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The Psychosocial and Clinical Outcomes of Surgery for Thyroid Eye Disease (TED)

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pp 357-362: **Appendix Q.** Reflective notes.

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DECLARATION

I, Sadie Wickwar, confirm that the work presented in this thesis is my own. Where information has been derived from other sources I confirm this has been indicated in the thesis.

LIST OF ABBREVIATIONS

ACT	Acceptance Commitment Therapy
AR1	First-order Autoregressive Structure
ARC	Appearance Research Collaboration
ATDs	Antithyroid Drugs
ATSCI	Attention to Social Comparison Information
B-FNE	Brief Fear of Negative Evaluation Questionnaire
BDD	Body Dysmorphic Disorder
BMEC	Birmingham and Midland Eye Centre
CAR	Centre for Appearance Research
CARSAL	Centre for Appearance Research Salience of Appearance Scale
CARVAL	Centre for Appearance Research Valence of Appearance Scale
CAS	Clinical Activity Scale
CASP	Critical Appraisal Skills Programme
CBT	Cognitive Behavioural Therapy
CHI-VFQ-25	Chinese National Eye Institute Visual Function Questionnaire
CI	Confidence Intervals
CONSORT	Consolidated Standards of Reporting Trials
COREQ	Consolidated Criteria for Reporting Qualitative Research
CT	Computerised Tomography
DAS24	Derriford Appearance Scale 24 Item Version
DV	Dependent Variable
E-TEDS	Expectations of TED Surgery Questionnaire
E-TEDS AC	E-TEDS Appearance Concerns Subscale
E-TEDS ISR	E-TEDS Intimacy and Social Relationships Subscale
E-TEDS VF	E-TEDS Visual Function Subscale
EL	Eyelid Lengthening
EMS	Eye Muscle Surgery
EQ-5D	European Quality of Life Questionnaire
ESSQ	Expectations of Strabismus Surgery Questionnaire
EUGOGO	European Group on Graves Orbitopathy
EuroQol	European Quality of Life Questionnaire
FNE	Fear of Negative Evaluation Questionnaire
GC	Glucocorticoid
GD	Graves’ Disease

GO	Graves’ Ophthalmopathy
GO-QLS	Graves Ophthalmopathy Quality of Life Scale
GO-QOL	Graves’ Ophthalmopathy Quality of Life Questionnaire
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HRQL	Health-Related Quality of Life
ICC	Intraclass Correlation
INCOM	Iowa-Netherlands Comparison Orientation Measure
IPA	Interpretative Phenomenological Analysis
IS	Intravenous Steroids
IV	Intravenous
IV	Independent Variable
KMO	Kaiser-Meyer-Olkin
LAR	Long-Acting Repeatable
LogMAR	Log of the Minimal Angle of Resolution
M	Mean
MCAR	Missing Completely at Random
MCID	Minimal Clinically Important Difference
MCS	Mental Component Summary Scale of the SF-36 and SF-12
MEH	Moorfields Eye Hospital London
MI	Multiple imputation
MLM	Multilevel Modelling
MMAT	Mixed Methods Appraisal Tool
MOS-24	Medical Outcomes Study Short Form General Health Survey
MRD	Marginal Reflex Distance
MSPSS	Multidimensional Scale of Perceived Social Support
N/A	Not Applicable
NEI VFQ-25	National Eye Institute Visual Function Questionnaire
NHS	National Health Service
NOSPECS	Classification of TED severity tool
OCD	Obsessive-Compulsive Disorder
OD	Orbital Decompression
OND	Optic Nerve Dysfunction
ONS	Office for National Statistics
OS	Oral Steroids

PAS	Patient Administration System
PCA	Principle Component Analysis
PCS	Physical Component Summary Scale of the SF-36 and SF-12
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist
PTSD	Post-Traumatic Stress Disorder
PTX	Pentoxifylline
R&D	Research & Development
RAI	Radioiodine
RAPD	Relative Afferent Pupillary Defect
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SD	Standard Deviation
SE	Standard Error
SF-12 ™	Medical Outcomes Study 12 Item Short Form Survey
SF-36 ™	Medical Outcomes Study 36 Item Short Form Survey
SIP	Sickness Impact Profile
SIST	Social Interaction Skills Training
SPK	Superficial Punctate Keratitis
SPSS	Statistical Package for Social Sciences
TAO	Thyroid-Associated Orbitopathy
TED	Thyroid Eye Disease
TED-QOL	Thyroid Eye Disease Quality of Life Questionnaire
TEDcT	Thyroid Eye Disease Charitable Trust
ThyPRO	Thyroid Specific Patient Reported Outcome Questionnaire
UK	United Kingdom
VAS	Visual Analog Scale
VIF	Variance Inflation Factor
WHO	World Health Organisation
WHOQoL	World Health Organisation Quality of Life Group

ABSTRACT

This study aimed to investigate whether quality of life in patients with thyroid eye disease (TED) improves as a result of having orbital decompression surgery and whether any demographic, clinical or psychosocial factors can predict which patients might benefit from this surgery.

One hundred and twenty three adults with TED were recruited from Moorfields Eye Hospital (MEH), London. Clinical measurements were taken by the clinical team at MEH and participants completed a range of psychosocial questionnaires prior to surgery and again 6 weeks and 6 months after surgery. The Appearance Research Collaboration's (ARC) framework of adjustment to living with a disfiguring condition was used to guide the study's measures and analysis. The Graves' Ophthalmopathy Quality of Life Questionnaire (GO-QOL; Terwee et al., 1998) was completed by participants at each time point and was the dependent variable in each hierarchical multiple regression model. Semi-structured interviews were conducted with fourteen patients from Birmingham and Midland Eye Centre (BMEC) to explore expectations of orbital decompression and thematic analysis was performed.

Prior to surgery, the regression model explained 55% of the variance in GO-QOL visual function scores and 75% of the variance in GO-QOL appearance scores. Although vision-related quality of life was associated with age and asymmetrical disease, it was intervening psychosocial processes that were more consistently associated with both vision- and appearance-related quality of life. Patients had high expectations for surgery to return them to the "normality" of their lives, and appearance, before TED. High expectations were often a result of great confidence and trust in surgeons and information they had accessed about the surgery online.

Significant improvements were found in all clinical characteristics following surgery and in most psychosocial variables. Vision-related quality of life did not change significantly until 6 months after surgery whilst appearance-related quality of life significantly improved 6 weeks post-surgery and continued to significantly increase 6 months post-surgery reaching a minimal clinically important difference (MCID). Ethnicity and a small number of clinical factors patients presented for surgery were unique predictors of the variance in change in vision-related quality of life and appearance-related quality of life. None of the changes in clinical or psychosocial outcomes significantly predicted change in vision-related quality of life. The hierarchical regression model explained 81% of the variance in change in appearance-related quality of life however, with improvement in personal evaluation of appearance uniquely predicting improvement in appearance-related quality of life.

Further research is required to establish whether expectations are met after surgery. Recommendations for clinical practice include routine psychological assessment and the provision of clear and comprehensible information about surgery. Patients with TED in the future would benefit from interventions targeting the intervening psychosocial processes identified by this thesis as amenable to change.

1. THYROID EYE DISEASE (TED)

1.1 PROLOGUE

The aim of this thesis is to investigate the psychosocial impact of thyroid eye disease (TED) and the clinical and psychosocial outcomes following orbital decompression surgery. In this chapter, a description of TED is provided along with information regarding its prevalence, the major signs and symptoms and risk factors for developing the disease. Clinical management will also be discussed, including current recommended clinical guidelines and a description of the surgical procedures offered to patients. Surgical approaches to TED will be described later in this chapter including orbital decompression surgery, which is the focus of this thesis.

1.2 DESCRIPTION

TED, also known as Graves’ ophthalmopathy (GO), thyroid-associated orbitopathy (TAO) and dysthyroid orbitopathy, is an autoimmune thyroid disorder that affects the eyes. TED is the most common cause of swelling and inflammation of the orbit in adults (Leatherbarrow, 2011). It is thought that this inflammation is caused by an autoimmune response against one or more autoantigens shared by the thyroid gland and orbital tissues (Bahn & Heufelder, 1993; Bahn, 2010) leading to an increase in volume of orbital fat, muscles and connective tissue (Orgiazzi & Ludgate, 2010). The exact link between thyroid disturbance and the eye tissues remains unclear, however, TED has been found to occur at the time of onset of hyperthyroidism in the majority of cases (Lazarus, 2012). Hyperthyroidism, or overactive thyroid gland, causes a variety of symptoms including sweating, increased metabolic rate manifesting as heat intolerance, weight loss, and palpitations (Weetman, 2000). Hyperthyroidism has been found to influence mood changes, including anxiety and depression (Bunevicius & Prange, 2006). Noticeable changes in the eyes can however precede, or develop as long as 5 years after, a diagnosis of hyperthyroidism and are not linked to the severity of thyroid problems (Lazarus, 2012).

1.3 PREVALENCE

Hyperthyroidism is more common in women than men, with figures estimating 77 women per 100,000 population per year compared to 14 men per 100,000 population per year developing the condition (Flynn et al., 2004). TED occurs mainly in patients with Graves' disease (GD), which is the most common type of hyperthyroidism (Lazarus, 2012). Estimates of the prevalence of TED in GD are between 25% and 50% (Bahn & Heufelder, 1993). Whilst it has been difficult to define the prevalence and incidence of TED in the UK as there are virtually no prevalence studies (Lazarus, 2012), TED has been reported to have an incidence of approximately 2.9 to 16 cases per 100,000 population per year in Olmsted County, Minnesota (Bartley, 1994) and 400,000 people are estimated to suffer from TED in the UK (Cawood, Moriarty, & O'Shea, 2004). As with hyperthyroidism, TED affects five times more women than men (Cawood, Moriarty, & O'Shea, 2004) and presents more commonly in adults between the ages of 30 and 50 years old (Bartley, 1994).

1.4 AETIOLOGY

Whilst the majority of cases of TED have been linked to GD, research into its causes continues (Lazarus, 2012). Some studies have found eye disease to develop after certain types of treatment for hyperthyroidism. For instance, Tallstedt et al. (1992) report the development and worsening of ophthalmopathy in 33% of patients treated with radioiodine, a proportion significantly higher than in patients treated with drugs and thyroidectomy combined.

A difficulty in diagnosing TED is found in around 5-10% of patients who have never had hyperthyroidism but do have other autoimmune thyroid disease, such as *hypo*thyroidism (Lazarus, 2012). Hypothyroidism, or underactive thyroid gland, causes persistent fatigue and often weight gain (Louwerens et al., 2012).

Other potential factors associated with the development of TED include environmental, hormonal, and genetic factors, as well as age (Bartalena, 2010). A large body of evidence has also shown close links between smoking and the onset of TED (Daumerie, 2010; Bartalena, 2010; Cawood, Moriarty & O'Shea, 2004; Thornton et al., 2007), with smokers or ex-smokers being four times more likely to develop TED (Cawood, Moriarty & O'Shea, 2004). Thornton et al. (2007) conducted a systematic review of the evidence for the link between smoking and TED and found a strong association, including a dose-response effect, and worse treatment outcomes in patients who smoke. However the mechanisms by which smoking affects TED are still unclear (Bartalena, 2010). Despite the plethora of research, studies on the underlying mechanisms for TED remain inconclusive (Bahn, 2000; Tallstedt et al., 1992).

1.5 SIGNS AND SYMPTOMS

The commonest early sign of TED is a noticeable change in the appearance of the eyes including swelling and redness of the orbits (Dickinson, 2010). This swelling of the tissues and fat behind the eyes pushes the eyes forward within the orbits, causing proptosis, or *exophthalmos*. Occasionally, the swelling is severe enough to compress the optic nerve and impair visual function (*optic neuropathy*) which, if left untreated, can cause partial or complete loss of vision (Terwee et al., 1998).

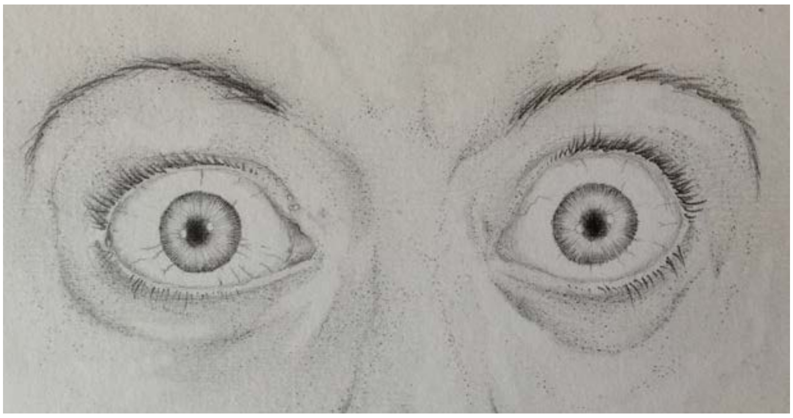


Figure 1. A patient with thyroid-related orbital inflammation and upper eyelid retraction

TED can occur in one eye (*unilateral*) or both eyes (*bilateral*). Kashkouli et al. (2011a) suggest that unilateral TED might be less common, but does not show any significant difference – in terms of severity of the condition, patient demographics, or duration of the disease – to bilateral TED. Wiersinga and colleagues (1989) suggest that establishing a diagnosis of unilateral TED may be more difficult, as these cases are more likely to resemble other causes of unilateral orbital inflammation and proptosis such as infection or orbital tumour. Patients with TED frequently face a delay in diagnosis, and experience an understandable level of anxiety over the cause of their proptosis. In a recent survey of patient experiences of services for TED, Estcourt et al. (2009) found that as many as 58% of patients were given a range of incorrect diagnoses for their eye symptoms, including conjunctivitis and allergies.

Upper eyelid retraction, which produces a marked ‘staring’ appearance, affects most patients at some stage during the disease (Figure 1). Another common sign is redness of the eyes that arises either from drying and irritation of the ocular surface, or from vascular congestion due to severe swelling of the orbital muscles causing disruption of blood flow (*hydraulic orbit*) (Rose, 2006). Corneal superficial punctate keratitis (SPK) is another sign of TED and involves the death of cells on the surface of the cornea causing dry eyes and redness (Miyata et al., 2003). Having severe proptosis, eyelid retraction, or both, can prevent an individual from closing their eyelids fully (particularly at night when trying to sleep) and this can lead to corneal exposure, ocular surface drying, and a propensity for recurrent infections (Schotthoefer & Wallace, 2007).

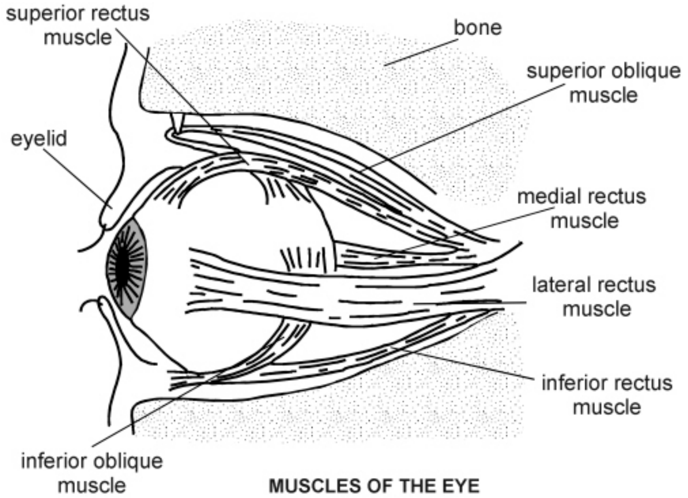


Figure 2. A diagram of the orbital muscles in a healthy adult eye (Kenny, 2010)

TED also causes tightness of the orbital muscles (Figure 2), which can restrict eye movements and cause double vision, or *diplopia*, which is the perception of two separate images (Perros, Neoh & Dickinson, 2009). Diplopia might occur only in secondary gaze when the eyes are deviated vertically or horizontally, in the absence of primary-gaze diplopia. For someone with primary gaze diplopia however, double vision is also experienced when gaze is fixated straight ahead. The onset of diplopia varies: for some patients this will start during progression of inflammation and for others it can first occur after orbital decompression surgery. Orbital decompression surgery is described in more detail in section 1.9 of this chapter.

1.6 DISEASE ACTIVITY

The duration of the development of TED can vary. The condition is unique amongst autoimmune diseases as it is self-limiting, with an “active” phase lasting up to two years, followed by an “inactive” phase (Verity & Rose, 2013). Inflammation of the orbital tissues underlies the active phase and is often characterised by a worsening of the eye condition with symptoms including pain, and ocular and eyelid redness (Dickinson, 2010; Terwee, 2000). After the active inflammation has peaked, there is generally a gradual decrease in its severity until it reaches stability (Terwee, 2000). This process is best illustrated by Rundle’s curve (Rundle, 1945), which describes two distinctive phases of the disease where the eyes reach a maximum level of protrusion, before a gradual reduction occurs until the eyes remain at a new, but stable, configuration (Figure 3).

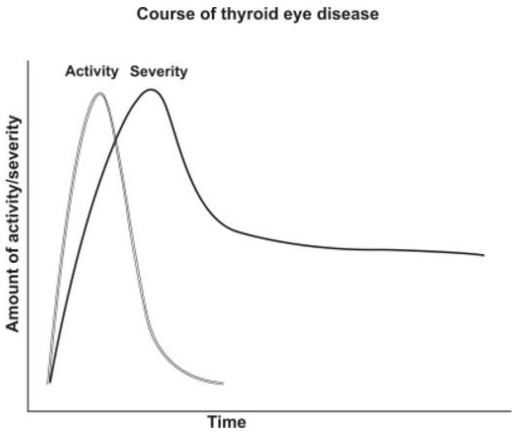


Figure 3. Rundle's (1945) curve illustrating the active and static phases of TED (Bothun et al., 2009)

The rate of development of proptosis and its stabilisation are variable between patients, but the eyes generally do not return to their former appearance (Rundle, 1945). The duration of the active phase varies between patients and as treatment decisions are influenced by disease stage, clinicians are advised to regularly monitor patients throughout the course of their illness to assess the activity of the disease. This is commonly implemented using the Clinical Activity Score (CAS; Mourits et al., 1989), which is a 10-item measure covering four of the five classical characteristics of inflammation in TED (pain, redness, swelling, and impaired ocular function) and gives a score of between 0 and 10 (Table 1). The development of the tool was based on the recognition of different levels of inflammation, different types of pain (for example one type can be from stretching the inflamed muscles when looking upwards), different areas of swelling (such as swelling overlying the whites of the eye) and different levels of impaired function, such as a decrease in eye movements (Mourits et al., 1989).

Table 1. The Clinical Activity Score (CAS; Mourits et al., 1989)

Pain	1 Painful, oppressive feeling on or behind the globe, during last 4 weeks 2 Pain on attempted up, side or down gaze, during the last 4 weeks
Redness	3 Redness of the eyelid(s) 4 Diffuse redness of conjunctiva, covering at least 1 quadrant
Swelling	5 Swelling of the eyelid(s) 6 Chemosis 7 Swollen caruncle 8 Increase of proptosis > 2mm during a period of 1-3 months
Impaired function	9 Decrease of eye movements in any direction >5 degrees during a period of 1-3 months 10 Decrease of visual acuity >1 line(s) on the Snellen chart (using a pinhole) during a period of 1-3 months

For each item present, 1 point is given. The sum of these points is the CAS

1.7 DISEASE SEVERITY

In the absence of pain, swelling, redness and double vision, ophthalmologists will look for signs of disease severity to establish the diagnosis of TED and indicate need for treatment. These include the degree of proptosis, impairment of visual acuity, and loss of colour vision (Dickinson, 2010). Normally the presence of optic neuropathy, severe proptosis, and/or primary-gaze diplopia is sufficient for the ophthalmologist to consider the disease to be severe (Marcocci et al., 2002).

Werner (1977) developed a classification tool to measure the severity of TED referred to as ‘NOSPECS’. This tool is widely used for the clinical assessment of changes in eye symptoms and signs of TED (Terwee, 2000). The tool classifies clinical signs and symptoms on a scale of 0 to 6; where 0 is **N**o physical signs or symptoms, 1 is **O**nly signs, 2 is **S**oft tissue involvement, 3 is **P**roptosis of 3 mm or more above the normal limit, 4 is **E**xtraocular muscle involvement, 5 is **C**orneal involvement, and 6 is **S**ight loss due to optic nerve involvement (Werner, 1977; Dickinson, 2010). For each class there are 4 grades which indicate the severity of the sign or symptom, where 0=0, a=1, b=2 and c=3. For example, under class 4 'extraocular muscle involvement', **0** indicates an absence of diplopia, **a** indicates intermittent (i.e. when tired), **b** indicates inconstant and **c** indicates constant. Patients can receive a maximum total score of 45 points (Terwee, 2000). It is estimated that 3 to 5% of patients have the severest forms of TED (Gerding et al., 1997). Being male and being over the age of 50 have been found to be associated with increased TED severity (Perros et al., 1993; Kendler, Lippa & Rootman, 1993), as has smoking (Vestergaard, 2002).

Levels of activity and severity of TED are used as indicators for treatment options. However, for patients who are misdiagnosed, or for those that experience a delay in their diagnosis, it can be months or in some cases years before they are referred for specialist treatment in the UK (Estcourt et al., 2009). Furthermore, it is likely that several treatments will be required over the course of TED, particularly if TED coincides with GD, and some treatments are ineffective. These issues will be discussed further in the following section of this chapter.

1.8 CLINICAL MANAGEMENT

1.8.1 Anti-thyroid treatment

Many patients with TED will have received prior monitoring and treatment for hyperthyroidism, which is most commonly treated with antithyroid drugs, partial or total removal of the thyroid gland (thyroidectomy) or radioiodine (iodine-131 therapy) (Yip, Lang & Lo, 2012). The first recommended action for patients with GD who smoke is to stop, so as to significantly reduce the risk of developing eye disease. Not only has the response to treatment for TED found to be lower in smokers, but it has also been found to be significantly slower (Eckstein et al., 2003).

Around 30% of newly referred patients with TED have moderate disease, and around 5% to 10% have severe disease (Bartalena, 2014). In the moderate to severe cases, a complex multidisciplinary disease management regime is usually required. For example, in cases where GD and TED overlap, it is necessary for patients to maintain simultaneous medical treatment for both aspects of the condition. However, there is little consensus over which treatment option works best and the optimum methods for measuring treatment efficacy, making it difficult to judge which is optimal (Prummel et al., 2003). However, it is considered essential that treatment follows a logical plan that aims to produce the best results for the patient (Yang & Perros, 2012). Generally ophthalmologists will diagnose TED as either moderate-to-severe – that is, patients without sight-threatening TED but with disease that interferes with daily life thereby justifying further treatment – or severe and sight-threatening (Prummel et al., 2003; Ezra & Rose, 2013). The types of treatment and the order in which they are offered will depend on this diagnosis (Al Mahrouqi, 2011).

TED will often not worsen once the patient has achieved a stable serum thyroxine level, known as the *euthyroid state* (Tallstedt et al., 2000). The majority of patients who subsequently develop TED will have mild ocular symptoms that will not necessarily require any further treatment, other than topical ocular lubricants to reduce dry eyes (Marcocci et al., 2002). For eyelid retraction and proptosis, patients are often recommended to use topical lubricants and, in severe cases, to tape their eyes shut at night to avoid corneal drying (Marcocci et al., 2002).

1.8.2 Steroids

A group of immunosuppressant steroids, known as *glucocorticoids* (GCs), are often effective at reducing thyroid-related inflammation in TED (Marcocci et al., 2002). The use of GCs during the active phase of TED has been found to prevent disease progression and reduce the total length of this phase (Terwee, 2000). Clinicians tend to initially treat patients with oral GCs (the most common being prednisolone) in high doses although the disease activity may increase once the dose has been reduced or withdrawn (Marcocci et al., 2002). There is some evidence that sight-threatening TED is most effectively treated with intravenous methylprednisolone, which is becoming more popular because of reduced side effects compared with oral medication (Kahaly et al., 2005; Aktaran et al., 2007).

1.8.3 Radiotherapy

Low-dose orbital radiotherapy might be administered alongside GCs, or as an alternative treatment if GCs are found to be ineffective (Marcocci et al., 2002). Orbital radiotherapy, which targets the soft tissues around the orbits directly, is found to be effective in over 60% of cases, particularly for optic neuropathy and inflammation (Marcocci et al., 2003). Radiotherapy has been used in the treatment for TED for over 60 years, although clinical trials have revealed conflicting results in terms of efficacy. A recent review suggests this treatment should be offered early, during the active phase, and is most effective when combined with GCs (Dolman & Rath, 2012).

1.8.4 Alternative drug therapies

In recent years, other drugs have begun to show some evidence of efficacy in reducing TED symptoms. Selenium, which is an anti-inflammatory agent and has the greatest concentration in the thyroid gland in healthy persons, has recently been found to be at reduced levels in patients with TED (Khong et al., 2014). Selenium is found at high concentration in brazil nuts and has been reported to increase immune functioning in patients with TED (Marcocci et al., 2011). It has been recommended as a supplement throughout the course of the condition, particularly in milder cases (Marcocci et al., 2011). Somatostatin analogues are growth hormone-inhibitors that can help to regulate the endocrine system; one type of somatostatin analogue commonly used to treat TED is octreotide (Dickinson et al., 2004) and is occasionally used for moderate disease. Rituximab is an antibody that depletes B-lymphocytes, a cell involved in active inflammation, and initial research has indicated its ability to improve TED by reducing inflammation and proptosis, (Minakaran & Ezra, 2013). Methotrexate – a drug more commonly used in the treatment of cancer or arthritis – has been evaluated for treatment of TED in patients who are intolerant to GCs (Strianese et al., 2014). Early findings have shown a reduction in CAS scores and improved ocular motility; however, further research is required before this medication can be introduced to regular treatment protocols (Strianese et al., 2014).

1.8.5 Surgery

Once TED has reached a stable phase, patients might be offered corrective surgery in order to preserve sight, improve appearance, or both. The ophthalmologist's decision to operate for TED, and when to do so, is influenced by a number of factors including disease activity, severity, and clinical preference. Most clinicians prefer to reduce the activity of TED using drugs or radiotherapy before considering surgery, although occasionally surgery might be required earlier in the course of the disease (Wiersinga & Kahaly, 2010).

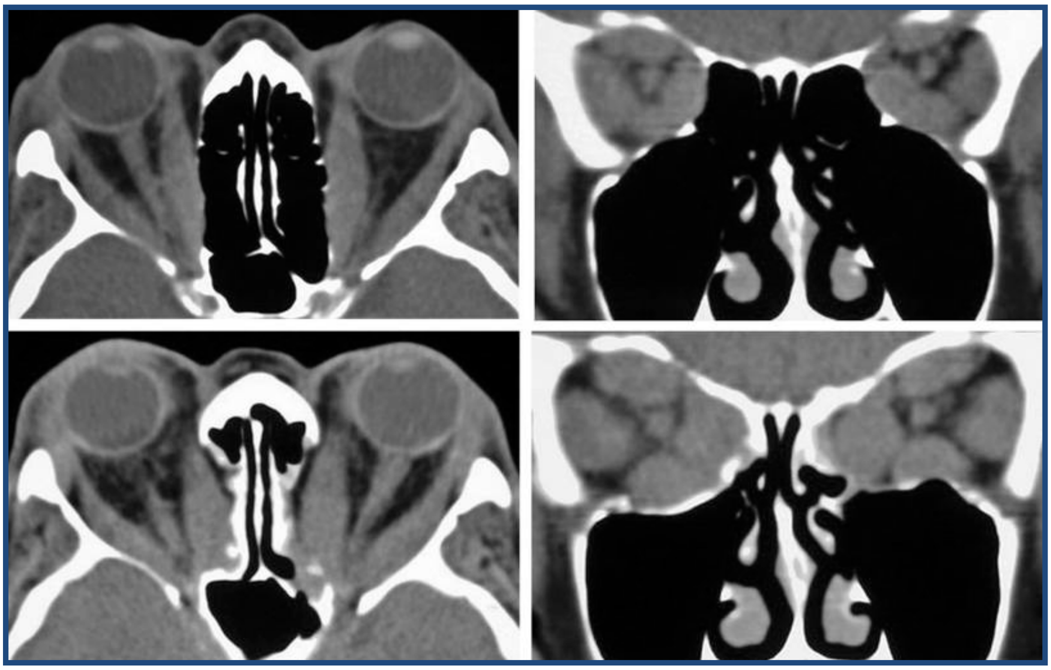
One or more of a number of surgical options are available, depending on the severity of TED. Orbital decompression involves removal of some of the bony walls of the eye sockets, to make space for the swollen muscles and retrobulbar tissues when the disease is inactive (Leong et al., 2009), for treatment of moderate or marked proptosis. It is also offered to patients with persistent optic nerve compression in order to save their sight (Boboridis & Bunce, 2011). Strabismus surgery, to correct ocular misalignment, is offered to patients with diplopia or to those with squint in the absence of double vision (Jellema et al., 2014). As the commonest residual sign of TED is upper eyelid retraction, many patients will undergo eyelid lengthening surgery that either lengthens the upper eyelid, lower eyelid, or both, to improve eye closure (Neoh & Eckstein, 2010). Some patients may require all three types of surgery and in these cases, the recommended sequence of performing the procedures is firstly orbital decompression, followed by strabismus surgery, and finally eyelid repositioning (Bartalena et al., 2008; Goldberg, 2008). Orbital decompression can affect motility as well as the level of lid retraction, with a number of studies reporting the worsening of diplopia after orbital decompression (Tallstedt et al., 2000; Baldeschi, 2010; EUGOGO et al., 2009), hence the recommendation to perform decompression before other types of corrective surgery.

1.9 ORBITAL DECOMPRESSION

Orbital decompression is a major procedure involving the removal of fat, bone, or a combination of both, from the orbits (EUGOGO et al., 2009), which in turn provides additional space to accommodate swollen orbital tissue (Figure 4). In most cases, orbital decompression is performed to improve the appearance of the eyes but, for a small number of patients with optic neuropathy, the procedure is used to restore sight

(Perros et al., 2012; EUGOGO et al., 2009). Decompression is occasionally performed to reduce pain with severe orbital inflammation (Tallstedt et al., 2000). Orbital decompression is the most common surgery offered to patients with severe TED (Perros et al., 2012).

Pre-decompression



Post-decompression

Figure 4. Computerised tomography (CT) scans showing the movement of orbital tissue from pre- to post-orbital decompression

Reduction in proptosis with bony orbital decompression is dependent on whether one, two, three or four walls are removed (Table 2). Lateral wall decompression (a one-wall approach), is one favoured option for patients with less severe proptosis, as it has been found to produce a lower risk of post-operative diplopia (Goldberg, 2008). In cases of severe proptosis, removal of bone from two or more walls is more appropriate, although four-wall decompression involving removal of the orbital roof is rarely performed (Verity & Rose, 2013).

Table 2. Types of orbital decompression and average recorded reduction in proptosis (adapted from Garrity, 1994)

Number of walls	Common approach to the orbit	Average proptosis reduction (mm)
1 wall	Lateral	3-5.7
	Medial	2.25
	Superior (roof)	9
2 wall	Transantral	3.4-5.5
	Translid (lateral + floor)	5
	Transfrontal	4
	Endoscopic (medial + floor)	1.5-4.4
3 wall	Endoscopic	3.2-7.7
4 wall		3-11.3

Specifically, two-wall decompression involves removal of either the medial wall and floor, or the medial and lateral walls and this results in around 3-6mm reduction in proptosis. Three-wall decompression involves removal of the medial wall, lateral wall and floor, this achieving around 3-8mm reduction in proptosis (Garrity, 1994). There are several evolving techniques that might be used during decompression surgery (Leong et al., 2009). The European Group for Graves' Orbitopathy (EUGOGO) found favourable results after surgery with a combination of bony wall and fat removal, and a larger reduction in proptosis after three-wall, as compared to two-wall, approaches (EUGOGO et al., 2009). However, removal of orbital fat has been found to result in some hollowing in the orbital structure in a small number of cases (Fichter, Krentz & Guthoff, 2013) and performing this type of decompression remains a matter of dispute (Boboridis & Bunce, 2011). Leong et al. (2009), in a recent systematic review of outcomes after decompression found that the transpalpebral-endoscopic approach resulted in the most significant reduction in proptosis.

