Men's beliefs about treatment for erectile dysfunction – What influences treatment use? A systematic Review

Running title: Systematic review: erectile dysfunction treatment.

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1. 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; HMIC; 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 4.4-76% for phosphodiesterase type 5 inhibitors, 18.6-79.9% for intracavernosal injections, 32-69.2% 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 health care profesionals (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 health care professionals with regards to supporting men to make better use of treatment.

2. 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 approximately 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 over 70 (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 the medication and its effect as well as the financial cost of treatment (19). Psychosocial explanations include performance anxiety, depression, varying arousal patterns and misaligned expectations between a man and his partner (20).

To date there has not been a synthesis of research investigating adherence to ED treatment. National guidelines for medication adherence (21) recognise that in order for health care professionals (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. The review will serve as a foundation to develop future interventions to facilitate ED treatment utilisation.

3. Material/Subjects and Methods

The protocol was registered on PROSPERO (reference CRD42015023341).

3.1 Search strategy

MEDLINE®, Embase, Cochrane Central Register of Controlled Trials, Health Management Information Consortium (HMIC), Health Technology Assessment, CINAHL plus with full text, PsychARTICLES, PsychINFO and Allied and Complementary Medicine (AMED) were searched from inception to August 2018 . English language key words and MeSH terms for ED, adherence and treatment for ED, were used and combined using Boolean logical operators (see Supplementary Information).

3.2 Inclusion Criteria

Studies had to meet the following criteria:

- Published in a peer reviewed journal in English
- Primary research of qualitative, quantitative or mixed methodologies
- Include an assessment of treatment utilisation
- Include an assessment of patient barriers and/or enablers to ED treatment utilisation
- Include participants who were
    - Men aged ≥18 years
    - Diagnosed with ED either using a validated diagnostic tool or by a relevant HCP i.e. a GP or urologist
    - Prescribed PDE5Is, ICI, US, VEDs or PP.

3.3 Exclusion Criteria

Systematic reviews, conference proceedings, commentary articles and letters were excluded.

3.4 Study Selection and Data Extraction

Articles were imported into Thomson Reuters Reference Manager v12.0 and duplicate records removed. Two authors (PW, AA) independently screened titles and abstracts to exclude ineligible

studies, followed by full-text screening of the remainder. Any disagreements were discussed with a third author (HM) to reach consensus. Data were extracted using an adapted Cochrane Data Extraction Form (22).

3.5 Quality Assessment

The QualSyst tool was employed to assess study quality due to its ability to cater for both qualitative and quantitative designs (23). Final scores were converted into a percentage where <50% indicates limited quality, 50–70%: adequate; 71–80%: good, and >80%: strong (24). Scoring was carried out by one author (PW) and checked by a second (AA).

3.6 Synthesis

A narrative synthesis, considered the most appropriate method of synthesising qualitative and quantitative evidence (25), was conducted. Barriers and enablers of treatment utilisation were classified into one of six categories:

- Demographic; age, gender, ethnicity, education.
- Clinical; nature of the condition and treatment; including side-effects and medication efficacy.
- Psychological and cognitive: individual-level processes and meanings that influence mental states such as depression, stress and beliefs about ED or its treatment.
- Social: social processes that impinge on the individual, such as relationship quality.
- Behavioural: observable behaviours (as opposed to internal events such as thinking), which can be objectively measured, such as the length of time before seeking help for ED.

Depending on the study, the percentage of overall participant's discontinuation, persistence or adherence was reported. Studies indicating the same barriers and enablers to treatment were grouped together and the number/percentage of participants reporting a particular barriers/enablers as being influential were reported (see supplementary material).

3.4 Terminology

The use of the term 'adherence' is synonymous with overlapping definitions, such as compliance and persistence. Studies of medication usage lack uniformity in definitions (26), therefore, due to the neutrality of its meaning, the current review will use the term 'treatment utilisation' to describe usage patterns.

4. Results

4.1 Literature search

A total of 3,232 papers were retrieved, 129 underwent full text screening and 50 studies were included (See Figure 1).

4.2 Study Characteristics

All studies used a quantitative study design (Table 1), except one that employed a mixed methodology. The qualitative component of this study was reported as frequency data and was therefore interpreted quantitatively (27). Study designs included retrospective (n=5) and prospective cohort designs (n=29), cross-sectional studies (n=8), randomised trials (n=5), a randomised control trial (n=1), quasi experimental study (n=1) as well as mixed-methodology (n=1). Almost one third of studies were conducted in the USA (n=15). Although all studies examined barriers/enablers to treatment utilisation, this was the primary focus for only 24 studies. Other studies' primary focus was ED treatment-related factors such as acceptability, safety, efficacy, satisfaction and tolerability (n=25) and one study focussed on help seeking behaviour (n=1).

Thirty-three studies (66%) focussed on PDE5I medication, twelve (24%) on ICI therapy, three (6%) on US and two (4%) on multiple treatments, of which one included PP. Studies were conducted between 1991 and 2017.

4.3 Participant characteristics

Data related to 14,371 men. Mean age, reported in 46 studies, ranged from 39.9-69.1 years. Five studies reported ethnicity (28-32), where 67.2-97.8% were classified as white/Caucasian. Seven

studies reported on relationship status (27, 29, 33-37), where 61.5–96.0% were described as having a partner (Table 2).

4.4 Clinical characteristics

Twenty-three studies (46.0%) used the International Index of Erectile Dysfunction (IIEF) (38) or the Sexual Health Inventory for Men (SHIM) (39) to assess ED severity, moderate ED was most prevalent (33.3-61.7%). ED duration, reported in 21 studies, ranged from 3-72 months. Twenty studies provided data on ED aetiology, 6.3-86% were classified as having organic ED, 5.0-36.3% psychogenic, and 15-71% as having mixed ED. Twenty studies reported on comorbidities; hypertension (5.0-51.9%) and diabetes (4.4-42.4%) were most commonly reported. Eight studies recruited exclusively men who had undergone a prostatectomy.

4.5 Study quality

Quality scores ranged from 41-100%, 7 (14%) were classified as limited, 22 (44%) as adequate, 4 (8%) as good and 17 (34%) as strong. Lower scores typically related to limited or no provision of definitions of outcome measure/s, neglecting information on power calculations, sample or effect sizes and not controlling for confounding variables.

4.6 Definitions of Treatment Utilisation

There were a variety of different definitions of treatment utilisation and discontinuation (Table 3). Due to the heterogeneity of definitions, synthesis was achieved through a top-down application of the following definitions;

- Adherence: conforming to recommendations made by the HCP with respect to timing, dosage, and frequency of medication utilisation.
- Persistence: continuing to take any amount of medication (26).
- Discontinuation: cessation of treatment.

Forty-four studies were classified as measuring discontinuation, three; persistence and three both adherence and persistence.

4.7 Measures of Treatment Utilisation

Thirty-four studies (68%) used self-report measures to investigate treatment utilisation including; questionnaires, patient diaries, consultations and telephone surveys (Table 3). Other methods included for example prescription records (n=2) and twelve studies did not report their method. No validated measures of treatment utilisation were used.

4.8 Rates of Treatment Utilisation

Rates of adherence to PDE5Is ranged from 59.6-70.2%, persistence from 64.9-100% and discontinuation from 4.4-76%. Follow-up periods varied from 3-48 months. ICI discontinuation rates ranged from 18.6-79.9%, in which follow-up ranged from 3-65 months. Discontinuation of US ranged from 32-69.2%, in which follow-up ranged from 9–27 months. The one study that explored PP, followed men over a 65 month period where 30% stopped having sex due to complications with the device itself or due to periphery reasons such as a lacking a partner or a loss of sexual interest (40).

It might be expected that longer follow-up periods infer higher rates of discontinuation or poorer adherence; no such pattern emerged. Similarly, there was no pattern of association between rates of treatment utilisation and sample size, study design, or country in which the study took place (Table 3).

4.9 Barriers and enablers of treatment utilisation

Thirty-seven studies (74%) used self-report measures to investigate barriers and enablers to treatment utilisation, mostly self-report questionnaires (Table 3). Other methods included clinical and demographic data (n=2) as well as prescription renewals (n=1). However, ten studies did not clarify their method. Less than half of included studies (n=18) examined whether there was a statistically significant relationship between potential barriers or enablers and treatment utilisation. The remaining 32 studies reported descriptive statistics only. For each barrier or enabler, descriptive data from relevant studies was combined and presented as a total percentage of participants across relevant studies. None of the studies used a validated measure or a theoretical approach to

investigate barriers and enablers to treatment utilisation. Based on the studies included, the following sections will consider the most widely reported barriers and enablers to ED treatment utilisation.

4.10 Demographic Factors

Sixteen studies (32%) examined the relationship between demographic factors and use of PDE5Is (n=12) or ICI treatment (n=4) (see Table 4).

Age

Twelve studies examined the relationship between age and PDE5I utilisation (29, 34-37, 41-47). One reported older age as a barrier, however, this was based on descriptive statistics (43). Eleven performed statistical analysis, for which findings were inconsistent. Three studies reported significantly higher rates of discontinuation for men over 60 years (31, 36, 44); however, older men were reported as being significantly more persistent and adherent according to two other studies (35, 42). Six studies reported a non-significant relationship (34, 37, 41, 45-47); as did studies focused on ICI treatment (48-50).

Education

Five studies investigated levels of education and PDE5I utilisation using inferential statistics (34, 37, 41-43). Results were conflicting. One study indicated that higher levels of education related to significantly higher rates of utilisation (34). However, after controlling for age, delay in seeking medical help, relationship status and SHIM score; one study reported the relationship to be non-significant (37). A further study reported a higher level of education relating to significantly higher rates of persistence but not adherence (43) and finally, two studies reported a non-significant relationship (41, 42).

Employment

Three studies explored the effects of employment on PDE5I utilisation (29, 41, 42). Full-time employment related to significantly higher rates of persistent (42) and adherence (41, 42) compared to being part-time, retired or unemployed. One study, however, reported the relationship to be non-significant (29).

Clinical factors

All fifty studies examined the relationship between one or more clinical factors and treatment utilisation (Table 4).

Treatment Ineffectiveness

Ineffectiveness of PDE5Is was explored by twenty-two studies (27-32, 35, 36, 43, 45, 46, 51-61), eleven on ICI treatment (40, 49, 61-69), four on US (61, 70-72) and one on PP (40).

PDE5I ineffectiveness related to hardness and duration of erection. Across all studies 12.1% (range: 0.2-60%) of participants reported ineffectiveness as a reason for discontinuation.

Ineffectiveness of ICIs related to inadequate erectile response and was explored using descriptive statistics by ten studies, where 15.2% (range: 5–39.3%) discontinued for such reasons. One study used inferential statistics and reported significantly higher rates of discontinuation where treatment was ineffective (49).

Ineffectiveness of US was characterised by insufficient erections as well as a lack of a consistent reliable response (70-72); 31.5% (range: 16-50.8%) of participants across studies discontinued for this reason. Finally, 4.7% of participants reported prosthesis malfunction as a reason for discontinuation (40).

Perceived side-effects

The experience of side-effects was reported in twenty-one studies focussed on PDE5Is (27, 29-32, 34-36, 45, 46, 51, 52, 54, 55, 59-61, 73-76), twelve on ICI (40, 48, 49, 61, 62, 64-69, 77), three on US (61, 71, 72) and one on PP (40).

Across 21 studies, 2.5% (range: 0.9-16%) of men discontinued PDE5Is due to side-effects, which included headaches, rhinitis, Peyronie's disease and chest pain. Three of these studies used statistical analysis, one of which found side-effects to be related to significantly higher rates of persistence (45). Similarly, where men reported side-effects to a HCP they were significantly less likely to discontinue treatment (35). However, one study reported the relationship to be non-significant (31).

ICI treatment side-effects included injection pain, priapism, Peyronie's disease and fibrosis of the penile shaft. Across twelve studies, side-effects were reported by 8.1% (range: 0.9-20.9%) of men as the reason for discontinuation. According to one study, side-effects related to significantly higher rates of discontinuation (49), however, a further study found no such relationship (48).

Side-effects of US included urethral pain and burning, where 15% (range: 7.4–32%) of men across studies reported side-effects as the reason for discontinuation. Finally, one study reported that infection or erosion was responsible for 9.4% of participants discontinuing PP (40).

