxiety		-0.12	0.24
HADS Depression		-0.04	0.68
BMQ Items			
BMQ Necessity		-0.18	0.05
BMQ Concerns		-0.23	0.01
SEAR Items			
SEAR Sexual relationship		-0.02	0.81
SEAR Self-efficacy		-0.09	0.32
SEAR Overall relationship		0	0.99
SEAR Confidence and self-esteem		-0.07	0.46
SEAR Total		-0.05	0.57
Brief COPE Items			
Brief COPE Self-sufficient coping		-0.04	0.69
Brief COPE Social support coping		-0.09	0.35
Brief COPE Avoidant coping		0.00	1.00
BEED-TQ			
Behavioural regulation	1) I have a plan or pattern with regards to using my ED treatment	0.04	0.69
Beliefs about capabilities	2) I feel confident that I am able to use my ED treatment	-0.02	0.86
Beliefs about consequences	3) I experience treatment side-effects as a consequence of my ED treatment	-0.11	0.23
	4) My ED treatment enables me to have a sexual relationship with my partner	-0.03	0.73
	5) My ED treatment improves my ability to get an erection	-0.08	0.41
	6) My ED treatment is quick to work upon using it	-0.08	0.44
	7) My ED treatment works effectively every time I take it.	-0.06	0.56

		r	p
Emotion Environmental context and resources	8) Taking ED treatment makes my sex life less spontaneous (R)	0.01	0.91
	9) The effect of my ED treatment (i.e. duration of erection does not last long enough (R)	0.03	0.76
	10) My ED treatment makes me feel more confident	0.00	0.99
	11) I find it difficult to pay for my ED treatment.	0.13	0.21
Goal	12) I have sought alternative treatments for my ED outside of the NHS (R)	-0.01	0.90
	13) I aim to have a sex life that does not rely on treatment.	-0.18	0.06
	14) My aim is to find a more natural/holistic solution to my ED	-0.04	0.67
	15) My aim is to use my treatment for ED as a rehabilitative measure	-0.04	0.69
Intention	16) Taking my ED treatment as prescribed is high on my list of priorities	-0.10	0.30
	17) I intend to take my treatment in the future	0.00	0.98
	18) If I think sex is likely then I will use my ED treatment	0.03	0.76
Knowledge	19) I know how to use my ED treatment, as prescribed, in order for it to work effectively	0.02	0.84
Memory, attention and decision processes	20) Decisions about whether to use my ED treatment are difficult to make (R)	-0.01	0.93
Optimism	21) I am optimistic that my ED treatment will make my ED better	0.14	0.17
Social Influence	22) I feel encouraged by my doctor/nurse to use my ED treatment	0.09	0.37
	23) I feel encouraged by my partner to use my ED treatment	0.10	0.31
	24) I have informed my partner that I use ED treatment	-0.06	0.54
Social professional role and identity SRM Domains	25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	0.13	0.21
	26) Using treatment for ED has a negative impact on my masculinity (R)	0.22	0.02
Cause	27) I know the cause of my ED	-0.08	0.40
Consequence	37) My ED is caused by physiological problems	-0.22	0.02
	38) My ED is caused by psychological problems	-0.12	0.23
	28) ED makes my partner feel frustrated (R)	-0.06	0.55
	29) ED means I am unable to have penetrative sex (R)	-0.02	0.85
	30) ED reduces my level of intimacy with my partner (R)	0.04	0.66
	31) I avoid sexual encounters because of my ED (R)	-0.05	0.60
	32) I lack confidence because of my ED (R)	-0.05	0.62
	33) My ED has had a negative effect on my relationship with my partner (R)	-0.11	0.25

		r	p
Emotion	34) Suffering from ED is stressful and traumatic (R)	-0.06	0.57
Timeline	35) ED is a long-term condition (R)	0.00	0.98
	36) I do not always experience ED, it is intermittent	-0.05	0.59

Appendix 29: Comparison of Means - Binary and categorical demographic independent variables and sexual attempts to ED treatment (t-tests and ANOVA)

		n	M(SD)	F	df	p
Age		11	2.27(2.20)	0.31	3, 112	0.82
	18 - 34	21	3.90(3.88)			
	35 - 54	74	3.59(5.53)			
	55 - 74	10	4.10(5.67)			
	>75	11	2.27(2.20)			
Education				0.71	3, 112	0.55
	No Qualifications	19	3.16(3.10)			
	Higher Education Qualification	36	4.58(7.43)			
	Secondary school and Further Education Qualification	47	3.09(3.76)			
	Other	14	3.14(2.63)			
		n	M(SD)	t	df	p
Ethnicity				0.40	114	0.64
	Caucasian	90	3.68(5.49)			
	Other	26	3.23(2.80)			
Sexuality				-1.48	114	0.14
	Heterosexual	100	3.37(5.06)			
	Other	16	5.31(4.59)			
Employment status				0.90	114	0.37
	Employed	62	4.10(6.01)			
	Retired, unemployed, other	54	3.11(3.39)			
Relationship status				0.09	114.00	0.93
	Married or in a relationship	93	3.70(5.07)			
	Divorced, single or other	23	3.26(5.14)			