Treatments for TED are not without their risks and side effects. For instance, weight gain and gastrointestinal problems are common among patients who are given systemic corticosteroids (Aktaran et al., 2007; Kahaly et al., 2005). Similarly, major surgery such as decompression can be associated with a number of side effects including induced diplopia, eyelid malposition, facial numbness, vision loss and, very rarely, cerebrospinal fluid leakage (Jernfors et al., 2007). EUGOGO et al. (2009) found that the three-wall approach had more complications than the two-wall (e.g. eyelid swelling), but that the coronal approach resulted in the most complications (e.g. paralysis of the frontal muscles lasting at least 3 months after surgery).

Further orbital decompression might be required in rare cases as, for example, where there has been disease recurrence, where the patient or clinician has a preference for sequential unilateral decompression, or where the results of the initial decompression are inadequate.

Given the uncertainty around the efficacy of many of the treatments for TED, and the cost of major procedures such as orbital decompression, it is important that those involved in the management of the disease inform the patient of the expected chances, and extent, of rehabilitation. It is also important that patients are aware of the risks and complications of proposed treatments.

1.10 SUMMARY

TED can cause a variety of unpleasant changes in the eyes that may require complex treatment from specialists within a multidisciplinary team. Multiple ophthalmic and systemic assessments need to be made by specialist clinicians, particularly endocrinologists and ophthalmologists, to gauge the phase and the severity of the disease, and to take urgent action where necessary. Patients are often required to adhere to a variety of medical treatments for variable periods, depending on disease duration and activity, before considering the option of one or more surgical interventions. For most patients, eye symptoms are mild and improve spontaneously, particularly when they become euthyroid and if they cease smoking. However, some patients develop severe TED, for whom treatments may be ineffective. As it can take many years before the disease stabilises and the sight and/or appearance is improved, it is important that patients should be aware of this from the time of diagnosis and to ensure their continued understanding throughout the course of the illness.

This chapter has introduced the appearance altering and functional symptoms of TED and the following chapter will describe and review what is currently known about the quality of life of patients with TED. A systematic review of the efficacy of different treatments, as described in this chapter, on patients’ well-being is presented in Chapter 3 of this thesis.

2. IMPACT OF TED ON QUALITY OF LIFE

2.1 PROLOGUE

As clinicians have sought to find out more about the causes of TED and further knowledge about how to effectively treat the disease and its symptoms, recent research has begun to examine how TED might impact on a patient’s psychological state and, ultimately, their quality of life. The aim of this chapter therefore is to describe the small body of research to date that has investigated the psychological impact of having TED. It does not include the impact of treatment, which will be reviewed in the next chapter. This chapter provides a description of the methods and measures that have been used by previous studies to examine the impact on both health-related quality of life (HRQL) and disease-specific quality of life.

2.2 CONCEPTUALISATION OF QUALITY OF LIFE

Quality of life is defined by the World Health Organisation (WHO) as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (The WHOQoL Group, 1995, p1405). Quality of life has been increasingly recognised by clinicians and researchers as an important measure in healthcare. Diseases often cause dysfunction and symptoms that can prevent an individual from carrying out activities of daily living (Kaplan & Ries, 2007), thus impacting on their overall quality of life.

Most healthcare researchers now conceptualise quality of life as having several distinct dimensions, including psychological, social, occupational, physical and cognitive (Ogden, 2004). Quality of life is therefore widely considered to be a multi-faceted concept that, when measured using valid and reliable tools, can quantify change in patients over the course of their illness and after treatment (Bradley, 2006) as well as provide some basis for cost-effectiveness evaluation (Kaplan & Ries, 2007). However, there remains disagreement amongst investigators over which aspects of quality of life should be evaluated in healthcare (Fayers & Machin, 2007). Quality of life, and more specifically HRQL, is now generally conceptualised as generic or disease specific. Generic HRQL refers to the study of aspects of quality of life that can be applied across patient groups, such as physical functioning, or emotional well-being. Disease-specific quality of life on the other hand refers to the aspects of quality of life unique to a particular condition.

2.3 MEASUREMENT OF QUALITY OF LIFE

Quality of life has become an increasingly popular construct to evaluate the impact of disease and its treatment. Generic HRQL instruments allow researchers to quantify the impact of a disease and compare this impact across different disease groups and healthy populations (Kaplan & Ries, 2007). Generic HRQL measures are useful to capture both physical and social aspects of illness beyond clinical changes as the result of medical care (Wilson & Cleary, 1995). By contrast, disease-specific quality of life measures do not allow for comparisons between different disease groups, but do tend to capture aspects of quality of life more specific to a particular disease population. HRQL encompasses the physical, psychological and social domains of health that are influenced by an individual's perceptions of health (Testa & Simonson, 1996) and a comprehensive measure should assess all of these domains. The following sections of the chapter will describe some of the HRQL measures that have been used to assess quality of life in patients with TED.

2.3.1 Generic health-related quality of life

A number of generic HRQL questionnaires have been used to assess quality of life in TED. The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36^{TM}) is one such measure that can be classified into the following eight health status subscales: physical functioning, role limitations due to physical problems, social functioning, bodily pain, emotional well-being, role limitations due to emotional problems, fatigue, and general health perception (Ware & Sherbourne, 1992). A physical component score (PCS) and a mental component score (MCS) are calculated and each is scored out of 100, with higher scores indicating better health (Ware, Koskinski & Keller, 1994). This measure has demonstrated high internal consistency and good reliability across patient groups (McHorney et al., 1994) including in TED as described later in this chapter.

The Sickness Impact Profile (SIP; Bergner et al., 1981) is another generic HRQL questionnaire consisting of 136 items that assess performance on a range of daily activities, for example; 'I am doing fewer social activities with groups of people'. It has been demonstrated to have high reliability, as well as good construct, convergent and discriminant validity (Bergner et al., 1981) and has been used to evaluate quality of life in TED as described in section 2.3.2 in this chapter.

The Euro Quality of Life questionnaire (EQ-5D; The EuroQoL Group, 1990) measures 5 domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. It also includes a Visual Analog Scale (VAS) rating of health that ranges between best imaginable health states and worst imaginable health states (Hurst et al., 1997). This measure has been validated within a variety of patient groups, including rheumatoid arthritis (Hurst et al., 1997), cardiac patients (Schweikert, Hahmann, & Leidl, 2006), and inflammatory bowel disease (König et al., 2002).

A constraint on all the generic global measures of HRQL is their lack of ability to capture the specific limitations that patients with TED might face. These include adjustment to the change in their appearance, and functional problems including double vision. While vision-specific questionnaires have been developed in recent years they, as with generic HRQL measures, tend not to include the issues specific to patients with TED, such as double vision. In response to the need for a questionnaire that captures such issues, TED-specific quality of life measures have begun to emerge, and will be described in the following section of this chapter.

2.3.2 Disease-specific quality of life

It is important to measure psychosocial outcomes in TED using comprehensive, validated questionnaires, to capture a broad range of issues relevant to the lives of patients with TED and to ensure that these constructs are being captured accurately. Generic HRQL measures, whilst useful for comparing quality of life outcomes for patients with TED to other chronic disease groups, are less helpful for detecting small clinically relevant changes in TED (Terwee et al., 1998). They are also often found not to include questions that are most important to the quality of life of patients with TED, such as changes in appearance, or double vision (Terwee et al., 1999).

A number of vision-specific quality of life questionnaires have recently emerged that were developed in the contexts of cataract and glaucoma. For example, the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) consists of 25 items that measure 12 health domains including general health, general vision, near vision, distance vision, and driving, and has been reported to be a reliable and valid measure (Mangione et al., 2001).

The Graves' Ophthalmopathy Quality of Life Questionnaire (GO-QOL) is the first tool to measure HRQL in patients with TED. It has two subscales that measure 1) visual functioning as a consequence of double vision and reduced visual acuity, and 2) psychosocial functioning as a result of changed appearance (Terwee et al, 1998). The questionnaire consists of 16 items in its original form and has been found to be highly reliable (Terwee et al., 1999). Construct validity has been demonstrated by correlations with the MOS-24 and SIP, and clinical measurements have been found to correlate well with the visual function subscale (Terwee et al., 1998; Terwee et al., 1999). The GO-QOL has been recommended for use in clinical trials as it is sensitive enough to detect a minimal clinically important difference (MCID); changes of 3 to 4 points can be interpreted as very small effects; 10 points as small to moderate effects and 20 points as a large effect (Terwee et al., 2001; EUGOGO et al., 2009).

Yeatts (2005) designed the Graves Ophthalmopathy Quality of Life Scale (GO-QLS), which measures quality of life related to perceptions of general health, mental health, social functioning, general visual functioning, and TED-specific visual functioning. Yeatts (2005) developed this 105-item measure by adapting items from the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12 $^{\text{TM}}$; Ware, Kosinski & Keller, 1996), Dermatology-Specific Quality of Life questionnaire (DSQL; Anderson & Rajagopalan, 1998), and the NEI-VFQ (Mangione et al., 2001).

Tehrani et al. (2004) developed a 90-item questionnaire based on 26 questions distributed to patients after surgery. Higher scores indicate lower overall contentment with surgical outcomes and quality of life. Validity was considered by the authors indirectly by the correlation between clinical post-surgical endpoints and quality of life scores, but no other reliability or validity testing has been reported in this or any other study. Furthermore, patients were not involved in the development of the measure so it is unclear if it captures aspects of post-surgical outcomes important to patients and their quality of life. As the questionnaire was not administered to patients prior to, as well as after, surgery it is unclear whether the questionnaire has captured clinically significant changes as a result of surgery.

One other questionnaire to assess quality of life in TED has recently been developed (TED-QOL; Fayers & Dolman, 2011) that consists of three items that ask “How is your eye disease currently affecting your overall quality of life/ your ability to carry out daily activities/ your satisfaction with your appearance?” The authors report this tool to be a valid and reliable measure of quality of life in TED (Fayers & Dolman, 2011). However, with only 3 items this questionnaire is designed to be used in busy hospital clinics as a “snap shot” rather than for developing our understanding of the areas of quality of life most impacted upon. This questionnaire also has yet to be used in any studies evaluating treatment for TED and therefore no MCID has been provided. Son et al. (2014) recently used this questionnaire to measure quality of life in Korean patients with TED and found there to be significant and substantial ceiling effects on all three items making it difficult to distinguish between the most affected patients. In follow-up interviews, two patients suggested a need for additional items (Son, Lee & Yoon, 2014).

It has been argued that the GO-QOL is not only the most valid and reliable measure of quality of life in TED but it has also been recommended to be used as a primary outcome measure in randomised controlled trials (Wiersinga, 2012). Furthermore, in a recent review of TED-specific HRQL tools the GO-QOL has been found to be the only tool that encompasses all the desired elements of a pre-to post-intervention quality of life assessment tool (Ridyard & Inkster, 2014). The GO-QOL is a short questionnaire enhancing its suitability for patients to complete in a short amount of time before and after their treatment, and its development involved asking patients which items they felt were most important to them (Terwee et al., 1999). Originally written in Dutch, the GO-QOL has been translated into a number of different languages including English, Korean (Choi et al., 2012) and German (Ponto et al., 2011). It has also been modified to suit the Australian population in a study by Park et al. (2004), who replaced an item about the effects of decreased visual function on cycling with two new items; one about effects on work, and another about effects on domestic duties.

2.4 QUALITY OF LIFE IN TED

It should be noted that the studies described in the following sections of this chapter have examined quality of life in patients with TED, rather than patients with Graves' disease (GD). There are mixed reports for quality of life in GD, with studies reporting diminished quality of life aspects when measured by the SF-36 TM (Abraham-Nordling et al., 2005; 2007) and using a GD-specific questionnaire (ThyPRO; Watt et al., 2014). However, Klaver et al. (2013) found no difference in the quality of life of people with thyroid dysfunction compared to people with normal thyroid levels. Importantly, further evidence suggests that quality of life improves after antithyroid drug treatment and thyroidectomy, i.e. when patients have become euthyroid (Ljunggren et al., 1998; Watt et al., 2014), with similar findings for mood (Kathol, Turner & Delahunt, 1986; Schreckenberger et al., 2006).

The SIP was used as an outcome measure in one of the first published studies to examine quality of life in TED. This study found that patients with TED scored lower in quality of life than patients with other chronic conditions including diabetes, emphysema and heart failure (Gerding et al., 1997).

Using the SF-36 TM, a number of authors have compared the quality of life scores of healthy control groups with scores from samples of patients with TED. They found that individuals with TED had poorer quality of life on all subscales of the SF-36 TM (Kahaly et al., 2002; Gerding et al., 1997; Lee et al., 2010). Egle et al. (1999) have reported that patients with TED with double vision are significantly more limited than patients without double vision on a number of SF-36 TM subscales. The SF-36 TM has been translated into several languages and the Korean version was used in a recent study that found patients with TED showed significantly lower SF-36 TM scores than an age- and sex-matched healthy control group (Lee et al., 2010).

Du et al. (2014) used the Chinese version of the NEI-VFQ-25 (CHI-VFQ-25; Du et al., 2014) to measure vision-related quality of life in 23 patients with optic neuropathy caused by TED and found that these patients were impaired in their daily roles and mental health. Bradley and colleagues (2006) distributed the NEI-VFQ-25 to 30 patients with TED and found that many scored at the ceiling level on most subscales, a finding reproduced by Du et al. (2014), arguing that the NEI VFQ-25 is potentially insensitive to detecting the severest ends of visual loss. Furthermore, in a qualitative study the authors found that more than two thirds of their sample discussed aspects of their TED that did not feature on the NEI VFQ-25. For example issues about their appearance were missing, suggesting it might not be a comprehensive measure for patients with TED (Bradley et al., 2006).

Using the GO-QLS, Yeatts (2005) found that patients with TED report greater impairment in physical and mental health, poorer self-image, more sleep, social and work impairment than healthy controls. However there appears to be no later study that has used this questionnaire, and validation data are not available. Furthermore, the length of this questionnaire makes it unsuitable for use in clinical settings (Wiersinga, 2012) and is likely to cause participant burden. This makes it difficult to conclude whether the GO-QLS is a suitable tool to measure disease-specific quality of life in TED.

Using the TED-QOL, Son et al. (2014) distinguished between the 3 items in this scale as conceptualising functional quality of life, appearance-related quality of life and “overall” quality of life and found that “overall” quality of life in patients with TED was poor. The authors found significant correlations between gender, soft tissue inflammation and proptosis and appearance-related quality of life, and correlations between age, inflammation and motility disorder and functional quality of life (Son, Lee & Yoon, 2014). However, this tool has not been rigorously evaluated for factorial structure so it is unclear if these 3 concepts are valid.

Since its development, a number of studies have used the GO-QOL to assess the impact of TED on patients’ lives. Such studies have highlighted the detrimental impact of TED on activities of daily living not only as a result of visual problems but also due to a change in appearance. Studies that have used the GO-QOL have found that TED causes limitations in daily functioning including reading, watching TV, driving, and moving both around the house and outdoors due to problems in visual function (Lin, Lee & Liao, 2014; Choi et al., 2012; Ponto et al., 2011; Park et al., 2004). Vision-related quality of life scores have been found to be poorer in moderate to severe, and sight-threatening TED (Ponto et al., 2011). The impact of a changed appearance due to TED has also been found to reduce quality of life, with GO-QOL appearance scores having been consistently found to be lower than visual function scores, suggesting that the impact of a change in appearance is even more substantial than the impact of visual problems (Lin, Lee & Liao, 2014; Choi et al., 2012; Park et al., 2004; Ponto et al., 2011).

2.5 SUMMARY

Patients with TED face a difficult journey in the management and treatment of their condition and must attend regular assessments from a multidisciplinary team of clinicians to ensure that they are given the appropriate treatment. Based on disease symptoms and severity alone, TED might not be classed as severe, but subjectively patients often report finding it difficult to adjust to the changes in visual function and appearance. Patients not only report limitations in their day-to-day activities because of visual problems, but also report poorer quality of life due to the change in the appearance of their eyes. A patient’s adjustment to their condition might be explained by intervening cognitive and psychosocial processes that will be individual to each patient. Once these are better understood and evaluated, it might be possible to improve psychosocial outcomes for patients with support interventions designed to target the appropriate cognitions, and prevent carrying out unnecessary medical treatments. There is still little research on the psychological impact of disfigurement to the eyes. TED-specific quality of life questionnaires such as the GO-QOL are likely to best capture the experiences specific to patients with TED and are recommended in research on the impact of the disease as well as its treatment. However, the majority of studies that have used the GO-QOL have only investigated the relationship with clinical factors; there appear to be no studies to date that have evaluated a range of intervening psychosocial factors that might account for some of the variability in quality of life.

This chapter has described research to date that has evaluated the impact of TED on quality of life and the following chapter will focus on the impact of treatment on quality of life outcomes.

3. THE IMPACT OF TREATMENT ON PSYCHOSOCIAL OUTCOMES IN TED: A SYSTEMATIC REVIEW OF THE LITERATURE

3.1 PROLOGUE

The first chapter of this thesis described the clinical features of TED and current treatment provisions offered to patients, which aim firstly to reduce symptoms and secondly to improve appearance and/or vision in patients with severe disease. Chapter 2 described how quality of life has been conceptualised and gave an overview of the literature to date that has reported the quality of life of patients with TED. These studies have found TED to have a detrimental impact on quality of life, due to both an altered appearance and double vision, with reductions found in self-confidence and daily activities (Terwee et al., 1998; Ponto et al., 2011; Choi et al., 2012; Kahaly et al., 2002; Gerding et al., 1997; Lee et al., 2010). Patients with TED have also been found to have poorer quality of life than other disease groups including diabetes, emphysema and heart failure (Gerding et al., 1997).

An important question is whether treatment for TED improves quality of life outcomes as well as clinical features. Treatment-induced changes in clinical outcomes, including proptosis, inflammation, swelling, and disease activity have been well documented in the literature (e.g. Marcocci et al., 2002; Marcocci et al., 2003; Rajendram et al. 2012; Boboridis & Bunce, 2011; Bartalena et al., 2008) but effects of treatment on quality of life have not yet received the same research interest. This issue is particularly important as there is some evidence to suggest that clinical characteristics do not correlate well with patients' reports of perceived visibility and the impact it has on daily living (Gerding et al., 1997; Terwee et al., 1998). This chapter therefore presents a systematic review that aimed to investigate the literature that has examined the impact of treatment for TED on quality of life outcomes.

3.2 BACKGROUND & RATIONALE FOR SYSTEMATIC REVIEW METHODOLOGY

Although clinical interest has traditionally focused on the improvement of clinical outcomes and physical complications of TED after treatment, far less research has explored the degree to which treatment improves a patient's feelings of well-being and their appearance concerns. There has been growing interest in the routine measurement of quality of life in patients with TED, with a number of TED-specific questionnaires now recommended for use in clinical settings (Fayers & Dolman, 2011; Terwee et al., 1999; Wiersinga, 2012; Yeatts, 2005) and to evaluate treatment efficacy. To date there has been no review that has systematically evaluated quality of life outcomes following the variety of treatments for TED.

Research studies vary greatly in their quality and methodological rigour but important healthcare decisions need to be made based on current evidence (Pai et al., 2004). This is best made available through systematic reviews, which synthesise the results from a number of sources in a systematic way and rigorously evaluate studies for quality. The findings from systematic reviews provide healthcare professionals with a clear picture of the evidence in relation to a particular treatment's efficacy and/or effectiveness at improving the outcomes concerned. A systematic review was therefore conducted on the research literature concerned with changes in psychosocial functioning after treatment for TED.

When this systematic review commenced, a number of narrative reviews were identified that had investigated quality of life in patients with TED. Watt et al. (2006) reviewed quality of life in patients with benign thyroid disorders including TED, and Estcourt and colleagues (2011) evaluated the impact of quality of care on quality of life in TED. There are also several reviews that have investigated quality of life in TED before and after immunosuppressant therapy, including intravenous GCs (Zang, Ponto, & Kahaly, 2011), a combination of GCs and orbital radiotherapy (Zoumalan et al., 2007) and various alternative types of immunotherapies (Douglas & Gupta, 2011), including one review that did not identify the specific type of immunosuppressant therapy (Wiersinga, Prummel & Terwee, 2004). A number of reviews have recently been published that have evaluated a variety of other treatments in terms of their impact on quality of life, but these are again narrative, not systematic reviews (Coulter et al. 2007; Fichter, Guthoff & Schittkowski, 2012; Eichorn et al., 2010; Gillespie, Smith, & Douglas, 2012; Marcocci, Altea, & Leo, 2012; Marcocci & Marin, 2012; Ponto & Kahaly, 2010; Terwee et al., 2003a; Wiersinga, 2012).

A number of systematic reviews have been conducted in order to establish the impact of radiotherapy (Bradley et al., 2008; Rajendram et al., 2012; Viani et al., 2012), orbital decompression (Boboridis & Bunce, 2011) and radioiodine therapy (RAI) compared to antithyroid drugs on the progression of eye disease for patients with GD (Acharya et al., 2008) on the quality of life of patients with TED. However, the study that reviewed orbital decompression found no evidence for quality of life improvement after surgery in the studies they reviewed (Boboridis & Bunce, 2011). Similarly, none of the few studies that examined the impact of radiotherapy on quality of life found any improvement (Bradley et al., 2008; Rajendram et al., 2012; Viani et al., 2012). In a study of radioiodine therapy patients with TED have not been distinguished from patients with GD on their quality of life (Acharya et al., 2008). However with the most recent study included in these reviews having been published in 2005, and with new treatments for TED continually emerging, an updated evaluation of the current evidence was deemed necessary for this thesis.

This is therefore the first systematic review to evaluate quality of life outcomes following a variety of treatments for TED. The present review only included studies that have evaluated such outcomes using validated and reliable measures as including such studies will increase the reliability of the evidence for treatment.

3.3 AIMS

The aim of the present review was to determine the quality of life outcomes of a range of medical treatments for TED including drug treatments, radiotherapy, and surgical interventions, and to report the findings using guidance from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist (PRISMA; Moher et al., 2009).

3.4 METHODS

3.4.1 Inclusion & exclusion criteria

Articles were restricted to those that had recruited adult patients with TED (>16 years), and had evaluated the impact of some form of clinical treatment for TED on quality of life. The tools used to measure quality of life needed to have been validated and the article published in a peer-reviewed journal and in English.

Studies were excluded from the review if they had been printed in a language other than English due to lack of resources to have such studies translated. Studies were also excluded if they did not include primary data (e.g. reviews of other studies) and if data from patients with TED could not be extracted, for example if a study included a sample of GD patients where data for patients with TED had not been analysed separately.

3.4.2 Literature search

A preliminary literature search was performed to aid the development of an effective search strategy. Suitable search terms were defined for the review based on the initial search and were discussed with and validated by a Consultant Ophthalmologist specialising in TED. The search strategy included terms related to quality of life outcomes in TED and medical terms (Appendix A). Relevant electronic databases were chosen for the literature search, which included Ovid MEDLINE, EMBASE, PubMed, PsycINFO, Web of Science, CINAHL, AMED, PsycARTICLES, and The Cochrane Library. SCOPUS was searched using the same search terms for any relevant unpublished grey literature including conference abstracts and PhD theses so that authors could be contacted in case any potentially relevant work had since been published.

The databases were first searched in September 2012. Once searches had been carried out, email alerts were implemented and prominent authors found within the search were contacted for any further unpublished work in the area, or to retrieve hard to find articles. Reviews identified by the searches were hand searched for relevant articles. The reference lists of all articles included in the current review were searched for any additional studies, as were those of existing similar reviews identified.

The current review was performed to inform the thesis, was submitted for publication in December 2013, and has since been published (Wickwar et al., 2014; Appendix B). As email alerts identified two further relevant papers for the review since this time, in August 2014 the search was conducted again using the original search terms in order to update the thesis. Whilst the search in 2012 was not limited by date, the 2014 update was restricted to identify papers published between

September 2012 and August 2014. The results of this updated search are reported in an addendum at the end of the current chapter (page 65).

A quantitative meta-analysis was not conducted as part of this review. Meta-analytic methods were considered inappropriate because of the heterogeneity among studies in terms of sample characteristics and because of the poor quality of the studies, which will be discussed further in section 3.5.2 of this chapter.

3.4.3 Study selection

Once searches had been conducted, clearly irrelevant titles were removed and if it was unclear from the title alone the abstracts were screened. All remaining articles were retrieved in full and screened for eligibility. A second reviewer crosschecked the relevance of the remaining articles and any disagreements were resolved in collaboration with a third reviewer until consensus was reached. The second and third reviewers had extensive experience in conducting and publishing systematic reviews.

3.4.4 Data extraction

A standardised data extraction form was developed for extraction of the relevant data from each of the final articles (Appendix C). This was piloted on five of the final articles and necessary amendments were made. Any amendments were applied to the first five articles to ensure consistent data were extracted. Once data had been extracted from all the articles and in order to validate the data extraction process, a second researcher performed data extraction on 20% of the final papers and the extractions were compared. Any disagreements were discussed between the two researchers until consensus was achieved.

3.4.5 Quality assessment

Bias is systematic error within a study’s results or inferences and can lead to underestimation or overestimation of the true effect of an intervention (Higgins & Altman, 2008). It can be caused by poor study design, misconduct in data collection and analysis, and poor quality reporting of methods and results (Centre for Reviews and Dissemination, 2009). There is a distinction between ‘risk of bias’ and ‘quality’, where a study may have been conducted to high standards yet still have a risk of bias, for example it might have been impossible to blind participants from the intervention. There may also be no risk of bias where a study lacks quality reporting such as a power calculation (Higgins & Altman, 2008). Assessments of the risk of bias are commonly referred to as *quality assessments*; it is important that alongside quality these assessments also consider potential sources of bias, such as attrition bias (Higgins & Altman, 2008) and therefore a reliable quality assessment tool should be used to assess each study in a systematic review.

A plethora of widely recognised tools exist and a number were considered for the present review. These included tools developed by the Critical Appraisal Skills Programme (CASP) for a variety of study designs, including CASP tools for RCTs and cohort studies (CASP, 2006), and the Mixed Methods Appraisal Tool (MMAT; Pluye, 2011). However for the purpose of the present systematic review a tool was required that incorporated all types of study design giving one overall quality score, where RCTs were considered the gold standard. Whilst the MMAT does provide an overall score it was designed for studies that use mixed methods designs, and the CASP tools give separate scores depending on study design. Therefore the quality index developed by Downs & Black (1998) was chosen as the most appropriate tool as it is highly regarded for use in systematic reviews (Wells & Littell, 2009), and it incorporates an evaluation of both quality and internal validity (control of bias an confounding). It consists of 27 items designed for use with both RCTs and observational studies and is composed of five subheadings: reporting, external validity, internal validity and power (Downs & Black, 1998). Nine of the items included the response options “yes” (1 point) or “no” (0 points), 16 items included the additional option “unable to determine” (0 points). One item included the response options “yes” (2 points) “partially” (1 point) or “no” (0 points). The final item asked “*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?*” and scores for this item ranged from 0 to 5 depending on power achieved. The software G*Power version 3.1.2 was used for this task where studies did not report a power calculation. The highest possible score for quality assessment was 32. The quality assessment was crosschecked by a second reviewer and a third reviewer was asked to review the process and final scores to reach agreement.

3.5 RESULTS

3.5.1 Description of the studies

The database searches identified 440 articles and 2 additional citations were retrieved from other sources; the email alerts received during the period of 4th June 2012 and 1st April 2013 identified one article and contact with key authors identified a further article. The search for grey literature in SCOPUS identified 88 unpublished references. Titles were searched for relevance and one conference abstract was identified as potentially relevant for the review. However, contact with the authors revealed that this article related only to pre-treatment impact of TED and did not include a post-treatment evaluation. A total of 259 titles and abstracts were screened. 71 citations were excluded at this stage (Figure 5). The full texts of 188 articles were retrieved and reviewed for inclusion. After review and consensus, a total of 13 articles remained with an additional 2 articles that were retrieved from the reference lists, resulting in 15 articles.

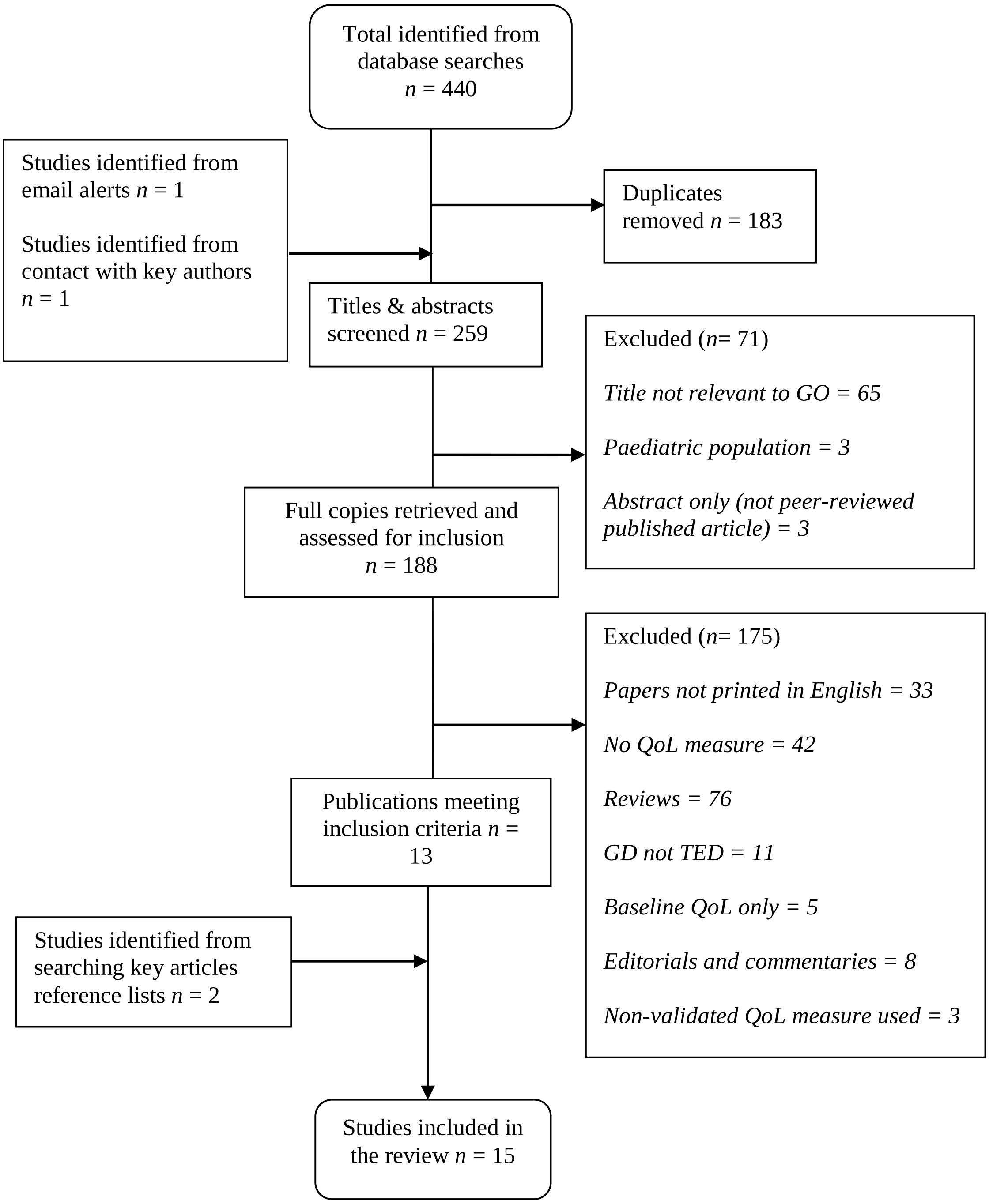


Figure 5. A flow chart showing each stage of the study selection process for the original search (in September 2012)

The characteristics of the included studies are shown in Table 3. The 15 articles included a total of 1433 patients with TED. Most participants were female (1,267; 88% of those reporting gender) although not all the studies reported genders (e.g. Kulig et al, 2009). Six of the studies were RCTs and 5 out of these 6 were double-blind randomised trials where the patients and treating clinicians were blind to the type of treatment (Bartalena et al, 2012; Dickinson et al, 2004; Marcocci et al, 2011; Prummel et al, 2004; Wémeau et al, 2005). One of the 6 trials was single-blind due to the nature of administering intravenous IV steroids (Kahaly et al., 2005). Three out of the final 15 studies compared pre-treatment quality of life in patients with TED to a healthy control group (Abraham-Nordling et al., 2010; Kulig et al., 2009; Terwee et al., 2002), 5 included a control group of patients with untreated TED (Dickinson et al., 2004; Marcocci et al., 2011; Prummel et al., 2004; Wémeau et al., 2005; Elberling et al., 2004) and the remaining studies had no group for comparison In addition, two studies compared patients with GD without eye symptoms to those with TED (Abraham-Nordling et al., 2010; Elberling et al., 2004).