Treatment-specific factors: ICI treatment

There were 7.2% (2.0-24%) of men across ten studies (40, 48, 49, 62-65, 68, 69, 77) who reported that they discontinued ICI treatment due to difficulty, inability, being unwilling to self-inject or needle phobia. This was associated with significantly higher rates of discontinuation in one of these studies (48).

4.11 Condition Specific Factors

ED aetiology

Five studies investigated the relationship between aetiology and PDE5I utilisation (29, 34, 35, 41, 43). Men with psychogenic as opposed to organic (34, 43) or venogenic as opposed to arteriogenic, diabetic or iatrogenic ED (35), reported significantly higher rates of persistence. Further studies however, did not replicate these findings (29, 41). In relation to ICI, aetiology that included an organic component was related to significantly higher rates of discontinuation (49).

ED severity

Of eight studies on PDE5Is, five found that less severe ED was associated with significantly higher rates of persistence (36, 37, 42, 43, 47) and adherence (43). However, three studies did not find such a relationship (29, 41, 46).

ED duration

Five studies investigated the relationship between duration of ED symptoms and PDE5I utilisation. Findings were conflicting, shorter duration of ED was reported as being related to significantly higher rates of discontinuation in one study (34), but to significantly higher rates of persistence (43, 45) and adherence (42) in three studies. Finally, one study found the relationship between ED duration and treatment utilisation to be non-significant (41).

Comorbid conditions

The effects of comorbid conditions were explored by eight studies on PDE5Is (29, 34, 36, 41, 42, 46, 55, 74) three on ICI treatment (40, 62, 65) and one on PP (40). Across three studies (55, 74, 78) 1.9% (range: 0.8-3.9%) of men discontinued PDE5Is due to comorbid conditions. A higher proportion of men suffering with comorbid hypertension were both more persistent and adherent than those without the condition (42). Similarly, men who had a BMI of ≥ 23 or more indicated significantly higher rates of persistence (34, 36). Conversely, participants with coronary artery disease (41) or who had undergone pelvic surgery (36) were significantly more likely to discontinue PDE5Is. Finally, four studies found no significant relationships (29, 34, 41, 46).

Across two studies (40, 65), 4.4% (range: 3.4-5.5%) of men discontinued ICIs due to comorbid conditions. A third study, using inferential statistics, reported the relationship as non-significant (62).

4.12 Psychological and Cognitive Factors

Twelve studies explored one or more psychological or cognitive factors in relation to treatment utilisation, nine on PDE5Is (27, 29, 31, 34-36, 45, 56, 78) and three on ICI (48, 67, 68).

Treatment Related Beliefs

In one study PDE5Is were discontinued by 23.4% of men as they caused personal conflict, although the study does not elaborate on its meaning (56). In addition, fear of drug dependency was reported by 3% of men (35) and a lack of confidence in medication by 0.1% (29). However, a lack of confidence in meication was reported as having a non-significant relationship with treatment utilisation according to one study (31). Potential harm to the heart was reported by 6.5% (range: 4-7.6%) of men across two studies (27, 35) and not being willing for one's sex life to depend on medication was reported by 3% (range: 0.4-7.4%) of men across three studies as reasons for discontinuation (29, 34, 78).

Psychosocial well-being

The effects of psychosocial factors were reported by two studies focussed on PDE5Is (27, 36) and one on ICI treatment (48). One study reported that 10.1% of men used PDE5Is only in "special moments" to prolong pleasure or to avoid and/or improve bad performance (27). Similarly, 8.1% of men reported using PDE5Is to improve their psychological and emotional state (27). A lack of self-esteem or self-confidence was given as a reason for PDE5I discontinuation by 0.8 and 11.4% of men (27, 36) and significantly higher rates of persistence to ICI treatment were also associated with higher levels of self-confidence and self-esteem (48).

4.13 Social Factors

Thirty-six studies investigated social factors and their effect on ED treatment utilisation, twenty four on PDE5Is (27-29, 31, 33-37, 41, 43, 45, 46, 51-55, 57, 58, 61, 73, 74, 78), nine on ICI (40, 48, 49, 62, 64-66, 69, 77), one on US (72) and PP (40).

Cost of Treatment

Across seventeen studies (27-29, 34-36, 43, 45, 46, 52-55, 61, 73, 74, 78) 6.6% (0.6-47.3%) of men discontinued PDE5Is due to high personal financial cost. Across three studies 4.6% (range: 4.4-5.5%) of men discontinued ICI treatment (40, 62, 65). Finally, 25.4% discontinued US due to cost (70). Studies were from a variety of countries including New Zealand (28), Portugal (27) Korea (34, 78),

Taiwan (45) and the USA (46, 52, 53), where some were multi-national (29, 31, 36, 42, 43, 56) (Table 1).

Related to Partner and Intimate relationship

Twenty-two studies focussed on PDE5Is (27-29, 31, 33-37, 40, 41, 45, 51-53, 55-58, 73, 74, 78) nine on ICI (40, 48, 49, 62, 64-66, 69, 77), one on US (72) and PP (40) explored couples' sexual relationship and treatment utilisation.

The most commonly reported factors were loss of libido or interest in the sexual relationship; reported by 6.6% (range: 0.6-17.3%) of men across nine studies focussed on PDE5Is (34, 35, 45, 52, 55, 58, 73, 74, 78), 8.8% (range: 6.9–30%) across four studies focussed on ICIs (40, 62, 65, 77) and 8.9% and 6.9% of men using US and PP, respectively (40, 72).

A partner's lack of interest in the sexual relationship was given as a reason for PDE5I discontinuation by 5.5% (1.2-9.8%) of men across five studies (27, 34, 45, 58, 74). A lack of emotional readiness for restoration of sexual activity was a reason for discontinuing PDE5Is for 5.5% (13.1-22.7%) of men in two studies (34, 78) and conflict within one's relationship by 4.1% (2.4-5.8%) of men in three studies (27, 28, 51). Conflict within one's relationship was also a reason for 1% discontinuing ICI (62). Low levels of satisfaction with one's sexual relationship, was associated with significantly higher rates of ICI discontinuation (49). Conversely, a better quality sexual relationship was associated with significantly higher rates of ICI persistence (48).

4.14 Behavioural Factors

Seven studies examined the effect of behavioural factors on treatment utilisation; six on PDE5Is (27, 33-37) and one on ICI treatment (49). Most commonly a lack of opportunity to engage in sexual intercourse was a reason for 0.9% (2-7.3%) of men to discontinue PDE5Is, across three studies (27, 35, 61). 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 (33, 36). Finally, less frequent masturbation was related to significantly higher levels of ICI treatment discontinuation (49).

5. Discussion

Rates of treatment discontinuation varied considerably across studies, from 4.4-76.0% for PDE5Is, 18.6-79.9% for ICI, 32.0-69.23% for US and 30% for PP. This may relate in part to limitations in operational definitions where less than a quarter of studies gave explicit definitions of treatment utilisation. Where provided, however, variation existed. These findings support a previous call for standardisation of adherence definitions to enable more accurate comparisons between studies (26). Other potential reasons for variation in utilisation rates identified by previous research include; differences in methodologies, adherence measures, treatment regimens, and patient characteristics (79).

In relation to barriers and enablers of treatment utilisation, no consistent findings were evident for demographic factors. However, clinical factors, examined by all studies included in this review, indicate treatment ineffectiveness and side-effects as the most prevalent reasons given for discontinuation.

Only twelve studies examined psychological or cognitive factors, which is surprising considering that psychogenic factors are the cause to some degree of nearly all cases of ED (80). In addition, there is a large body of research which highlights the importance of patient beliefs in relation to a range of acute and chronic conditions and their respective treatments (81-83). Such beliefs have been found to predict adherence in a variety of chronic conditions (84) and are amenable to change which can improve adherence (85). None of the studies included in this review utilised psychological theory to guide their investigations, therefore, future research would benefit from employing psychological theory to advance our understanding of barriers and enablers to ED treatment utilisation.

A widely reported social factor was treatment cost (n=21), however, it was not explored by any of the studies using inferential statistics. Therefore, it is difficult to ascertain the extent to which other factors, such as employment status, play a role. Additionally, studies originated from a variety of countries involving a variety of health care systems. In the UK, for example, guidance provided by the Department of Health restricts prescription of ED treatments to those patients who meet specific criteria, meaning that, for example, those men with ED who additionally suffer with diabetes, multiple sclerosis or Parkinson's disease can receive treatment on the NHS for ED (86). Previously, if a patient did not meet such criteria, then the patient incurred a personal cost for treatment. However, with the advent of cheaper medicines becoming available (87), in 2014, legislation was introduced removing the restrictions on NHS prescribing of generic sildenafil. This enabled HCP's the ability to prescribe generic sildenafil for all men with ED on NHS prescription (88). Finally, more recently, Sildenfil has been made available in UK pharmacies for men who wish to purchase the treatment over-the counter (89). It is beyond the scope of this review to consider the impact of varying procurement methods on ED treatment utilisation, however, this remains an important consideration for future research.

Loss of libido in men and their partners and its relationship with ED treatment discontinuation was also a widely reported social factor. It is possible that loss of libido was underreported as other factors potentially overlap, such as a lack of emotional readiness for restoration of sexual activity and conflict within one's relationship. Furthermore, loss of libido and ED are both symptoms of testosterone deficiency (90), but studies did not report potential causes of low libido in their participants. The causes of low or a lack of libido are important considerations for HCP's to consider when providing treatment for ED as successful treatment of other conditions such as testosterone deficiency may influence successful treatment with regards to ED. Although treatment ineffectiveness was the most frequently reported barrier to utilisation, operational definitions were absent. Therefore it is possible that a treatment could potentially be described as 'ineffective' due to other factors such as loss of libido or conflict within one's relationship. Underlying factors such as

these may have been overlooked and therefore, future research would benefit from investigating individual perceptions of ineffectiveness which, in turn, could enable HCPs to provide appropriate support, potentially reducing discontinuation.

It is important to note that results of the current review indicate that men who reported side-effects to a HCP were significantly less likely to discontinue treatment. This suggests that there is potential for HCP's to influence utilisation rates. As discussed, perceived ineffectivness of treatment has a subjective element and therefore requires exploration with a given patient. We would recommended that if men report that their treatment is ineffective, prescribers seek to identify and clarify any misconceptions patients may have in relation to their treatment. This would enable the possibility of exploring beliefs about medication with patients where changing treatments or altering doses in line with any insights that arise could potentially increase ED treatment utilisation. Additionallly, exploring the quality of patients' intimate relationships may indicate the necessity for additional treatments, for example psychosexual counselling, which could potentially work in conjunction with medication/devices and increase treatment utilsiation.

There were methodological limitations with respect to the studies included. Descriptive statistics were used by 32 studies and only 8 used multivariate statistics to analyse data. Therefore, a substantial amount of frequency data was included, which can indicate the prevalence of a barrier or enabler, but not their unique impact on utilisation when others are taken into account.

There was an absence of reliable and validated measures with respect to rates of treatment utilisation, as well as barriers and enablers to utilisation. Although there is no 'gold standard' to measuring treatment adherence (91), there are a variety of validated treatment adherence measures (92). However, existing measures of treatment adherence are potentially unsuitable for assessing ED treatments; taken predominantly on demand. Therefore, this review highlights the need for a validated measure of ED treatment utilisation and echoes the call for simple, valid and

reliable methods for detecting the prevalence and types of non-adherence to enable the possibility of building effective and targeted adherence interventions (85) .

The methods used to ask men about barriers and enablers to treatment utilisation varied considerably. Use of open-ended questions may result in some barriers or enablers being under-reported if they are not asked about specifically. In order to understand barriers and enablers to ED treatment utilisation, future studies would benefit from using a design that are 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 has several limitations. The inclusion of only published manuscripts introduces the possibility of publication bias and resources dictated that articles were published in English. Due to the nature of some of the barriers and enablers, allocation to one of the overarching themes was not always straight forward. For example, loss of libido was classified as a social factor; however, this is likely to have psychological and/or physiological components. The quality of findings of any systematic review relies in part on the quality of the studies included and although study quality varied, 58% were classified as either 'limited' or 'adequate'. In general, there was an under-reporting of important participant data such as ED duration, ED severity, relationship status, levels of employment and levels of education.