Appendix 30: Bivariate correlations for sexual attempts in the last 4 weeks and continuous independent variables

		r	p
Clinical Characteristics			
Total number of comorbidities		0.14	0.17
ED duration (Months)		-	0.15
		0.14	
ED severity (IIEF-5)		0.18	0.05
IPQ Items			
IPQ: consequences		0.05	0.61
IPQ: timeline		0.01	0.88
IPQ: personal control		-	0.2
		0.12	
IPQ: treatment control		0.02	0.83
IPQ: identity		0.06	0.53
IPQ: Illness concern		0.01	0.95
IPQ: coherence		-	0.96
		0.01	
IPQ: emotional representation		0	0.97
HADS Items			
HADS Anxiety		0.15	0.11
HADS Depression		0.12	0.23
BMQ Items			
BMQ Necessity		.298	0.00
BMQ Concerns		0.13	0.15
SEAR Items			
SEAR Sexual relationship		.226	0.01
SEAR Self-efficacy		0.15	0.12
SEAR Overall relationship		-	0.64
		0.04	
SEAR Confidence and self-esteem		0.11	0.26
Brief COPE Items			
Brief COPE Self-sufficient coping		-0.1	0.29
Brief COPE Social support coping		0.04	0.67
Brief COPE Avoidant coping		0.02	0.81
BEED-TQ Items			
Behavioural regulation	1) I have a plan or pattern with regards to using my ED treatment	-	0.14
		0.14	
Beliefs about capabilities	2) feel confident that I am able to use my ED treatment	-	0.28
		0.12	
Beliefs about consequences	3) I experience treatment side-effects as a consequence of my ED treatment	-	0.96
		0.01	
	4) My ED treatment enables me to have a sexual relationship with my partner	0.19	0.06

		r	p
Emotion Environmental context and resources	5) My ED treatment improves my ability to get an erection	0.09	0.39
	6) My ED treatment is quick to work upon using it	0.11	0.29
	7) My ED treatment works effectively every time I take it.	0.04	0.73
	8) Taking ED treatment makes my sex life less spontaneous (R)	0.05	0.62
	9) The effect of my ED treatment (i.e. duration of erection does not last long enough (R)	0.02	0.87
	10) My ED treatment makes me feel more confident	0.06	0.55
	11) I find it difficult to pay for my ED treatment.	0.00	0.99
	12) I have sought alternative treatments for my ED outside of the NHS (R)	- 0.14	0.16
	13) I aim to have a sex life that does not rely on treatment.	0.15	0.13
	14) My aim is to find a more natural/holistic solution to my ED	0.17	0.10
	15) My aim is to use my treatment for ED as a rehabilitative measure	- 0.03	0.76
Goal	16) Taking my ED treatment as prescribed is high on my list of priorities	0.02	0.89
	17) I intend to take my treatment in the future	0.10	0.30
	18) If I think sex is likely then I will use my ED treatment	- 0.02	0.87
Intention	19) I know how to use my ED treatment, as prescribed, in order for it to work effectively	- 0.04	0.74
	20) Decisions about whether to use my ED treatment are difficult to make (R)	- 0.18	0.12
Knowledge			
Memory, attention and decision processes			
Optimism	21) I am optimistic that my ED treatment will make my ED better	- 0.04	0.70
Social Influence	22) I feel encouraged by my doctor/nurse to use my ED treatment	- 0.05	0.66
	23) I feel encouraged by my partner to use my ED treatment	- 0.09	0.35
	24) I have informed my partner that I use ED treatment	- 0.10	0.30
	25) My doctor or nurse has provided me with adequate instructions about how to use my ED treatment correctly	- 0.11	0.30
	26) Using treatment for ED has a negative impact on my masculinity (R)	- 0.23	0.03
Social professional role and identity			
SRM Domains			
Cause	27) I know the cause of my ED	0.04	0.72
	37) My ED is caused by physiological problems	0.04	0.72

		r	p
Consequence	38) My ED is caused by psychological problems	0.04	0.68
	28) ED makes my partner feel frustrated (R)	-	0.92
		0.01	
	29) ED means I am unable to have penetrative sex (R)	0.03	0.77
	30) ED reduces my level of intimacy with my partner (R)	0.04	0.70
	31) I avoid sexual encounters because of my ED (R)	0.00	0.99
Emotion	32) I lack confidence because of my ED (R)	0.03	0.80
	33) My ED has had a negative effect on my relationship with my partner (R)	-	0.31
		0.10	
Timeline	34) Suffering from ED is stressful and traumatic (R)	0.01	0.94
	35) ED is a long-term condition (R)	-	0.88
		0.01	
	36) I do not always experience ED, it is intermittent	0.18	0.07