Despite 6 RCTs being identified by the searches, a meta-analysis on this RCT sub-group was not possible due to the heterogeneity of studies, such that different quality of life measures were used, one study did not report quality of life data (Wémeau et al., 2005) and two studies were described as RCTs but did not include a control group (Bartalena et al., 2012; Kahaly et al., 2005).

Table 3. The main characteristics of the studies included in the systematic review

Authors	***Country***	***Design***	***Control group***	***Sample population***	***Sample size***	***Exclusion criteria***	***Treatment type(s) & administration***	***Follow-up periods***
Bartalena *et al.*, (2012)	The Netherlands, Belgium, France, Italy, Switzerland, and Greece	RCT	No	Moderate to severe, active TED	159	CAS <3, optic neuropathy, patients not recommended for GC therapy, pregnancy, no informed consent, increased liver enzymes by a factor of 2 or more above upper normal limits.	Three different doses of IV GC: 2.25g (low dose), 4.98g (middle dose), 7.47g (high dose)	6, 12 and 24 weeks
Dickinson *et al.*, (2004)	UK & Germany	RCT	Yes	Moderately severe, active TED	50	Patients with sight-threatening disease (NOSPECS 5b, 5c, or 6)	Octreotide-LAR (30 mg by injection at 4 week intervals); placebo (prepared in ampoules of same volume and appearance as octreotide-LAR).	16, 32, 44, and 56 weeks
Kahaly *et al.*, (2005)	Germany	RCT	No	Untreated, active, severe TED	70	Not reported	Oral GC (cumulative dose of 4.0g after 12 weeks); IV GC (cumulative dose of 4.5g).	12 and 24 weeks

Marcocci *et al.*, (2011)	Holland, Germany, Switzerland, Italy, Greece	RCT	Yes	Mild TED	152	NOSPECS class 2c1, exophthalmos >22 mm, diplopia and/or ocular torticollis, mono-ocular duction in any direction of < 20º, optic neuropathy, pregnancy, drug and/or alcohol abuse, severe concomitant illness, inability to comply with study protocol, no informed consent, current use of selenium- or PTX-containing preparations.	Selenium (100 µg orally twice daily for 6 months); PTX (600 mg orally twice daily for 6 months); placebo (tablets twice a day for 6 months that looked identical to selenium and PTX)	12, 24, and 48 weeks
Prummel *et al.*, (2004)	Holland	RCT	Yes	Mild and previously untreated TED	88	Severe periorbital swelling, proptosis > 25 mm, moderate or severe motility disturbances, or any sign of optic neuropathy), contraindications for radiotherapy (mostly diabetes), severe concomitant disease, no informed consent	Orbital radiotherapy (2 Gy daily over 2 weeks); sham irradiation (patients underwent the same procedures and the sound of the accelerator was simulated)	12, 24, and 48 weeks
Wémeau *et al.*, (2005)	France	RCT	Yes	Mild, active TED	51	Any other eye problem, gallstones, a history of treatment with systemic corticosteroids, immunosuppressive drugs, radiotherapy, or chemotherapy.	Octreotide-LAR (2ml treatments by IM injection); placebo (2 ml treatments by IM injection)	4 week intervals throughout the 16 week treatment period, and again 24 weeks after the beginning of treatment

Abraham-Nordling *et al.*, (2010)	Sweden	Prospective randomised trial	Healthy (did not receive treatment so only compared at one time point)	Graves' hyperthyroidism	313 GD patients. 41 patients had TED on entry into treatment groups. 76 patients developed TED during the study (diagnosed during post-treatment assessments).	Previous history of treatments with ATDs, I^{131}, thyroid surgery, severe TED requiring treatment with corticosteroids, incipient toxic crisis, large goiters, coronary heart disease, pregnancy, breast-feeding, pregnancy planned within following 2 years	Methimazole; radioiodine (one dose aiming for an absorbed dose of 120Gy)	12 and 24 weeks, 24 and 36 months (48 months if eye symptoms continued to develop/ deteriorate)
Aktaran *et al.*, (2007)	Turkey	Prospective, randomised, single-blind trial	No	Active, moderately severe TED	52	Corneal involvement (exposure keratitis, corneal ulceration, clouding or necrosis), patients not recommended for GC therapy, patients who had already been treated with GCs, surgery or radiotherapy.	IV GC (cumulative dose of 4.5g); high dose oral GC (cumulative dose of 4 g)	12 weeks
EUGOGO *et al.*, (2009)	11 European centres: Holland, Italy, Greece, UK, Germany, France, Switzerland	Prospective cohort	No	Inactive TED, patients seeking surgery	118	Not reported	OD (17 different approaches)	12 weeks
Terwee *et al.*, (2001)	Holland	Prospective cohort	No	TED	164; radiotherapy (n=23), OD for sight loss (n=10), OD for proptosis (n=38), EMS (n=31), EL (n=43), and blepharoplasty (n=19).	Not reported	Orbital radiotherapy; OD; EMS; EL; blepharoplasty (dose and administration of each not reported)	12 weeks after surgery, 24 weeks after radiotherapy

Terwee *et al.*, (2002)	Holland	Cross sectional	Healthy (did not receive treatment so only compared at one time point)	Patients with TED who had started radiotherapy treatment	163	Not reported	Orbital radiotherapy; oral GC (prednisone); a combination of both immunosuppressive treatments (dose and administration not reported)	Duration of follow-up was calculated as the time between the first visit to the clinic and the follow-up visit; average follow-up was 11.7 years
Kashkouli *et al.*, (2009)	Iran	Cross-sectional	No	TED	61	Absence of clinical and biochemical euthyroid state, presence of other chronic disorders such as diabetes mellitus, incomplete follow-up, and incomplete questionnaires (more than 10% missing data).	"Corticosteroids" (dose and administration not reported)	24 weeks
Kashkouli *et al.*, (2011b)	Iran	Cross-sectional	No	TED	67	Absence of clinical and biochemical euthyroid state, presence of other chronic disorders such as diabetes mellitus, and incomplete follow-up	"Steroids" (dose, type and administration not reported); OD (specific type not reported)	24 weeks
Elberling *et al.*, (2004)	Denmark	Before and after study	Yes	Newly diagnosed, and untreated patients with Graves' thyrotoxicosis	27 GD patients. 9 patients with toxic GD also had signs or symptoms of TED as classified by NOSPECS on entry into study	Unable to read Danish, prior thyroid disease or psychiatric disorders, neurologic disorders known to influence neuropsychiatric functions, and other co-morbidities	Methimazole (dose and administration not reported)	48 weeks

Kulig *et al.*, (2009)	Not stated - authors are in Poland & Denmark	Before and after study	Healthy (did not receive treatment so only compared at one time point)	Progressive infiltrative TED	29	Other autoimmunological disease, administration of oral steroids before hospital admission, treatment by means of orbital irradiation only or cyclical administration of methylprednisolone only, patients whose treatment was ceased because of complications, cessation of oral treatment with prednisone, patient’s refusal to be examined after completing the full therapy, relapsing form of TED	Combined IV GC and orbital radiotherapy (6 cycles of IV methylpred. sodium succinate)	6 weeks
Beleslin et al.. (2014)	*Not stated - authors are in Serbia*	*Before and after study*	*No*	*Active, moderate-to-severe TED*	*50*	*Contraindication to GCs*	*IV GC (500mg repeated after 48 hours). Oral GCs started on the 3rd day.*	*24 weeks*
Fichter, Krentz & Guthoff (2013)	*Germany*	*Before and after study*	*No*	*Moderate-to-severe TED*	*11*	*Prior orbital decompression surgery*	*Lateral wall decompression*	*12 and 24 weeks*
Jellema et al., (2014)	*Not stated - authors are in The Netherlands*	*Before and after study*	*No*	*Euthyroid TED*	*28*	*Patients with pre-existent strabismus, suppression and/or vision <0.2 in one or both eyes*	*Strabismus surgery for diplopia*	*Between 8 and 16 weeks*

A total of 14 treatments were evaluated (Table 3): methimazole, radioiodine (RAI), intravenous (IV) glucocorticoids (methylprednisolone), oral glucocorticoids (methylprednisolone, prednisone and an unspecified corticosteroid), orbital radiotherapy, a combination of radiotherapy and oral glucocorticoids, a combination of radiotherapy and IV glucocorticoids, octreotide-LAR, selenium, pentoxifylline (PTX), orbital decompression, eye muscle surgery (for strabismus), eyelid lengthening, and blepharoplasty. Three studies reported administering, in addition to the main drug evaluated in the trial, methimazole and other anti-thyroid drugs in order to stabilize thyroid function (Dickinson et al., 2004; Prummel et al., 2004; Wémeau et al., 2005). Unfortunately the efficacy of the main treatment in each of these studies might have been overestimated (or underestimated) if methimazole independently alters eye symptoms and quality of life outcomes. The additional papers from the August 2014 search did not identify any further treatments. Their characteristics have been included in Table 3 in italics.

Quality of life was a primary outcome measure in 7 out of 15 articles (Abraham-Nordling et al., 2010; Elberling et al., 2004; Kashkouli et al., 2009; Kashkouli et al., 2011b; Kulig et al., 2009; Terwee et al., 2001; Terwee et al., 2002) and secondary to clinical outcomes in the remaining 8 (Aktaran et al., 2007; Dickinson et al., 2004; EUGOGO et al., 2009; Kahaly et al., 2005; Marcocci et al., 2011; Prummel et al., 2004; Wémeau et al., 2005; Bartalena et al., 2012), The SF-36^{TM} was used as an outcome measure in 8 studies (Abraham-Nordling et al., 2010; Elberling et al., 2004; Kahaly et al., 2005; Kulig et al., 2009; Prummel et al., 2004; Terwee et al., 2001; Terwee et al., 2002; Wémeau et al., 2005). Prummel et al. (2004) and Terwee et al. (2001) used the Sickness Index Profile (SIP) and each study used only 3 of the subscales; social interaction, household management and leisure pastimes and recreation. Prummel et al. (2004) used the full version of the EQ-5D and Terwee et al. (2001; 2002) used the visual analogue scale. Aktaran et al. (2007) and Kashkouli et al. (2009) used the Australian version of the GO-QOL; Kashkouli et al. (2009) removed one item about education and counselling. Kashkouli et al. (2011b) modified the original version into Farsi. The remaining 8 studies used the original version of the GO-QOL (Bartalena et al., 2012; Dickinson et al., 2004; EUGOGO et al., 2009; Marcocci et al., 2011; Prummel et al., 2004; Terwee et al., 2001; Terwee et al., 2002; Wémeau et al., 2005).

3.5.2 Quality assessment

The results of the quality assessment (Downs & Black, 1998) indicated that study quality varied considerably (mean = 20/32; range 14/32 to 31/32), with higher scores indicating superior quality (Appendix D). The most common issues relating to quality were omission of details about recruitment (such as exclusion criteria, sources of recruitment, or participant characteristics), the use of incorrect statistical analysis or lack of such analysis, the lack of either the reporting of statistical power, or inadequate recruitment to reach statistical power and the descriptions of treatment and its administration were often inadequate.

In particular, some articles did not clearly describe patient characteristics (e.g. smoking status), making it difficult to assess whether those that took part were representative of the population they were recruited from. Details that were commonly omitted included how many patients were approached to take part and why those that declined chose not to take part. For example, “The total number of patients that met the inclusion criteria is not known, but the reported cases were 482” (Abraham-Nordling et al., 2010, p.652). Dickinson et al. (2004) did not report how many patients were recruited from each study site, or any details about the recruitment period. It is therefore unclear whether patients in different intervention groups were recruited from the same centre or not; if patients in one treatment group were recruited from different populations this may have biased the results for that particular treatment.

Some studies lacked statistical comparison between treatments making it unclear what impact these treatments had on quality of life. For example no statistical analysis was conducted in Terwee et al. (2002), while Wémeau et al. (2005) did not report which statistical analysis was used to compare quality of life outcomes just that no difference was found between octreotide-LAR and placebo. Terwee et al. (2002) did not describe how they adjusted for different lengths of treatment follow up over 11 years, or indeed whether this was done at all. EUGOGO et al. (2009) also failed to report any statistical findings for the difference in GO-QOL subscale scores from pre- to post-decompression although they report conducting statistical analyses. These authors have also only presented the seven most frequently used procedures; it is unclear what the results were for the other ten types of orbital decompression. The scale of random variability in the data of the majority of the studies is not clear, as SDs were frequently not reported by studies (Abraham-Nordling et al., 2010; Aktaran et al., 2007; Dickinson et al., 2004; Kahaly et al., 2005; Kashkouli et al., 2009; Kashkouli et al.; 2011b).

3.5.3 Methimazole

Abraham-Nordling et al. (2010) found no significant difference, at any point between baseline and 4 years after treatment, in the physical or mental health-related quality of life subscale scores between patients who received RAI and those that received methimazole, a standard anti-thyroid drug given to all patients with GD. Both groups did, however, experience a significant improvement in quality of life after treatment and at 3 to 48 months after treatment the quality of life scores for physical health were equal to those of a Swedish general population reference group. Notably however, it was not until the 12-month follow-up that mental health subscale scores were found to reach the same average for the reference population. This study also compared patients with GD with and without TED, and found that patients with TED 2 years after methimazole treatment had significantly worse physical health-related quality of life as compared to patients without eye disease. At one year follow up, the authors found “no clear correlation” (p.655) between objective eye scores and physical health or mental health subscale scores, however correlation coefficients were not provided. Elberling et al. (2004) found that, after a year of methimazole treatment, patients with GD (both those with and those without TED) had significantly lower mental and physical quality of life as compared to a healthy control group from the general population; these authors did not examine the differences between patients with GD with and without TED.

3.5.4 Orbital radiotherapy

Using the GO-QOL, Prummel et al. (2004) reported that a year after orbital radiotherapy patietns had similar quality of life scores to those receiving placebo radiotherapy, although the comparison was only descriptive. Terwee et al. (2001) did not find a significant improvement in the visual functioning subscale of GO-QOL at 6 months after radiotherapy ($p=0.05$). Compared to orbital decompression, eye muscle surgery, eyelid lengthening or blepharoplasty, orbital radiotherapy led to the least improvement in appearance-related quality of life (Terwee et al., 2001). In a cross-sectional study looking at long-term quality of life outcomes (up to 11 years) Terwee et al. (2002) compared SF-36^{TM} scores for patients who had received radiotherapy, steroids (or both treatments) with the scores for patients who completed the SF-36^{TM} before the start of radiotherapy or orbital surgery. They found that the treated group experienced significantly better quality of life than those newly diagnosed, except on the physical functioning and general health perceptions subscales. The treated group also reported significantly better quality of life on the GO-QOL appearance and visual function subscales. Notably these findings are for "GO patients after treatment" and are not reported by treatment type. The radiotherapy group experienced worse functional quality of life than the steroid treated group, but scored better on the GO-QOL appearance subscale. It is important to note, however, that no analysis of statistical significance was reported for this finding.

3.5.5 Systemic corticosteroids

Using the SF-36™, Kahaly et al. (2005) reported a significant improvement in physical and mental health-related quality of life after IV methylprednisolone, but no significant changes after oral methylprednisolone. Bartalena et al. (2012) found that after 12 weeks of medium or high-dose IV methylprednisolone, there was a significant improvement in the GO-QOL visual function subscale, and a significant improvement in appearance-related quality of life for those on low dose therapy. Likewise, Aktaran et al. (2007) found that, after 3 months, 85% of the IV steroid group experienced significant improvements in vision-related quality of life and 81% had an improvement in the appearance subscale. In a group receiving oral steroids, 76% showed improvement in visual function subscale scores and 78% showed improvement in appearance subscale scores. IV treatment led to significantly more improvements in quality of life scores than oral therapy (Aktaran et al., 2007).

Of the participants in the study by Terwee et al. (2002), 32% received prednisone, although it is unclear if this was oral or IV treatment. As compared to those receiving radiotherapy, participants who received prednisone had a better overall quality of life, with the exception of the appearance subscale of GO-QOL and the SF-36™ vitality score. Kashkouli et al. (2009; 2011b) studied the effects of corticosteroids on quality of life, but the method of administration is unclear in both studies. In 2009 the authors reported the change in mean scores from baseline to 6 months after treatment and suggest significant improvement in both GO-QOL subscale scores. In the later study, both GO-QOL visual function and appearance subscales significantly improved after steroids, this contrasting with orbital decompression whereby only the appearance subscale scores improved. In both the steroid and the decompression groups, over two-thirds achieved the minimum clinically important difference in quality of life, with no significant difference between the two groups. In both studies Kashkouli et al. failed to show any significant relationship between quality of life scores (before and after treatment) and clinical variables (including duration of disease, severity, or activity) (Kashkouli et al., 2009; Kashkouli et al., 2011b).

Kulig et al. (2009) reported that patients with TED had significantly reduced quality of life, assessed by the SF-36™, as compared with a healthy group of volunteers from the general population. They found that radiotherapy, combined with IV methylprednisolone, improved quality of life in relation to physical functioning, bodily pain and vitality; it is unclear if these changes were statistically significant however. The authors also found no correlation between quality of life and demographic or clinical variables. The authors have not reported the correlation coefficients found, however.

3.5.6 Long-acting octreotide (octreotide-LAR)

Dickinson et al. (2004) reported a significant improvement in visual-related quality of life from pre-treatment to 16 weeks after administration of octreotide and a significant improvement in appearance-related quality of life at 32 and 54 week follow-up, however significance levels were not reported. Wémeau et al. (2005) used both the SF-36™ and GO-QOL but merely report no significant changes in either quality of life score after treatment. Exact data was not presented.

3.5.7 Pentoxifylline and selenium

Marcocci et al. (2011) found no significant difference between the placebo and pentoxifylline on any of the GO-QOL subscales at 6 and 12 months after treatment. A significantly greater proportion of patients in the selenium group did exhibit an improvement in quality of life at 6 months, compared with those receiving a placebo (Marcocci et al., 2011). An improvement of 6 or more points on the appearance subscale was reported in 84% of those taking selenium, 72% on the visual function subscale and 81% in overall scores. Selenium led to a significant reduction in deterioration of quality of life (as compared with those given placebo). Selenium had a beneficial effect on quality of life that continued up to 6 months after treatment finished, both over time and when compared to the placebo group. However, the authors appear not to have analysed the differences in quality of life improvements between the pentoxifylline and selenium groups (Marcocci et al., 2011).

3.5.8 Surgery

EUGOGO et al. (2009) investigated the impact of 18 different approaches to orbital decompression on quality of life using the GO-QOL. They reported improvements in the appearance subscale scores of between 17.4 and 39.9 points in all treatments, except for the translid and endoscopic approaches to decompression, in which the change was no more than 1.8 points. Although no significance testing was performed, improvements appear to be substantial for a number of approaches, with many changes in scores reaching a minimal clinically important difference (MCID) for the GO-QOL (Table 4). Although the coronal approach led to the biggest improvement in appearance related quality of life, this approach caused the most frequent and serious complications.

Terwee et al. (2001) reported a significant improvement in the GO-QOL visual function subscale where orbital decompression was performed for sight loss and an improvement in the appearance subscale when decompression was performed for disfiguring proptosis. The authors have highlighted that improvement on the GO-QOL can be seen in either the visual function subscale, or appearance subscale, or both, depending on the type of treatment (2001). For example the effect size for decompression for sight loss in the GO-QOL visual function subscale is 0.9 and the effect size for decompression for appearance in the GO-QOL appearance subscale is 0.45; for the SF-36™ physical and mental health subscales these are 0.15 and 0.13, respectively. Eyelid lengthening resulted in a lower mean change in appearance-related quality of life compared to the other treatments, although this was not significant. Blepharoplasty (which included 8 patients who had eyelid lengthening at the same surgery) led to significant improvements in the appearance subscale, these improvements being comparable to those after orbital decompression (Terwee et al., 2001).

Table 4. Scores representing the mean change and standard deviations from pre-treatment to post-treatment follow-up for each quality of life outcome measure

Treatment	Author	N	Length of follow up	GO-QOL Visual Function†	GO-QOL Appearance†	SF-36^{TM} Mental Component Score†	SF-36^{TM} Physical Component Score†	EuroQol†
Methimazole	Abraham-Nordling et al. (2010) *N.B Authors did not test for statistical significance*	145	48 months	-	-	21*♦	16*♦	-
	Elberling et al. (2004)	30	12 months	-	-	8.1*♦ **	8.6* ♦**	-
RAI	Abraham-Nordling et al. (2010)	163	48 months	-	-	17*♦	14*♦	-
Radiotherapy	Terwee et al. (2001)	23	6 months	8.1 (18.6)**	2 (17.9)	-	-	-
	Prummel et al. (2004)	26	12 months	8.2 (15.8)	6.7 (17.2)	-	-	1.2 (14.5)
	Terwee et al. (2002) *N.B authors combined treatment scores*	21	Various	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*

IV Methylpred.	Bartalena et al. (2012) *N.B HD group showed the biggest change in mean scores*	52	3 months	12.8 (7.2; 18.3) ** ♦	9 (4.5; 13.5) ** ♦	-	-	-
	Kahaly et al. (2005)	35	3 months	-	-	0.5‡ **	0.4‡ **	-
	Aktaran et al. (2007)	25	3 months	*Not Reported*	*Not Reported*	-	-	-
Oral Methylpred.	Aktaran et al. (2007)	27	3 months	*Not Reported*	*Not Reported*	-	-	-
	Terwee et al. (2002) *N.B authors combined treatment scores*	52	Various	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*
	Kahaly et al. (2005)	35	6 months	-	-	0.3 **	0.1	-
Other GCs	Kashkouli et al. (2009) *N.B authors combined treatment scores*	61	6 months	*Not Reported*	*Not Reported*	-	-	-
	Kashkouli et al. (2011b)	61	6 months	20.1 **♦	24.4 **♦	-	-	-
	Beleslin et al. (2014)	***50***	***Not reported***	***Not reported****	***Not reported***	-	-	-

Radiotherapy & GCs combined	Terwee et al. (2002) *N.B authors combined treatment scores*	90	Various	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*
	Kulig et al. (2009) *N.B authors combined treatment scores*	29	6 weeks	-	-	*Not Reported*	*Not Reported*	-
Octreotide-LAR	Dickinson et al. (2004)	23	14 months	*Not Reported*	*Not Reported*	-	-	-
	Wémeau et al. (2005)	26	6 months	*Not Reported*	*Not Reported*	*Not Reported*	*Not Reported*	-
PTX	Marcocci et al. (2011) *N.B Authors did not test for statistical significance*	48	12 months	-0.64	-0.9	-	-	-
Selenium	Marcocci et al. (2011) *N.B Authors did not test for statistical significance*	54	12 months	11 (15.3)♦	12.6 (11.8)♦	-	-	-
OD (sight loss)	Terwee et al. (2001)	10	3 months	20.3 (19.5) **♦	4 (9.3)	-	-	-

	Kashkouli et al. (2011b)	6	6 months	34.6♦	36 **♦	-	-	-
OD (exophthalmos)	Terwee et al. (2001)	38	3 months	3.2 (23.9)	11 (15.5) **♦	-	-	-
	EUGOGO et al. (2009) *Swinging eyelid transcar (3 wall)*	26	3 months	17.5 (20.8)♦	17.4 (24.5)♦	-	-	-
	Coronal (3 wall)	14	3 months	-1.7 (35.9)	39.9 (27)♦	-	-	-
	Translid endo (3 wall)	14	3 months	-0.8 (9.5)	1.8 (9.5)	-	-	-
	Swinging eyelid transcar (2 wall)	25	3 months	8.5 (20.9)	19.9 (22.9)♦	-	-	-
	Transcon transcar (2 wall)	18	3 months	7.9 (21.8)	9.7 (18.9)	-	-	-
	Endo (2 wall)	10	3 months	2.3 (30)	34.5 (30.4)♦	-	-	-
	Translid (2 wall)	11	3 months	13.6 (18.7)♦	22.1 (25.3)♦	-	-	-

OD (both)	***Fichter et al. (2013)***	***11***	***6 months***	***34.9**♦***	***24**♦***	-	-	-
EMS	Terwee et al. (2001)	31	3 months	2.8 (25.4)	2.6 (22.2)	-	-	-
	Jellema et al. (2014)	***28***	***2-4 months***	***20**♦***	***9**♦***	-	-	-
EL	Terwee et al. (2001)	43	3 months	3.7 (15)♦	4.2 (13.9) **♦	-	-	-
Bleph.	Terwee et al. (2001)	19	3 months	0.2 (19.7)	10.2 (17.5) **♦	-	-	-

** Findings were statistically significant

♦ Minimal clinically important difference (MCID) achieved

*Scores include GD and TED patients combined,

‡ Authors reported change in age- and gender-adjusted z scores for the SF-36

† Scale runs from 0 to 100 (higher scores indicate better QoL outcomes)

3.5.9 The relationship between clinical & psychosocial factors

A number of the studies investigated the relationship between clinical and psychosocial outcomes and all report finding no statistically significant relationship. Abraham-Nordling et al. (2010) found that at 1 year post-treatment follow-up, there was no significant relationship between SF-36 scores and scores on clinical measures, although correlation coefficients were not provided. Kashkouli et al. (2009) conducted a linear regression analysis and Spearman’s correlation test finding no significant correlation between the duration of thyroid dysfunction, or the duration, severity, or activity of TED and quality of life scores both before and after treatment. However, correlation coefficients were not been provided. Kashkouli et al. (2011b) reported that they found no statistically significant effect of disease duration on TED severity and activity on quality of life scores before or after treatment.

Kulig et al. (2009) reported finding no correlation between disease activity as measured by the CAS and quality of life; however correlation coefficients were not reported in this paper. Terwee et al. (2001) found low correlation coefficients between changes in GO-QOL subscale scores and changes in clinical characteristics. For the GO-QOL visual function subscale these include $r = 0.27$ for visual acuity and $r = 0.27$ for diplopia and for the GO-QOL psychosocial function subscale these were $r = 0.04$ for lid aperture, $r = 0.25$ for proptosis and $r = 0.28$ for soft tissue involvement. Where a correlation coefficient of 0.1 is considered small, 0.3 is considered moderate and 0.5 large (Cohen, 1992); these findings suggest that only small to moderate relationships exist. Terwee et al. (2002) report that 45% of patients with diplopia scored on average 6 points lower on the GO-QOL visual function subscale and 7 points lower on the psychosocial function subscale compared to patients with no diplopia. However the authors did not use correlational statistical tests to examine the relationship between clinical and psychosocial factors making it unclear what conclusion can be drawn from these findings.

3.6 ADDENDUM

In order to ensure that the systematic review was up to date at the time of the submission of the thesis the original search used was repeated and identified a further 95 papers. Screening of titles identified 37 clearly irrelevant papers. Screening of abstracts identified 1 commentary, 15 reviews, 2 articles published in a foreign language and one conference abstract. Of the remaining 39 articles, 16 investigated aspects of GD that did not include patients with TED, 16 investigated TED but did not include quality of life measures, 3 measured quality of life in TED but not after treatment and 1 measured patient satisfaction after treatment that did not include a validated quality of life measure. The final 3 articles met the original inclusion criteria for the systematic review (Fichter, Krentz & Guthoff, 2013; Jellema et al., 2014; Beleslin et al., 2014) and were included in this updated version of the systematic review to assess whether any conclusion should be revised.

Quality of life was a primary outcome measure in one of the additional studies (Jellema et al., 2014) and a secondary outcome measure in the other two additional studies (Fichter et al., 2013; Beleslin et al., 2014). All three studies used the original Dutch version of the GO-QOL. Using the Downs & Black (1998) quality assessment tool, the results of the quality assessment indicated that none of the studies fell outside of the range found in the 2012 review (see page 54). Fichter et al. (2013) received a score of 16 out of 32 in the quality assessment and the other two studies (Beleslin et al., 2014; Jellema et al., 2014) received a score of 18 out of 32.

The results of the three additional studies in terms of mean change scores from pre- to post-treatment can be seen in Table 4, with these studies highlighted in italics. Beleslin et al. (2014) measured differences in GO-QOL scores pre to post-administration of systematic GCs and reported a statistically significant improvement in GO-QOL visual function scores; but the improvement in GO-QOL appearance scores was not found to be statistically significant. However, as this study involved administering IV methylprednisolone followed by a tapering of doses of oral prednisone (Beleslin et al., 2014), it is unclear which of these two treatments was being evaluated in terms of quality of life. Furthermore, it was reported that follow up measurements were taken at monthly intervals, but the authors have failed to report the follow-up time point at which GO-QOL scores were compared to baseline scores.

Fichter et al. (2013) examined the impact of lateral wall decompression on 11 patients and found significant improvements in both visual-function and appearance subscales at 3 month follow-up, with a further statistically significant improvement in the visual-function subscale 6 months after surgery.

Jellema et al. (2014) measured quality of life before and after strabismus surgery for TED and found statistically significant improvements in both vision-related and appearance-related quality of life after strabismus surgery. The largest improvement was seen in vision-related quality of life, which was the only subscale to reach a MCID (Table 4). A moderate significant correlation was found between the visual-function score and field of binocular single vision (BSV) after surgery ($r = 0.417$, $p = 0.034$).

These most up-to-date three studies therefore did not substantially alter the conclusions of the published systematic review.

3.7 DISCUSSION

This is the first systematic review to evaluate the impact of treatment including drugs, radiotherapy and surgery on quality of life in patients with TED.

In summary, radiotherapy was found to improve vision-related quality of life but had the least improvement in appearance-related quality of life compared to surgery, which had the best appearance-related quality of life outcome. IV methylprednisolone led to better quality of life outcomes than oral methylprednisolone and, even at low doses the former improved appearance-related quality of life. These studies also reported fewer adverse effects for IV corticosteroids as compared to oral, thereby making IV steroids a more favourable treatment both clinically and psychologically.

Long-term benefits in quality of life were found for octreotide-LAR, methimazole and selenium at up to 4 years after treatment. Eyelid lengthening and blepharoplasty were both found to improve appearance-related quality of life, although these findings need to be considered in light of the poor quality in reporting of these studies. Orbital decompression was found to have a larger effect on vision-related quality of life when it was performed for failing vision and a larger effect on appearance-related quality of life when surgery was performed for aesthetic improvement.

The reporting of participant characteristics varied greatly between studies and this potentially introduced bias, with many studies failing to report disease severity (Elberling et al., 2004) or previous treatments (Elberling et al., 2004; Kashkouli et al., 2009). The severity of TED and prior treatment are important clinical factors that might contribute to a patient's psychosocial adjustment and their subsequent quality of life. The reporting of smoking status also varied, with only 6 of 15 studies reporting this data. Smoking is an important factor in the onset and severity of TED and the response of TED to treatment. Therefore smoking status might affect both the clinical and psychological quality of life outcomes. A recent systematic review provides some evidence for this contention (Thornton et al., 2007).

Although this is not always possible in health research, the inclusion of a "no treatment" control group varied between RCTs, with a third of the RCTs included in this review being conducted without a control group. Where particularly important confounding variables have not been accounted for – such as whether patients smoked, or if they were taking treatments additional to that under investigation – this could potentially affect the results of these studies. Limitations of some of these studies make it impossible to give definite recommendations about the most effective treatments for improving quality of life. Furthermore not all of the studies reviewed included the TED-specific GO-QOL as a measure of quality of life in the population of interest. Generic HRQL measures, such as the SF-36™, include items that are considered too broad to capture the specific experiences of patients with TED, unlike the GO-QOL, which is able to detect clinically important changes in scores from baseline to post-treatment follow-up (Terwee et al., 2001). Despite the GO-QOL being recommended as an independent primary outcome measure in TED clinical trials (Terwee et al., 2001; Wiersinga, 2012), not all of the reviewed studies included this measure.