In conclusion, treatment ineffectiveness, side-effects, the quality of one's intimate relationship as well as the cost of treatment emerged as important barriers to treatment utilisation. There is a need for study designs to be more rigorous as well as a greater focus on the impact of psychosocial factors. Beliefs about ED and its treatment are potentially modifiable, offering an opportunity to improve treatment utilisation and the quality of life of both men and their partners. Therefore, based on the results of this review, future research would benefit from identifying modifiable factors e.g. beliefs about medication, which could be targeted by interventions to help improve utilisation through the use of a more theoretically informed, evidence-based approach.

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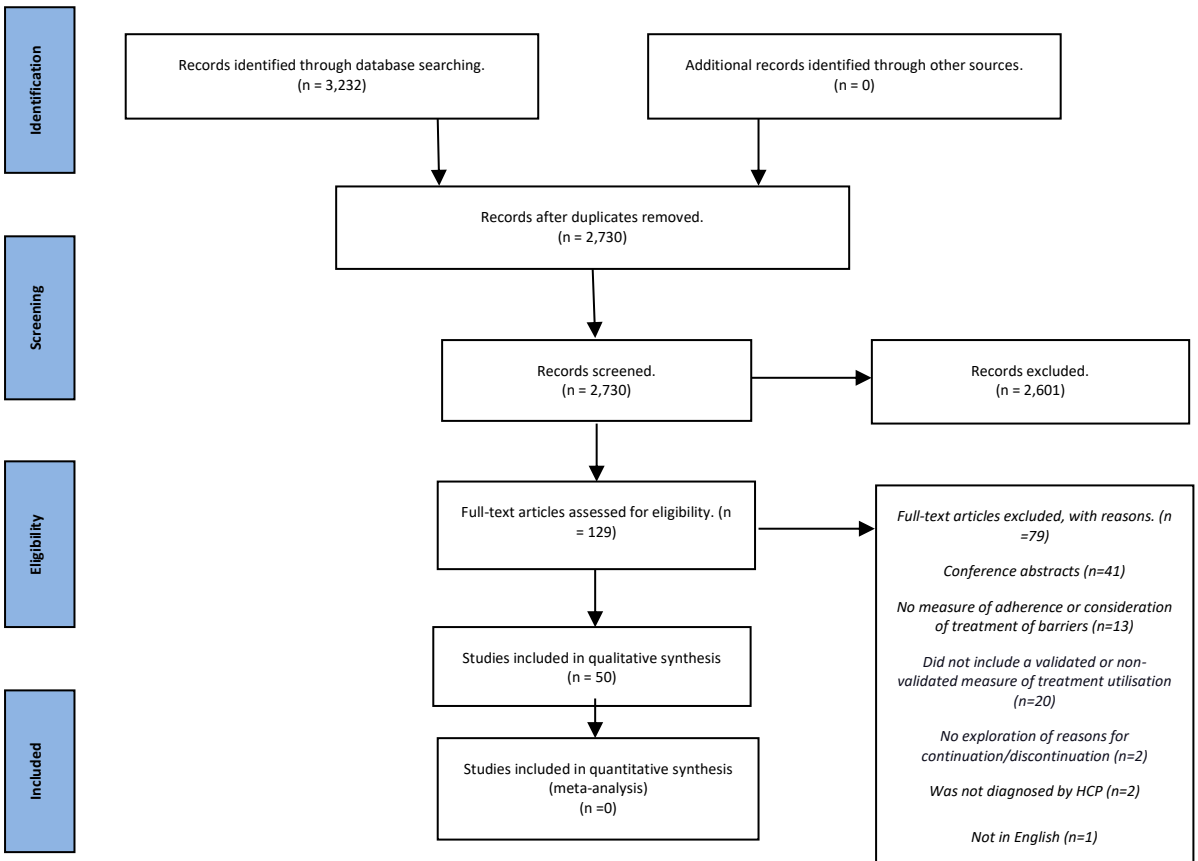
Figure 1: PRISMA flowchart



699 Table 1: Study characteristics

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
ICI treatment							
Alvarez et al. (1998)(63)	Europe, South Africa	Evaluate the long-term safety and efficacy.	Prospective cohort study	Aprostadil 20 mg/mL	6 months	848	70%
Armstrong et al (1994)(64)	N. Ireland	To identify factors contributing to patient drop-out from an ICI programme.	Cross-sectional study	NR	n/a	30	45%
Gerber and Levine (1991)(65)	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	41%
Irwin & Kata (1994)(77)	USA	To determine acceptance and durability of treatment.	Prospective cohort study	Aprostadil (mean dosage) = 23 ug (range 5-30 ug).	6 months	60	45%
Kunelius et al (1999)(66)	Finland	To assess the long-term outcome of treatment and overall patient satisfaction with their sexual life.	Retrospective cohort study	NR	36 months	69	54%
Lehmann et al (1999)(48)	Switzerland	To clarify the reasons why experience with self-injection therapy for ED shows high dropout rates.	Retrospective cohort study	Alprostadil 2-mL	M=16 (3-64 months)	86	59%
Perimenis et al (2001)(67)	Greece	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	64%
Polito et al (2012)(68)	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	68%
Purvis et al (1999)(50)	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	64%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Raina et al (2003a)(57)	USA	Investigate drug efficacy in patients following RP.	Retrospective 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	73%
Rowland et al (1999)(49)	USA	Explore satisfaction with and dropout from ICI use.	Prospective cohort study	NR	M=9 months	119	73%
Sung et al (2014)(62)	Korea	To investigate the rate of withdrawal and its associated reasons.	Cross-sectional	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	82%
PDE5I medication							
Bai et al (2015)(59)	China	To compare treatment preference, efficacy, and tolerability of sildenafil and tadalafil for treating erectile dysfunction (ED)	Randomised Trial	(1) 20-mg tadalafil and then 100-mg sildenafil (2) 100-mg sildenafil and then 20-mg tadalafi	7 Months	383	91%
Buvat et al (2013)(31)	France, Greece, Portugal, Germany, UK	To evaluate the effects of initiating treatment with Tadalafil OaD, Tadalafil PRN, or sildenafil PRN on treatment utilisation.	Randomised Trial	(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	82%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Buvat et al (2014)(29)	Germany, France, Italy, Greece	To evaluate treatment continuation, effectiveness and tolerability of Tadalafil OaD.	Prospective cohort study	Tadalafil OaD 5-mg	6 months	778	100%
Cairoli et al (2014)(41)	Brazil	To characterize persistence and adherence to PDE5I on-demand therapy over 6 months	Prospective cohort study	NR	6 months	104	81%
Carvalheira et al (2012)(35)	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	68%
Carvalheira et al (2014)(27)	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	65%
Choi et al (2014)(60)	China	To investigate the sustainable effect of 5-mg alternate-day tadalafil versus 5-mg once-daily tadalafil	Randomised Trial	(1) Tadalafil) 5-mg once-daily (2) Tadalafil) (5-mg alternate-day	3 months	180	61%
Cimen et al (2009)(73)	Turkey	Retrospective evaluation of ED patients who were recommended a PDE5I treatment in terms of patient satisfaction.	Cross-sectional Study	NR	n/a	345	55%
Conaglen & Conaglen (2012)(28	New Zealand	To evaluate factors influencing adherence to, or discontinuation of, oral ED medications.	Retrospective cohort study	NR	12 months	155	64%
El-Galley et al (2001)(51)	USA, Saudi Arabia	Evaluation of the long-term efficacy of Sildenafil	Prospective cohort study	NR	24 months	200	54%
El-Meliegy et al (2013)(42)	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	95%
Fagelman et al (2001)(52)	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	54%
Green and Martin (2000)(53)	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	45%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Incrocci et al (2003)(54)	Netherlands	To determine the efficacy of Sildenafil citrate in patients with ED after three-dimensional conformal external beam radiotherapy.	Quasi experimental	50 mg for 2 weeks increasing to 100 mg if necessary.	24 months	50	64%
Jiann et al (2006)(45)	Taiwan	To assess treatment compliance and reasons for dropout.	Cross-sectional Study	NR	M=36 months	434	64%
Kim et al (2014)(34)	Korea	To identify characteristics of ED patients who discontinued PDE5I medication.	Cross-sectional Study	NR	n/a	485	91%
Kim et al (2015)(32)	USA	To evaluate whether TAD-OaD provides similar efficacy in men with ED who had previously demonstrated a partial response to PRN PDE5I therapy.	RCT	(1) Placebo, (2) Tadalafil 2.5 mg (uptitrated to tadalafil 5mg after 4 weeks) (3) Tadalafil 5mg OaD	3 months	623	93%
Klotz et al (2005)(74)	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	41%
Lee et al (2010)(46)	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	61%
Li et al (2016)(76)	China	To assess the efficacy of tadalafil de-escalation in the therapeutic effects of psychogenic ED	Randomised Trial	(1) 5 mg of tadalafil per day; Group 2: 20 mg tadalafil per day (for 1 month) followed by 10 mg per day (for the 2nd month) and 5 mg for the third month.	3 months	86	61%
Ljunggren et al (2008)(55)	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.	Prospective cohort study	NR	M=27 months	138	45%
Mazzola et al (2013)(33)	USA	To explore the link between erection hardness and treatment adherence.	Prospective cohort study	Sildenafil, 100 mg	17 +/- 4 months	186	82%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
McMurray (2007)(30)	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	54%
Montorsi et al (2004)(56)	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	68%
Raina et al (2003b)(57)	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	73%
Ricardi et al (2010)(75)	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.	Randomised Trial	Tadalafil 20 mg PRN (arm A) or Tadalafil 5 mg OaD (arm B)	3 months	52	93%
Roumeguere et al (2008)(36)	Austria/Belgium/Denmark /Greece/Iceland/Netherla nds/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	100%
Rubio-Aurioles et al (2013)(43)	Brazil, Mexico, Venezuela	Investigate the factors that may be predictive for PDE5I persistence and adherence.	Prospective cohort study	NR	6 months 6 months	511	100%
Salonia et al (2008a)(58)	Italy	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	82%
Salonia et al (2008b)(37)	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	91%
Sato et al (2007)(47)	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	68%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Son et al (2004)(78)	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	41%
Souverein et al (2002)(44)	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	86%
Urethral Suppository							
Mulhall et al (2001)(70)	USA	To determine the consistency of a successful response to a urethral suppository (Aprostadil)	Prospective cohort study	Aprostadil 1000 mg	M=9 months	68	73%
Raina et al (2007)(72)	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	61%
Raina et al (2005)(71)	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.	Retrospective cohort study	Aprostadil 250 mg flexible to 500 or 1000 mg dose of urethral suppository, if needed	M=27 +/- 14 months	54	82%
Multiple Treatments							
Panach-Navarretea et al (2017)(61)	Spain	To describe the medium and long-term satisfaction and adherence of pharmacological treatments in ED	Cross-sectional	NR	NA	250	85%
Sexton et al (1998)(40)	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	54%

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701 *ICI: Intracavernousal injection therapy; M: mean; OaD: once a day; PP: penile prosthesis; PRN: on demand; RAP: robotic assisted prostatectomy; RCT: randomised control trial; US: Urethral suppository*

702 Table 2: Participant Characteristics

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
ICI treatment							
Alvarez et al. (1998)(63)	52	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)(64)	50.5	NR	NR	NR	NR	NR	NR
Gerber and Levine (1991)(65)	NR	NR	NR	NR	NR	NR	NR
Irwin & Kata (1994)(77)	64	NR	NR	NR	NR	NR	NR
Kunelius et al (1999)(66)	60.5	NR	NR	NR	Vasculogenic: 30 (28) Psychogenic: 31 (29) Neurologic: 8 (7)	NR	NR
Lehmann et al (1999)(48)	58 (10)	NR	NR	NR	Organic: 52 (60) Mixed: 23 (27) Psychogenic: 11 (13)	NR	NR
Perimenis et al (2001)(67)	54.85	NR	NR	NR	NR	28	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Polito et al (2012)(68)	64.6 (6.5)	NR	NR	NR	NR	NR	M=No ED (=/> 20): 212 (77.6%)
Purvis et al (1999)(50)	57	NR	NR	NR	Vascular: 33% Idiopathic: 31% Psychogenic: 26% Neurologic: 7% Endocrine: 3%	NR	NR
Raina et al (2003a)(57)	60.4 (6.3)	NR	NR	NR	NR	NR	Sev: 68%
Rowland et al (1999)(49)	58	NR	NR	NR	NR	41	NR
Sung et al (2014)(62)	61.8 (7.9)	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

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
PDE5I medication							
Bai et al (2015)(59)	39.94 (11.00)	NR	NR	Diab: 17 (4.4), Hyp 19 (5.0)	Organic: 24 (6.3), Mixed: 272 (71.0)	≥3 to <12 164 (42.8), ≥12 219 (57.2)	Mi 131 (34.2), Mod 133 (34.7), Sev 119 (31.1)
Buvat et al (2013)(31)	53.03 (11.66)	White 753 (97.8), Black/African American 10 (1.3), Multiple 1 (0.1)	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)
Buvat et al (2014)(29)	57	Caucasian 523(67.2), Other 4(0.5)	Married 639(65.9), Partnered/living together 120(12.4)	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(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Cairoli et al (2014)(41)	57.8 (10.9)	NR	NR	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 (2012)(35)	56.30 (11.44)	NR	Married: 65.4% Divorced/separated: 18.3% Single: 10.4% Common law: 3.1% Widowed: 2.8%	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
Carvalheira et al (2014)(27)	55.8 (11.11)	NR	Married: 61.5% Divorced/separated: 20.3% Single: 12.2% Common law: 4.1% Widowed: 2.0%	NR	Venogenic:31% Arteriogenic: 23% Psychogenic: 18% Iatrogenic: 13% Neurogenic: 8% Diabetic: 7%	NR	NR
Choi et al (2014)(60)	56.8	NR	NR	Underlying disease 42 (29.1)	NR	NR	Mod – Sev 180 (100)
Cimen et al (2009)(73)	56 (11.2)	NR	NR	Diab: 21.7%, Hyper: 16.1%, CVD: 4.7%	NR	27.7	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Conaglen & Conaglen (2012)(28	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
El-Galley et al (2001)(51)	58 (10)	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
El-Meliegy et al (2013)(42)	49.6 (12.03)	NR	NR	Hyp: 222 (45), Diab: 209 (42.4), Ob: 104 142 (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)

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Fagelman et al (2001)(52)	54.1	NR	NR	NR	NR	44	NR
Green and Martin (2000)(53)	40.4	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)(54)	68	NR	NR	Diab and/or Hyp 13%	NR	NR	NR
Jiann et al (2006)(45)	66.8 (9.8)	NR	NR	NR	NR	NR	NR
Kim et al (2014)(34)	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)	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: 228 (47.0), Mod: 224 (46.2) Sev: 33 (6.8)
Kim et al (2015)(32)	57.6 (10.4)	Caucasian: 517 (83.0), Black/African American: 88 (14.1), Asian: 8 (1.3), Other: 9 (1.4)	NR	NR	Psychogenic: 31 (5.0) Organic 297 (47.7) Mixed 217 (34.8) Unknown 78 (12.5)	<1 year 39 (6.3) ≥ 1 year 584 (93.7)	Mi/Mod: 123 (19.7) Mod: 472 (75.8), Sev: 28 (4.5)

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Klotz et al (2005)(74)	60.5	NR	NR	Hyp: 40%, Diab: 16%	Organic: 202 (86)	NR	M=Mi-Mod 17
Lee et al (2010)(46)	57.8 (7.0)	NR	NR	NR	NR	NR	Mi 22
Li et al (2016)(76)	24.55 (3.8)				Psychogenic: 86 (100)		Mi 15 (16.6) Mod 30 (33.3) Sev 45 (50)
Ljunggren et al (2008)(55)	60 (7)	NR	NR	NR	Organic: 40 (32%) Psychogenic: 23 (18%) Mixed: 64 (50%)	60	NR
Mazzola et al (2013)(33)	61 (22)	NR	Partnered: 63%	Hyper: 36%, Dys: 38%, CAD: 16%, Diab: 15%	NR	26	Mi 25%, Mod 45%, Sev 30%,
McMurray (2007)(30)	58.2	White: 873 (89.2), Black: 68 (6.9), Asian: 8 (0.8), Other: 30 (3.1)	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)(56)	NR	NR	NR	NR	NR	NR	NR
Raina et al (2003b)(57)	NR	NR	NR	NR	NR	NR	Sev: 68%
Ricardi et al (2010)(75)	69.1	NR	NR	NR	NR	12	Sev: 88.9%

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Roumeguere et al (2008)(36)	56.5 (11.1)	NR	Currently has a partner 1504 (96)	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)
Rubio-Aurioles et al (2013)(43)	53.2 (12.4)	NR	NR	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 (2008a)(58)	51.8 (12.7)	NR	No stable sexual relationship: 38 (16.45) Stable sexual relationship >12 months: 193 (83.5)	NR	NR	NR	M=Mi-Mod: 13.75
Salonia et al (2008b)(37)	53; 10.3 51.4; 13.5	NR	NR	NR	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Sato et al (2007)(47)	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)(78)	54.6	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)
Souverein et al (2002)(44)	57.2 (10.74)	NR	NR	NR	NR	NR	NR
Urethral Suppository							
Mulhall et al (2001)(70)	46.5 (14.6)	NR	NR	Diab: 11% , Hyp: 29%, Hyperch: 21%, A History of cigarette smoking: 31%	NR	NR	NR
Raina et al (2007)(72)	55.6 (3.78)	NR	NR	NR	NR	NR	Sev: 19.65 (mean)
Raina et al (2005)(71)	63.7 (5.6)	NR	NR	NR	NR	NR	Sev: 68%
Multiple Treatments							

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
Panach-Navarretea et al (2017)(61)	57.09 (10.63)	NR	NR	Hyp: 115 (46), Diab: 70 (28), Dys: 92 (36.8) Smkr; Yes 79 (31.6)/No 71 (28.4)/Former smkr 97 (38.8), CHD: 27 (10.8), Ldis: 24 (9.6), VasD: 14 (5.6), DigD: 19 (7.6), Endo: 27 (10.8), Neuro: 22 (8.8); OncH: 27 (10.8), PS: 16 (6.4)	NR	NR	NR
Sexton et al (1998)(40)	58.5	NR	NR	NR	NR	NR	NR

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; DigD: Digestive disease; Dys: Dyslipidaemia; Endo: Endocrinopathy; Hyperch: Hypercholesterolemia; Hyp: hypertension; Hyperl: hyperlipidaemia; Hypog: Hypogonadism; IHD; Ischemic heart disease: IO: Intrapelvic operation; LUTS: Lower Urinary Tract Symptoms; Ldis: Lung disease; M: mean; Mi: mild; Mod: moderate; Neuro: Neuropathy; N: normal; NR: Not recorded; NR; Ob: obesity; Onco: Oncologic History; 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; Smkr: Smoker; VasD: Vascular disease

708 Table 3: Measures of Utilisation and Treatment Barriers and enablers

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
ICI treatment						
Alvarez et al. (1998)(63)	PD	Reasons for discontinuation were collected monthly.	NR	PD	After each injection: date, time, volume of injection and dose were recorded by the patient.	34% (D)
Armstrong et al (1994)(64)	SRQ	Qs: Reasons for withdrawal from treatment were collected via predefined questions.	NR	SRQ	Qs: covering home injection use including period of time.	64% (D)
Gerber and Levine (1991)(65)	Cons	Patients returned every 3 months and were questioned regarding erectile response, pain after injection and frequency of use.	NR	Cons	Qs: covering frequency of prostaglandin E1 use.	72% (D)
Irwin & Kata (1994)(77)	Cons	Patients were given monthly follow-up visits scheduled to evaluate the patients' acceptance and usage patterns	NR	NR	Monthly follow-up visits to evaluate patients' acceptance and usage pattern.	60% (D)
Kunelius et al (1999)(66)	SRQ	Qs: Patients were invited to a check-up after three years after they had been started on ICI treatment and were sent a questionnaire prior to the appointment.	NR	SRQ	Qs: aspects of sexual function and possible problems with Aprostadil self-injection.	46%.4 (D)
Lehmann et al (1999)(48)	Int & Cons	Included objective and subjective variables which included barriers to treatment use.	NR	Int & Cons	Qs: covering the number of injections used.	20% (D)
Perimenis et al (2001)(67)	NR	NR	NR	NR	NR	42.5% (D)
Polito et al (2012)(68)	SRQ	Qs: multiple choice questions including: lack of, disappointment with the effects, Injection pain/problems with the injection (difficulty/fear), Cost of the drug.	NR	NR	NR	18.6% (D)
Purvis et al (1999)(50)	SRQ	Qs: Twenty eight questions were asked which were multiple choice in the majority of cases.	NR	SRQ	NR	38.6% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Raina et al (2003a)(57)	NR	NR	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)(49)	SRQ	Qs: including as section for participants who had discontinued ICI treatment.	NR	SRQ	Qs: items pertained to how ICI was used, its effectiveness, and the patient's general satisfaction.	40% (D)
Sung et al (2014)(62)	TS	Participants were asked about reasons for discontinuation.	NR	TS	Qs: multiple responses.	79.9% (D)
PDE5I medication						
Bai et al (2015)(59)	NR	NR	NR	NR	NR	tadalafil 20mg: 13.7% (D) Sildenafil 100-mg: 10.3% (D)
Buvat et al (2013)(31)	Cons	Time to discontinuation was measured by the number of days from randomization up to discontinuation of treatment. Secondary outcomes included patients who switched and discontinued treatment and were asked about reasons for switches and discontinuations.	NR	Cons	NR	Tadalafil OaD:52% (D) Tadalafil PRN:42% (D) Sildenafil PRN:67% (D)
Buvat et al (2014)(29)	TS	Patients who had no visit within 4–6 months after baseline were followed up with a telephone follow-up call.	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)
Cairoli et al (2014)(41)	SRQ	A questionnaire administered at 1, 3, and 6 months post baseline.	P=≥ 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)
Carvalheira et al (2012)(35)	TS	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?	NR	SRQ	Qs: quantitative and qualitative variables and including frequency and duration of PDE5 use.	48.9% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Carvalheira et al (2014)(27)	SRQ	Qs: 29-item questionnaire including open ended questions with regards to utilisation of PDE5Is.	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)
Choi et al (2014)(60)	NR	NR	NR	NR	NR	Tadalafil OaD: 18.9% (D) Tadalafil alternate-day: 21.1% (D)
Cimen et al (2009)(73)	TS	Patients were called by phone and asked to answer questions on the phone including questions regarding reasons for discontinuation.	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)(28	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.	D=stopping medication taking	Int	Qs: details of frequency of usage and reasons for discontinuation of use.	33% (D)
El-Galley et al (2001)(51)	TS	Participants were contacted by telephone. Patients who ended treatment were asked about the main reason for discontinuation.	P=Continued use	TS	NR	48% (D)
El-Meliegy et al (2013)(42)	SRQ	Outcomes were assessed at baseline and at 1, 3, and 6 months after treatment initiation.	P=≥ 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)(52)	SRQ	Qs: At follow-up visits, the patients were given a questionnaire and then interviewed	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)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Green and Martin (2000)(53)	SRQ / TS	The initial forty patients were followed for a two-year interval either by follow-up clinic visits or telephone interviews.	NR	SRQ / TS	At follow-up clinic visits or telephone interviews.	32.5% (D)
Incrocci et al (2003)(54)	SRQ	Qs: evaluate their current sexual functioning and to ask about sildenafil use.	NR	SRQ	Qs: current sexual functioning and use of sildenafil.	76% (D)
Jiann et al (2006)(45)	SRQ	Qs: multiple choice questions in regard to reasons for discontinuation.	NR	SRQ	Qs: marital status, ED duration, frequency of sexual intercourse, history and current status of usage.	57% (D)
Kim et al (2014)(34)	SRQ	Qs: questionnaire had multiple choice questions regarding discontinuation.	D=not taken PDE5i in the past 1 year	SRQ	Qs: characteristics and treatment of ED.	23.9% (D)
Kim et al (2015)(32)	NR	NR	NR	NR	NR	Placebo: 9.1% (D) Tadalafil 2.5 mg (pptrated: 10.1% (D) tadalafil 5mg OaD: 8.7% (D)
Klotz et al (2005)(74)	TS	The reasons for abandonment were determined by a telephone survey.	D=no 2nd prescription within 6 months	PR	NR	31% (D)
Lee et al (2010)(46)	TS	Reasons for discontinuing PDE5I therapy were recorded by asking each patient..	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)
Li et al (2016)(76)	NR	NR	NR	NR	NR	Tadalafil 5 mg: 4.4% (D) Tadalafil de-escalation: 4.4% (D)
Ljunggren et al (2008)(55)	TS	Participants were contacted by telephone and asked questions regarding reasons for discontinuation.	NR	Int	Qs: current treatment, frequency of use, change of treatment, reason for change, and reason for discontinuation.	14.2% (D)
Mazzola et al (2013)(33)	Cons	On follow-up, patients were questioned regarding continued use of PDE5.	D=stopping medication taking	NR	Qs: regarding continued use of PDE5Is.	67% (P)
McMurray (2007)(30)	NR	At yearly intervals changes in dosing or temporary or permanent discontinuation were recorded.	NR	PD	Compliance was assessed by medication diaries and by continued study participation.	40% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Montorsi et al (2004)(56)	Cons	At patient visits, blood pressure and pulse, adverse events, concomitant medications and the reason for dose modification were recorded.	NR	Cons	NR	21% (D)
Raina et al (2003b)(57)	SRQ	Qs: focussed on sexual satisfaction of the patients' spouses/partners 3 years after the first survey to assess long-term efficacy and compliance.	NR	CR	Data collected: drug efficacy, dose, frequency, compliance, return of erections, new side-effects.	27% (D)
Ricardi et al (2010)(75)	NR	NR	P=taking at least 70% of doses	NR	NR	Arm A (20-mg tadalafil PRN): 86% (P) Arm B: (tadalafil 5-mg OaD): 100% (P)
Roumeguere et al (2008)(36)	SRQ	Qs: 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.	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)(43)	SRQ	Qs: 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.	P=≥ 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)
Salonia et al (2008a)(58)	SRQ	Qs: At the 18-mo follow-up, patients were asked to complete a multiple-choice global assessment questionnaire (GAQ) regarding specific reasons for eventual therapy discontinuation.	NR	SRQ	Patients were asked to complete a multiple-choice GAQ	72.6% (D)
Salonia et al (2008b)(37)	Clin, demog data	Patients were subdivided into two groups according to their compliance.	NR	Cons	Data gathered included patient compliance with the suggested PDE5.	42% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Sato et al (2007)(47)	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.	NR	SRQ, Int, Cons	NR	48% (D)
Son et al (2004)(78)	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.	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)(44)	PR	The date of sildenafil discontinuation was defined as the last sildenafil prescription date plus the number of tablets dispensed.	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)
Urethral Suppository						
Mulhall et al (2001)(70)	SRQ	Qs: 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.	NR	SRQ	Qs: to determine whether they were continuing to use MUSE as a treatment.	69.2% (D)
Raina et al (2007)(72)	NR	NR	NR	NR	NR	32 (D)
Raina et al (2005)(71)	NR	NR	NR	CR	Data gathered: treatment effect, frequency of use, duration of erection following treatment and side-effects.	52 (D)
Multiple Treatment						
Panach-Navarretea et al (2017)(61)	TS	To collect information about the use (including time of use) and dropout (including reason) of the prescribed treatment.	NR	TS	To collect information about the use (including time of use) and dropout (including reason) of the prescribed treatment.	1st PDE5I: 62.07% (D) Other PDE5I: 41.94% (D) US: 69.23% (D) ICI: 65.11% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Sexton et al (1998)(40)	TS	Telephone interviews were conducted with all patients to determine levels and frequency of sexual activity, current form of therapy and reasons for discontinuing therapy, side-effects and overall satisfaction.	NR	NR	NR	ICI:59%(D) PP:30%(D)