It is worth noting the limited number of studies that have examined quality of life after treatment, particularly in relation to orbital decompression. Given how costly and physically invasive such procedures are, this is somewhat surprising.

This review has also shown that the relationship between clinical and psychosocial outcomes remains unclear in TED. For instance, Kulig et al. (2009) and Kashkouli et al. (2011b) failed to find a relationship between demographic or clinical factors and quality of life either before or after treatment, but Terwee et al. (2001) found small to moderate relationships. There are a number of early studies that suggest that a relationship does exist, for example Yeatts (2005) found a correlation between quality of life and the objective severity of TED characteristics such as diplopia and dry eye symptoms. However, the tool used to measure quality of life in this population – the Graves Ophthalmopathy Quality of Life Scale (GO-QLS) – had been developed by choosing the items that correlated highly with clinical severity so this finding would be expected (Yeatts, 2005). Park et al. (2004) found that poorer quality of life was associated with more severe disease; however the authors conclude that their research might have been overrepresented by severe cases. Interestingly, Moss (2005) has described a possible ‘U’ shaped curve where at the extreme ends of severity, i.e. in the least and most severe cases, objective and subjective ratings would be likely to correlate. Choi et al. (2012) provide some evidence for this relationship having found that GO-QOL visual function and appearance scores were significantly negatively correlated with clinical characteristics including soft tissue involvement, proptosis, severity score (NOSPECS) and activity (CAS). Although a number of studies included in this review searched for relationships between clinical and psychosocial outcomes, no such relationship was found either before or after treatment. This supports Terwee et al.’s (2003) study that investigated the discrepancy between clinicians’, laypersons’ and patients’ ratings of the severity of their TED and found that patients tended to overrate, and endocrinologists underrate, TED severity. Between-group agreement was found to be highest between ophthalmologists and laypersons; interestingly, not between clinicians and the patients themselves (Terwee et al., 2003b). It might be that psychological processes rather than objective clinical measurements can better explain quality of life variability in patients with visibly disfiguring conditions (Thompson, 2012), with some previous research supporting this notion in TED

(Gerding et al., 1997; Terwee et al., 1998). However, there remain few studies that have investigated this relationship specifically in TED and, with mixed findings to date, further research is needed.

The exclusion of 33 foreign language articles could be a limitation of this review as one of these studies measured quality of life pre- and post-orbital radiotherapy using the GO-QOL (Nasr et al., 2010) and may have been eligible to include in the present findings if there was capacity to consider studies using languages other than English.

3.8 CONCLUSIONS

The present review has brought together the results of a range of treatments for TED on quality of life. Whilst major treatments such as surgery do appear to improve quality of life, other non-invasive treatments, such as IV steroids, may have a similar impact and lead to long-term benefits. There remain only 3 studies that have investigated how major surgery impacts on the quality of life of patients over the longer term, i.e. after 3 months. It is striking to note how few participants were included in these studies.

This is the first systematic review to evaluate the impact of treatment including drugs, orbital radiotherapy and surgery on quality of life for patients with TED. The findings of the present review are based on a systematic search for existing literature and predefined inclusion and exclusion criteria. The studies included in the review have been assessed for quality and a narrative synthesis of the effects of a variety of treatments for TED on quality of life outcomes has been provided. The studies that have been included have assessed both clinical outcomes (e.g. proptosis, disease activity and diplopia) as well as psychosocial outcomes. However, details of the clinical changes have not been reported, as the focus of the present review was to assess the impact of treatment on psychosocial measures after a variety of treatments and not to report clinical changes. What the review has found however is that recent findings for the relationship between demographic and clinical characteristics, and quality of life, have been mixed and remain inconclusive.

4. ADJUSTMENT TO LIVING WITH A DISFIGURING CONDITION: THEORETICAL FOUNDATIONS

4.1 PROLOGUE

One in 111 people are living with a facial disfigurement in the UK today (Changing Faces, 2013). Frances MacGregor was one of the first researchers to investigate psychological adjustment associated with living with a facial disfigurement using mainly qualitative methods. MacGregor made a significant contribution to the area through her work dating back to the 1950s that found social prejudices experienced by individuals with facial disfigurements had an impact on their psychosocial adjustment (MacGregor, 1951; MacGregor, 1990). Ray Bull and colleagues made further early contributions to ideas about the social impact of living with a visible difference in the late 1970s, including issues of perceived attractiveness (Bull, 1979; Bull & Brooking, 1986), stereotyping (Rumsey, Bull & Gahagan, 1986), and impact on social interactions (Rumsey & Bull, 1986). Since this, research in the field has grown to look not only at the social impact of living with a disfigurement but also the psychosocial effects, and the impact of rehabilitative treatment. A number of researchers have begun to develop theories, to incorporate the social, clinical, demographic and psychosocial factors that help explain adjustment to living with a disfiguring condition and this chapter outlines some of these and their relevance to this thesis.

4.2 TERMINOLOGY

With a rise in societal and media interest in body image and disfigurements, the terminology used has changed in recent years. The word ‘deformity’ was commonly used to describe an unusual feature in appearance, but has since been thought to have negative connotations around being misshapen or abnormal. The term ‘disfigurement’ is a universal term used amongst researchers in the appearance literature as it can be used succinctly to describe a range of changes and differences in appearance. However, it is considered important that this term is used as a noun, e.g. ‘a facial disfigurement’, rather than an adjective, e.g. ‘a disfigured face’ (Griffey & Castle, 2009). Increasingly, people with appearance-altering conditions prefer to use the term ‘visible difference’ or the medical name of their condition (Griffey &

Castle, 2009). Therefore in the following thesis the term ‘disfigurement’ will be used as a noun and used interchangeably with the terms ‘visible difference’ and when being specific the term ‘TED’ will be used.

4.3 A FRAMEWORK TO EXAMINE FACTORS THAT MAY ACCOUNT FOR VARIATIONS IN ADJUSTMENT

Concern about appearance is widespread across the general population and tends to involve concern about a particular body feature; with the nose, weight and skin disorders being the most common complaint (Harris & Carr, 2001). It has been repeatedly found that people with a visible difference experience higher levels of psychosocial distress, including anxiety, depression and social avoidance, than the general population (Rumsey, Clarke & Musa, 2002; Rumsey, Clarke & White, 2003; Rumsey et al., 2004). However, levels of distress vary between individuals with a disfigurement and some even report adjusting positively (Rumsey et al., 2004; Thompson, 2012). This chapter will describe some of the main explanatory variables that have been found to account for this variability in adjustment to appearance-altering conditions.

The Appearance Research Collaboration (ARC; 2008) proposed a framework that aims to draw together the key constructs believed to explain the variability in adjustment to living with a disfigurement, in order to drive further research into disfiguring conditions (Thompson, 2012; Figure 6). This framework was seen as a useful guide in planning the research into the quality of life in patients with TED described in this thesis.

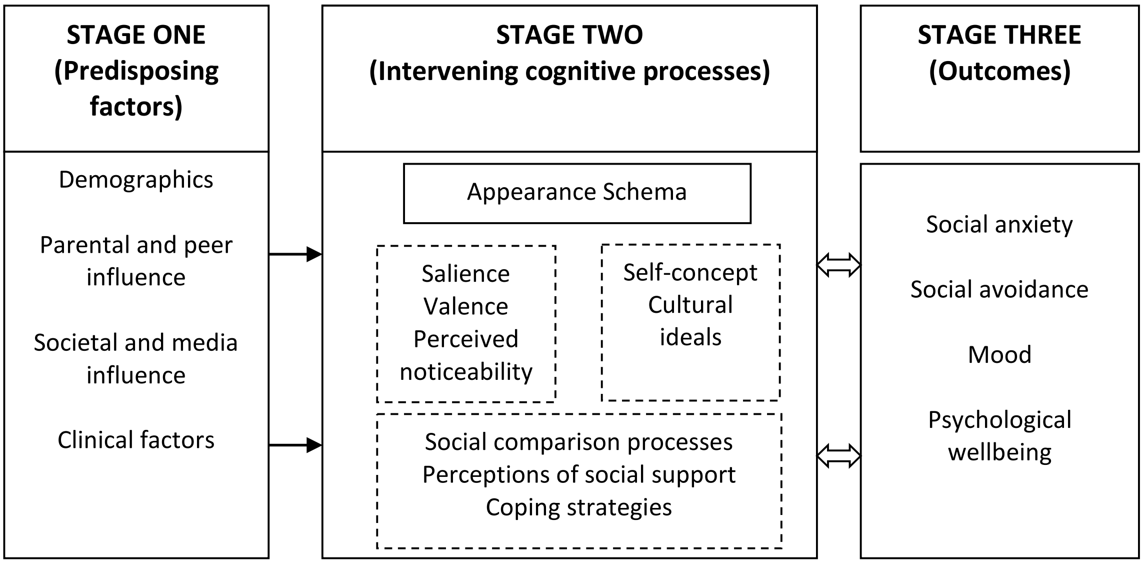


Figure 6. A working framework containing the constructs demonstrated to be involved in psychological adjustment to appearance-altering conditions (adapted from ARC, 2008)

4.3.1 Predisposing factors

The first element of the framework is the social context in which adjustment takes place, comprising of predisposing factors including demographic characteristics, socioeconomic factors, societal and media influence and clinical factors (ARC, 2008). As these are likely to have varying influences on each individual and thus play a part in adjustment, it is argued that these factors are important but are less amenable to intervention (Thompson, 2012). It has been argued that the predominant focus of research on adjustment to appearance should be the intervening cognitive processes and behavioural outcomes, which can be targeted within interventions (ARC, 2008; Thompson, 2012).

4.3.1.1 Demographics

The level of appearance concern within the general population has been reported to be high, with prevalence in both genders being highest during the early twenties. However among women in the general population concern often does not reduce until older age (Harris & Carr, 2001). In those with a visible difference, as with the general population, generalised and appearance-related distress usually reduces with age (ARC, 2008), with younger people experiencing the highest levels of anxiety and distress (Rumsey et al., 2003; James et al., 2011). Research specific to disfiguring eye conditions has however found older age to be associated with greater levels of depression in people with strabismus (McBain et al., 2014). These contradictory findings are reflected in a review by Thompson and Kent (2001). They found mixed reports for the relationship between age and adjustment, concluding that wide variation in individual responses within all age groups have been found (Thompson & Kent, 2001; Thompson, 2012).

Women with a disfigurement have been found to experience higher levels of appearance related distress than men (Rumsey et al., 2003; James et al., 2011). In the largest scale study to date investigating predictors of positive adjustment to living with a disfigurement, The ARC (2008) found that women not only had significantly more appearance-related distress, but also higher levels of general anxiety and depression than men. Research into psychosocial adjustment to burns has suggested that the gender difference may be reflected in the meaning the genders attach to having a visible difference. Women with burn injuries have been found to be more prone to a sense of loss from a changed appearance, whereas men experience more difficulty in adjusting to an altered identity from limitations in physical functioning (Andreasen & Norris, 1972; Brown et al., 1988).

Findings for these factors have to date been mixed and appearance researchers argue that demographic characteristics add little to understanding the process of adjustment (Thompson & Kent, 2001). Furthermore they maintain that demographic, societal and media influences are either not possible or more difficult to change in interventions targeted at increasing psychosocial adjustment (Moss & Rosser, 2012; Thompson, 2012).

4.3.1.2 Clinical factors

Moss and Rosser (2012) suggest that when searching for explanations for the variability in adjustment to a visible difference, it is external characteristics, such as size and noticeability that are the first factors that come to mind. This assumption is often inherent in clinical practice and patients with more severe conditions might be offered surgery to ‘correct’ their appearance by reducing the objective size and noticeability of the feature (Moss, 2005). Research has provided some support for this claim, for example Tebble, Thomas and Price (2004) found a significant relationship between length of facial scar and psychological distress.

Moss (2005) has argued that objective (clinical) severity shows a small ‘U’ shaped effect whereby those with the *minimal* and *most* severe differences in appearance had adjusted more positively and were less psychologically distressed than those with moderate levels. It was hypothesised that patients with conditions of moderate severity face less predictable social interactions as their condition might be noticed on some occasions but not others, making it difficult for the individual to develop consistent and effective coping strategies (Moss, 2005). Many other studies have found that levels of psychosocial distress associated with having a disfigurement are not well predicted by severity (Rumsey, Clarke & White, 2003; Rumsey et al., 2004; Thompson & Kent, 2001).

The location of a disfigurement has been found in some studies to play a role in adjustment. Moss and Rosser (2012) suggest that disfigurements to less visible body sites require different methods of interpersonal management to visible sites, such as the face. As the face is central to communicating and recognising others, changes to facial appearance have been considered a major life crisis (Rumsey, 2004; Lansdown et al., 1997). The eyes are the most prominent facial feature and influence perceived attractiveness and communication with others (Clarke & Wyn-Williams, 2000; Borwick & Khanche, 2012). As the eyes play a central role in communication, people who have a disfigurement to the eyes would be expected to have particular difficulty in social interaction and this has been supported in the literature (Clarke et al., 2003). People with conditions affecting the appearance of the eyes report high levels of perceived noticeability (Clarke & Wyn-Williams, 2000; McBain et al., 2014), and fear of negative evaluations from others (McBain et al., 2013; Richards et al., 2014) leading to high levels of social anxiety and social avoidance (Clarke & Wyn-Williams, 2000). This may also be the case in TED, where patients report difficult social interactions and issues in communicating with others (Jensen & Harder, 2011).

Symptoms and their severity tend to guide treatment decisions in the care of patients with TED. There are a number of previous studies that have suggested that a relationship exists between subjective and objective reports of TED severity (see section 3.7, page 67 for a full description). However, limitations in the methodologies of some studies make it difficult to conclude the presence of a relationship. For example, quality of life questionnaires have been designed by choosing items that correlate highly with clinical severity (e.g. Yeatts, 2005) and clinical measurements are not always collected at the same time as quality of life scores (e.g. Park et al., 2004).

A number of studies have found that patients’ subjective reports of the severity of TED and its impact on daily life are not consistently associated with objective measures of symptom severity (Gerding et al., 1997; Terwee et al., 1998). Wiersinga (2012) suggested that quality of life outcomes may not correlate with clinical characteristics in TED because patients’ perceptions of their health and daily functioning are influenced by their individual characteristics and environment and less determined by the objective severity of their illness. As clinical and demographic factors appear to explain only a small amount of the variance in psychosocial adjustment it is therefore possible that psychological processes rather than objective clinical measurements may better explain quality of life variability in this condition (Thompson, 2012). However there remain few studies that have investigated this relationship in TED and further research is needed to examine this question.

4.3.2 Intervening cognitive processes

The second element of the framework focuses on the intervening psychological processes that might contribute to adjustment and help explain the variability seen in patients, including appearance-related beliefs and socio-cognitive processes. Researchers in this area now commonly accept adjustment as a complex interaction of physical, socio-cultural and psychosocial factors (Clarke et al., 2003; James et al., 2011) and suggest that these factors should be taken into account when treating patients with disfiguring conditions. Furthermore, as these factors are more amenable to change through psychological interventions they are the key drivers for a body of appearance research that is attempting to establish what interventions should focus on to improve outcomes for individuals with a disfigurement.

4.3.2.1 Appearance schemas

We all form images of our bodies and the processes by which we do have received much attention in recent years. Body image has begun to be recognised as a multidimensional concept that includes thoughts, feelings and attitudes towards one's own body (Thompson et al., 1999). Body image has been researched from a range of psychological approaches, including cognitive-behavioural theory (Cash, 2002) and an information-processing perspective (Rosser, Moss & Rumsey, 2010). Within these perspectives is the idea that the self-concept is an information-processing network that is comprised of thoughts about aspects of the self (Moss & Carr, 2004). Cash, Melnyk and Hrabosky (2004) have suggested that greater schematic investment in appearance leads to larger self-ideal discrepancies (i.e. poor psychosocial adjustment), greater idealisation of media or cultural ideals, and particularly for women, this can impact on body image quality of life.

Recent research has begun to examine the links between individual body image perceptions and images portrayed in the media. For example, body dissatisfaction has been found to come from an individual being personally unable to match unrealistic body image ideals portrayed in the media (Halliwell & Diedrichs, 2012). Another relationship between media exposure and body dissatisfaction has been found where higher levels of exposure are associated with increased levels of body image disturbance (Botta, 2003). However, the links between the media, body dissatisfaction and body image disturbances are beyond the scope of this thesis and will not be examined in more detail.

4.3.2.2 Salience, valence and perceived noticeability

Preferential attention towards appearance, or *attentional biases,* can lead to appearance-related information being processed more quickly (Rosser, Moss & Rumsey, 2010). Some of these have been identified by Moss and Carr (2004) who have integrated social-cognitive theories to propose that within the multi-faceted self-concept some aspects such as appearance are more central, or *salient*, leading to an increase in the speed of processing of information relevant to these aspects. Salience of appearance has been found to inhibit adjustment if there is a discrepancy between appearance-related information and the view of one's own appearance (Moss & Rosser, 2012). Interpretative biases towards appearance-related information can, for the individual highly concerned about appearance, create a world dominated by appearance-relevant information (Rosser, Moss & Rumsey, 2010). The interpretation of ambiguous stimuli as appearance-related has been associated with levels of appearance concern (Rosser, Moss & Rumsey, 2010).

According to Moss and Rosser (2012) the appearance self-schema also encompasses the emotional evaluation of one's own appearance (valence), as well as the extent to which appearance-related information is more easily processed (salience). Valence can be seen in the degree to which an individual invests in the maintenance of their appearance (Thompson, 2012). Self-objectification theory (Friedrickson & Roberts, 1997) has demonstrated the detrimental impact of having a negative internalised representation of the self in relation to appearance including continuous monitoring of outward appearance, and seeing the self as void of other characteristics unrelated to the body (Moss & Rosser, 2012). These biases and beliefs are highly variable between individuals. Variation in appearance-related social anxiety and avoidance has been found to be significantly associated with variation in subjective evaluation of appearance (valence) in patients with ocular prostheses (McBain et al., 2013) and ptosis (Richards et al., 2014), and in a large sample of patients with disfiguring conditions assessed by The ARC (2008). Furthermore, McBain et al (2014) found poorer psychosocial functioning in strabismus to be associated with patients placing high value on appearance (salience).

Findings about perceived noticeability to date have been mixed. There is significant research that suggests that people with visible differences tend to perceive their differences as more noticeable than when measured objectively. For instance perceptions of particularly high noticeability have been found amongst individuals with head and neck cancer, skin conditions, and those seeking elective plastic surgery for appearance concerns, but less so for people with burns (Rumsey, Clarke & White, 2003). Perceptions of high noticeability have also been found in patients with strabismus (Jackson, Morris & Gleeson, 2013; McBain et al., 2014). More specifically to the current population, Terwee et al. (2003b) found that patients with TED tend to overrate and clinicians underrate the severity of their eye symptoms, including severe eyelid swelling and proptosis. Moss (2005) argues that surgery for a disfiguring condition would only result in patient satisfaction and reduced appearance-related distress if it reduced the individual's perception of the noticeability of their condition, such that their appearance became “normal”. Some initial findings for treatment in the context of disfiguring eye conditions suggest that patients' perceived noticeability of their condition is significantly reduced after strabismus surgery (Jackson, Moss & Gleeson, 2013); however when compared to clinician ratings of improvement, clinicians rate improvement after this surgery as far greater than patients themselves (Beauchamp et al., 2005).

4.3.2.3 Fear of negative evaluation from others

The negative evaluation of an individual based on one of their personal characteristics is likely to result in stigma. Stigma is a powerful social concept that involves a person being "disqualified from full social acceptance" (Goffman, 1963 p9). Stigma can influence an individual's social identity. *Felt* stigma refers to the fear of discrimination and can result in feelings of embarrassment and shame, whereas *enacted* stigma refers to actual discrimination from others in society (Scambler, 2007). Stigmatisation of an individual may arise from a number of perceptions including fear of contamination, pity, reduced competence of the individual or reduced morality (West & Hardy, 2007). A number of these perceptions have been found to contribute to the stigmatisation of individuals with facial disfigurements. For example, the "what is beautiful is good" stereotype has been demonstrated where subjects have assigned more favourable personality traits and successful life outcomes to individuals perceived as highly attractive (Dion, Berscheid &Walster, 1972). This effect has been observed more recently in the context of disfigurement to the eyes. When shown photographs, lay people have rated individuals with strabismus unfavourably, perceiving them as less competent, less likely to find a partner (Mojon-Azzi et al., 2008), and, for women in particular, less likely to succeed in job applications (Mojon-Azzi & Mojon, 2009). Furthermore, Pilivian and colleagues (1975) found that bystanders were significantly less likely to help an individual with a visible birthmark they observed collapsing on a New York subway than an unmarked individual.

It is therefore unsurprising that people with disfiguring conditions fear the negative evaluations of others, particularly if they have had prior experience of feeling or actually being discriminated against. Fearing negative evaluations can have a significant impact on psychological adjustment. This fear has been found to significantly predict appearance-related adjustment in people with head and neck cancer (Clarke et al., 2014). Leary et al. (1998) also found that perceptions of stigmatisation interacted with severity of psoriasis, concluding that the impact of severity of psoriasis was moderated by the extent to which patients were concerned about others' negative evaluations.

In particular, disfigurements to the eyes have been linked to high levels of concern about the negative perceptions of other people (Richards et al., 2014). Studies evaluating the impact of disfiguring eye conditions have found that it is predominantly a combination of the appearance-related cognitive processes described above that are associated with and predict adjustment, including perceived noticeability, fear of negative evaluations, subjective evaluation of appearance and the value placed on appearance (McBain et al., 2013; McBain et al., 2014; Clarke & Wyn-Williams, 2000; Clarke et al., 2003). Indicating that psychosocial adjustment to living with a disfiguring eye condition is not well predicted by clinical severity, aetiology, or duration of the condition, but rather intervening cognitive processes, individual to each person.

4.3.2.4 Social comparisons

As well as appearance-related processes, socio-cognitive processes have also been found to significantly impact on adjustment to living with a disfigurement. The majority of people engage in some form of self-comparison in order to acquire further information about the self (Gibbons & Buunk, 1999). However, researchers have suggested that interest in the self can increase with uncertainty, and periods of stress or change in particular have been found to increase the frequency with which people compare themselves to others (Aspinwall & Taylor, 1993; Taylor, Buunk & Aspinwall, 1990; Aspinwall, 1997). It could be argued that acquiring a disfiguring condition as TED could be such a time and in turn that an increase in social comparisons could impact on adjustment. In support of this hypothesis, Halliwell (2002) found poorer psychological adjustment to be associated with a greater tendency to make appearance-related comparisons with others (Halliwell, 2002). Some research has even supported this finding in the context of ophthalmology: a greater tendency to make social comparisons has been found in patients with ptosis, TED, strabismus, ocular cancer and trauma (James et al., 2011). Furthermore, women with disfiguring eye conditions have been found to demonstrate a greater tendency to make social comparisons than men (James et al., 2011). However, James et al.'s (2011) study only recruited four patients with TED, and with no indication of the association between social comparisons and quality of life. Further research in this area is required to establish the relationship between adjustment and social comparison in TED.

When individuals feel under threat, social comparison processes can include explicit self-evaluation against another less fortunate (downward comparisons) or seeking affiliation with more fortunate others (upward comparisons) which serve to ameliorate self-esteem, and help individuals feel more hopeful about their situation (Taylor & Lobel, 1989). Commonly reported by people who show positive adjustment to having a disfigurement is the use of downward comparisons, which have been found to boost self-regard (DeVellis et al., 1990; Egan et al., 2011).

4.3.2.5 Perceptions of social support

Although people with a disfigurement report negative social interactions, perceptions of positive social support have been found to improve adjustment (Rumsey et al., 2004). Rumsey et al. (2004) found that when people with a disfigurement feel more supported by others, the less visible they feel their condition is to other people and the less worried they are about their appearance. Similarly, The ARC (2008) found that greater satisfaction with social support was associated with less appearance-related social anxiety and avoidance, and to significantly predict lower levels of anxiety and depression. However, findings within specific conditions have been mixed, and the types of social support received might impact on subsequent adjustment to living with a visible difference. For example Egan et al. (2011) found that for people who had been living with a visible difference since childhood, a lack of support from family had formed an increased sense of independence, and social support from friends and significant partners had increased a sense of acceptance and boosted self-esteem. Deno et al. (2012) also found that whilst social support from friends lowered social distress in patients affected by head and neck cancer, it also increased *emotional* distress (Deno et al., 2012).

Specific to those with a disfiguring eye condition, having less support from friends but more support from family was found to predict greater levels of anxiety and depression in strabismus; however social support did not predict the variability in quality of life in this population (McBain et al., 2014). No studies to date have examined perceptions of social support in patients with TED and how this might help to explain variability in quality of life in this patient group. Therefore, further research in this area is warranted to establish whether the various areas of social support impact on quality of life in TED.

4.3.2.6 Coping strategies

A number of categorisations of coping strategies have been proposed in psychology, including emotion-focused and problem-focused styles (Lazarus, 1993). However, further coping strategies have been identified in relation to adjustment to a disfiguring condition. Thompson and Kent (2001) have described ‘self-presentation’ coping strategies that include behavioural and cognitive strategies that involve attempting to maintain self-esteem against the impact of others’ comments, for example by dealing with the comments, avoiding social situations altogether, or concealing the disfigurement. Egan et al. (2011) reported that patients who adjust positively to living with a visible difference use active coping strategies that involve distractions, practical solutions, and focusing on other aspects of their lives than appearance. Other coping strategies used by some individuals with a visible difference are proactive social skills including staying calm, politely confronting negative reactions, and trying to educate others about their noticeable feature (Partridge, 1990). One study that evaluated coping styles used by patients with TED reported that negative coping styles were used, including depressive coping, withdrawal, and trivialising and that these were associated with poorer quality of life (Kahaly et al., 2005).

4.3.2.7 Expectations of treatment outcomes

Expectations of healthcare outcomes are complex psychological processes influenced by a range of individual perceptions, and as a consequence are likely to vary from patient to patient. What an individual with a disfiguring disease expects from their treatment could be a significant predictor of not only their quality of life but also how they adjust to changes in their appearance. Although this variable was not included in the ARC (2008) framework, some initial research has begun to make links between expectations of rehabilitative surgery for disfiguring conditions and psychological wellbeing.

Most patients attend a clinical appointment with specific expectations about the medical care they are about to receive (Dawn & Lee, 2004) and such expectations have been linked to satisfaction with treatment outcomes, particularly in situations when these have not been met. When patients are listed for surgery to alter appearance it is normally because they cannot be treated with alternative, less invasive treatments and as such patients are likely to have pre-conceptions and expectations about the effectiveness of surgery and its impact. Indeed, patients' expectations before surgery have been linked to satisfaction with post-surgical outcomes (Dawn & Lee, 2004; Finlay, Atkinson & Moos, 1995; Finlay et al., 1995; Pager, 2004; Bhty, 1999). Research suggests that unrealistic expectations, for example in orthognathic surgery that aims to restructure the jaw can lead to dissatisfaction (Kiyak, Vitaliano & Crinean, 1988). Clinical outcomes such as more scarring than expected, can also lead to patient dissatisfaction with their treatment (Dawn & Lee, 2004). Conversely, patients who are highly anxious preoperatively about the outcome may find that surgery exceeds their expectations (Pager, 2004). Hence expectations appear to play an important role in psychosocial well-being and the impact of treatment.

With regards to living with a visible difference, what a patient expects from their treatment in terms of changes in their appearance could therefore be a major factor in the variability in patients' quality of life. Previous research on expectations has focused on a variety of surgical procedures, including cataract surgery, orthognathic surgery and surgeries for cancer treatment, but to date few studies have examined the expectations of patients with disfiguring eye conditions. One recent study has examined the expectations of patients with strabismus seeking to have their eyes realigned through strabismus surgery and found that less than 3% of their sample expected surgery to worsen their condition, despite the fact that typically only 24% of patients are realigned after surgery and 61% still report double vision post-surgery (McBain et al., *in press*). One qualitative study in TED reported that patients can have unrealistic expectations that surgery will enable them to go back to the life they had before their TED (Estcourt et al., 2008), but no further research has been conducted in this condition.

4.3.3 Outcomes

The final element of the ARC framework (ARC, 2008; Thompson, 2012) is the observable impact of disfiguring conditions in behaviour or psychosocial adjustment. In the original version of the framework described by ARC (2008) levels of appearance-related social anxiety, social avoidance, and mood are considered key outcomes along with psychological well-being.

4.3.3.1 Social anxiety and social avoidance

Not only are cognitive factors related to the self-concept associated with adjustment, but research also indicates that individual factors associated with social interactions also play a part in adjustment. The majority of difficulties that people with a visible difference are faced with relate to social interactions (Rumsey et al., 2004). Some authors argue that people are simply curious or feel unskilled in coping with a social situation with someone who has a visible difference (Partridge, 1990; Rumsey et al., 2004). However, studies have found extremely negative perceptions of people with facial disfigurements, including that they are less honest, less trustworthy, less intelligent, and less capable (Rankin & Borah, 2003) among other perceptions described in section 4.3.2.3 of this chapter. Thus, stigmatisation has a number of implications for social interaction. Studies have shown that individuals with visible differences face stigmatisation and as a result both feel and display awkwardness in social situations (Newell, 2000). Frances Macgregor, over decades of research on the social implications of having a facial disfigurement, found that many people experienced distress and damage to their self-esteem as a result of the reactive behaviour of others they came into contact with (1974; 1990). Individuals with an unusual facial appearance are labelled as different from other members of society and treated as such (MacGregor, 1974). The *felt* stigma of individuals with facial disfigurements may therefore translate into the avoidance of social situations.

The type of condition causing a visible difference has also been found to influence levels of social anxiety. People with burns have been found to report lower levels of worry about their appearance and less appearance-related social anxiety than patients with variable dermatological conditions, maxillofacial injuries, and those seeking elective plastic surgery (Rumsey et al., 2003; Rumsey et al., 2004). Particularly high levels of appearance-related anxiety and low mood have been found in populations electing to have cosmetic surgery on a feature they are concerned with (Rumsey et al., 2004). In a number of cases this has been linked to a psychiatric disorder that is associated with preoccupation with parts of the body that are objectively non-impaired or have minimal irregularity known as “body dysmorphic disorder”, or BDD (Castle, Honigman & Phillips, 2002).

Conversely, the positive adjustment of a number of people with long-standing burns has been linked to the development of positive coping strategies (Rumsey et al., 2004; Partridge, 2006). People with disfiguring eye conditions report considerable appearance-related social anxiety and avoidance (Clarke et al., 2003), which is often associated with a fear of negative evaluation from others and poorer subjective evaluation of appearance (McBain et al., 2013; Richards et al., 2014).

Thompson and Kent (2001) suggest that social avoidance is common amongst individuals with a visible difference. Rumsey, Clarke and Musa (2002) have found that as many as 72% report avoiding a number of activities that involve exposing their condition, including swimming and socialising. Newell (2000) proposed the *fear avoidance* model to explain this behaviour, whereby avoidance is prompted by fear of negative social situations and leads to a reduction in social activities, with more and more situations that might be trivial to others being deemed as threatening, such as walking outdoors. This explanation has been supported in a number of contexts, including facial disfigurements caused by cancer (Bonanno & Esmaeli, 2012; Konradsen et al., 2012), and skin, eye, and rheumatic conditions (Rumsey et al., 2004).

Rumsey et al. (2000) found high levels of social avoidance in patients with visible eye conditions including avoiding having photos taken and situations that required them to make eye contact with others, such as meeting new people. These ideas have recently been supported in studies involving patients with TED. Using interviews, Jensen and Harder (2011) found that the change in appearance caused by TED had affected central aspects of patients’ lives including facial communication, involvement with others, and maintenance of social relationships, leading to social withdrawal. Respondents felt that their eyes had become ‘uncontrollable’ due to protrusion and reduced mobility, making simple activities such as shopping or walking through crowds difficult and an inability to express emotions during interactions with others often misinterpreting their facial expressions (Jensen & Harder, 2011). Estcourt et al. (2008) also found that TED leads to an altered sense of identity, which in some cases caused depression, and in many cases social isolation.