709 *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*
710 *questionnaire; TS: telephone survey; Y: year*

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714 Table 4: Treatment barriers and enablers

	Factor	TT	Descriptive results	Inferential results
Demographic	**Age**			
	Being of older age	PDE5I	**(-):** 43	**(0):** 34,37,41,45,46,47 **(-):** 29,36,44 **(+):** 35,42
		ICI		**(0):** 48,49,50
	Education			
	Higher level of education	PDE5I		**(0):** 41,42 **(+):** 34,37,43(P, not A),
	Employment			
	Being in FT employment	PDE5I		**(0):** 29 **(+):** 41 (A, not P),42(A/P),
Clinical	**Related to Treatment**			
	Medication Ineffective	PDE5I	**(-):** 27,28,29,30,31,32,35,36,43,45,46,51,52,53,54,55,56,57,58,59,60,61	31; - ***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 Sidl PRN
		ICI	**(-):** 40,61,62,63,64,65,66,67,68,69,	**(-):** 49
		US	**(-):** 61,70,71,72	
		PP	**(-):** 40	
	Side-effects/Fear of side-effects	PDE5I	**(-);** 27,29,30,32,34,36,46,51,52,54,55,59,60,61,73,74,75,76	**(0):** 31 **(**between PDE5Is) **(+):** 35; **(**Men who reported side-effects were less likely to discontinue treatment) **(-):** 45
		ICI	**(-):** 40,61,62,64,65,66,67,68,69,77	**(0):** 48 **(-):** 49
		US	**(-):** 61,71,72	
		PP	**(-):** 40	
	Medication lacks spontaneity	PDE5I	**(-):** 34,35,78	
		ICI	**(-):** 40, 62	
		US	**(-):** 70	
	Specific to PDE5I Treatment			
	Initial treatment	PDE5I		**(0):** 41
	Having a history of ED treatment utilization	PDE5I		**(0):** 62 **(+):** 44

	Factor	TT	Descriptive results	Inferential results
	Using; Tadalafil/Sildenafil or Vardenafil	PDE5I		42; **(0):** Tad Vs Sild **(0):** Tad Vs Sild **(+):** Using Sild at initial prescription rather than Vard 43; **(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		**(+):** 36; Having good toleration for treatment after 1 month was associated with sig continued utilisation.
	Higher incidence of trying dose titration	PDE5I		**(+):** 45
	Having a dose greater than 50mg	PDE5I		**(+):** 45
	Short window of time in which the drug is effective	PDE5I		31; **(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):** 31 **(**Tad OaD Vs Sild PRN Vs Tad PRN)
	Specific to ICI Treatment			
	Administration	ICI	**(-):** 40,49,62,63,64,65,68,69,77	**(-):** 48
	Type of vasoactive substance	ICI		**(-):** 49
	Disposable 1ml syringe	ICI	**(0):** 50	
	Fully automatic RFSU pistol	ICI	**(0):** 50	
	Manual Injection (d-penn) as opposed to semi-automatic BD pistol	ICI	**(0):** 50	
	Using papaverine-phentolamine (15 mg; 0.5 mg)	ICI	**(0):** 50	
	Using;Low dose Aprostadil (0 ± 10 mg)/High dose Aprostadil (0 ± 20 mg)/TRIMIX/D-penn Aprostadil	ICI	**(0):** 50	
	Condition Specific Factors			
	Aetiology	PDE5I	**(+):** 43 (psychogenic associated with continuation)	**(0):** 29,41 **(-):** 34 **(**psychogenic associated with discontinuation) **(+):** 35 (venogenic associated with continuation compared to arteriogenic /diabetes/iatrogenic)
		ICI		**(-):** 49 **(**ED including an organic component)
	Having more severe levels of ED	PDE5I		**(0):** 29,41,46 **(-):** 36,37,42,43,47
	A shift of =/> 2 or a score of 4 on the erection hardness score (EHS)	PDE5I		**(+):** 33
	Shorter Duration of ED symptoms	PDE5I		**(-):** 34 **(+):** 43 (≥ 4 years versus <1 year; P=+, A=0),42 (<1 year P=0, A=+), 45 **(0):** 41 (P=0, A=0)
	Comorbidities			
	Due to the effects of co-morbidities	PDE5I	**(+):** 42 **(**Hypertension) **(-):** 55,74 (tumor/hip prosthesis),78	**(0):** 29,46 (BMI score/Charlson Comorbidity Index score). 34;

	Factor	TT	Descriptive results	Inferential results
				(0): Number of comorbidities/Stress/Smoking/alcohol **(+):** Sig increase in utilisation by those of higher weight and those with a BMI of ≥ 23 41; **(0):** Diabetes Mellitus/Dyslipidemi/Hypertension/Depression **(+):** Those with Coronary artery disease had sig higher rates of utilisation. **(+):** 36 (Sig increase in utilisation by those with pelvic surgery)
		ICI	**(-):** 40,65	**(0):** 62 (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	**(-):** 40	
	Illness (ongoing health issues, deteriorating health or recent injuries or operations	PDE5I	**(-):** 28,36	
		ICI	**(-):** 63,64	
	Other medications and treatments			
	Due to other Medications and Treatments	PDE5I	**(-):** 34	44; **(-):** 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		31; **(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		**(-):** 49
	Penile rigidity adequate for sexual intercourse	ICI		**(+):** 62
	Premature ejaculation	ICI		**(-):** 49
Psychological and	**Treatment Related Beliefs**			
	Lack of confidence in medication	PDE5I	**(-):** 29	**(0):** 31 (Tad OaD/Tad PRN/Sild PRN)
	Fear of drug dependency	PDE5I	**(-):** 35	
	Fear that medication is harmful for the heart	PDE5I	**(-):** 27,35	
	Averse to taking medication	PDE5I	**(-):** 27	
	Medication caused personal conflict	PDE5I	**(-):** 56	
	Don't want to take a pill everyday	PDE5I	**(-):** 29	31; **(0):** Tad PRN vs Sild PRN **(-):** Tad OaD sig increased discontinuation compared to Tad PRN/Sild PRN

	Factor	TT	Descriptive results	Inferential results
	Prefer a pill every day, not on demand	PDE5I		31; **(0):** Tad PRN vs Sil PRN **(+):** 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	**(-):** 29,34,78	31; **(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	**(-):** 27,45	
	Forgetting to buy or to get medical prescription	PDE5I	**(-):** 27	
	Satisfaction with treatment	ICI		**(+):** 48
	Disappointed with treatment	ICI	**(-):** 67,68	
	Would recommend treatment to a friend	ICI		**(+):** 48
	Psychosocial Well-being			
	Lack of self-confidence/self-esteem	PDE5I	**(-):** 27,36	
		ICI		**(-):** 48
	Improve Sexual performance	PDE5I		**(+):** 27
	To improve psychological and emotional state	PDE5I	**(+):** 27	
Social	**Cost of Treatment**			
	Cost	PDE5I	**(-):** 28,27,29,34,35,36,43,45,46,52,53,54,55,61,73,74,78	
		ICI	**(-):** 40,62,65,	
		US	**(-):** 70	
	Related to Partner and Intimate relationship			
	Loss of libido/interest in sex	PDE5I	**(-):** 34,35,45,52,55,58,73,74,78	
		ICI	**(-):** 40,62,65,77	
		US	**(-):** 72	
		PP	**(-):** 40	
	Partner lack of interest in sexual relationship	PDE5I	**(-):** 34,45,58,74 **(+):** 27	
	Lack of emotional readiness for restoration of sexual activity	PDE5I	**(-):** 34,78	
	Higher level of Partners sexual activity	PDE5I		**(0):** 27
	Conflicts within one's relationship	PDE5I	**(-):** 27,28,51	
		ICI	**(-):** 62	
	Low satisfaction with sex life	ICI		**(-):** 49
	Better quality of sexual relationship	ICI		**(+):** 48
	Person within the dyad who most often initiated sexual activity	ICI		**(0):** 49
	Partner Related			
	Partner's difficulty in accepting treatment	PDE5I	**(-):** 27,29,36	**(0):** 31
		ICI	**(-):** 66	
	Partner satisfaction with treatment (reported by patient)	ICI		**(+):** 48
	Partner aware of and involved in the use of treatment	PDE5I		**(+):** 27