The concept of appearance concern in relation to social anxiety and social avoidance has been captured in a recent tool that has been developed to measure levels of appearance-related distress. The Derriford Appearance Scale (DAS24; Carr, Moss & Harris, 2005) is a 24-item scale measuring the impact of appearance-related distress on social anxiety and social avoidance. In a recent study investigating mood and quality of life in patients with strabismus, the DAS24 was found to predict anxiety, depression, and both functional and psychosocial quality of life (McBain et al., 2014).

4.3.3.2 Mood

Mood is placed in the ARC (2008) framework as an observable outcome of adjusting to having a visible difference. The impact of having a disfigurement on mood has been evaluated in strabismus, where higher levels of anxiety were associated with more concerns about treatment, greater fear of negative evaluation from others, greater social anxiety and social avoidance, and less support from friends. Greater levels of depression were predicted by greater social anxiety and social avoidance, less support from friends and more support from family (McBain et al., 2014).

Levels of anxious and depressed mood have been widely investigated in patients with TED, although specific predictors of mood have not yet been considered. Wong and Yu (2013) found the current prevalence of anxiety or depressive disorders in a sample of 124 patients with TED as 19%. Kahaly et al. (2005) used the Hospital Anxiety and Depression Scale (HADS) and found clinical levels of anxiety in as many as 40.2% and clinical levels of depression in 22% of patients with TED.

Mood has been found to be a strong, significant predictor of quality of life in the contexts of other health conditions, including multiple sclerosis (Karatepe et al., 2011), diabetes (Goldney et al., 2004), and myocardial infarction (Mayou et al., 2000) as well as in strabismus (McBain et al., 2014). It has also been found to be significantly associated with quality of life in patients with TED (Kahaly et al., 2005). Because mood appears central to quality of life, it is necessary to gain a full understanding of influences on quality of life, including evaluating mood as a predictor of quality of life. It is possible that low mood could lead to poorer quality of life as it interferes with the ability and desire to engage in activities of daily living. An alternative explanation of the relationship is that poor quality of life drives mood, and this relationship requires further evaluation in TED in order to establish links.

4.3.3.3 Quality of life

Whilst the original framework considers social anxiety and avoidance, and mood, as outcomes of adjustment, it can be argued that these are also cognitions that might influence quality of life. They could therefore be used to try to explain overall quality of life by including them as intervening psychosocial processes in the ARC framework (2008). The authors of the framework argue that appearance-related social anxiety and avoidance, and mood, could be equally well placed as intervening cognitive processes in stage two of the model (Figure 6, page 73) when applying the model to research investigating the impact of living with a visible difference on quality of life (Thompson, 2012).

The ARC (2008) framework has recently been used to explore which of the above factors might help to explain variability in quality of life across a number of disfiguring eye conditions including ocular prosthesis (McBain et al., 2013) strabismus (McBain et al., 2014) and ptosis (Richards et al., 2014), but to date has not been used to explore the psychosocial impact of TED, or outcomes after orbital decompression surgery. McBain et al. (2013) and Richards et al. (2014) investigated the association of a number of the constructs described in this chapter with social anxiety and avoidance, and mood. McBain et al. (2014) investigated their ability to predict quality of life in strabismus and found poorer visual function-related quality of life to be associated with greater fear of negative evaluations, and greater social anxiety and avoidance. Psychosocial quality of life was significantly associated with more perceived noticeability, greater social anxiety and avoidance, and placing a higher value on appearance (McBain et al., 2014), as mentioned previously.

4.4 INVESTIGATING THE PSYCHOSOCIAL IMPACT OF TED

Whilst quality of life measures have been developed to encapsulate patient life experiences, as described in Chapter 2, a number of other psychosocial variables might also play a role in adjustment to TED. Literature on the psychological impact of disfiguring conditions might help to indicate some of the factors that could be associated with patients' adjustment to TED and the variability in adjustment. The framework developed by the ARC (2008) captures the possible relationship between constructs that have been developed in recent years in relation to appearance schemas, appearance processing, and social anxiety and social avoidance, and how these might interact to influence quality of life outcomes. With the exception of James et al.'s (2011) study that included a small number of patients with TED, there has been no research to date that has used the ARC framework as a model to investigate the specific pathways that predict adjustment to living with TED.

4.5 SUMMARY

It has been widely documented that having a visible disfigurement can have a profound psychological impact, but there are some who adjust positively. The experience of living with a disfigurement appears to be multifaceted and involves cultural, societal and individual factors. For this reason there is wide variability in adjustment and research has moved towards understanding what factors might predict how well, or indeed poorly, patients with a range of disfiguring conditions, might adjust.

A number of theories and models have been developed from health, social and clinical psychology research that attempt to explain individual differences in appearance concern and subjective adjustment to changes in appearance. Moss and Rosser (2012) have encouraged researchers to integrate the empirical evidence and theories described in this chapter in order to construct more holistic models that can be applied in context. The socio-cultural environment has been found to impact on levels of appearance concern in the general population and in populations of people with disfiguring conditions, however these factors are relatively impermeable and difficult to target in interventions to improve outcomes. There have been mixed findings in the ability of clinical severity to predict adjustment. This relationship certainly requires further exploration in TED. Particularly as emphasis is placed on surgical procedures to reduce the noticeability of the condition and improve objective measures of appearance. Research investigating the impact of the type and location of the disfigurement has been mixed, although there is some evidence that more prominent conditions affecting the face, and in particular the eyes, may lead to higher levels of social anxiety and social avoidance. Therefore, for individuals living with a visible difference such as TED, appearance schemas and social-cognitions might better explain adjustment than demographic or clinical factors. There remains less evidence as yet for the role that intervening cognitive processes in adjustment to a change in appearance due to TED.

The framework proposed by the ARC (2008) is intended to drive further research that will test specific pathways and to determine precise relationships between predictor variables (Thompson, 2012). Developers of this framework argue that its ability to predict both short-term and longer-term adjustment to a sudden change in appearance needs to be explored further, in a range of appearance-altering conditions (ARC, 2008; Harcourt & Rumsey, 2012). An adapted version of the ARC (2008) framework will therefore be used in this thesis to investigate other factors that might predict quality of life of patients with TED. Specifically, some initial research has supported the conceptualisation of appearance-related social anxiety and avoidance, and mood, to be cognitive processes that can predict adjustment and therefore the studies within this thesis has conceptualised these as predictors of quality of life, rather than as outcomes.

5. METHODS

5.1 PROLOGUE

The systematic review in Chapter 3 of this thesis highlighted the limited research into the psychosocial outcomes of treatment for TED, particularly the impact of major surgery that aims to improve appearance and vision. Orbital decompression surgery has to date been assessed in terms of changes in quality of life from pre- to post-surgery in only 5 studies. Three of these studies included small sample sizes (Terwee et al., 2001; Kashkouli et al., 2011b; Fichter et al., 2013), one study failed to use a validated TED-specific quality of life outcome measure (Tehrani et al., 2004), and one study excluded patients with optic neuropathy (EUGOGO et al., 2009). Considering the cost of performing major surgery such as orbital decompression, and the lack of evidence to date for the effectiveness of this surgery in terms of quality of life and psychosocial improvement, this was considered an important area for further investigation.

5.2 AIMS

The overall aim of this thesis was to understand the impact that TED and decompression surgery have on quality of life.

Through the use of both quantitative and qualitative methods, this study aimed to answer the following research questions:

(1) What demographic, clinical and psychosocial factors are associated with quality of life in patients presenting for orbital decompression surgery?
(2) What are patients’ expectations of orbital decompression surgery, what influences these expectations, and do they impact on quality of life?
(3) Does quality of life change from pre- to post-surgery?
(4) Which clinical and intervening psychosocial factors change from pre- to post-surgery?
(5) What demographic, clinical and psychosocial patient characteristics at baseline predict change in quality of life from pre- to post- surgery?
(6) Which changes in clinical and psychosocial factors from pre- to post-surgery predict change in quality of life from pre- to post-surgery?

5.3 PREDICTIONS

Based on the literature described in Chapters 2, 3 and 4 of this thesis, and utilising the ARC (2008) framework of adjustment to disfiguring conditions the following predictions were made:

- There will be large variations in quality of life between patients with TED and that intervening psychosocial processes will better explain this variation than demographic or clinical factors.
- Both vision-related and appearance-related quality of life will improve significantly from pre- to post-decompression surgery in patients with TED.
- It is expected that both clinical and psychosocial factors will improve significantly postoperatively.
- However, as double vision has been found to worsen in some post-decompression, it is expected that in this sub-group of patients, vision-related quality of life may not improve significantly.
- Improvements in intervening psychosocial processes will drive improvements in appearance-related quality of life. As there may not be improvements in double vision, it is not expected that changes in these areas will drive changes in vision-related quality of life.

5.4 DESIGN

A mixed methods design was employed for the pre-surgical assessment. A prospective cross-sectional design was used to answer research question (1). Qualitative methods were employed to answer question (2), which involved the use of semi-structured interviews. Within-subjects repeated measures designs were used to answer questions (3), (4), (5) and (6).

5.4.1 Rationale for using a mixed methods approach

Combining quantitative and qualitative methodology to explore the same research problem has increased in popularity in healthcare research over recent years (Curry et al., 2013). A recent review has attempted to define mixed methods research, with over 19 different definitions currently being used (Johnson, Onwuegbuzie & Turner, 2007). Based on the analysis of the definitions, Johnson and colleagues (2007) proposed that mixed methods research “combines elements of qualitative and quantitative research approaches (e.g. use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding" (Johnson et al., 2007, p.123).

The emphasis in the current study has been on the results of the quantitative study, with the qualitative study embedded within the quantitative research, in order to complement and enhance the findings. Curry and colleagues (2013) have described this method as the *concurrent embedded approach,* whereby quantitative and qualitative data collection occurs simultaneously, and one component is more dominant. Following the data collection and analysis of each study, interpretation of the embedded results is required. O'Cathain, Murphy and Nicholl (2008) argue that integration of the findings from each method is a key part of using mixed methods and one that is often missing in mixed methods healthcare research. *Triangulation* is one advantage of embedding qualitative studies within quantitative research as it involves the researcher using multiple methods and comparing the results of each method to see what similarities and differences have emerged (Guion, Diehl & McDonald, 2011).

5.5 ETHICAL APPROVAL

Full ethical approval for both the quantitative and qualitative studies was obtained from the North London Research Ethics Committee (REC reference 11/H0724/6). Relevant approvals were also gained from the Research & Development (R&D) teams at the two research sites: Moorfields Eye Hospital (MEH) and Birmingham and Midland Eye Centre (BMEC). All participants provided written informed consent.

5.6 SAMPLE SIZE CALCULATIONS

For the research questions (1), (5) and (6) an a priori sample size calculation was performed using the software G*Power (version 3.1.7; Faul et al., 2009). Effect sizes of 0.45 and 0.9 were specified for the GO-QOL appearance and GO-QOL visual function subscales, respectively, and α at 0.05. Between 64 and 97 patients would need to be recruited to achieve a power of 90% when using linear multiple regression analysis (to find the R^2 deviation from zero) with 33 predictor variables. Assuming an attrition rate of 20% at each follow-up a sample size of between 90 and 135 was recommended. The effect size and attrition rate estimation was based on a group of

48 patients with TED using the GO-QOL to evaluate quality of life pre- and post-orbital decompression (Terwee et al., 2001). The number of predictor variables was based on the number measured for the cross-sectional pre-surgery study described in this thesis. Another suggestion for study designs involving multiple regression analysis is to recruit 10 participants per predictor variable (Field, 2009). Therefore 330 participants would be required for the present study if all the variables assessed at baseline were to be included into the analysis.

For research questions (3) and (4), literature was consulted for guidance on appropriate sample sizes for measuring change over time using multilevel modelling (MLM) analyses. Calculating the sample size required for MLM and subsequent power achieved is complicated by the various factors involved in this type of analysis and as such there is currently no rule of thumb (Field, 2009). However, Kreft and de Leuuw (1998) suggest that there should be no less than 20 patients for every level introduced into the model, whilst Tabachnick and Fidell (2007) suggest 60 for each level. As the data was structured to account for two levels (see section 5.10.4.2 of this chapter), a sample size of between 40 and 120 was required.

The sample size for the **qualitative** study used to explore research question (2) was determined by the saturation of themes during the interviews. In order to ensure a reasonable sample size was achieved for the aims of the research, guidance for operationalising data saturation from Francis et al. (2010) was followed. This involved setting an initial recruitment target and estimating how many further interviews would be needed before no new themes emerged, and applying a ‘stopping criterion’ of the number of consecutive interviews that elicited no new themes or ideas (Francis et al., 2010). Therefore for this study, an initial target of 10 interviews was set, with an estimation that a further 5 would be needed before no new themes emerged and a ‘stopping criterion’ of 2 consecutive interviews that did not elicit any new themes or ideas before recruitment ended.

5.7 RECRUITMENT

5.7.1 Inclusion & exclusion criteria

To be eligible to take part in the studies the following inclusion criteria were used:

- Patients diagnosed with TED by a Consultant Ophthalmologist
- Aged 18 years or over
- Patients listed for orbital decompression surgery
- A comprehensive understanding of written and spoken English, as determined by the patient’s Consultant Ophthalmologist.

Patients were excluded if they were identified as suffering from psychiatric or co-morbid health conditions that rendered them too ill or distressed to take part in the study, as determined by their Consultant Ophthalmologist.

5.7.2 Identification procedure

All participants included in the **quantitative** studies were patients at MEH, under the care of one of three Consultant Ophthalmologists. Eligible patients were initially identified either by the consultant who listed them for surgery or from surgery lists that were screened weekly on the electronic Patient Administration System (PAS) at MEH. Potential participants were either approached on the day of their outpatient appointment when they were listed for surgery, or contacted directly after this appointment. All eligible patients who agreed to take part in the study, were given a study information sheet that they kept (Appendix E), along with a consent form that was to be given to the researcher once signed (Appendix F) and stored in a locked cabinet in a secured office. Participants were also given a questionnaire pack (Appendix G) that they were given the option of completing at home or in the waiting room. Three participants completed the questionnaire in the waiting room and the remainder completed it at home. Participants recruited during their outpatient’s appointment took the information and questionnaire pack home, giving them time to decide if they wanted to take part, and were able to call the researcher with any questions about the study. Information and questionnaire packs were posted to patients identified from surgery lists; this was followed by a telephone call 7 to 14 days later. All patients were given a Freepost envelope to return the signed consent form and completed questionnaire pack.

Patients who did not return the consent form and questionnaire within 4 weeks of invitation were followed up with a telephone call before their surgery. Any patients that could not be contacted by telephone were sent a reminder letter about the study from the researcher and then again 6 weeks later from their Consultant

Ophthalmologist, at which point if they still did not respond it was assumed they did not want to take part. General Practitioners (GPs) were informed of their patients' participation in the study by letter (Appendix H).

With approximately 80 orbital decompression operations being performed at MEH per year (MEH Performance Information, 2013) and a sample size requirement for the quantitative study of 141, it was decided that every eligible patient recruited at MEH would be required for the quantitative study. Furthermore, it was felt that the questionnaires included in the quantitative study might influence participants' responses during an interview about their surgery for TED. Therefore BMEC was enrolled as an additional recruitment site for the **qualitative** study and approval from BMEC R&D to carry out the research onsite was received on 17th October 2012.

The inclusion and exclusion criteria described in section 5.7.1 were applied to the identification of patients for the qualitative study. Eligible patients were identified by a clinical researcher at BMEC and asked if they wished to take part in the study during the outpatient appointment in which they were listed for orbital decompression surgery. Participants were given an information sheet (Appendix I) and consent form (Appendix J) to take home and asked if they minded being contacted to arrange an interview. Any patients that verbally expressed an interest in taking part in this initial consultation were followed up with a telephone call 2 to 7 days later to arrange a suitable time for interviewing.

5.8 ASSESSMENT PROCEDURE FOR THE QUANTITATIVE STUDY

Participants were asked to complete questionnaires at 3 time points; before surgery, 6 weeks after surgery, and 6 months after surgery. The follow-ups coincided with the usual protocol for post-surgery outpatient appointments. Patients who attended these appointments were given questionnaire packs in clinic to fill in either in the waiting room or at home. Follow-up questionnaire packs were posted to patients who did not attend their outpatient appointment. The same reminder protocol described in section 5.7.2 was used for any participants who did not respond to post-surgery questionnaires.

Clinical measures were first obtained by a Consultant Ophthalmologist at the outpatient appointment where patients were listed for surgery (a copy of the data collection form can be found in Appendix K). A post-surgery version of the form was completed by an ophthalmologist at the 6 week and 6 month follow-up appointments. This included some additional items described in section 5.8.1.4 of this chapter. The schedule of the assessments can be seen in Table 5 below.

Table 5. Schedule of assessments for the study including measures taken at each time point

		Baseline	6 weeks	6 months
Demographics	Gender, Age, Marital Status, Ethnicity	x		
Clinical variables	Thyroid function	x		
	Treatment history	x		
	Duration of disease	x		
	Laterality of disease and surgery	x		
	Corneal SPK	x	x	x
	Visual acuity	x	x	x
	Disease activity	x	x	x
	Double vision	x	x	x
	Eyelid retraction	x	x	x
	Optic neuropathy	x	x	x
	Hydraulic orbit	x	x	x
	Lagophthalmos	x	x	x
	Proptosis in mm	x	x	x
	Smoking	x	x	x
	Further surgery		x	x
Psychosocial variables	Fear of negative evaluation (BFNE)	x	x	x
	Social comparison (INCOM)	x	x	x
	Perceptions of social support (MSPSS)	x	x	x
	Expectations of outcome (E-TEDS)	x	x	x
	Appearance-related distress (DAS24)	x	x	x
	Appearance valence and salience (CARSAL & CARVAL)	x	x	x
	Perceived visibility	x	x	x
	Mood (HADS)	x	x	x
	Quality of life (GO-QOL)	x	x	x
	Satisfaction with surgery			x
	Side effects from surgery			x
	Satisfaction with pre-operative information			x

5.8.1 Measures

As the theoretical underpinnings for the study lay within appearance and socio-cognitive approaches, the analysis framework and selection of measures to include in the study were based on these.

5.8.1.1 Predisposing factors

5.8.1.1.1 Demographics

The ARC (2008) framework suggests that demographic factors might play an important role in psychological adjustment to living with a disfiguring condition. The questionnaire pack given to patients prior to surgery asked them to answer the following demographic questions at this time point only:

- Age
- Gender
- Ethnic background: The options were based on the Office for National Statistics (ONS) 11 categories of ethnicity classification (ONS, 2003).
- Relationship status: This was recorded using 6 response options: married, divorced, widowed, single, living with partner, other.

5.8.1.1.2 Clinical

The following measures were taken by an Ophthalmologist at **baseline only for each eye**:

Thyroid function: Thyroid function was measured according to stability with a yes or no response.

Disease duration: This was determined by the participants' medical files and was recorded in months.

Treatment history: Whether patients had previously received 1) immunosuppressants (e.g. steroids), 2) radiotherapy, 3) orbital surgery (e.g. eyelid surgery or orbital decompression) was recorded with a yes or no response for each.

Laterality of TED & planned surgery: Whether disease was in one eye (unilateral), or both eyes (bilateral) was measured. Patients with bilateral disease usually undergo bilateral orbital decompression; however at MEH patients are able to opt to have surgery in one eye at a time, so laterality of surgery was also measured.

Smoking: Current smoking status was measured with a yes or no response.

It was important to measure the presence, or change, in a number of clinical factors. The following were therefore measured **at all 3 time points**:

Disease activity: The Clinical Activity Scale (CAS; Mourits et al., 1997) was used to provide a score on the presence and level of disease activity (Table 1, Chapter 1, page 22).

Visual acuity: Visual acuity was measured for each eye using a Snellen Chart (Snellen, 1862); a universally accepted tool that involves reading letters of different sizes on each line, one eye at a time, from a 6 metre distance (Hussain et al., 2006). The result was converted to the log of the minimal angle of resolution (LogMAR) as recent studies have suggested this measurement is more accurate and lends itself better to statistical analysis (Hussain et al., 2006; Rosser, Laidlaw & Murdoch, 2001). LogMAR values range between -0.20 and 2.1 when converted from Snellen scores. A score of 2.2 was assigned to patients with vision only of counting fingers, hand movements, perception of light and non-perception of light. A "worst eye analysis" was conducted on the visual acuity data in order to control the number of variables in the study. Numerous previous studies in eye research have performed a worst eye analysis to deal with large amounts of ophthalmic data (McBain et al., 2014; Miserocchi et al., 2011; Katz, Zeger & Liang, 1994). The worst eye was identified using the highest exophthalmometry reading and using subsequent measurements for this eye only for exophthalmometry, LogMAR and eyelid retraction.

Optic neuropathy: Whether sight had been lost due to compression of the optic nerve was measured using the Ishihara colour test, which has been found to be highly effective at detecting colour deficiency (Birch, 1997). The most widely used colour deficiency test, it involves patients identifying a number printed in coloured dots that is surrounded by dots of a different colour and elicits colour blindness. In addition, testing for a relative afferent pupillary defect (RAPD) was used, known as the ‘swinging light test’. This test measures differences in the response of the pupils of the eyes to light. In a normal swinging light test (no RAPD) the pupils of both eyes constrict equally. In an abnormal test (presence of a RAPD) there is less pupil constriction in the eye with optic nerve disease (Broadway, 2012).

Proptosis: Projection of eyes from the lateral rim of the eye socket was measured in millimetres (mm) using an exophthalmometer. Exophalmometry readings for the worst eye were used in the analysis.

Marginal reflex distance: Marginal reflex distance 1 (MRD1), or upper eyelid retraction, was measured using the distance from the pupil centre to the upper eyelid in mm. Marginal reflex distance 2 (MRD2), or lower eye lid retraction, was measured using the distance from pupil centre to lower eyelid in mm. These measurements indicate the level of exposure of the whites of the eyes (scleral show) and the inability to close the eyes fully (lagophthalmos). MRD1 and MRD2 for the worst eye were used in the analysis. As described for LogMAR (page 122), the worst eye was identified using the highest exophthalmometry reading.

Corneal superficial punctate keratitis (SPK): The presence or absence of cell death on the surface of the cornea causing dry eyes and redness was detected using fluorescein staining.

Hydraulic orbit: Hydraulic orbit, or raised pressure behind the eyes caused by tightening and swelling of the orbital muscles and tissue, was measured in terms of presence or absence.

Double vision: Double vision, or diplopia, was measured in terms of presence (including constant diplopia, or in up or down gazes only), or absence.

The following measure was taken at the 6 week and 6 month **post-surgery follow-ups only**:

Further surgery: It was recorded whether patients where likely to need further surgery after their orbital decompression, including strabismus surgery to correct misalignment of the eyes and double vision, eyelid surgery, or further decompression in the non-operated eye if unilateral surgery was performed.

5.8.1.2 Intervening cognitive processes

A number of self-report questionnaires were chosen for this study that were based on the ARC (2008) framework of adjustment to living with a disfigurement (described in Chapter 4, section 4.3). These questionnaires were all completed by the participant. Section 4.4 of Chapter 4 (page 88) provides a rationale for the particular variables chosen for this study.

5.8.1.2.1 The Brief Fear of Negative Evaluation scale (BFNE; Leary, 1983)

The BFNE examines the extent to which an individual is concerned by other peoples' opinions of them. A validated brief 12-item version of the full Fear of Negative Evaluation scale (FNE), originally developed by Watson & Friend (1969), was used. This brief version correlates highly with the original scale ($\alpha = 0.96$; Leary, 1983). Example items include "I am afraid that others will not approve of me" and "I am frequently afraid of people noticing my shortcomings". Responses are on a 5 point Likert scale from 1 ('Not at all characteristic of me') to 5 ('Extremely characteristic of me'). Four of the items are positively worded and are reverse scored. One total score is calculated, with a lowest possible score of 12 and highest score of 60. Higher scores indicate greater fear of negative evaluation from others.

This brief version of the original scale was preferred in order to keep the length of the questionnaire pack to a minimum and reduce participant burden. There has been some criticism that, because of the complexity of some items, the BFNE may be more appropriate as a two-factor measure of positively worded items (BFNE-S) and negatively worded items (BFNE-R) (Rodenbaugh et al., 2004). However, the inter-item correlation for the BNFE-S is poorer than the 12-item BFNE ($r = .72$; Carleton et al., 2011). The 12-item measure has been found to have excellent inter-item reliability ($\alpha = .97$) and test-retest reliability ($r = .94$) and the ability to discriminate between patients with social phobia than a group of non-clinical community controls (Collins et al., 2005). The BFNE has also been used in previous studies that have evaluated the psychosocial impact of living with a disfiguring eye condition (ARC, 2008; James et al., 2011; McBain et al., 2014) and was therefore considered most appropriate for use in the current study.

5.8.1.2.2 Iowa-Netherlands Comparison Orientation Measure (INCOM; Gibbons & Buunk, 1999)

The INCOM is an 11-item scale that measures how well respondents feel they are doing in life when comparing his or herself to others. Example items include “I always like to know what others in a similar situation would do” and “I often like to talk with others about mutual opinions and experiences”. Responses are on a 5-point Likert scale ranging from ‘strongly disagree’ (1 point) to ‘strongly agree’ (5 points), 2 items are reverse scored. A total score is calculated, with a lowest possible score of 11 and the highest 55. Higher scores indicate a greater tendency to make social comparisons. The scale has been demonstrated to have good internal consistency ($\alpha = 0.83$) and correlates well with similar measures, including the Attention to Social Comparison Information (ATSCI) Scale (r=0.66) (Gibbons & Buunk, 1999). The INCOM has also previously been used in the literature examining adjustment to living with a visible difference (ARC, 2008; James et al., 2011; McBain et al., 2014).

5.8.1.2.3 Multidimensional Scale of Perceived Social Support (MSPSS; Zimet et al., 1988)

This 12-item scale measures subjective levels of social support from three sources: family, friends and significant others. Example items include “I get the emotional help and support I need from my family” and “There is a special person in my life who cares about my feelings”. Responses are on a 7-point Likert scale ranging from 1 (‘Very strongly disagree’) to 7 (‘Very strongly agree’). There are three subscales, with possible scores ranging from 4 to 20 on each subscale (friends, family, and significant others), with higher scores indicating greater perceived social support. The overall scale has good internal consistency (α=0.88) and test-retest reliability (r=0.85) (Zimet et al., 1988), and the factor structure has been supported with excellent internal reliability of each of the 3 subscales: α’s of .91, .89, and .91 were found for the Friends, Family and Significant Others subscale, respectively (Canty-Mitchell & Zimet, 2000). This measure has been used in a study that used the ARC (2008) framework to explore adjustment to strabismus (McBain et al., 2014).

5.8.1.2.4 Development of an Expectations of TED Surgery Questionnaire (E-TEDS)

In the absence of a disease specific measure, assessment of patients' expectations of post-surgical outcomes was undertaken using an adapted version of the Expectations of Strabismus Surgery Questionnaire (ESSQ; McBain et al., *in press*). The ESSQ has three subscales and has been found to have high internal reliability in all subscales (Cronbach's alphas range from 0.76 to 0.89; McBain et al., *in press*). No similar questionnaire currently exists in TED.

One aim of this part of the thesis was therefore to develop a brief measure to quantitatively assess patient expectations before TED surgery. A description of the initial stages of the questionnaire's development will be provided in this chapter and the results of the final questionnaire will be presented in Chapter 6, section 6.6.4.

Three phases of questionnaire development were implemented: item generation and selection, reduction of the items to produce a reliable questionnaire, and validation of the measure. Similar measures developed for other facial disfigurements were consulted for important areas and for item wording (McBain et al., *in press*; Finlay, Atkinson & Moos, 1995). Relevant issues pertaining to expectations of corrective surgery were extracted and these extractions were used to generate items for the new questionnaire. For the present thesis, a literature review of adjustment to living with TED (Chapter 3) was conducted. This identified key articles that reported areas specific to the impact TED has on patients' lives and that were used to establish relevance of the items generated for the TED-specific expectations questionnaire. Participants were asked to complete the new questionnaire as part of the cross-sectional study described in this chapter.

Responses from participants were subjected to a principle component analysis (PCA) using IBM SPSS for Windows (version 21). A PCA helps the analyst determine the number of psychological concepts, or *factors*, present in a questionnaire. The suitability of the data for factor analysis was investigated prior to performing the PCA. The Kaiser-Meyer-Olkin (KMO; Kaiser, 1970) measure of sampling adequacy, Bartlett's Test of Sphericity and the correlation matrix provided in the SPSS output are used to indicate whether characteristics of the dataset are appropriate for PCA.

Guidelines suggest that correlation coefficients for each item in the correlation matrix should not be below 0.3 (Pallant, 2007).

Another way of determining the number of factors to retain is Parallel Analysis, which involves inspection of the eigenvalues obtained and comparing them with a randomly generated dataset the same size. The statistical programme Monte Carlo PCA for Parallel Analysis 2.3 (Watkins, 2000) was used to generate the random dataset. The number of items was entered into the programme, along with the number of participants, and the number of replications. It has been recommended to specify 100 replications for PCA (Pallant, 2007).

Once the number of factors had been established, these were interpreted using a factor rotation. Ideally the rotation will show a simple structure where each item loads strongly onto one factor, and that each factor is represented by a number of strongly loading items (i.e. more than 3) (Pallant, 2007). A number of methods of rotation are available and a balance between interpretability and reliability is sought. Orthogonal rotation does not provide correlations between factors but offers easier interpreting and describing of the results (Tabachnick & Fidell, 2007). Oblique rotation is recommended for use when constructs are likely to be correlated (normally based on previous theory), but can have disadvantages when trying to interpret the results (Tabachnick & Fidell, 2007). The most commonly used rotation technique is direct oblimin, which offers a range of correlations between factors and is recommended by Pallant (2007). Therefore the direct oblimin rotation was chosen for the PCA of the current questionnaire.

Once the structure of the questionnaire had been established using PCA, the internal consistency was checked by ensuring that Cronbach’s alphas were above 0.7 (Pallant, 2007). To ensure that the questionnaire measured what it aimed to measure conceptually, content validity analysis was employed, i.e. the extent that the items represented each construct being measured and covered the potential range of that construct (Field, 2009). This was achieved through a review of the questionnaire by experts in the area: four Consultant Ophthalmic Surgeons, a Professor of Health Psychology a Health Psychologist, and a patient with TED.

The final questionnaire was composed of 23 items and three subscales: expectations of post-surgery visual functioning (11 items), intimacy and social relationships (5 items), and appearance-related concerns (7 items). A full description of the results for the development of the measure is provided in Chapter 6, section 6.6.4. Participants were instructed to rate how they expected surgery to change the various aspects of their lives including for instance “my vision” and “the appearance of my eyes” on a Likert scale from 1 (‘Made considerably worse’) to 5 (‘Considerably improve’). The total score for each subscale was a mean of the responses, such that the possible scores for each subscale ranged from 1 to 5. As this assessed pre-surgery expectations participants only completed the questionnaire at baseline. Cronbach’s alpha and other reliability assessments to ensure the suitability of this questionnaire in TED are also reported in Chapter 6, section 6.6.4.3.

5.8.1.2.5 Derriford Appearance Scale short form (DAS24; Carr, Moss & Harris, 2005)

The DAS24 is a 24-item scale measuring the impact of appearance related distress and concern on social anxiety and social avoidance. Responses for each item range from 0 to 4, with response options varying between items. Where an item relates to the intensity of emotional response, the categories ‘extremely’ to ‘not at all’ are used, whereas other items relate to the frequency of behaviours brought on by self-consciousness require an ‘almost always’ to ‘never/almost never’ response (Moss, Harris & Carr, 2004). For example, the item “I am self-conscious about my feature” has response options on a Likert scale from 0 (‘Never/ almost never’) to 4 (‘Almost always’), and the item “How distressed do you get when going to social events?” ranges from 0 (‘Not at all’) to 4 (‘Extremely’).