	Factor	TT	Descriptive results	Inferential results
	Having no partner	PDE5I	**(-):** 28,36,53,57	**(+):** 33 (having a partner)
		ICI	**(-):** 40,64,69,77	
		PP	**(-):** 40	
	Marital Status/Relationship Status	PDE5I		**(0):** 34,37,41
		ICI		**(0):** 49
	Living with partner	PDE5I		**(0):** 34
	Longer duration of living arrangement	PDE5I		**(-):** 31
	Length of marriage/relationship	PDE5I		**(0):** 34,37
		ICI		**(0):** 49
	Geographical distance from partner	PDE5I	**(-):** 27	
	Partner being of younger age (=/>10 years younger)	PDE5I		**(0):** 34 **(+):** 33
	Partners illness	ICI	**(-):** 66	
Behavioral	**Help seeking**			
	Length of time before seeking help for ED	PDE5I		**(0):** 37
	Personal behavior			
	Lower frequency of masturbation	ICI		**(-):** 49
	Related to sexual relationship			
	Lack of opportunity for sexual intercourse	PDE5I	**(-):** 27,35,61	
		ICI	**(-):** 61	
		US	**(-):** 61	
	Pre-treatment sexual activity (=/>4 times per month)	PDE5I		**(+): 33**
	Greater No of sexual attempts in the first month of treatment	PDE5I		**(+):** 36
	Life style			
	Level of exercise	PDE5I		**(0):** 34

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

1.1 Supplementary Material

Prisma Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
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.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
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.	4
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.	4
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.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp. Material p 4-7
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).	5
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.	5

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
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.	5 Supp. Material p 8-47

Section/topic	#	Checklist item	Reported on page #
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).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
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.	6 Figure 1 - PRISMA flowchart
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.	6 Table 1 – Study Characteristics
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).	N/A
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.	9 Table 4 – Treatment barriers and enablers
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A

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).	15-18
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).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
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.	18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

1.1.1 Systematic Review Search Terms

General Terms		
Erectile Dysfunction	**Adherence**	**Treatment for ED**
Erectile Dysfunction*	Medication AND (adher* OR -use OR taking)	PDE5 Inhibitor*
Impoten*	(complian* OR non-complian*)	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?complian*	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

1.1.2 Barriers and Enablers to Treatment Utilisation

	Factor	Treatment type	Barrier to treatment utilization *Descriptive results* (n (%) reporting reason for discontinuation unless otherwise stated)	Barrier to treatment utilization *Inferential results*	Enabler of treatment utilization *Inferential results*	Non-significant *Inferential results*
Demographic	**Age**					
	Being of older age	PDE5I	**Rubio-Aurioles (2013)#** **(P)** Higher rates of persistence in younger men (mean age of 52.3 years versus 54.9 years for non-persistent patients). **(A)** Higher rates of adherence in younger men (mean age of 52.1 years versus 55.5 years for non-adherent patients).	**Buvat (2014):** >65 y significantly higher rates of discontinuation than those ≤65 y (p=0.038). **Roumeguere (2008):** >60 y significantly higher rates of discontinuation than those 51-60 y (OR = 1.88; 95% CI: 1.18–2.99; P = 0.008) **Souverein (2002):** =/>60 y significantly higher rates of discontinuation than <60 y (RR 1.71 (95% CI: 1.20 – 2.44).	**Carvalheira (2012)** Older men less likely to discontinue (OR = 0.956, p =0.005). **El-Meliegy (2013)#** Older men were likely to be both more persistent (P) (OR =1.03, p=0.002) and adherent (A) (OR =1.02, 0.034)	**Cairoli (2014) (P) (A)** **Jiann (2006)** **Kim et al (2014)** **Lee et al (2010)** **Salonia (2008b)** **Sato et al (2007)**

		ICI				**Purvis (1999)** **Lehmann (1999)** **Rowland (1999)**
	Education					
	Higher level of education	PDE5I			**Kim et al (2014)** Significantly greater discontinuation for middle school graduate or below compared to high school graduate or above p=0.049. OR: 0.48, p= 0.05 **Rubio-Aurioles (2013)** **(P)** Significant higher rates of persistence for primary, secondary or tertiary education in comparison with no education) p=0.047	**Cairoli (2014) (P)(A)** **Rubio-Aurioles (2013) (A)** Postgraduate Vs no formal education **(P)(A)** Primary education Vs formal education **(P)(A)** Secondary education Vs formal education **(P)(A)** Tertiary education Vs formal education **(P)(A)**

					Salonia (2008b) high education group indicated significantly higher rates of persistence compared to patients in the low education group UVA: OR = 2.46, p=0.005	University education Vs formal education **(P)(A)** **Salonia (2008b)** higher level of education not significant using **MVA**
	Employment					
	Being in FT employment	PDE5I		Overall work status	**El-Meliegy (2013)** **(P):** FT employment was related to a significantly higher rates of persistence p= 0.010 **(P):** being employed FT opposed to being unemployed was associated with significantly higher rates of persistence OR: 0.28, p=0.024 **(P):** being employed FT as opposed to retired was associated with significantly higher rates of persistence OR: 0.411, p=0.009 **(A):** FT employment was related to a significantly higher rates of adherence p= 0.006	**Buvat (2014)** Pensioner/retired vs. employed/student Unable to work vs. employed/student Unemployed/other vs. employed/student **Cairoli (2014) (P)** FT/PT/retired/unemployed **El-Meliegy (2013)** **(P)** FT as opposed to PT **(A)** FT as opposed to Unemployed

					(A): being employed FT opposed to PT was associated with significantly higher rates of adherence OR: 0.59 p=0.007 **(A):** being employed FT as opposed to retired was associated with significantly higher rates of adherence OR: 0.411, p= 0.010 **Cairoli (2014)** **(A)** Being employed FT compared to part time, retired, unemployed significantly increased adherence p=0.022	
	Other					
	Height / Residential area / Occupation / Number of children	PDE5I				**Kim (2014)**
	Being of Catholic religion	PDE5I		**Kim (2014)** Continuers 24 (20.7), discontinuers 36 (9.8), p=0.015 OR: 2.31, p=0.01		**Kim (2014)** Protestant Buddhist

						Other
	Ethnic background	PDE5I		Buvat (2014) France vs. Germany 0.045 HR 1.62 (1.01, 2.59) Italy vs. Germany 0.022 HR 0.41 (0.19, 0.87) Greece vs. Germany 0.010 HR 0.32 (0.13, 0.75)		**Cairoli (2014)** *Black* *African American* *White*
Clinical	**Related to Treatment**					
	Medication Ineffective	PDE5I	**Bai (2015)#** *Ineffective:* Tad 1 (3.8) **Buvat (2013)#** *Hardness of erection:* Tad OaD: 55 (21.4)	**Buvat (2013)** *Duration of erection* Tad OaD was related to significantly increased persistence compared Sild PRN: p=0.035 Tad PRN was related to significantly increased persistence compared Sil PRN: p=0.003		**Buvat (2013)** *Hardness of erection* Tad OaD vs. Sild PRN Tad PRN vs Sil PRN Tad OaD vs. Tad PRN *Duration of erection*

			Tad PRN: 46 (18.3) Sild PRN: 55 (21.1) *Duration of erection* Tad OaD: 11 (4.3) Tad PRN: 7 (12.8) Sild PRN: 24 (9.2) **Buvat (2014)# Total: 35 (4.4)** *Hardness of erection:* 33 (4.2) *Duration of erection:* 2 (0.2) **Carvalheira (2012)#** 61 (38.1) **Carvalheira (2014)#:** 23 (15.5) **Choi (2014)# Total: 14 (15.5)** Insufficient response: Tad OaD: 5 (5.5) Tad alternative days: 9 (10) **Conaglen (2012)#** 1 (0.6)			OaD vs. Tad PRN

			El-Galley (2001)# 14 (7) **Fagelman (2001)#** 64 (39) **Green (1999)#** *Minimal response:* 6 (15) **Incrocci (2003)#:** 30 (60) **Jiann (2006)#** 104 (23.9) **Kim (2015**)# Tad 2.5mg; 2 (0.9) **Lee (2010)#** 8 (15) **Ljunggren (2008)#** 3 (2.3) **McMurray (2007)# Total 52 (7.5)** *Year 1:* 22 (2.2) *Year 2:* 19 (2.3) *Year 3:* 14 (1.9) *Year 4:* 7 (1.1) **Montorsi (2004)#** 173 (23.8) **Panache Navarrete (2017)#** 90 (38.8)			

			Raina (2003b)# 5 (10.4) **Roumeguere (2008)#: 38 (**2.4) **Rubio-Aurioles (2013)#** *Tad:*60 (19.0) *Sild:* 17 (15.0) *Vard:*13 (17.0) **Salonia (2008a)#** 28 (54.9)			
		ICI	**Alvarez (1998)#** 69 (8.0) **Armstrong (1994)#** 3 (10.0) **Gerber (1991)#** *Inadequate erectile response* 9 (12.5) **Kunelius (1999)#** 9 (13.0) **Panache Navarrete (2017)#** 11 (39.3) **Perimenis (2001)#**3 (7.5) **Polito (2012)#** 33 (12) **Raina (2003a)#** 18 (17.6)	**Rowland (1999)** Those that reported a lack of efficacy were more likely to discontinue p=0.009.		

			Sung (2014)# 111 (37) **Sexton (1998)#:** 16 (18.3)			
		US	**Mulhall (2001)#** 30 (50.8) **Panache Navarrete (2017)#** 14 (28) **Raina (2005)#** 16 (29.6) **Raina (2007)#:** 9 (16.0)			
		PP	**Sexton (1998)#** *Malfunction:* 2 (4.7)			
	Side-effects/Fear of side-effects	PDE5I	**Bai (2015)#** *Adverse event* Tad 20mg: 3 (0.9) **Buvat (2014) #** Total: 23 (2.9) *Adverse event;* 22 (2.8) *Un-wanted spontaneous erections* 1 (0.1) **Carvalheira (2014)#:** Fear of/side effects 15 (10.1)	**Jiann (2006)** A higher incidence of adverse events in continuers than discontinuers 63% and 47% respectively, p=0.01	**Carvalheira (2012):** Men who reported side-effects were less likely to discontinue treatment OR: 0.396, p=0.002.	**Buvat (2013)** *Un-wanted spontaneous erections* / *Adverse event* Tad OaD Tad PRN Sild PRN

			Choi (2014)# Total: 5 (4.5) *Side effects;* Tad OaD: 3 (2.7) Tad alternate days: 2 (1.8) **Cimen (2009)#** 4 (1.3) **El-Galley (2001)#** Total: 10 (8) *Side-effects:* 2 (1.6) *Worsened Peyronie's disease:* 2 (1.6) *Un-wanted spontaneous erections* 6 (4.8) **Fagelman (2001)#** Total: 13 (6.9) *Side-effects: 7 (3.1)* *Peyronie's disease: 3 (1.9)* *Chest pain: 3 (1.9)* **Incrocci (2003)#:** 8 (16) **Kim (2014)#** 19 (3.9)			

			Kim (2015)# Total: 6 (2.8) Tad 2.5mg: 3 (1.4) Tad 5mg: 3 (1.4) **Klotz (2005)#** *Adverse (headache and rhinitis)* 4 (1.7) **Lee (2010)#** 4 (7.5) **Li (2016)# Total: 4 (4.6)** Tad 5mg : headache and dyspepsia: 1 (1.15) Myalgia: 1 (1.15) Tad 20mg: Headache/back pain: 1 (1.15) Flushing and headache: 1 (1.15) **Ljunggren (2008)#** 3 (2.4) **McMurray (2007)#** *Total*: 11 (1.3) **Year 1:** 5 (0.5)			

			Year 2: 2 (0.2) **Year 3:** 1 (0.1) **Year 4:** 3 (0.5) **Panache Navarrete (2017)#** Fear of/ADR:13 (6.4) **Ricardi (2010)#** *Intolerable adverse events*: 3 (5.78) *Headache:* 1 (1.9) *Anaphylactic reaction:* 1 (1.9) **Roumeguere (2008)#:** 23 (1.4)			
		ICI	**Armstrong (1994)#** 1 (3.0) **Gerber (1991)#:** *pain due to injection:* 12 (16.6) **Irwin (1994)#** *pain:* 2 (3.3) **Kunelius (1999)#:** Total: 7 (10.1)	**Rowland (1999)** Those that discontinued were more likely to report side-effects p=0.038		**Lehmann (1999)** *Pain from injection* *Aching pain in corpus cavernosum* *New scar tissue* *Bleeding from injection site* *Secondary penile deviation*