A total score is calculated and ranges from 11 to 96, with lower scores representing lower levels of social anxiety and social avoidance. As the focus of the present study was the impact of the appearance of the eyes, respondents were told to focus on this area. It was made clear to participants in the questionnaire instructions that some items might not be relevant to them and to circle the “N/A” if this was the case. This measure demonstrates high internal consistency (α = .92), good test-retest reliability (*r*=0.82) (Carr, Moss & Harris, 2005) and excellent criterion validity with the DAS59 (*r*=0.88) (Moss, 2010). It also discriminates well between those concerned, and those not concerned, about their appearance in different patient groups and between clinical and non-clinical samples (Moss, 2010). The DAS24 has been used widely in previous studies evaluating the impact of living with disfiguring conditions (ARC, 2008; James et al., 2011; Jackson et al., 2006; Clarke et al., 2003).

5.8.1.2.6 Valence of Appearance scale (CARVAL; Moss & Rosser, 2012)

The CARVAL is an 8-item measure of how an individual evaluates his or her own physical appearance. Example items include “I don’t like the way I look” and “The way I look makes me feel good about myself”. Responses range from 1 (‘Strongly disagree’) to 6 (‘Strongly agree’), five of the items are reverse scored, and one total score is calculated that can range from 6 to 36. Higher scores indicate a more negative self-evaluation of appearance. The scale has been found to demonstrate high internal consistency (Pearson’s *r* correlations between 0.72 and 0.84), good construct validity, and strong test-retest reliability (*r*=0.89) (Moss & Rosser, 2012).

5.8.1.2.7 Salience of Appearance scale (CARSAL; Moss & Rosser, 2012)

The CARSAL is a 5-item measure of the extent to which physical appearance is important to the individual. Example items include “I am usually conscious of my appearance” and “I don’t usually give much thought to my appearance”. Responses are on a 6-point Likert scale ranging from 1 (‘Strongly disagree’) to 6 (‘Strongly agree’), three items are reverse scored. A total score is calculated and ranges from 5 to 30; higher scores indicate greater value placed on appearance. The CARSAL has demonstrated good internal consistency (Pearson’s *r* correlations between 0.74 and 0.81), construct validity, and good test-retest reliability (*r*=0.74) (Moss & Rosser, 2012).

5.8.1.2.8 Perceived Visibility of TED

This is a single item measure of how visible participants feel their proptosis is to other people: Responses were on a 7-point Likert scale ranging from 1 (‘Not at all visible’) to 7 (‘Extremely visible’). Similar single item measures have been used to assess visibility in other disfiguring conditions (Moss, 2005; ARC, 2008), including strabismus (Jackson et al., 2006; McBain et al., 2014).

5.8.1.2.9 Hospital Anxiety & Depression scale (HADS; Zigmond & Snaith, 1983)

The HADS is a 14-item questionnaire designed to screen for depression and anxiety in patients with physical health problems. It is made up of two subscales; anxiety and depression. Example items include “I look forward with enjoyment to things” and “I get sudden feelings of panic”. Responses range from 0 to 3 for each item; 8 items were reverse scored.

The two subscale scores are calculated and the total scores for each range from 0 to 21. Higher scores indicating greater levels of anxious or depressed mood. For each subscale scores of 0 to 7 are considered to be in the ‘normal’ range, scores of 8 to10 suggest moderate levels of anxiety or depression and scores of 11 or over are considered as highly indicative of cases of clinical anxiety or depression (Zigmond & Snaith, 1983). This tool has demonstrated high internal consistency (r=0.76 to 0.41 for anxiety scale items and r=0.60 to 0.30 for depression scale items) and good reliability (Zigmond & Snaith, 1983).

The HADS has been used previously in studies evaluating the impact of living with a disfigurement (Jackson et al., 2006; James et al., 2011; Clarke et al., 2003). Whilst mood has been used in previous studies as an outcome of adjustment, including the ARC (2008) study, the HADS anxiety and depression subscales scores were used as predictors of quality of life in the present study. This has been discussed in more detail in section 4.3.3.2.

5.8.1.3 Primary outcome measure

5.8.1.3.1 Graves Ophthalmopathy Quality of Life questionnaire (GO-QOL; Terwee et al., 1998)

The 17-item GO-QOL measures quality of life in patients with TED (Terwee et al., 1998; 1999). Example items include “During the past week, to what extent were you limited in reading, because of your thyroid eye disease?” and “Do you feel that you are stared at in the streets because of your thyroid eye disease?” The measure consists of two subscales: vision-related quality of life and appearance-related quality of life. Responses for each item are on a 3-point Likert scale; ‘severely limited' (1 point), 'a little limited' (2 points) or 'not at all limited' (3 points); with a higher score on each subscale indicating better health.

The GO-QOL has been translated from Dutch into eight other languages including English, French, German, Greek, Italian, Spanish, Russian and more recently, Korean (Wiersinga et al., 2012; Choi et al., 2012). Being able to cycle is important for Dutch patients but in a recent translation for the Australian population, Park et al. (2004) replaced the item about bicycling with two items about limitations in work and carrying out domestic duties. These authors also recognised that not all patients have a driving licence or current employment and in such cases respondents were able to answer 'not applicable' (Park et al., 2004). Therefore in this study for the two items "During the past week, to what extent were you limited in driving/ at work?" it was possible to answer 'not applicable'.

The present study has therefore used the GO-QOL Australian version (Park et al., 2004) but excluded the additional two items in this version about patient education and counselling, which are not included in total scores. Subscales were calculated following guidelines from the authors (Terwee et al., 2001). These are: raw score - number of items in subscale / (2 x number of items in subscale) x 100 (Park et al., 2004). Where data were missing, the guidelines from the original authors of the questionnaire (Terwee et al., 2001) were followed to calculate total scores for the remaining completed items. These are: where there are missing values for some items, total scores are calculated for the remaining completed items. The transformation used for the present study was adjusted to: total score = (raw score – #)/2 X # X 100 where # is the number of completed items. When more than half of the items within a subscale were missing the total score was not calculated. The GO-QOL has been found to be a valid and reliable measure with high internal consistency (α=0.86 for the visual function scale and α=0.82 for the appearance scale; Terwee et al., 2001). The GO-QOL has many advantages over using a generic quality of life measure as it is designed to capture issues specific to patients with TED (Terwee et al., 1998), including the ability to detect a MCID in changes in scores from pre- to post-treatment. A change in GO-QOL scores of 10 to 20 points after decompression surgery is suggested as the MCID (Terwee et al., 2001).

5.8.1.4 *Individual follow up items*

A small number of single items were used at the end of the 6 month post-surgery questionnaire to assess patient satisfaction with their surgical outcomes in 3 areas: satisfaction with surgery, satisfaction with pre-operative information, and side effects from surgery. These items were used for descriptive purposes to complement the main findings from the study.

5.8.1.4.1 Satisfaction with surgery:

Three single items measured overall regret (“Do you regret having surgery?”), satisfaction with the procedure (“Knowing what you do now, would you go through the operation again?”), and likelihood of recommending the operation (“Would you recommend the operation to others?”). Responses for each item ranged from 1 (‘Yes definitely’, or ‘Yes, with no hesitation’) to 4 (‘Not at all’ or ‘Certainly not’).

5.8.1.4.2 Side effects:

Side effects were measured using 4 items, each asked patients how much pain, swelling, scarring, and redness they experienced as a result of surgery. Likert scale responses ranged from 0 (‘No pain/ swelling/ scars/ redness’) to 10 (‘Severe pain/ swelling/ scars/ redness’), shown in Figure 7. Participants were also asked how they would compare each of the side effects to what was expected before surgery, from 1 (‘Much less than expected’) to 5 (‘Much worse than expected’).

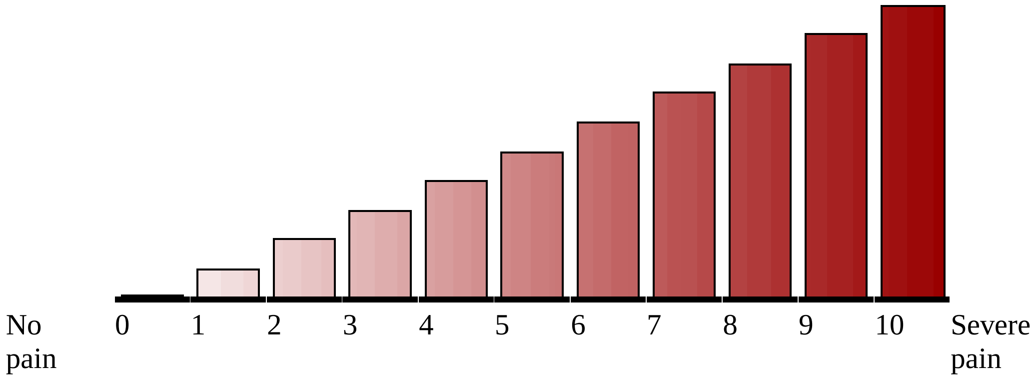


Figure 7. The 10-point rating scale used to measure side effects

5.8.1.4.3 Preoperative information:

Participants were also asked if they were given the right amount of information preoperatively, with response options of ‘Too much’, ‘The right amount’, or ‘Too little’.

5.9 ASSESSMENT PROCEDURE FOR THE QUALITATIVE STUDY

5.9.1.1 Location of the interviews

All interviews were either held in a seminar room in the research department at BMEC, or at the patient's home if they could not easily access the hospital. Safety protocols were carried out when interviews were conducted in the patient's home: the researcher called a member of the supervisory panel before and after each interview. A code word was agreed that the researcher would use if there were any concerns that alerted the supervisor. Fortunately, there were no safety concerns at any time during these interviews. A total of 11 interviews took place in the research department at BMEC and 3 interviews took place in participants' homes. Two of the participants interviewed at BMEC brought their partner, who contributed to the interviews. During one of the home interviews the participants' daughter came into the room for a short while, but did not contribute to the interview.

5.9.1.2 Topic guide

Semi-structured interviewing methods were chosen for this study. Semi-structured interviews allow for more elaboration from the respondent and are favoured by researchers for their balance of the ability of participants to discuss matters important to them and the interviewer having some control through the use of topic guides (Shauver & Chung, 2010). The researcher in collaboration with the supervisory team developed an interview schedule (Appendix L) that included topics based on previous research on patient expectations of surgery (Klassen et al., 2008; Bhty, 1999; Bramwell, Morland & Garden, 2007) and from experience gained whilst recruiting patients with TED for the quantitative study described in this chapter. The use of the interview schedule provided some structure to the interview but questions were designed to be used as prompts rather than a specific format for the interview. This enabled the interview to be directed by ideas brought forward by the participant (Murray & Chamberlain, 1999). Prior to their interview participants were instructed that the researcher had some prompting questions but that these were not fixed and that further questioning depended on their answers to previous questions. The first pre-surgery interview was used to test the utility of the interview schedule, and some changes were made as a result of this first interview (Figure 8). The pilot interview was included in the analysis for this study to avoid losing any valuable data.

All interviews were conducted by the researcher and digitally recorded using an Olympus DS-30 digital voice recorder. The length of the interview depended greatly on the willingness of the interviewee to go into detail about their views and experiences. Prompts were used to elicit further detail about particularly important areas, but equally participants were free to give as much detail as they chose and were not pushed into any topic that they were uncomfortable or unwilling to talk about.

Topics: *current impact of illness on daily activities; current feelings about appearance; treatment options; personal reasons for having surgery; goals for surgery/ outcomes; motivation for going forward with surgery; any influences that others have had on their decision to go for surgery; any events related to appearance that might have had an impact on decision to have surgery; what preparations might they have made for surgery; what are they expecting about outcomes*

Example questions (to be used as a general guideline):

Introduction

1) Can you tell me about the impact TED might have had on your daily life?
   Prompt: Can you tell me about the impact TED might have had on your appearance?
   Prompt: Can you tell me about the impact that TED might have had on how you feel about yourself?

Motivation(s) for having surgery

2) When did you first start thinking about having surgery?
3) Did you consider alternative treatment options? If so, reasons for choosing surgery over others
4) What do you feel your reasons might be for having surgery?
5) Could you tell me what is motivating you to have this surgery?
6) Are there any particular goals you hope to achieve by having surgery?
7) Can you tell me if anything has influenced your decision to have surgery?
8) Could you tell me about what you might have done to prepare for your surgery, or that you plan on doing to prepare before your surgery?

Information about surgery

9) Can you tell me about the information you have been given about your surgery?
   Prompt: By your doctor/ surgeon, nurses, any other healthcare professional?
10) Can you tell me if you have tried to find out more about orbital decompression surgery? If so, where did you look?
11) What do you feel about the information you have been given, or that you have found, about your surgery?
    Prompt: What about the quantity?
12) Can you describe what you expect from the surgery based on the information you have been given, or that you have found?
    Prompt: On the day of surgery, leaving hospital, recovery?

Expectations of surgery

13) Can you tell me what outcomes you might be expecting from your surgery?
    Prompt: Appearance outcomes? Daily life outcomes?

Figure 8. The final topic guide used in the qualitative study to explore patients' expectations of orbital decompression

5.9.1.3 Consent

Participants were asked to bring their consent forms on the day of their interviews and were asked to sign these if they were happy to take part in the study. At the beginning of each pre-surgery interview, participants were also given a demographic details questionnaire, which asked for their gender, age, ethnic background, relationship status, employment status, highest qualification, duration of TED, and surgical history (Appendix M).

Although this information was provided in the information sheet given to patients when they were approached for the study (Appendix I) participants were reminded at the beginning of each interview that any their interviews would be kept confidential, data would be stored in a locked cabinet in a secured office and that any names they gave during interviews would be kept anonymous during transcriptions. All participants were asked for permission to audio record the interview and given an alternative option for the interviewer to make notes if they weren’t happy to be audio recorded. All patients gave their consent to interviews being recorded digitally, however.

5.10 STATISTICAL ANALYSIS

All statistical analyses were performed using the statistical package IBM SPSS for Windows (version 21) for the quantitative study.

5.10.1 Data screening

A process of data cleaning was carried out after all the data had been entered and before any data analysis was performed. Guidelines for data screening and cleaning by Pallant (2007) were used, which involved examining the ranges of scores for each continuous variable to check they fell within possible ranges for each questionnaire item, and checking frequencies of categorical variables to ensure these were within normal limits. Missing data was flagged using the code ‘999’. For the GO-QOL ‘not applicable’ responses, the code ‘555’ was used to distinguish these scores from genuine item omissions. Any potential errors in the data were corrected where necessary during the screening process, for example by returning to raw data if required.

5.10.2 Missing data

Missing data is a common problem in medical and social science research, especially with longitudinal designs. Levels of missing data were analysed using Little's Missing Completely at Random (MCAR) test (Pallant, 2007) to check that there were no systematic differences between the missing values and the observed values.

A missing value analysis conducted at item level involved analysing patterns of missing data to find out how much information would be lost if a listwise deletion was used at baseline; i.e. how much data is to be imputed. The results of the missing data analysis are reported in Chapter 6, section 6.4, page 127. The DAS24 was introduced into the questionnaire pack approximately 6 months into the study following an ethics amendment and therefore items from this measure were missing for a number of participants at baseline.

At baseline multiple imputation (MI) was used to retain as much data as possible (Koutroumanou & Wade, 2012; Rubin, 1987). Any participants with over 50% missing data at baseline however were removed from the analysis on research question (1). In addition, any participants with over 50% missing data for the entire dataset were removed from the analyses concerned with research questions (3), (4), (5) and (6). MI at item level was performed on the data for the cross-sectional study. This was to enhance the accuracy of the re-calculated scale scores, and constraints and rounding were used to ensure that the imputed item level data was meaningful and corresponded to possible values. Analysis using a multiply imputed data set allows for uncertainty about missing data by using several plausible datasets, and appropriately combining the results obtained from all the datasets (Sterne et al., 2009). MI is an iterative approach that calculates imputations based on the information available from scores available for each participants; using 10 imputations therefore increases the accuracy of the study results (Rubin & Schafer, 1990).

For this study a total of 10 imputed datasets were produced and pooled results from all 10 datasets were used in the baseline analysis. Subscale scores were re-calculated using the imputed items. For the GO-QOL, answers of 'not applicable' were retained and subscale raw scores and transformations were calculated as guided by the original authors of this measure (Terwee et al., 2001).

5.10.3 Data exploration

5.10.3.1 Normality and outliers

Normality was assessed using histograms and normal probability plots. Pallant (2007) describes normal data as having a symmetrical, bell-shaped curve with the greatest frequency of scores in the middle, i.e. around the mean. Normal probability plots display the observed value for each score plotted against the expected value from the normal distribution, and a straight line should be seen if the distribution is normal (Pallant, 2007).

Normality was also assessed in terms of skewness and kurtosis in the data. Skewness refers to the symmetry in the distribution and kurtosis provides information about how peaked in the middle the data are (Pallant, 2007). The Shapiro-Wilk test, which is recommended for smaller samples, was used to assess whether the distribution deviated from a comparable normal distribution (Field, 2009), with a significant result indicating non-normality. However, Field (2009) warns of the sensitivity of this test to capture even small deviations from normality and a significant result may not be enough to indicate bias in statistical analyses. Therefore the results of this test were considered alongside distribution plots and histograms. One option for dealing with non-normality is to perform transformations on these scales. However by transforming the data you do not only change the hypothesis being tested but also the constructs that were originally measured and this reduces the interpretability of the results (Grayson, 2004). Therefore, transformations were avoided for this study and non-parametric statistical analyses were used instead, which are widely recommended (Field, 2009).

The imputed dataset generated 10 histograms in total: one for each dataset. Assessing normality data for 10 imputations therefore involved checking the results from the first imputation, provided that there were no great differences between the results from each imputation.

Outliers were assessed by first checking the tail ends of the distribution from each histogram. Boxplots were also generated for each scale score and assessed for extreme values more than 1.5 box-lengths from the edge of the box, indicated by an asterisk (Pallant, 2007). Outliers can pose a problem if they influence overall results, however there is disagreement amongst researchers about how to deal with outliers and a number of options are available (Tabachnick & Fidell, 2007). Removing the participants from the analyses is one option but this would only be beneficial if it is certain that the case is not from the population intended to sample (Field, 2009). Furthermore, removing participants due to random outlying scores would result in a significant reduction in sample size and it was felt for this study that the data may still provide useful information about relationships between variables and therefore any outliers were retained in the analyses.

5.10.3.2 Internal reliability of scales and subscales

All the measures included in the study were assessed for reliability using Cronbach's alpha with scores above 0.7 indicating acceptable levels of reliability (Pallant, 2007).

5.10.4 Data analysis

5.10.4.1 Research question (1): Which factors are associated with quality of life in patients with TED presenting for surgery?

Hierarchical multiple regressions were used to investigate research question 1. Hierarchical multiple regressions require that all predictor variables are either continuous or categorical with two categories, or they are dummy coded to be made binary. Therefore categorical predictor variables with more than two groups were dummy coded where appropriate. If there were extremely few participants in a third group, the groups were collapsed into two, for example "white" and "non-white" for ethnicity.

The hierarchy used to enter the predictors into the regression was based on the ARC (2008) framework of adjustment to disfiguring conditions (Figure 9). Entered into block 1 were the demographic variables, clinical variables formed block 2, socio-cognitive processes (fear of negative evaluation, social comparisons and perceived social support) were entered in block 3, expectations were entered in block 4 and appearance related cognitions (social anxiety and social avoidance, salience and valence of appearance, and perceived visibility of TED) were entered in block 5. Levels of anxiety and depression were entered into block 6. Each of the GO-QOL subscales were the outcome variables, or dependent variables (DVs).

Entry rather than *stepwise* methods were used as stepwise methods will not necessarily produce the best model if there are redundant predictors, rather the model is purely statistically driven and carries an inflated risk of creating results from chance features in the data (Judd, Clelland & Ryan, 2009; Tabachnick & Fidell, 2007). Effect sizes for multiple regression (Cohen's f^2) were calculated: a value of 0.02 is considered a small effect, 0.15 is considered a medium effect, and 0.35 is considered a large effect (Cohen, 1992).

Thirty six predictor variables in total were measured in the quantitative study and guidelines suggest 10 participants per predictor variable are required to reach power for hierarchical multiple regression (Field, 2009). Following guidelines that suggest reducing the number of predictor variables when using smaller sample sizes (Harrell, Lee & Mark, 1996), univariate linear regression analyses were first performed to determine whether a predictor variable (IV) was significantly associated with each dependent variable (DV) and thus should be entered into the hierarchical regression.

The IVs were examined for multicollinearity, linearity and homoscedasticity. Multicollinearity occurs when two predictor variables are highly correlated ($r > .90$) and poses a problem in multiple regression as it becomes impossible to assess the individual importance of a predictor (Field, 2009). Multicollinearity is also identified using the VIF scores provided in SPSS output from the regression analyses. VIF values above 10 indicate multicollinearity and it is advised that the variable with the highest VIF value is removed from the regression (Field, 2009). A further requirement of hierarchical multiple regression is that each IV has a linear relationship with the DV (Field, 2009). After each hierarchical regression was performed, assumptions of the model were checked to ensure that the model generalised beyond the sample (Field, 2009). This involved assessing the histograms and normal probability plots of the saved residuals to check for normal distributions. Violations of these assumptions would weaken the results of the regression analyses, but not invalidate them.

PREDISPOSING FACTORS		**INTERVENING PSYCHOLOGICAL PROCESSES**				**OUTCOMES**
Demographic (BLOCK 1)	**Clinical (BLOCK 2)**	**Socio-cognitive Factors (BLOCK 3)**	**Expectations (BLOCK 4)**	**Appearance-specific Cognitions (BLOCK 5)**	**Mood (BLOCK 6)**	**Quality of Life**
Age Gender Ethnicity Relationship status	Disease duration Smoking Previous treatments Thyroid function Laterality of TED Laterality of surgery Optic neuropathy LogMAR Exophthalmos Asymmetry Corneal SPK Hydraulic orbit MRD1 MRD2 Diplopia CAS score	Fear of negative evaluation (BFNE) Social comparisons (INCOM) Perceptions of social support (MSPSS)	E-TEDS appearance concern E-TEDS visual function E-TEDS intimacy and social relationships	Appearance-related social anxiety & avoidance (DAS24) Evaluation of own appearance (CARVAL) Salience of appearance (CARSAL) Perceived visibility	Anxiety (HADS) Depression (HADS)	GO-QOL visual function GO-QOL appearance

Figure 9. The potential variables to be used in the hierarchical multiple regression used for the analysis of research questions (1) and (4). Note that the analysis for research question (5) did not include the E-TEDS subscales. Framework adapted from ARC (2008)

5.10.4.2 Research questions (3) and (4): Which clinical and intervening psychosocial factors change after surgery?

To assess change over time from pre- to post-surgery, a multilevel modelling (MLM) approach was employed. This method of analysis takes into account the non-independence of scores given on the same questionnaire by the same participant at different time points, i.e. that data points are more similar within individuals over time than they are between individuals (Cartwright, Traviss & Blance, 2012). MLM approaches are recommended when data has been collected from individuals on more than one occasion, as multilevel models imply that scores are clustered within each individual.

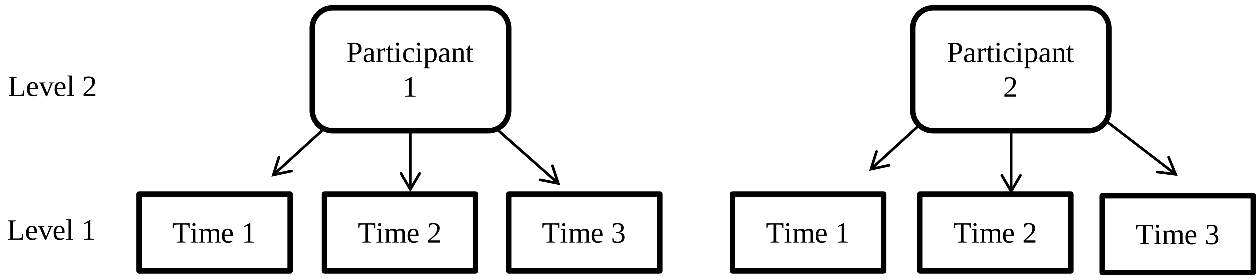


Figure 10. The hierarchical structure used to model the data for research question (3): which clinical and psychosocial factors change over time?

Heck and colleagues (2014) have made recommendations for dealing with longitudinal data using MLM in SPSS that were used to guide this analysis. Firstly, data was restructured into a higher level (level 2, or participant-level) arrangement that recognised the hierarchical structure of the data (Figure 10) which resulted in each participant having three rows of observations, each row indicating a time point.

For the continuous scales, an unconditional model (that did not account for the effects of time) was first applied that allowed intercepts to vary by participants and simultaneously allowed assessment of the proportion of variance at level 2 (the participant level). The intraclass correlation (ICC) estimates the amount of variance in the outcome that can be explained by between-participant variance and the higher this statistic, the more similar the units (i.e. substantial variability exits between participants) (Heck, Thomas & Tabata, 2014). The ICC indicates whether the higher level grouping affects estimates in a way that makes MLM suitable for this data. A cut-off score of 0.05 is used, with an ICC smaller than this suggesting little advantage in conducting MLM (Heck, Thomas & Tabata, 2014). MLM was performed for all variables with ICCs higher than 0.05, with each scale score as the dependent variable and with the effect of time controlled for. To measure the standardised effect size of the fixed effect of time, partial eta squared (ŋ^{2}p) was calculated, which is recommended for use when no other covariates are entered (Lakens, 2013).

As effects of repeated measures (i.e. time) were used in the MLM, a covariance structure was chosen to specify the model parameters. A number of options for this were available in SPSS, including the *diagonal* variance structure, which assumes all variances at each time point are heterogenous, the *unstructured* option, which assumes covariance are unpredictable, and the *first-order autoregressive structure* (AR1), which takes into account the correlation between repeated measures and assumes that whilst scores between the first two time points are likely to be correlated, scores become less correlated over time (Field, 2009). An autoregressive structure (AR1) was therefore chosen to model the correlation structure of within participant effects for this analysis, as scores at adjacent time points were likely to be correlated and are not assumed to be heterogeneous or unpredictable within each participant.

Change over time within each of the intervening psychosocial process variables and continuous clinical variables (exophthalmos, asymmetry, visual acuity, disease activity, and eyelid retraction) were also assessed using adjusted mean scores with time entered as a categorical variable in the SPSS command. Effect sizes were calculated for the effects of time again using partial eta squared (ŋ^2_p), as described above. To examine whether significant change was seen between baseline and 6 week follow-up, baseline and 6 month follow-up, and between the 6 week and 6 month follow-ups, pairwise comparisons were performed on the adjusted mean scores. Pairwise comparisons can compare all possible time point combinations whilst controlling for family wise error rates (i.e. the inflated error from conducting several statistical tests on the same data) by correcting the level of significance for each test so that the overall Type 1 error rate across comparisons remains at 0.05 (Field, 2009). When MLM is performed SPSS provides standard error values rather than standard deviations. Standard deviations were therefore manually calculated using the formula: [SE * √n] where the standard error was multiplied by the square root of the sample size (Higgins & Green, 2011).

To assess change over time in the categorical variables (optic neuropathy, diplopia, hydraulic orbit and corneal SPK), a variation of MLM designed specifically for repeated measures categorical outcomes was applied. This also involved calculating ICCs and entering time into the model as an ordinal variable. The log odds of the intercept was used to identify the predicted probability of having optic neuropathy, diplopia, hydraulic orbit and corneal SPK at each time point, a significant result would indicate whether the likelihood of having one of these clinical factors at baseline and 6 weeks, or baseline and 6 months, decreased (Heck, Scott & Tabata, 2012). SPSS produced a β value, which represents the log odds coefficients, and the effect size for odds ratios, Exp(β), which represents exponentiated log odds (Field, 2009). These two values were used to assess the probability of any of these variables being present from one time point to another (Heck, Scott & Tabata, 2012). Results of these analyses are reported in Chapter 9.

5.10.4.3 *Research question (5): Do baseline factors predict change on quality of life from pre- to post-surgery?*

Change over time was calculated using residualised change scores. This involved conducting a linear regression in which the 6-month score on a variable was predicted from the baseline score and the standardised residuals produced by SPSS were saved as new variables. This method has been used widely in health research to measure relationships between variables over time (e.g. Crocker et al., 2006; Sallis et al., 1999; Barerra, Toobert & Strrycker, 2012). Residualised change scores are recommended over raw change scores as they are able to describe the direction or magnitude of change from baseline to follow-up whilst removing the dependency from the baseline score. By contrast, raw scores mean that participants are more likely to have a positive direction of change if they start low and a negative direction of change if they start high (Fleeson, 2007).

In order to establish pre-surgical predictors of change in quality of life, residualised change scores were calculated for vision- and appearance-related quality of life.

Following this, two further hierarchical multiple regressions were performed, with change in quality of life subscale as the DV and baseline predictors as the IVs. Baseline variables that were found to be significantly associated with the changes in quality of life in univariate linear regressions were entered into the model. Again, the ARC (2008) framework was used as a guide to model entry into the regression and predictors were entered in the same blocks as for research question (1), and shown in Figure 9.

Assumptions of multicollinearity, linearity and homoscedasticity were checked following these regressions as described in section 5.10.4.

5.10.4.4 *Research question (6): Which changes over time in clinical and psychosocial factors predict change in quality of life over time?*

Residualised change scores were calculated for each of the intervening psychosocial variables from pre- to post-surgery. These were then assessed for significant predictive value against change in the DVs. Baseline variables that were not expected to change but may expect to have some effect on quality of life, including age, gender, ethnicity, thyroid function, previous treatment, laterality of TED and surgery, and smoking, were entered into the first stage of the regression if they were found to be associated with a change in quality of life in the univariate regressions described in section 5.10.4.3 to control for any significant effects of these variables at baseline.

The same model was applied for entering predictors into the regression as for research questions (1) and (4). The procedures to check the assumptions of the regression models for research question (1) (described in section 5.10.4) were repeated after the analysis for research question (5).

Results of the analysis for questions (4), (5) and (6) are reported in Chapter 9.

5.11 QUALITATIVE ANALYSIS

The data generated from the semi-structured interviews were analysed using thematic analysis (Braun & Clarke, 2006).

Thematic analysis was chosen as the most appropriate method for this study. Interpretative Phenomenological Analysis (IPA) was not chosen as it is concerned with capturing in-depth the lived experience of an individual (Smith, 1996) and is suited to smaller numbers of homogenous participants (between 3 and 6) due to the depth of understanding individuals rather than a group of patients (Smith et al., 2009). Grounded theory aims to develop a new theory from the data (Strauss & Corbin, 1990), which was not the overall aim of this study. Framework analysis (Ritchie & Spencer, 1994) involves a similar set of phases as thematic analysis to systematically identify themes, however thematic analysis has been widely used in previous qualitative research on patient expectations of surgery and hospital care (Estcourt, 2008; Bhty, 1999; Bramwell, Morland & Garden, 2007) and was deemed a well-suited approach for this topic and the aims of this research study.

There exist two approaches to thematic analysis: an inductive, data-driven approach that allows the research question to evolve through the coding process, and a theoretical, top-down approach that uses previous theory to code the data (Braun & Clarke, 2006). A theory-driven approach was taken for this study as previous research was used to generate specific research questions and objectives. Theory-driven code development is the most common approach in social science research (Boyatzis, 1998).

Thematic analysis involves searching across the dataset to identify, analyse and report patterns within the data (Braun & Clarke, 2006). The specific steps used to analyse the data are described in the following sections. Clarke and Braun (2013) urge investigators not to view these steps as linear, where one phase needs to be completed before moving onto the next; rather the analysis is a recursive process.

5.11.1.1 Familiarisation with the data

Firstly, audio files were played back to ensure accuracy of the written transcriptions and for familiarisation of the data. At this point any identifiable names were changed. Any reference to other individual’s names that could potentially identify them was replaced with a generic description, for example [the surgeon] replaced any reference to surgeon’s names and [daughter] replaced the interviewee’s daughter’s name. All medical terms were checked against published clinical articles to ensure correct spellings. Transcriptions were read and re-read, initially to become familiar with the breadth and depth of the content, and later to read the data in an active way, where any initial meanings and possible patterns were noted. Transcripts were uploaded into NVivo version 10 for Windows (QSR International, 2014).

5.11.1.2 Coding

The coding process was considered part of the data analysis as it involved the production of initial codes from features in the data that the researcher found interesting (Braun & Clark, 2006). Data items that appeared across the data set were considered ‘patterns’ and were thus coded (Marks & Yardley, 2004). To collate data extracts within each code, NVivo version 10 was used by adding extracts of text to ‘nodes’ defined by the researcher. Individual extracts were coded into as many codes as they fitted.

Boyatzis (1998) describes a good thematic code as one that “captures the qualitative richness of the phenomenon” (p.31) and that would be likely to produce high inter-rater reliability and validity. Five key elements of the good thematic code are the use of a label, a definition of the characteristic of concern, a description of when to use the code, a description of any qualifications or exclusions to identify the code and giving examples of the code to avoid confusion (Boyatzis, 1998). Therefore these guidelines were followed during coding for the present study.

Using Boyatzis’ (1998) guidelines each label was conceptually meaningful, clear, concise and close to the data, i.e. one that avoided any interpretation of the data at this stage. Marks and Yardley (2004) also suggest that coding categories form a hierarchy with higher-level categories and sub-categories within these. For example, for the present study a higher level category was ‘impact of having TED’ (reduced to ‘impact’), as this was commonly discussed by interviewees, and the lower level category was the particular area of impact, such as ‘employment’, which formed the code ‘impact-employment’.

Each transcript was examined a second time to identify any further codes (Braun & Clarke, 2006). The resulting codes were collated into a thematic coding framework and labels, descriptions, qualifications or exclusions and examples were given for each. The transcripts were then read a third time to check the accuracy of the first stage of coding and to apply any codes identified during later transcripts. After this process the thematic coding framework was reviewed and any entirely overlapping codes merged to form one code. The descriptions for each code within the ‘Thematic Coding Framework’ (Appendix N) were used to guide consistency in meaning within each code. Any clearly irrelevant extracts at this stage were ‘uncoded’ using a command in NVivo in order to keep the data within each code consistent. The data within each code was finalised and ready for the process of identifying themes.

In order to validate the coding process, a second researcher with experience in thematic analysis was asked to independently code 20% of the interviews. These codes were compared to the original coding and any discrepancies were discussed until consensus was reached.

5.11.1.3 Searching for themes

Codes were reviewed and combined into broader, overarching *themes*. A theme was defined as a coherent and meaningful pattern within the data relevant to the research question (Clarke & Braun, 2013). An initial thematic map was drawn to organise codes into themes that they fitted into (Braun & Clarke, 2006). At this point any relationships between codes, themes, and different levels of themes, or sub-themes were identified. This phase ended with candidate themes, sub-themes, and all the data extracts that were coded into these.

5.11.1.4 Reviewing themes

The next phase involved reviewing these themes against the data extracts to ensure that data within themes cohered together meaningfully (Braun & Clark, 2006).
The entire dataset was read again to check that the themes accurately described the patterns in the data, and to code any additional data within themes that was missed in earlier coding stages (Braun & Clark, 2006). A final thematic map was developed that visually represented the themes and the relationship between themes (Figure 16).

5.11.1.5 Defining and naming themes

Once the thematic map was finalised theme names were checked for accuracy in defining what each theme was about. Braun and Clark (2006) suggest that names of themes should be concise and immediately give a sense of what the theme is about and this guideline was implemented for the current study. This phase continued into conducting and reporting the detailed analysis.

5.11.1.6 Validation of the methodology

Validity has a different meaning in qualitative research and rather than judge the statistical validity of a qualitative study, it is more useful to judge how rigorous methodology has been applied (Shauver & Chung, 2012). There is a need for qualitative researchers to be transparent in their methods. Tong, Sainsbury and Craig (2007) developed the Consolidated Criteria for Reporting Qualitative Research (COREQ); a 32-item checklist designed to guide quality reporting of qualitative methods and results. The COREQ was used for the present study. As is good practice for most qualitative approaches, notes were taken during interviews and the analytic process that identified the position of the researcher in the research process and any factors that might have influenced participants' responses (Mauthner & Doucet, 2003).

A reflexive account has been reported in Chapter 7, section 7.5. The researcher used this account to recognise their own values, interests and views when transcribing and analysing the data. A reflexive account can increase the validity of qualitative findings as the researcher is encouraged to be transparent in all their decisions regarding data collection and analysis (Mauthner & Doucet, 2003). The researcher kept notes during each interview and the analytic process that described any factors that the researcher felt might have influenced the interviewee, and their own analysis of the data (Appendix Q).

The results of this study have been provided in Chapter 7.

6. WHAT FACTORS ARE ASSOCIATED WITH QUALITY OF LIFE IN PATIENTS WITH TED PRESENTING FOR ORBITAL DECOMPRESSION SURGERY?

6.1 PROLOGUE

This chapter presents the results from a cross-sectional study investigating the demographic, clinical and psychosocial factors associated with quality of life in people with TED. Baseline characteristics of the patients approached and recruited to the study are presented, including the sample size and reasons for not taking part, followed by the demographic and clinical characteristics of those who completed a baseline questionnaire. The missing data analysis will also be provided, along with normality of the scales and subscales and internal reliability of each measure.

As there is currently no questionnaire that assesses the expectations of patients with TED about their upcoming surgery, the development and validation of a questionnaire designed to measure this area will also be described below (Section 6.6.4)

6.2 SUMMARY OF ANALYSIS

Two multiple hierarchical regression analyses were conducted in order to establish whether the variables measured prior to surgery were significantly associated with vision-related and appearance-related quality of life. The results from these analyses will be reported in section 6.7 of this chapter.

6.3 RECRUITMENT

During the recruitment period (from September 2011 to July 2013), a total of 192 potentially eligible patients were identified and were invited to take part in the study. Of these, 119 (62%) patients were approached in the outpatient clinic and all took home the information sheet, consent form and baseline questionnaire. An additional 73 patients were identified on surgery lists from the PAS system at MEH and were contacted by telephone about the study. Patients who expressed an interest in taking part over the phone were posted information sheets, consent forms and baseline questionnaire packs. Of all the patients approached (n=192), 60 (31.3%) were followed up by phone or letter as they did not respond to the initial invitation within 4 weeks. A number of the invited patients did not take part in the study. Fourteen

(7.3%) had their surgery cancelled and not re-booked during the period of recruitment, 15 (7.8%) declined to take part giving reasons such as not having time or feeling too ill to take part (see Table 6 for specific reasons), and 28 (14.6%) did not return consent forms despite confirming their willingness to take part in the study. One patient (0.5%) was misclassified as being listed for orbital decompression for TED on the PAS system.

Table 6. Reasons given by participants for declining to take part in the study

Reasons given by patients for declining to take part	**Number (%)**
Too ill from TED and other health problems	2(13.3%)
Emergency surgery, too little time to complete questionnaire	2(13.3%)
Partner did not feel patient would be well enough	1(6.7%)
Not interested in taking part in research	2(13.3%)
Did not want additional stress of filling in lots of forms	8(53.3%)
Total	**15(100%)**

Of the 135 (70.3%) patients who consented; 3 (1.6%) did not return their baseline questionnaire despite responding positively to reminders, 1 (0.7%) did not have time to fill in the questionnaire as their surgery for optic neuropathy was an emergency and occurred on the following day, 1 (0.7%) patient had their surgery cancelled and not re-booked, 5 (2.6%) baseline questionnaires were lost in the post, and two (1%) patients had their surgery cancelled as they were found to have a condition other than TED during biopsies. A total of 123 (64%) participants consented to take part in the study and returned the questionnaire prior to surgery.

6.4 MISSING DATA

A total of 149 items were to be completed for the cross-sectional study; 131 by the participant and 18 by the consultant ophthalmologist. The item level analysis revealed that a total of 2,183 values were missing (11.91%). Two participants (1.6%) were found to have high levels of missing data (i.e. greater than 50%); 9 (7.32%) participants had no missing data. The two participants with high levels of missing data were removed from the analyses as there was a risk that imputing over 50% missing data would give inaccurate results.

The MCAR test was not significant at item level ($\chi^2 = 7126.656$, $df = 8177$, $p = 1.000$) meaning that the data were missing completely at random. Therefore multiple imputation at item level was considered appropriate (IBM, 2011). Following the data imputations, scale scores for the psychosocial variables were re-calculated. The analyses described in this chapter were conducted on each of the 10 imputed datasets and the results were pooled. This provides valid inferences as this process averages over the distribution of the missing data given the observed values (Sterne et al., 2009).

6.5 DATA ASSUMPTIONS

6.5.1 Scale reliability

All scales and subscales of the psychosocial questionnaires used in the study showed excellent internal reliability as Cronbach’s α scores were over 0.7 (Table 7). Therefore no items needed to be removed and original scales and subscales were retained for the analysis. The internal reliability of the subscales for the E-TEDS are presented in Table 12, page 139.

Table 7. Number of items and internal reliability for each scale and subscale in the cross-sectional

Scale & subscale	N	No. of items	Cronbach’s α
HADS Anxiety	121	7	0.88
HADS Depression	121	7	0.83
DAS24	121	24	0.86
GOQOL Visual function	121	9	0.90
GOQOL Appearance	121	8	0.86
CARSAL	121	5	0.82
CARVAL	121	8	0.83
MSPSS Friends	121	4	0.93
MSPSS Family	121	4	0.92
MSPSS Significant other	121	4	0.97
BFNE	121	12	0.86
INCOM	121	11	0.86

6.5.2 Normality

The histograms and normal probability plots indicated that normal distributions were observed for the majority of the variables; however for the CARSAL, CARVAL, perceived visibility, and the three MSPSS subscales, data appeared skewed to the right (towards higher scores). The Shapiro-Wilk statistic was also significant (p<0.05) for all scales and subscales apart from age, BFNE and INCOM, suggesting a violation of the assumption of normality. As transformations are often complex and result in non-interpretable data (as described in section 5.10.3.1, page 114), scores were not transformed and therefore non-parametric tests were undertaken where necessary.

6.6 SAMPLE CHARACTERISTICS

6.6.1 Demographic & clinical factors

The age of the participants ranged from 22 to 79 years, with a mean of 47.1 years (SD=12.32). The majority of the sample was female (72.7%). Ethnicity was originally categorised into 11 groups as described in Chapter 5 section 5.8.1.1.1. However due to small numbers of participants in some groups this was collapsed into three groups: White, Asian and Black. The majority of participants were White (78.5%), married or living with a partner (60%), and had bilateral disease and stable thyroid function. Twenty-two (18.2%) patients with bilateral disease were having unilateral surgery due to either a preference to have one eye operated on at a time, or because their bilateral TED was asymmetrical and consultations with their surgeon resulted in the decision to operate on the most severely proptosed eye first in an attempt to achieve symmetry from a single operation.

Table 8. Descriptive statistics of the demographic and clinical variables of the sample (n=121)

Variable	n (%)	Range	Mean±SD
Age (years)		22-79	47.1±12.32
Gender			
Male	33(27.3)		
Female	88(72.7)		
Ethnicity			
Asian	11(9.1)		
White British/Irish/Other	95(78.5)		
Black African/Caribbean/Other	15(12.4)		
Relationship Status			
Married/Living with partner	73(60)		
Single/Other	48(40)		
Disease duration (months)		4-336	62.01±42
Laterality of TED			
Bilateral	101(83.4)		
Unilateral	20(16.6)		
Laterality of planned surgery			
Bilateral	79(65)		
Unilateral	42(35)		
Treatment history			
Previous immunosuppressants	58(48)		
Previous radiotherapy	18(15)		
Previous surgery	14(11.6)		
Thyroid function			
Stable	106(87.6)		
Unstable	15(12.4)		
Visual acuity (LogMAR conversion)		0-2	0.1±0.4
Corneal SPK	39(32)		
Hydraulic orbit	25(21)		
Optic neuropathy	15(12.4)		
Diplopia	62(51.2)		
Marginal reflex distance 1 (mm)		1.5-13	5.92±2.1
Marginal reflex distance 2 (mm)		4-11	6.73±1.4
Exophthalmometry (mm)		15-33	23.7±2.67
Asymmetry (mm)		0-8	1.8±1.8
CAS		0-9	1.12±1.9
Smokers	38(31.4)		

Disease duration ranged from 4 to 336 months (median 42 months, or 3.5 years). Almost half the sample (48%) had previously received immunosuppressant therapy, a small group of patients had received previous radiotherapy (15%) and previous surgery (11.6%); with 8 having had previous eyelid lowering (6.6%) and 6 previous orbital decompression (5%). Half the sample was experiencing double vision at the time of surgery (51.2%), around a third had corneal SPK, (32%), and just over 10% had optic neuropathy. Around a third of the sample was smokers (31.4%). The mean CAS score for this sample was low, with 84.3% of the sample scoring between 0 and 3which indicates non-active TED.

6.6.2 Intervening psychosocial factors

Table 9 summarises the mean scores on each of the intervening cognitive psychosocial variables, and the outcome variables.

Table 9. Mean scores for the psychosocial measures the present sample (n=121)

Variable	Min	Max	Max Possible	M	SD
BFNE	14	60	60	38	9.16
INCOM	16	54	55	36	7.2
MSPSS Family	4	20	20	15.3	4.5
MSPSS Friends	4	20	20	15.2	4.2
MSPSS Significant other	4	20	20	15.6	5.2
CARSAL	5	30	30	25.2	4.7
CARVAL	11	48	48	38.7	8.4
DAS24	22	83	96	51.3	13.1
Men (n=33)	22	83	96	50.7	15
Women (n=88)	22	83	96	51.6	12.4
Visibility	1	7	7	5.7	1.5
HADS Depression	1	21	21	9.2	4.9
HADS Anxiety	0	19	21	7.6	4.7
GOQOL Appearance	0	93.8	100	36.3	24.1
GOQOL Visual function	2.8	100	100	64	26.7

Mean scores indicate this sample generally experienced fear of negative evaluation from others, a high tendency to make social comparisons, and high levels of appearance-related social anxiety and avoidance. There was no significant difference between men and women in their appearance-related social anxiety and social avoidance (DAS24) *t*(223) = -0.29, *p* = 0.772, which was found to have a small effect *r* = 0.05. The mean score for depression in this sample was 9.2 (SD=4.9) and anxiety was 7.6 (SD=4.7). It was found that 25.6% of the sample experienced probable clinically relevant levels of depression and over a third (37%) experienced probably clinically relevant levels of anxiety. Twenty-five (20.7%) of the sample were experiencing clinical levels of both anxiety and depression.

6.6.3 Quality of life

This sample was found to have relatively low mean GO-QOL appearance scores, although vision-related quality of life was not as low. Of note are the large standard deviations for these subscales indicating that the variation in scores between participants was considerable, with some patients scoring on the extremely low end of the scale, particular for GO-QOL appearance.

6.6.4 Expectations of TED Surgery Questionnaire (E-TEDS)

6.6.4.1 Item generation

Following the item selection process described in Chapter 5, section 5.8.1.2.4 of this thesis, a total of 26 items were pooled that covered three different conceptual areas of expectation: visual functioning, intimacy and social relationships, and appearance-related concerns. All 121 participants completed these items on a 5-point Likert scale ranging from 1 (‘Considerably improve’) to 5 (‘Made considerably worse’). The questionnaire instructed participants to “rate how you expect surgery to change various aspects of your life”.

6.6.4.2 Item reduction

The KMO for the original 26 items was 0.95, exceeding the recommended value of 0.6 (Pallant, 2007). Bartlett’s Test of Sphericity was statistically significant (p<0.001) and the correlation matrix revealed coefficients that were all above 0.3, supporting the factorability of the correlation matrix. The only exception to this was in the case of the item “The relationship with my eye doctor” which showed slightly weaker correlations with the other scale items (*r*s were between 0.26 and 0.50).
The PCA revealed the presence of three factors with eigenvalues above 1 and an inspection of the screeplot (Appendix O) showed a clear break between the second and third factors, further indicating the presence of three factors. The 26 items

loaded relatively strongly onto three distinct factors in the *component matrix*, with more than three items on each, which further supported the three factor solution. To aid the interpretation of these factors an oblimin rotation was performed, which showed that all items loaded strongly onto three distinct factors (Appendix P). It was felt that these factors confirmed the three key areas for expectations of upcoming surgery; visual function, appearance-related concerns and intimacy and social relationships, also reflecting the previous measures of expectations that were consulted in the item generation phase (McBain et al., *in press*; Finlay, Atkinson & Moos, 1995).

Inspecting the pattern matrix further, two items loading onto the factor representing expectations about appearance-related concerns did not fit well conceptually. These were “My dry eyes” and “My headaches/ eye pain”, which are more likely representations of visual functioning. Along with the item “The relationship with my eye doctor”, which showed slightly weaker correlations with the other items in the correlation matrix, these items were removed. In order to assess the suitability and factorability of the 23 items, the PCA process was repeated. Inspection of the correlation matrix this time showed that all coefficients were 0.3 and above. KMO was 0.94 and Bartlett’s Test of Sphericity reached significance ($p < 0.001$), supporting the factorability of the correlation matrix. The PCA again revealed the presence of three factors with eigenvalues above 1 and the total variance explained by this three factor solution was 76%.

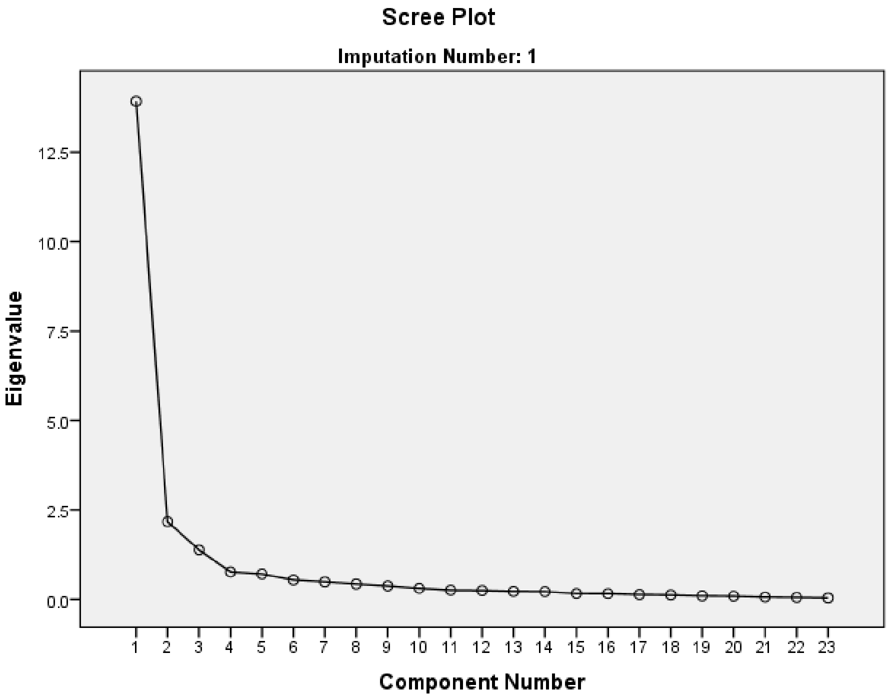


Figure 11. A screeplot showing the presence of factors for the Principle Component Analysis (PCA)

The majority of the items loaded strongly onto only one factor, however the item "My ability to make new friends" loaded onto two factors; intimacy and social relationships (r=0.48) and appearance-related concerns (r=0.52). After a discussion with a second researcher who developed the ESSQ (HM) it was agreed that "My ability to make new friends" should be included in the intimacy and social relationships subscale as this made more conceptual sense. Three items that loaded onto two factors were retained in the factor that made conceptual sense i.e. "My ability to move around the house" and "My double vision" were retained in the visual functioning subscale and "My ability to form new intimate relationships" was retained in the intimacy and social relationships subscale. There were moderate correlations between the factors measuring visual function and appearance concern (r=0.58), between appearance concern and intimacy and social relationships (r=-0.44) and between visual function and intimacy and social relationships (r=0.43), further supporting the use of three factors and 23 items.

Table.10. Pattern and structure matrix of E-TEDS following Principle Component Analysis (PCA) with oblimin rotation

Item	**Pattern Coefficients**			**Structure Coefficients**		
	Factor 1	**Factor 2**	**Factor 3**	**Factor 1**	**Factor 2**	**Factor 3**
5. Move around the house	**0.96**	-0.31		**0.92**	0.65	0.41
6. Perform domestic duties	**0.96**			**0.91**	0.64	0.40
9. Watch TV T1	**0.85**			**0.91**	0.6	0.39
4. Drive	**0.83**			**0.89**	0.38	0.49
10. Use the computer	**0.82**			**0.88**	0.34	0.49
8. Read	**0.82**			**0.87**	0.59	0.43
12. Walk outdoors	**0.79**			**0.85**	0.69	0.54
1. Vision	**0.76**			**0.84**	0.61	0.32
7. Engage in my hobby or pastime	**0.64**			**0.80**	0.49	
13. Double vision	**0.61**			**0.74**	0.59	0.41
11. Work at my usual job	**0.59**			**0.74**	0.60	0.32
23. Mask the changes in my appearance		**0.90**		0.67	**0.93**	0.55
22. Willingness to appear in photographs		**0.83**		0.60	**0.92**	0.51
15. Self confidence		**0.77**		0.60	**0.90**	0.62
2. Appearance of my eyes		**0.77**		0.69	**0.90**	0.41
21. Other people's reactions to my TED		**0.76**		0.53	**0.90**	0.39
3. Appearance of my face	0.30	**0.68**		0.72	**0.88**	0.49
14. Ability to obtain a job		**0.53**		0.55	**0.76**	0.72
16. Ability to make new friends		0.52	**0.48**	0.46	0.66	**0.41**
18. Relationship with my family			**0.85**	0.44	0.41	**0.88**

19. Relationship with my current friends		**0.85**	0.35	0.46	**0.87**
20. Relationship with my current partner/wife/husband		**0.70**	0.39	0.38	**0.75**
17. Ability to form new intimate relationships	0.33	**0.44**	0.52	0.60	**0.64**

The 23 item Expectations of TED Surgery Questionnaire (E-TEDS) consisted of three subscales. Expectations of visual functioning (VF) was made up of 11 items, intimacy and social relationships (ISR) contained 5 items, and appearance-related concerns (AC) contained 7 items. Responses on each item were mean scored for each subscale, with possible mean scores ranging from 1 to 5. Consultation with the authors of the ESSQ resulted in a suggested cut-off of mean scores of 1 to 2 (inclusive) indicated that patients expected surgery to make visual functioning, intimacy and social relationships, and appearance-related concerns worse, scores of >2 to <4 indicated that patients expected these areas to remain the same after surgery, and scores of 4 or above indicated that patients expected these areas to improve after their surgery. Mean scores in this sample were 3.5 (SD=1.2) for AC, 3.3 (SD=0.9) for VF, and 3.2 (SD=0.8) for ISR.

Table 11. The 23-item Expectations of TED Surgery Questionnaire (E-TEDS)

Using the five point scale below please rate how you expect surgery to change various aspects of your life.					
	Made considerably worse	**Made worse**	**Remained the same**	**Improve**	**Considerably improve**
1. My vision	1	2	3	4	5
2. The appearance of my eyes	1	2	3	4	5
3. The appearance of my face	1	2	3	4	5
4. My ability to drive	1	2	3	4	5
5. My ability to move around the house	1	2	3	4	5
6. My ability to perform domestic duties (e.g. cooking and cleaning)	1	2	3	4	5
7. My ability to engage in my hobby or pastime	1	2	3	4	5
8. My ability to read	1	2	3	4	5
9. My ability to watch TV	1	2	3	4	5
10. My ability to	1	2	3	4	5

use the computer					
11. **My ability to work at my usual job**	1	2	3	4	5
12. **My ability to walk outdoors**	1	2	3	4	5
13. **My double vision**	1	2	3	4	5
14. **My ability to obtain a job**	1	2	3	4	5
15. **My self confidence**	1	2	3	4	5
16. **My ability to make new friends**	1	2	3	4	5
17. **My ability to form new intimate relationships**	1	2	3	4	5
18. **The relationship with my family**	1	2	3	4	5
19. **The relationship with my current friends**	1	2	3	4	5
20. **The relationship with my current partner/ wife/ husband**	1	2	3	4	5
21. **Other people's reactions to my TED**	1	2	3	4	5
22. **My willingness to appear in photographs because of my TED**	1	2	3	4	5
23. **My desire to mask the changes in my appearance as a result of my TED**	1	2	3	4	5

6.6.4.3 Validity and reliability

Four Consultant Ophthalmic Surgeons, a Professor of Health Psychology, a Health Psychologist and a patient with TED reviewed the items of the E-TEDS. There was consistent agreement between the experts that the items reflected the concepts represented by the subscales, the experiences of patients with TED, and were medically accurate, thus achieving content validity.

Internal reliability of the subscales was high with Cronbach's alphas all above 0.7 (Table 12).

Table 12. Internal reliability of the E-TEDS subscales

Scale & subscale	N	No. of items	Cronbach's α
Expectations appearance concern	121	7	0.958
Expectations visual function	121	11	0.964
Expectations intimacy and social relationship	121	5	0.871

6.7 FACTORS ASSOCIATED WITH QUALITY OF LIFE IN TED

This section of the thesis describes the results of two hierarchical multiple regressions that were performed to assess the ability of the demographic, clinical, intervening cognitive process and mood variables described to predict the variance in GO-QOL visual function and appearance subscales. A full description of the method used is described in section 5.10.4 (page 115) and Figure 9 shows the regression model used.

6.7.1 GO-QOL visual function

As described in Chapter 5, section 5.10.4, univariate linear regressions were performed for each IV to determine whether it predicted the DV before entering only significant predictors into a hierarchical multiple regression.

These initial univariate regressions found that ten of the 36 variables significantly predicted GO-QOL visual functioning: age ($F_{(1,119)}=16.65$, $p<0.001$, $f^2=0.14$), optic neuropathy ($F_{(1,119)}=15.77$, $p<0.001$, $f^2=0.15$), worse eye LogMAR ($F_{(1,119)}=15.58$, $p<0.001$, $f^2=0.12$), previous immunosuppressant therapy ($F_{(1,119)}=11.13$, $p=0.001$, $f^2=0.09$), asymmetrical TED ($F_{(1,119)}=6.12$, $p=0.015$, $f^2=0.05$), hydraulic orbit ($F_{(1,119)}=9.22$, $p=0.003$, $f^2=0.06$), diplopia ($F_{(1,119)}=7.77$, $p=0.006$, $f^2=0.07$), CAS ($F_{(1,119)}=6.22$, $p=0.014$, $f^2=0.05$), social anxiety and avoidance ($F_{(1,119)}=3.95$,

p=0.049, f^2 =0.06), anxious mood ($F_{(1,119)}$=12.87, p<0.001, f^2 =0.11), and depressed mood ($F_{(1,119)}$=41.63, p<0.001, f^2 =0.36).

When entering these variables in the order of entry described in section 5.10.4, 55% of the observed sample variation in GO-QOL visual function was accounted for by the regression model (adjusted R^2=0.45, $F_{(1,119)}$=9.89, p<0.001, f^2 = 0.8). Beta coefficients indicated that age, asymmetrical TED and depression all made significant unique contributions to the model (Table 13). Poorer quality of life was associated with being older, having asymmetrical proptosis and more depressed mood.

Table 13. Results of the hierarchical multiple regression model used to identify predictors of GO-QOL visual function

	B	SE B	*t*	*p*
Step 1				
Constant	**98.16**	**9.53**	**10.30**	**.000****
Age	**-0.79**	**0.20**	**-4.03**	**.000****
Step 2				
Constant	**94.07**	**9.84**	**9.56**	**.000****
Age	-0.39	0.21	-1.85	.065
LogMAR	**-15.88**	**7.65**	**-2.08**	**.038***
CAS	-0.84	1.49	-0.56	.574
Asymmetry	-2.55	1.30	-1.96	.050
Optic neuropathy	-6.01	12.07	-0.50	.620
Hydraulic orbit	0.92	7.69	0.12	.904
Previous immunomodulation	-8.13	5.20	-1.57	.118
Diplopia	-6.16	5.05	-1.22	.222
Step 3				
Constant	**129.01**	**14.78**	**8.73**	**.000****
Age	**-0.54**	**0.21**	**-2.60**	**.009***
LogMAR	**-14.72**	**7.41**	**-1.99**	**.047***
CAS	-1.64	1.47	-1.12	.265
Asymmetry	**-2.96**	**1.27**	**-2.34**	**.019***
Optic neuropathy	-4.68	11.44	-0.41	.684
Hydraulic orbit	2.15	7.45	0.29	.773
Previous immunomodulation	-5.17	4.99	-1.04	.300
Diplopia	-5.63	4.86	-1.16	.247
DAS24	**-0.56**	**0.18**	**-3.06**	**.002***
Step 4				
Constant	**119.49**	**13.78**	**8.67**	**.000****
Age	**-0.50**	**0.19**	**-2.63**	**.009***
LogMAR	-11.28	6.45	-1.75	.080
CAS	-1.92	1.31	-1.46	.144
Asymmetry	**-2.25**	**1.13**	**-2.00**	**.046***
Optic neuropathy	-4.09	9.54	-0.43	.669
Hydraulic orbit	2.55	6.47	0.39	.694
Previous immunomodulation	-6.79	4.90	-1.38	.168
Diplopia	-4.39	4.29	-1.02	.307
DAS24	0.05	0.21	0.23	.815
HADS Anxiety	-0.69	0.58	-1.20	.231
HADS Depression	**-2.41**	**0.59**	**-4.10**	**.000****

Note: $R^2 = .12$ for Step 1 ($p < 0.001$), $R^2 = .28$ for Step 2 ($p < 0.05$), $R^2 = .40$ for Step 3 ($p < 0.001$), $R^2 = .55$ for Step 4 ($p < 0.001$)

*$p<0.05$, **$p<0.001$

A post-hoc power calculation conducted in G*Power 3.1.2 indicated that for 10 predictor variables, a sample size of 121, and an effect size of 0.8, 100% power was achieved.

6.7.2 GO-QOL appearance

The preliminary univariate linear regressions found 13 variables significantly predicted GO-QOL appearance: age ($F_{(1,119)}$=5.42, p=0.022, f^2 = 0.05), gender ($F_{(1,119)}$ =8.13, p=0.005, f^2 = 0.07), previous eyelid or orbital surgery ($F_{(1,119)}$ =5.55, p=0.020, f^2 =0.06), family support ($F_{(1,119)}$=5.12, p=0.025, f^2 = 0.04), support from friends ($F_{(1,119)}$=7.39, p=0.008, f^2 =0.06), fear of negative evaluation ($F_{(1,119)}$=58.76, p<0.001, f^2 =0.52), social comparison ($F_{(1,119)}$=12.23, p=0.001, f^2 =0.11), DAS24 ($F_{(1,119)}$=60.03, p<0.001, f^2 =0.59), salience of appearance ($F_{(1,119)}$=64.65, p<0.001, f^2 =0.51), valence of appearance ($F_{(1,119)}$=98.86, p<0.001, f^2 =0.76), perceived visibility ($F_{(1,119)}$=27.47, p<0.001, f^2 =0.24), anxious mood ($F_{(1,119)}$=42.25, p<0.001, f^2 = 0.39), and depressed mood ($F_{(1,119)}$=70.50, p<0.001, f^2 =0.57).

When entering the variables in the same method of entry as described in section 5.10.4 (page 115) and Figure 8, 75% of the observed sample variation in GO-QOL appearance was accounted for by the regression model (adjusted R^2=0.70, $F_{(13,107)}$=20.70, p<0.001, f^2 = 2.3). Beta coefficients indicated that gender, appearance-related social anxiety and social avoidance, salience of appearance, valence of appearance, perceived visibility of TED and depression all made significant contributions to the model (Table 14). Poorer appearance-related quality of life was associated with being female, having greater appearance-related social anxiety and avoidance, greater value being placed on appearance, a more negative evaluation of appearance, greater perceived visibility of TED, and being more depressed.