			Fibrosis in the penile shaft 3 (4.3%) *Pain after injection* 4 (5.8%) **Panache Navarrete (2017)#** Fear of/ADR 9 (20.9) **Perimenis (2001)#** *Peyronie's disease:*1 (2.5) **Polito (2012)#** *Injection pain:* 23 (8.4) **Raina (2003a)#** *Priapism:* 1 (0.9) **Sexton (1998)#** *Side-effects:* 12 (23) **Sung (2014)#** *Adverse side-effects:* 16 (4.4)			*Erection lasting longer than desired* *Priapism*
		US	**Panache Navarrete (2017)#**			

			Fear of/ADR 16 (32) **Raina (2007)#** *urethral pain and/or burning:* 4 (7.4) **Raina (2005)#** *urethral pain and/or burning:* 4 (7.4)			
		PP	**Sexton (1998)#:** *Infection or erosion:* 4 (9.4)			
	Medication lacks spontaneity	PDE5I	**Carvalheira (2012)#** 14 (2.6) **Kim (2014)#** 11 (2.2) **Son (2004)#** 2 (1.2)			
		ICI	**Sexton (1998)#** 14 (16.1) **Sung (2014)#** 43 **(**14.6)			
		US	**Mulhall (2001)#** 20 (34.0)			
	Specific to ICI Treatment					
	Administration	ICI	**Alvarez (1998) #** Inability/unwilling to self-inject: 18 (2.0)	**Lehmann et al (1999)**		

			Armstrong (1994)# *reluctance to use injections/difficulty with technique/method regarded as unacceptable:* 7 (24.0) **Gerber (1991)#** *did not like injections:* 7 (9.7) **Irwin (1994)#** Total: 4 (6.65) *physical limitations:* 3 (5) *needle phobia:* 1 (1.65) **Polito (2012) #** *difficulty, fear, pain when using injections*: 18 (15) **Raina (2003a)#** Total: 12 (11.8) *fear of injections:* 6 (5.9) *troublesome procedure:* 6 (5.9) **Rowland (1999)#** *procedural aspects surrounding the injection:* 10 (8.4)	The effort to prepare and inject was substantial for those who discontinued, p=0.001.		

			Sexton (1998)# *Total*: 9 (10.3) *Fear of needles or injection procedure:* 5 (5.7) *manual dexterity:* 4 (4.6) **Sung (2014)#** *inconvenience of use* 43 (14.6)			
	Type of vasoactive substance	ICI				**Rowland (1999)** *No difference across vasoactive treatments.*
	Disposable 1ml syringe	ICI	**Purvis (1999)#** *Did not influence the decision to use the treatment.*			
	Fully automatic RFSU pistol	ICI	**Purvis (1999)#** *Did not influence the decision to use the treatment.*			
	Manual Injection (d-penn) as opposed to semi-automatic BD pistol	ICI	**Purvis (1999)#** *Discontinuers: 35.3%, compared to 27.7% continuing*			

			semi-automatic BD pistol (13.1% compared to 23.7% continuing)			
	Using papaverine-phentolamine (15 mg; 0.5 mg)	ICI	**Purvis (1999)#** *Continuers 24.3%, discontinuers 14.6% (n=766)*			
	Using; - Low dose Aprostadil (0 ± 10 mg) - High dose Aprostadil (0 ± 20 mg) -TRIMIX - D-penn Aprostadil	ICI	**Purvis (1999)#** *Did not influence the decision to use the treatment.*			
	Specific to PDE5I medication					
	Initial treatment	PDE5I				**Cairoli (2014) (P) (A)** *Tad/Sild/Vard*

	Having a history of ED treatment utilization	PDE5I			**Souverein (2002)** Discontinuation was less frequent among patients with a history of ED treatment use compared with those with no prior history: 28.6% and 43.9% respectively. Adjusted RR 0.48 (95% CI: 0.31 – 0.76).	**Sung (2014)**
	Using Tadalafil, Sildenafil or Vardenafil	PDE5I			**El-Meliegy (2013)** **(P)** using Sild at initial prescription rather than Vard was associated with increased persistence OR: 0.450, p=0.023 **(A)** using Sild at initial prescription rather than Vard was associated with increased adherence OR: 0.42, p= 0.015 **Rubio-Aurioles (2013)** **(P)** Tad was associated with increased persistence when compared to Sild OR: 1.6 p=0.006. **(A)** Tad was associated with increased adherence when compared to Sild OR: 1.3, p=0.021.	**El-Meliegy (2013)** **(P)** Using Tad as opposed to Sild **(A)** Using Tad as opposed to Sild **Rubio-Aurioles (2013)** **(P)** Using Sild as opposed to Vard **(A)** Using Sild as opposed to Vard

	Able to tolerate treatment at 1 month	PDE5I			**Roumeguer (2008)** Toleration of treatment after 1 month (N = 1,350; 98% of total) was associated with continued use compared to patients who did not well tolerated at 1 month (N = 31; 2% of total): adjusted OR = 9.47; 95% CI: 4.04–22.18; P < 0.0001).	
	Higher incidence of trying dose titration	PDE5I			**Jiann (2006)** Dose titration was associated with significantly higher rates of continuation p=<0.01	
	Having a dose greater than 50mg	PDE5I			**Jiann (2006)** Having doses greater than 50mg was associated with significantly higher rates of continuation p=<0.01	**Jiann (2006)** *Having a responding dose greater than 50mg*
	Short window of time in which the drug is effective	PDE5I	**Buvat (2013)#** Tad OaD: 0 (0.0) Tad PRN: 1 (0.4) Sild PRN: 11 (4.2)	**Buvat (2013)** Significantly higher rates of continuation for those using; -Tad OaD compared to those using Sild PRN p=<0.001		**Buvat (2013)** Tad OaD compared to Tad PRN

				- Tad PRN compared to those using Sil PRN: p=0.006		
	Slow onset of action	PDE5I	**Buvat (2013)#** Tad OaD: 9 (3.5) Tad PRN: 5 (2.0) Sild PRN: 10 (3.8) **Buvat (2014)#** 3 (0.4)			**Buvat (2013)** Tad OaD vs. Sild PRN Tad PRN vs Sil PRN Tad OaD vs. Tad PRN
	Condition Specific Factors					
	Aetiology	PDE5I	***Psychogenic ED as opposed to organic:*** **Rubio-Aurioles (2013)#** **(P)** Higher rates of persistence for men with ED of psychogenic aetiology (79 persistent patients [23.2%] versus 15 non-persistent patients [8.9%]). **(A)** Higher rates of adherence for men with ED of psychogenic aetiology (78, [22.6%] of adherent patients versus 16 [9.8%] of patients who were non-adherent).	***Psychogenic ED as opposed to organic:*** **Kim (2014)** *Psychogenic ED:* The proportion of the patients with psychogenic ED in the discontinuation group (47.4%) was significantly greater than in the continuation group (32.8%) (P¼0.004). ***Venogenic ED opposed to Arteriogenic, Diabetic and Iatrogenic etiologies:***		**Buvat (2014)** **Cairoli (2014) (P) (A)**

				Carvalheira (2012): Compared to venogenic aetiology participants with the following aetiologies indicated significantly higher rates of discontinuation; arteriogenic OR = 3.4, P = 0.01 diabetes OR = 6.9, P = 0.001 iatrogenic OR = 7.5, P < 0.001.		
		ICI				**Rowland (1999)** *ED including an organic component*
	Having more severe levels of ED	PDE5I		**El-Meliegy (2013)** **(P)** Having moderate as opposed to severe was associated with increased persistence 0.017. **Roumeguer (2008)** Patients with lower ED severity were more likely to continue compared to severe ED: - normal ED (adjusted OR = 6.88; 95% CI: 3.68–12.86; *P* < 0.0001);		**Buvat (2014)** Mild Moderate severe **Cairoli (2014) (P) (A)** Mild Moderate severe

				- mild ED (adjusted OR = 7.83; 95% CI: 4.25–14.44; *P* < 0.0001); - moderate ED (adjusted OR = 2.06; 95% CI: 1.01–4.19; *P* = 0.05). **Rubio-Aurioles (2013)** **(P)** Moderate as opposed to severe ED was associated with higher rates of persistence OR: 0.6, p=0.029 **(A)** Mild and Moderate as opposed to severe ED was associated with higher rates of adherence OR: 0.5, p=0.037 and OR: 0.5, p=0.016 respectively. **Salonia (2008b)** Compliant patients indicated a significantly greater SHIM score i.e. had less severe ED: UVA: p=0.01 / MVA: p=0.01. **Sato (2007)** Patients with lower ED severity were more likely to continue compared to severe ED HR: 0.960 CI: 0.931–0.990, p=0.025		**El-Meliegy (2013)** **(P)** having mild as opposed to severe ED **(A)** having mild OR moderate as opposed to severe ED **Rubio-Aurioles (2013)** **(P)** having mild as opposed to severe ED **Lee (2010)** SHIM score

	A shift of =/> 2 or a score of 4 on the erection hardness score (EHS)	PDE5I			**Mazzola (2013)** Significantly higher rates of continuation were reported for those with such a score on the EHS, p= <0.001	
	Shorter duration of ED symptoms	PDE5I		**Jiann (2006):** Those that continued had a shorter duration of ED (49.6 ±77.5 months) opposed to those that discontinued (52.5 ± 50.0), p=<0.05 **Rubio-Aurioles (2013)** **(A)** Those that were adherent had a shorter duration of ED symptoms (those that had ED symptomology for ≥ 4 years compared to those that had ED symptomology for <1 year) OR: 0.4 p=0.004	**El-Meliegy (2013):** **(A)** Those who were adherent had a longer duration of ED (31.0 versus 24.0 years) OR:1.008 **Kim (2014)** Those that persisted had a longer duration of ED (m=5.13±3.87 years, sd) compared to those with a shorter duration (m=4.22 ± 3.33 years, sd) p=0.026. OR: 0.93, p=0.03	**Cairoli (2014) (P) (A)** **El-Meliegy (2013) P** **Rubio-Aurioles (2013)** **(P) (A)** 1–2 years versus < 1 year **(P) (A)** 2–4 years versus <1 year **(P)** ≥ 4 years versus <1 year
	Comorbidities					
	Due to the effects of co-morbidities	PDE5I	**El-Meliegy (2013)#** *Hypertension*	**Cairoli (2014)** *Coronary artery disease*	**Roumeguer (2008)** *Pelvic surgery* Treatment was continued by 71% of the patients with a history of pelvic surgery	**Buvat (2014)** *Co-morbid conditions* **Cairoli (2014) (P) (A)**

			(P) Higher proportion of persistent patients had hypertension (154 [48.1%] versus 68 [39.3%]) **(A)** A higher proportion of adherent patients had hypertension (146 [49.7%] versus 76 [38.2%]) **Klotz (2005)#** *tumour/hip prosthesis:* 3 (1.3) **Ljunggren (2008)#** *co-morbid conditions:* 1 (0.8) **Son (2004)#** *co-morbid conditions:* 6 (3.9)	those with the condition had higher rates of discontinuation p=0.002	(N = 48) vs. 88% of those with no history (adjusted OR = 0.40; 95% CI: 0.18–0.93; P = 0.03). **Kim (2014)** *BMI* Those with a BMI of ≥ 23 were more likely to continue(273, 85.3%) compared to those that discontinued (75, 72.1), p=0.002 Overall participants who had a higher BMI (kg/m2; m=24.60 ± 2.38, sd) were more likely to continue compared to those that discontinued (m=23.99 ± 2.60, sd) p=0.019. OR: 0.92, p=0.09 *Weight (kg)* Those who continued had a higher weight (m=71.93 ± 8.55, sd) compared to those that discontinued (m=69.37±8.95, sd) p=0.006	*Diabetes Mellitus* *Dyslipidemia* *Hypertension* *Depression* **Kim (2014)** *Number of comorbidities* *Stress* *Smoking* *alcohol*. **Lee (2010)** *BMI score* *CACI (Charlson Comorbidity Index) score*
		ICI	**Gerber (1991)#** *Developed a significant inter-current illness*: 4 (5.5)			**Sung (2014)** DM Hypertension

			Sexton (1998)# *co-morbid conditions:* 3 (3.4)			Cardiovascular disease Cerebrovascular attack Previous radical pelvic surgery including prostatectomy and cystectomy unilateral or bilateral nerve sparing prostatectomy Previous pelvic radiotherapy
		PP	**Sexton (1998)#** *co-morbid conditions:* 1 (2.3)			
	Illness (ongoing health issues, deteriorating health or recent injuries or operations	PDE5I	**Conaglen (2012)#** 13 (8.4) **Roumeguere (2008)#** 14 (1.1)			
		ICI	**Alvarez (1998)#** 36 (4.0) **Armstrong (1994)#** 4 (13.0)			
	Other medications and treatments					
	Due to other Medications and Treatments	PDE5I	**Kim (2014)#** More important to treat other conditions: 7 (1.4)	**Souverein (2002)** Discontinuing was highest among patients using:	**Souverein (2002)** *Lipid-lowering drugs*	**Souverein (2002)** antihypertensive agents oral anticoagulants

				incontinence materials: 85.7%; adjusted RR 2.61, 95% CI: 1.41 – 4.83 *antidepressants:* 80.0%; adjusted RR 3.41, 95% CI: 1.19 – 9.77) *nitrate therapy* 73.9%, adjusted RR 2.23, 95% CI: 1.30 – 3.82. *Insulin* adjusted RR 1.71, 95%CI: 1.06 – 2.93.	Were associated with increased continuation; adjusted RR 0.59, 95% CI: 0.36 – 0.97.	low dose acetylsalicylic acid benign prostatic hyperplasia products
	Other clinical factors					
	Type of physician	PDE5I		**Buvat (2014)** Those diagnosed by a GP rather than a urologist showed significantly higher levels of continuation OR: 0.27 (0.12, 0.56) p= <0.001		**Buvat (2014)** Endocrinologist diabetologist urologist Other

	-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)** More patients were able to achieve penile rigidity adequate for sexual intercourse in the continuing group than in the withdrawal group: 94.9% vs. 51.5%, respectively, p< 0.001.	

	Premature ejaculation	ICI		**Rowland (1999):** Higher rates of drop out in those with co-existent premature ejaculation: OR: 2.29, p=0.026		
Psychological and Cognitive	**Treatment Related Beleifs**					
	Lack of confidence in medication	PDE5I	**Buvat (2014)#** 1 (0.1)			**Buvat (2013)** Tad OaD Tad PRN Sild PRN
	Fear of drug dependency	PDE5I	**Carvalheira (2012)#** 10 (3.0)			
	Fear that medication is harmful for the heart	PDE5I	**Carvalheira (2012)#** 25 (7.6) **Carvalheira (2014)#:** 6 (4.0)			

	Averse to taking medication	PDE5I	**Carvalheira (2014)#:** 7 (4.7)			
	Medication caused personal conflict	PDE5I	**Montorsi (2004)#** 94 (12.9)			
	Don't want to take a pill everyday	PDE5I	**Buvat (2014)#** 12 (1.5)	**Buvat (2013)** -Higher rates of discontinuation for those taking Tad OaD compared with Sild PRN: p= <0.001 -Higher rates of discontinuation for those taking Tad OaD compared with Tad PRN: p=<0.001		**Buvat (2013)** Tad PRN vs Sild PRN
	Prefer a pill every day, not on demand	PDE5I		**Buvat (2013)** -Higher rates of discontinuation for those taking Sild PRN compared to Tad OaD, p= <0.001 - Higher rates of discontinuation for those taking Tad PRN compared to Tad OaD , p=<0.001		**Buvat (2013)** Tad PRN vs Sil PRN

	Not willing for sex life to depend on medication/medication controls sex life	PDE5I	**Buvat (2014)#** 3 (0.4) **Kim et al (2014)#** 36 (7.4) **Son et al (2004)#** 4 (2.5)	**Buvat (2013)** Higher rates of discontinuation for those taking Sild PRN compared to those taking Tad OaD, p= 0.015		**Buvat (2013)** Tad PRN vs Sil PRN Tad OaD vs. Tad PRN
	Inconvenience/embarrassment in obtaining medication	PDE5I	**Carvalheira (2012)#** 4 (1.2) **Jiann (2006)#** 71 (16.3)			
	Forgetting to buy or to get medical prescription	PDE5I	**Carvalheira (2014)#:** 3 (2.0)			
	Satisfaction with treatment	ICI			**Lehmann (1999):** Continuers were more satisfied with treatment than those who discontinued, p=0.02	
	Disappointed with treatment	ICI	**Perimenis (2001)#** 7 (17.5) **Polito (2012)#** 33 (12)			
	Would recommend treatment to a friend	ICI			**Lehmann (1999):** A higher proportion of those who continued would recommend the	

					treatment to a friend (continuers 65, 94.0%), discontinuers 7, 41.0%), p=0.01	
	Psychosocial Well-being					
	Lack of self-confidence/self-esteem	PDE5I	**Carvalheira (2014)#:** 17 (11.4) **Roumeguere (2008)#:** 12 (0.8)			
		ICI			**Lehmann (1999)** Continuers showed increased levels of self-esteem p=0.012	
	Improve Sexual performance	PDE5I	**Carvalheira (2014)#** *Total*: 25 (16.8) *To avoid bad performance* 15 (10.1) *To improve performance* 10 (6.7)			
	To improve psychological and emotional state	PDE5I	**Carvalheira (2014)# 12** (8.1)			
Social	**Partner related**					
	Having a partner	PDE5I			**Mazzola (2013)**	

					Having a partner was reported as significantly Increasing persistence: p= <0.01	
	Having no partner	PDE5I	**Conaglen (2012)#** 4 (2.6) **Green (1999)#:** 5 (12.5) **Raina (2003b)#** 1 (2.0) **Roumeguere (2008)#:** 27 (1.7)			
		ICI	**Armstrong (1994)#** 4 (13.0) **Irwin (1994)#:** 9 (15) **Raina (2003a)#** 4 (3.9) **Sexton (1998)#:** 10 (11.5)			
		PP	**Sexton (1998)#:** 3 (6.97)			
	Marital Status/Relationship Status	PDE5I				**Cairoli (2014) (P)(A)** **Kim et al (2014)** **Salonia (2008b)**
		ICI				**Rowland (1999)**
	Living with partner	PDE5I				**Kim (2014)**

	Longer duration of living arrangement	PDE5I		**Buvat (2014)** associated with an increased risk of treatment discontinuation, p=0.019		
	Length of marriage/relation ship	PDE5I				**Kim (2014)** **Salonia (2008b)**
		ICI				**Rowland (1999)**
	Geographical distance from partner	PDE5I	**Carvalheira (2014)#:** 13 (8.7)			
	Partner being of younger age (=/>10 years younger)	PDE5I			**Mazzola (2013)** Having a partner =/>10 years younger increased persistence significantly, p= <0.01	**Kim et al (2014)**
	Partners illness	ICI	**Kunelius (1999)#:** 2 (2.9)			
	Personal					
	For extra marital relations	PDE5I			**Carvalheira (2014):** 8.1%	
	Work commitments	ICI	**Armstrong (1994)#** 1 (3.3)			

	Cost of Treatment					
	Cost	PDE5I	**Buvat (2014)#** 16 (2.0) **Carvalheira (2012)#** 22 (6.7) **Carvalheira (2014)#:** 8 (5.4) **Cimen (2009)#** 51 (16.5) **Conaglen (2012)#** 18 (11.6) **Fagelman (2001)#** 5 (0.6) **Green (1999)#:** 2 (5) **Incrocci (2003)#:** 12 (24) **Jiann (2006)#** 93 (21.4) **Kim (2014)#** 31 (6.4) **Klotz (2005)#** 9 (3.8) **Lee (2010)#** 24 (45.3) **Ljunggren (2008)#** 1 (0.8) **Panache Naverette (2017)#** 20 (8.62) **Roumeguere (2008)#** 34 (2.2)			

			Rubio-Aurioles (2013)# *Total:* 161 (31.5) *Tad:*117 (37.0) *Sild:*26 (23.0) *Vard:*18 (25.0) **Son (2004)#** 2 (1.2)			
		ICI	**Sung (2014)#** 13 (4.4) **Gerber (1991)#:** 4 (5.5) **Sexton (1998)#:** 4 (4.6)			
		US	**Mulhall (2001)#** 14 (25.4)			
	Related to sexual relationship					
	Loss of libido/interest in sex	PDE5I	**Carvalheira (2012)#** 8 (2.4) **Cimen (2009)#** 18 (5.8) **Fagelman (2001)#** 1 (0.6) **Jiann (2006)#** 75 (17.3) **Klotz et al (2005)#** *Lack of opportunity or desire* 33 (14.1)			

			Kim (2014)# 9 (1.8) **Ljunggren (2008)#** 1 (0.8) **Salonia (2008a)#** 1 (1.9) **Son et al (2004)#** 2 (1.2)			
		ICI	**Irwin (1994)#** 18 (30) **Sung (2014)#** 16 (5.4) **Gerber (1991)#** 5 (6.9) **Sexton (1998)#** 6 (6.9)			
		US	**Raina (2007)#:**5 (8.9)			
		PP	**Sexton (1998)#** 3 (6.9)			
	Partner lack of interest in sexual relationship	PDE5I	**Carvalheira (2014)#:** 9 (6.0) ***Lack of emotional and physical stimulus by the partner increased utilisation of treatment.*** **Jiann (2006)#** 36 (8.2) **Kim (2014)#** 6 (1.2) **Klotz (2005)#** 19 (8.1) **Salonia (2008a)#** 5 (9.8)			

	Lack of emotional readiness for restoration of sexual activity	PDE5I	**Kim (2014)#** 15 (13.1) **Son (2004)#** Total: 20 (12.8) *Of partner:* 12 (7.7) *Of patient:* 8 (5.1)			
	Partners level of sexual activity	PDE5I				**Carvalheira (2012)**
	Conflicts within one's relationship	PDE5I	**Carvalheira (2014)#:** 5 (3.3) **Conaglen (2012)#** 9 (5.8) **El-Galley (2001)#** 2 (2.4)			
		ICI	**Sung (2014)#** 3 (1.0)			
	Low satisfaction with sex life	ICI		**Rowland (1999):** Higher rates of drop out associated with a lower level of satisfaction with one's current sexual life OR: 1.24, p= 0.054		
	Better quality of sexual relationship	ICI			**Lehmann (1999):** Continuers 63 (91.0) reported better quality of sexual relationship than discontinuers 5 (30.0) p=0.001	

	Person within the dyad who most often initiated sexual activity	ICI				**Rowland (1999)**
	Partner's difficulty in accepting treatment	PDE5I	**Buvat (2014)#** 5 (0.6) **Carvalheira (2014)#:** 5 (3.3) **Roumeguere (2008)#:** 12 (0.8)			**Buvat (2013)** Tad OaD Sild PRN Tad PRN
		ICI	**Kunelius (1999)#:** 2 (2.9)			
	Partner satisfaction with treatment (reported by patient)	ICI			**Lehmann (1999):** Those that persisted were more significantly more satisfied with treatment p=0.02	
	Partner aware of and involved in the use of treatment	PDE5I			**Carvalheira (2012):** Continuers were less likely to discontinue compared with men whose partner was not involved in the treatment OR: 0.345, p= 0.01	

Behavioral	**Help seeking**					
	Length of time before seeking help for ED	PDE5I				**Salonia (2008b)**
	Personal behavior					
	Lower frequency of masturbation	ICI		**Rowland (1999):** Higher rates of drop out indicated for those with a lower frequency. OR: 1.35, p=0.027		
	Related to sexual relationship					
	Lack of opportunity for sexual intercourse	PDE5I	**Carvalheira (2012)#** 18 (5.5) **Carvalheira (2014)#:** 3 (2.0) **Panache Naverette (2017)#** 17 (7.3)			
		ICI	**Panache Naverette (2017)#** 3 (6.9%)			
		US	**Panache Naverette (2017)#** 2 (4%)			
	Pre-treatment sexual activity (	PDE5I			**Mazzola (2013)**	

	=/>4 times per month)				Pretreatment sexual activity increased persistence significantly, p= <0.001	
	Greater No of sexual attempts in the first month of treatment	PDE5I			**Roumeguere (2008):** Patients with a greater number of sexual attempts in the first month were significantly more likely to continue the treatment at 12 months (adjusted OR = 1.09; 95% CI: 1.03–1.16; P = 0.003).	
	Life style					
	Level of exercise	PDE5I				**Kim (2014)**