Table 14. Results of the hierarchical multiple regression model use to identify predictors of GO-QOL appearance

	B	**SE B**	***t***	***p***
Step 1				
Constant	12.40	8.40	1.48	.140
Age	**0.43**	**0.17**	**2.51**	**.012***
Gender	**14.04**	**4.68**	**3.00**	**.003***
Step 2				
Constant	16.04	8.52	1.88	.060
Age	**0.39**	**0.17**	**2.30**	**.022***
Gender	**13.43**	**4.62**	**2.91**	**.004***
Previous surgery	**-14.89**	**6.76**	**-2.20**	**.028***
Step 3				
Constant	**54.38**	**15.75**	**3.45**	**.001***
Age	0.22	0.15	1.50	.133
Gender	**11.97**	**3.93**	**3.04**	**.002***
Previous surgery	-5.52	6.53	-0.85	.399
BFNE	**-1.29**	**0.24**	**-5.29**	**.000****
INCOM	0.03	0.30	0.11	.915
MSPSS Family	0.13	0.45	0.30	.765
MSPSS Friends	**0.97**	**0.49**	**1.97**	**.049***
Step 4				
Constant	**134.27**	**14.30**	**9.39**	**.000****
Age	0.05	0.11	0.43	.666
Gender	**8.41**	**3.07**	**2.74**	**.006***
Previous surgery	-5.62	5.20	-1.08	.283
BFNE	-0.21	0.22	-0.93	.354
INCOM	0.05	0.24	0.19	.849
MSPSS Family	-0.08	0.34	-0.22	.823
MSPSS Friends	**0.76**	**0.38**	**1.99**	**.047***
DAS24	**-0.54**	**0.12**	**-4.34**	**.000****
CARSAL	**-1.40**	**0.34**	**-4.12**	**.000****
CARVAL	**-0.69**	**0.22**	**-3.19**	**.001***
Perceived visibility	**-2.89**	**0.99**	**-2.92**	**.004***
Step 5				
Constant	**132.09**	**13.84**	**9.55**	**.000****
Age	0.11	0.11	0.94	.346
Gender	**6.56**	**3.02**	**2.17**	**0.03***
Previous surgery	-5.04	5.08	-0.99	.325
BFNE	-0.23	0.22	-1.03	.302
INCOM	0.01	0.23	0.06	.950
MSPSS Family	-0.29	0.34	-0.87	.382
MSPSS Friends	0.56	0.37	1.53	.127
DAS24	**-0.39**	**0.13**	**-2.93**	**0.004***

CARSAL	**-1.23**	**0.33**	**-3.69**	**0.000****
CARVAL	**-0.58**	**0.21**	**-2.76**	**0.006***
Perceived visibility	**-2.75**	**0.96**	**-2.86**	**0.004***
HADS Anxiety	-0.05	0.39	-0.14	.891
HADS Depression	**-1.12**	**0.43**	**-2.60**	**0.009***

Note: $R^2 = .11$ for Step 1 ($p < 0.05$), $R^2 = .15$ for Step 2 ($p < 0.05$), $R^2 = .43$ for Step 3 ($p < 0.001$), $R^2 = .71$ for Step 4 ($p < 0.001$), $R^2 = .75$ for Step 5 ($p < 0.05$)
*$p < 0.05$, **$p < 0.001$

A post-hoc power calculation conducted in G*Power 3.1.2 indicated that for 13 predictor variables, a sample size of 121, and an effect size of 2.3, 100% power was achieved.

6.7.3 Regression assumptions

The VIF and tolerance statistics for all 10 imputations were inspected as a pooled result was not produced by SPSS. All tolerance values were above 0.2 and VIF values were well below 10. Therefore it can safely be concluded that there was no multicollinearity within the data for either model. Furthermore, the residuals were inspected using histogram and normal probability plots and showed a normal distribution for both the GO-QOL subscales with a mean of 0.

6.8 DISCUSSION

This study investigated the demographic, clinical and individual psychosocial factors that might predict quality of life in a sample of patients with TED presenting for orbital decompression surgery. Factors associated with quality of life were identified using hierarchical multiple regression analyses. It was found that prior to surgery a range of demographic, clinical and psychosocial factors were associated with both vision-related and appearance-related quality of life. The representativeness of the study sample in comparison to other TED samples and the wider population of patients with TED will now be discussed. Following this, the results of the present study will be discussed in relation to previous research in section 6.8.2, and a discussion of the strengths and weaknesses of this study will be provided in section 6.8.3.

6.8.1 Representativeness of the study sample

6.8.1.1 Demographic & clinical factors

The demographic composition of the study sample was similar to the general TED population. The percentage of females in this study reflects the percentage from other TED studies in the UK (Edmunds, Huntbach & Durrani, 2014), and orbital decompression surgery in non-UK samples (Terwee et al., 2001; Tehrani et al., 2004). In terms of the mean age of the sample, the present study is comparable to other studies evaluating orbital decompression surgery (EUGOGO et al., 2009; Terwee et al., 2001). The literature on ethnic differences in TED is limited, however the current study presents an ethnic distribution that is comparable to another UK sample of TED patients (Edmunds, Huntbach & Durrani, 2014). Audit data from MEH suggests that approximately 46% of patients with TED referred to MEH between the period of August 2013 and July 2014 were White (MEH Performance Information, 2014), making the current study sample skewed towards those of White ethnicity, thus potentially reducing the generalizability of these findings to the wider population of patients with TED at MEH. This may have occurred in part due to the exclusion of patients who were not English speaking because of using questionnaires that required a fluent understanding of psychological concepts in English.

Disease duration varied greatly between participants, with a range similar to TED samples in previous studies investigating quality of life (Terwee et al., 1998; Terwee et al., 2001; Terwee et al., 2002). The large range may be in part due to the difficulty in diagnosing TED for some, particularly for patients with unilateral disease (Wiersinga et al., 1989). This might also be because orbital decompression surgery is only offered in a small number of TED speciality clinics and some patients have anecdotally reported that their GP was not aware of this corrective surgery available to them through the NHS and so did not seek further treatment for several years. Whilst others are identified quickly and if they live near to MEH (a specialty clinic), they would be more likely to be referred rapidly. Perros et al. (2012) indeed found that patients who lived further away from a specialty clinic were significantly less likely to have orbital decompression surgery than patients registered to primary care trusts closer to those clinics.

The proportion of patients in this study with unilateral TED was similar to previous TED populations (Kashkouli et al., 2011b). Previous studies investigating quality of life in patients with TED undergoing orbital decompression surgery have not reported stability of thyroid function, but the proportion in this sample with unstable thyroid function was lower than in previous patient groups (Ponto et al., 2011). However, as orbital decompression surgery is normally only offered to patients once GD has been controlled through antithyroid drugs or thyroidectomy, this would make sense for this sample. The majority of the patients in this study had a CAS score lower than 3, indicating inactive TED, which would be expected in patients listed for orbital decompression surgery, as this surgery tends only to be offered to patients whose TED has "burnt out", or reached a phase of stability. The high exophthalmometry readings in this sample are comparable to other samples of patients with TED before decompression surgery (EUGOGO et al., 2009; Terwee et al., 2002). The high number of patients in this sample with diplopia is also similar for patients with TED seeking surgery (EUGOGO et al., 2009; Terwee et al., 2002), as is the proportion of patients with optic neuropathy (Edmunds, Huntbach & Durrani, 2014; Perros et al., 1993).

6.8.1.2 Socio-cognitive factors

Participants in this sample scored 9 points higher on the fear of negative evaluation measure (BFNE; Leary, 1983), than a published normal threshold for a non-clinical community sample (Collins et al., 2005). The scores were, however, similar to samples of patients with psoriasis (Leary et al., 1998) and panic disorder (Collins et al., 2005), but lower than patients with identified social phobia (Collins et al., 2005; Weeks et al., 2005). This suggests that fear of negative evaluation was particularly high in patients with TED, but comparable to other visible conditions including ptosis (Richards et al., 2014) and strabismus (McBain et al., 2014).

The mean scores on the social comparison measure (INCOM; Gibbons & Buunk, 1999) indicated the tendency of this sample to make social comparisons is comparable to a group of patients with a range of ophthalmic conditions (n=98) including ptosis, TED, strabismus, ocular cancer and trauma (James et al., 2011), although not as high as a sample of US college students (Gibbons & Buunk, 1999).

The latter may be particularly influenced by social pressure and their age is also likely to be an important influence on the tendency for social comparison.

Scores on the perceptions of social support (MSPSS; Zimet et al., 1988) subscales Family, Friends, and Significant Other are particularly high relative to the general population with scores approximately 10 points higher on each subscale than a general population sample (Zimet et al., 1988). This may be due to patients being dependent and relying on support from loved ones, particularly if vision has had an impact on activities of daily life, and if changes in appearance have led to social withdrawal.

6.8.1.3 Appearance-specific cognitions

Mean appearance-related social anxiety and avoidance (DAS24; Carr, Moss & Harris, 2005) scores were high, particularly when compared to normative data from the general population (Harris & Carr, 2001). Scores were also higher in this sample than in patients who had identified themselves as having a particular concern about a feature of their head and neck region and their nose, as shown in Figure 12 (Carr, Moss & Harris, 2005). Normative data on the DAS24 for men and women are available (Carr, Moss & Harris, 2005) and scores in this sample are higher than men and women in the general population (Figure 12). In particular, men with TED scored almost twice as high as men from the general population (Carr, Moss & Harris, 2005). Scores for this sample are also around 10 points higher for both men and women than a sample of patients with a range of ophthalmic concerns (James et al., 2011) and are comparable to a sample of individuals having elective plastic surgery (Rumsey et al., 2004).

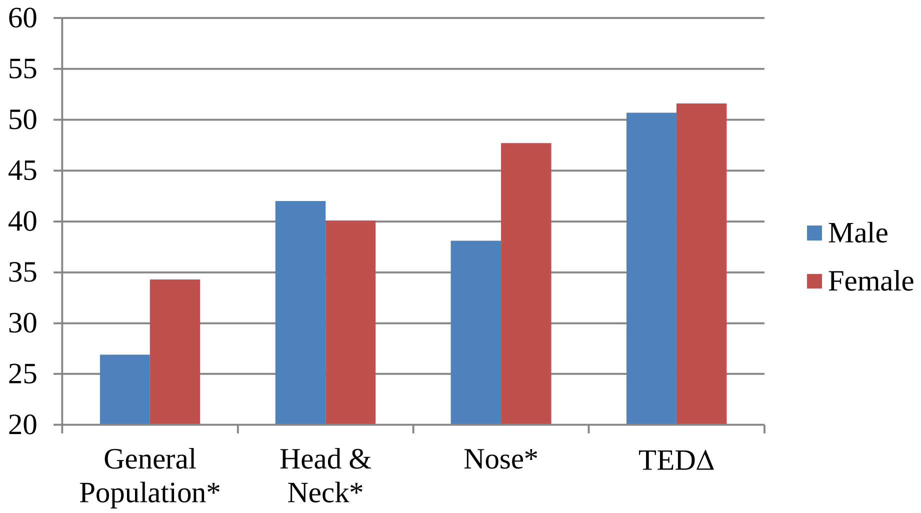


Figure 12. DAS24 scores for men and women at baseline for the current study (Δ) compared to norm values from Carr, Moss & Harris (2005) (*)

As the salience and valence of appearance scales (CARSAL and CARVAL; Moss & Rosser, 2012) used in this study were amended versions that have only recently been published (Moss & Rosser, 2012), there are no normative values for these two measures available. In terms of perceived visibility, participants reported that their TED was highly visible to others, with a mean score of 5.7 and 43% of the sample rating visibility as a 7 (the highest possible score), and only 1 patient (1%) reporting perceived visibility to be a 1 (the lowest possible score). The same scale has been used in a recent study evaluating quality of life in strabismus and participants in this study perceived TED to be more visible than strabismus (McBain et al., 2014).

6.8.1.4 Mood

The mean anxiety scores (HADS; Zigmond & Snaith, 1983) for the current sample were higher than a UK general population (Crawford et al., 2001) and patients with strabismus (McBain et al., 2014; Jackson et al., 2006), and other facial disfigurements (Martin & Newell, 2004). Mean depression scores (HADS; Zigmond & Snaith, 1983) in this sample were higher than for patients with other disfigurements including those caused by rheumatic conditions, burns, head and neck cancer, and dermatological conditions, but lower than patients having plastic surgery (Rumsey et al., 2004).

The high levels of possible clinical caseness in this sample (25.6% of depression and 37% of anxiety) were far higher than the 3% clinical levels of anxiety and 1% clinical depression in the general population (Crawford et al., 2001). The percentages were however similar for depression and less for anxiety compared to a sample of individuals with facial disfigurements (Martin & Newell, 2004). A lower proportion of this sample of patients with TED were found to have possible clinical levels of anxiety than a German group of patients with TED, although depression levels were higher in the current sample (Kahaly et al., 2005).

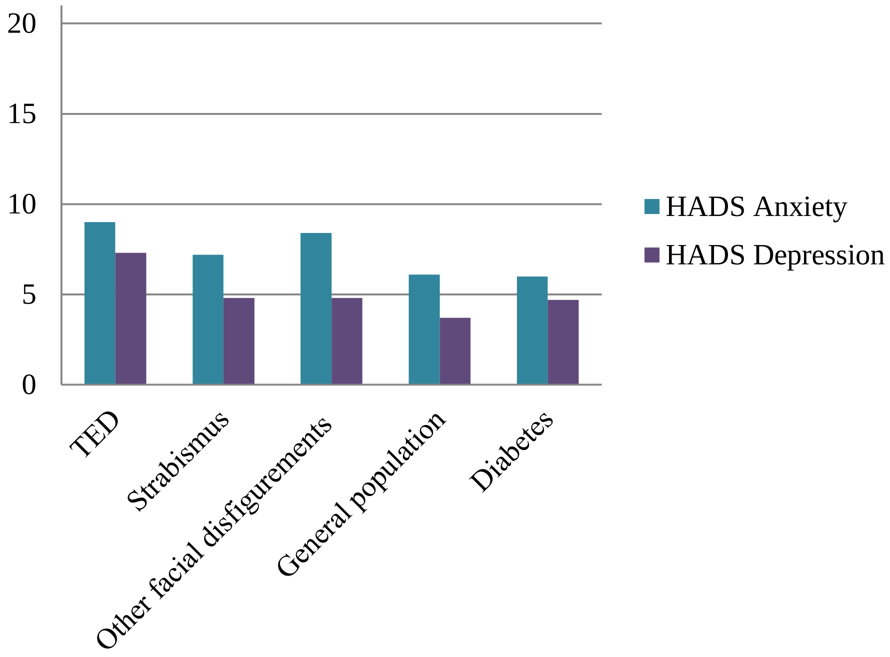


Figure 13. Bar chart displaying mean HADS subscale scores from this sample compared to normative scores from other populations

It remains possible that other psychological co-morbidities not assessed in this study could have explained the high percentage of possible clinical mood disorders. For example, Wong & Yu (2013) found that as many as 32% of TED patients had a current psychiatric disorder including panic disorder, agoraphobia, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD), all of which affect mood.

6.8.1.5 Quality of life

Quality of life in relation to visual functioning in this sample was comparable to a Dutch sample of 38 patients having orbital decompression for proptosis evaluated in the development of the GO-QOL (Terwee et al. 2001). Appearance-related quality of life in the present sample was, however, found to be several points lower than in the Dutch study (Figure 14).

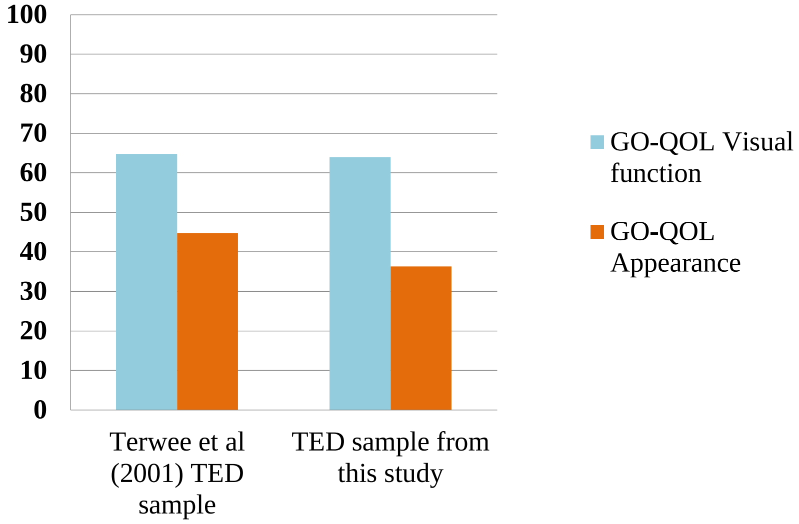


Figure 14. GO-QOL subscale scores for the current sample at baseline compared to scores from a previously studied TED sample (Terwee et al., 2001)

Large variation was found between patients in their visual function and appearance-related quality of life suggesting that whilst some patients adjusted well, others were on the extreme end of the scale. For some, TED had had a detrimental impact on their activities of daily living and perceptions of their appearance. This is in line with a number of previous studies (Jensen & Harder, 2001; Estcourt et al., 2008; Ponto et al., 2011; Choi et al., 2012). However, the current study investigated this phenomenon further by exploring the potential for intervening psychosocial processes to better explain quality of life than clinical and demographic factors.

6.8.2 Factors associated with quality of life in TED

It has been widely documented that individuals with facial disfigurements can experience poor psychological adjustment as a result of changes in appearance. Research in recent years has begun to challenge the idea that psychosocial adjustment can be predicted from clinical severity alone, and it is now considered that the experience of living with a facial disfigurement as multifaceted and involving societal and individual factors. A number, but not all, of the measures selected for this study were significantly associated with quality of life as predicted.. This section of the thesis presents the results of the analyses and discusses them in relation to previous literature.

6.8.2.1 Demographic factors

Demographic factors were found to predict quality of life in this sample, with older adults with TED experiencing poorer vision-related quality of life than younger patients. This finding contradicts previous studies that have reported appearance related distress, anxiety and depression to generally reduce with age in people with disfiguring conditions (ARC, 2008; Rumsey et al., 2003; James et al., 2011). In contrast the finding in this study corresponds to that in strabismus where being older has been found to be associated with increased levels of depression (McBain et al., 2014). It is also consonant with a study in TED, where older patients were found to have poorer visual related quality of life (Terwee et al., 1999). The similarity in these findings which are specific to the eyes and visual system might suggest that the general finding in disfigurement research in relation to age and depression is not supported where eyes are involved. However, a more plausible suggestion is that the relationship is related to severity as older age is one factor that is associated with more severe TED (Kendler, Lippa & Rootman, 1993).

Appearance-related quality of life was significantly associated with gender. One previous study in TED involving the development of the GO-QOL also found females to report more problems in appearance-related quality of life (Terwee et al., 1999). Being female has been found to be associated with poorer appearance-related quality of life in other disfiguring conditions (Rumsey et al., 2003; James et al., 2011; ARC, 2008). It might be that for women, the eyes are more central in perceived attractiveness and changes in appearance to the eyes have had a detrimental influence on self-confidence and willingness to appear in photographs. Concealment of TED has been found to be common in women in previous TED studies (Estcourt et al., 2008; Jensen & Harder, 2010; Terwee et al., 1999) and this sample of patients appear to be no exception.

6.8.2.2 Clinical factors

Asymmetrical disease was found to predict vision-related quality of life. Visual function has been found to be associated with eye symmetry, or lack thereof, and the degree of burden from this factor, individual to each patient, has been found to influence GO-QOL scores in a previous TED study (Terwee et al., 1999). Of note, no other clinical variables accounted for the variance in either visual function or appearance-related quality of life. Intervening cognitive processes explained more variance in quality of life than the clinical factors included in this study. This is in contrast to other studies in TED that have found a significant relationship between clinical and psychological factors, although there are methodological flaws in these studies that may have biased the results, (See Chapter 4, section 4.3.1.2) (Yeatts, 2005; Park et al., 2004; Son et al., 2014).

6.8.2.3 Intervening psychosocial factors

It was predominantly the intervening psychosocial factors that explained the variance in appearance-related quality of life in this study. The finding that increased appearance-related social anxiety and avoidance predicts poorer visual related and appearance related quality of life is supported by a recent study in strabismus. In the strabismus study social anxiety and social avoidance scores were significantly associated with both function and psychosocial quality of life (McBain et al., 2014). Another study has found that people with disfiguring conditions commonly avoid social activities that involve exposing their condition to others (Rumsey, Clarke & Musa, 2002). The issue of exposure would have significant implications for patients with disfiguring eye conditions where they are often met with questions, comments and staring from others (Clarke, 1998; Clarke et al., 2000; Jensen & Harder, 2001; Estcourt et al., 2008). Some previous studies have conceptualised appearance-related social anxiety and avoidance to be behavioural *outcomes* in adjusting to having a disfiguring condition (e.g. Richards et al., 2014). However, the results of this study, in addition to McBain et al.’s (2014), support the notion that these are intervening cognitive factors that strongly predict quality of life adjustment. Increased importance of appearance-related information, as well as having a poorer evaluation of one’s own appearance, were also found to significantly predict quality of life in this sample. This also supports the findings of McBain et al. (2014) for patients with strabismus. Appearance-related quality of life was also predicted by a tendency to perceive one’s own TED to be highly visible to others. In a recent study investigating perceptions of TED severity in different groups of observers, in addition to patients themselves, Terwee et al. (2003b) found that clinicians tended to underrate, and patients overrate, the severity of TED. Perceptions of particularly high noticeability have also been found in patients with strabismus (McBain et al., 2014), head and neck cancer, skin conditions, and individuals seeking elective plastic surgery for appearance concerns (Rumsey, Clarke & White, 2003).

Expectations about upcoming rehabilitative surgery for a disfiguring condition are understandably high (Dawn & Lee, 2004; Kiyak, Vitaliano & Crinean, 1988; Estcourt et al., 2008). Estcourt et al. (2008) investigated the well-being of patients with TED in a recent qualitative study and found patients to have unrealistically high expectations that surgery will enable them to return to the life they had before TED. This was the first study in TED to measure patients’ expectations of surgery and developed the E-TEDS questionnaire to achieve this task. Furthermore, this was the first study to the researcher’s knowledge that has tested the potential for expectations to explain variability in adjustment using the ARC (2008) framework. However, expectations for post-surgical visual function, appearance concerns, or intimacy and social relationship outcomes were not associated with quality of life in this sample. There may be issues with measuring quality of life in relation to patients’ expectations. A recent literature review has highlighted that expectations are complex, highly specific to each patient and are closely related to people’s relationships to their changing environments (Carr, Gibson & Robinson, 2001). Thus expectations may change over time and over the course of their illness trajectory.

Depression was found to be a strong predictor of both visual function and appearance-related quality of life. This is consistent with quality of life in other chronic disease groups, including diabetes (Goldney et al., 2004), multiple sclerosis (Karatepe et al., 2011) and myocardial infarction (Mayou et al., 2000) as well as in strabismus (McBain et al., 2014).

To conclude, this is one of the largest sample of patients with TED assessed on quality of life to date, and the only study to have investigated the potential of a range of intervening cognitive processes to explain quality of life in this patient group. Appearance-related quality of life was found to be particularly poor in this sample, but variation was found in both appearance and vision-related quality of life. This variation was predominantly accounted for by intervening cognitive processes as opposed to clinical severity, activity, treatment history or duration of the condition. There was some evidence that age and asymmetrical disease might predict vision-related quality of life in patients with TED. A higher proportion of possible caseness of anxiety and depression was found in this population than other patients with other facial disfigurements, and depression was found to be a strong significant predictor of both visual function and appearance-related quality of life.

This highlights the importance of measuring levels of depression and quality of life in this patient group prior to surgery. It would be valuable for clinicians to be aware of the significant detrimental impact of having TED on patients' lives, and the ability of psychosocial processes individual to each patient to predict who adjust particularly poorly, over and above clinical factors, so that they may be examined in the clinical interview, and appropriate intervention and support provided.

6.8.3 Strengths and weaknesses of the study

This cross-sectional study found a range of demographic, clinical and intervening psychosocial processes variables were associated with quality of life in this TED sample. However, as the design was cross-sectional, it is difficult to establish causal direction for the factors that are associated with quality of life. Longitudinal studies that follow patients up over time are needed to identify predictors of quality of life.

An adequately powered sample size of 121 was reached for this study making this one of the largest samples in any TED study. Sufficient power was also achieved for to find an effect for the hierarchical multiple regression analyses. The sample was representative of the wider TED population in terms of age, gender distribution, and indicators of activity and severity, but not for ethnicity.

The DVs for this study were found to be non-normally distributed, which can pose a problem when conducting regressions analyses, as generalising findings from the model beyond the sample becomes difficult (Field, 2009). These can be dealt with by transforming the data, but transformations are not without their own limitations and often produce results that are non-interpretable (Grayson, 2004), thus were avoided in this study. The non-normally distributed DVs may therefore have weakened the results of the current study. However, the normality of the residuals were also checked after the regressions were performed and these were found to be satisfactory.

The Expectations of TED Surgery Questionnaires (E-TEDS) was developed for the purposes of examining patient expectations of orbital decompressions surgery in this cross-sectional study. It was assessed for internal reliability and content validity, both of which were found to be high. However validity and reliability of the measure should be further established to confirm the robustness of the measure, including test-retest measures to ensure the stability of what is measures over time, and discriminant validity checks against measures that theoretically measure different, or the same, concepts (Pallant, 2007). The cut-off scores indicating expectations to be made worse, remain the same, or improve that have been suggested in this chapter also need further testing to establish their suitability.

This is one of few studies to examine quality of life in patients presenting for orbital decompression in the UK using the GO-QOL and to systematically examine demographic, clinical and psychosocial predictors of adjustment to TED. The findings from this study have a number of implications for clinical practice, which are described in more detail in Chapter 10 section 10.3.

7. A QUALITATIVE STUDY OF PATIENT EXPECTATIONS OF ORBITAL DECOMPRESSION SURGERY FOR TED

7.1 PROLOGUE

The previous chapter of this thesis described the results of a cross-sectional study investigating the demographic, clinical and psychosocial factors associated with quality of life of patients with TED presenting for orbital decompression surgery. This study found that intervening cognitive processes predominantly were associated with quality of life in this patient group, rather than clinical factors. It has been discussed in Chapter 4 of this thesis (section 4.3.2.7) that expectations of treatment are likely to impact on adjustment to having a disfiguring disease. Expectations were thus measured in the cross-sectional quantitative study described in Chapter 6 in relation to their association with quality of life. However, expectations for medical care are complex and are worthy of more in-depth exploration. The present chapter outlines the results of a qualitative study that explored patients’ expectations of orbital decompression surgery further. Semi-structured interviewing and thematic analysis were used to further our understanding of the expectations patients had about their upcoming decompression surgery for TED.

To date only two studies have used qualitative methods to explore the patient perspective in TED and both investigated the impact of TED on well-being (Jensen & Harder, 2011; Estcourt et al., 2008). One study highlighted the difficulty people with TED face in communicating with others and maintaining social relationships, thus they tend to withdraw socially (Jensen & Harder, 2011). The other study reported that some patients have unrealistic expectations that surgery will enable them to go back to the life they had before their TED (Estcourt et al., 2008). To date, no studies have explored this issue further. This is therefore the first study to specifically investigate patient expectations of the impact of surgery for TED.

7.2 AIMS & OBJECTIVES

This study used semi-structured interviews with the objective of capturing the views and experiences of patients with TED approaching surgery regarding:

- *Their expectations of the outcome of orbital decompression surgery, or of the actual procedure*
- *The factors that might influence their expectations*

A full description of the study design, procedure and analytic methods are described in Chapter 5, sections 5.4, 5.9, and 5.11 respectively.

7.3 RESULTS

7.3.1 Sample characteristics

A total of 22 patients were identified as being eligible for this study and were approached by the clinical researcher at BMEC between October 2012 and February 2014. Of these, 3 could not be contacted by telephone after multiple attempts. Of the 19 patients contacted by telephone, 5 could not attend an interview prior to surgery because of other commitments. Fourteen patients in total were interviewed. This is considered to be a sample size deemed adequate for theory-based interview studies (Francis et al., 2010), and importantly at which point no new themes were emerging from the interviews, i.e. data saturation was reached. The characteristics of the patients who took part in interviews can be seen in Table 15.

Table 15. Characteristics of the patients who took part in semi-structured interviews

ID*	Gender	Ethnic background	Age	Marital status	Employment	Education (or equivalent)	Disease duration (months)	Laterality of TED	Diplopia	Previous treatment¥
01	F	British	53	Married	Full time	GCSE	12	Bilateral	Yes	OS
02	M	British	64	Married	Full time	GCSE	480	Bilateral	No	RAI; OD
03	M	British	71	Single	Retired	GCSE	12	Unilateral	Yes	OS
04	F	British	76	Married	Retired	HE Degree	144	Bilateral	No	N
05	M	British	29	Single	Full time	A Level	36	Bilateral	No	RAI; OD
06	F	Chinese	37	Married	Full time	Postgraduate Degree	36	Bilateral	No	OS; OD
08	F	British	44	Married	Homemaker	GCSE	42	Bilateral	Yes	RAI; OS
13	F	Caribbean	34	Single	Unemployed	A Level	30	Bilateral	Yes	N
16	M	British	53	Married	Full time	GCSE	24	Bilateral	Yes	OS
17	F	British	47	Divorced	Full time	GCSE	10	Bilateral	No	RT; IS
18	F	British	55	Married	Semi-Retired	HE Degree	24	Bilateral	Yes	IS; OS
19	F	African	37	Married	Student	GCSE	24	Bilateral	Yes	N
20	F	British	38	Married	Homemaker	None	14	Bilateral	Yes	OS
21	F	Pakistani	23	Lives with partner	Full time	HE Degree	18	Bilateral	No	N

* ID – Identification number

¥No treatment, N; radioiodine therapy, RAI; oral steroids, OS; intravenous steroids, IS; radiotherapy RT; decompression surgery on one eye, OD

7.3.2 Interviews

The interviews lasted between 16 and 101 minutes. The pilot interview was retained for the thematic analysis, as the data generated was relevant to the research questions. The pilot interview led to small alterations in the topic guide to include some additional areas deemed to be important to be raised in further interviews. The final topic guide can be seen in Figure 8, page 111.

7.3.3 Coding

Thematic analysis was used to code the transcripts, a description of which can be found in Chapter 5, section 5.11.1.2 (page 121). A comprehensive thematic coding framework was developed during the initial stages of coding (as described in section 5.11.1.2, page 123) and was applied and re-applied to all the data transcripts until no new codes were generated and all relevant extracts of data had been coded. An independent researcher with a health psychology background coded three of the interview transcripts without prior knowledge of the thematic coding framework. The coding of these transcripts were compared to those previously coded by the current researcher and no major inconsistencies were found. The only discrepancies were the second researcher used the codes "attitudes towards surgery", and "avoidance of additional information". After a discussion it was agreed that "attitudes towards surgery" had been captured in the original coding framework, as either "confidence in the surgical process" or "fear of surgery", and "avoiding information" had been captured in the original coding framework as "information about orbital decompression".

7.3.4 Themes

A thematic map was developed during phase 4 of the thematic analysis, or reviewing of the themes (Figure 16). Two overarching processes were identified within the data; the first referred to dialogue regarding the factors which influenced the formation of expectations, and the other was about the expectations of the surgery and its outcomes. Overarching themes have been identified in previous qualitative research investigating experiences of living with rheumatoid arthritis, with further themes, and sub-themes, within these overarching processes (Flurey, 2012).

Three main themes were identified within the process of *forming expectations*: (1) consequences of living with TED, (2) influence of others, and (3) impact of information about the surgery. Four main themes were identified within the *expectations themselves*: (1) expectations about the surgical process, (2) expectations about recovery, (3) expectations about post-surgical appearance outcomes; and (4) expectations about post-surgical functional outcomes. Within these themes were a number of sub-themes (Figure 15), which will be described, along with their evidence, in the following sections.

Theme -	**Consequences of living with TED**
Theme -	**Influence of others**
Theme -	**Impact of information**
Sub-theme:	Sources of information
Sub-theme:	Degree of understanding
Theme -	**The surgical process**
Sub-theme:	Risk perception
Sub-theme:	Confidence in surgeons and healthcare system
Sub-theme:	Timing of surgery
Theme -	**Recovery**
Theme -	**Appearance outcomes**
Sub-theme:	Vague expectations
Sub-theme:	Social interaction
Sub-theme:	Restoring normality
Sub-theme:	Timeline to rehabilitation
Theme -	**Functional outcomes**

Figure 15. The final themes and sub-themes identified during thematic analysis

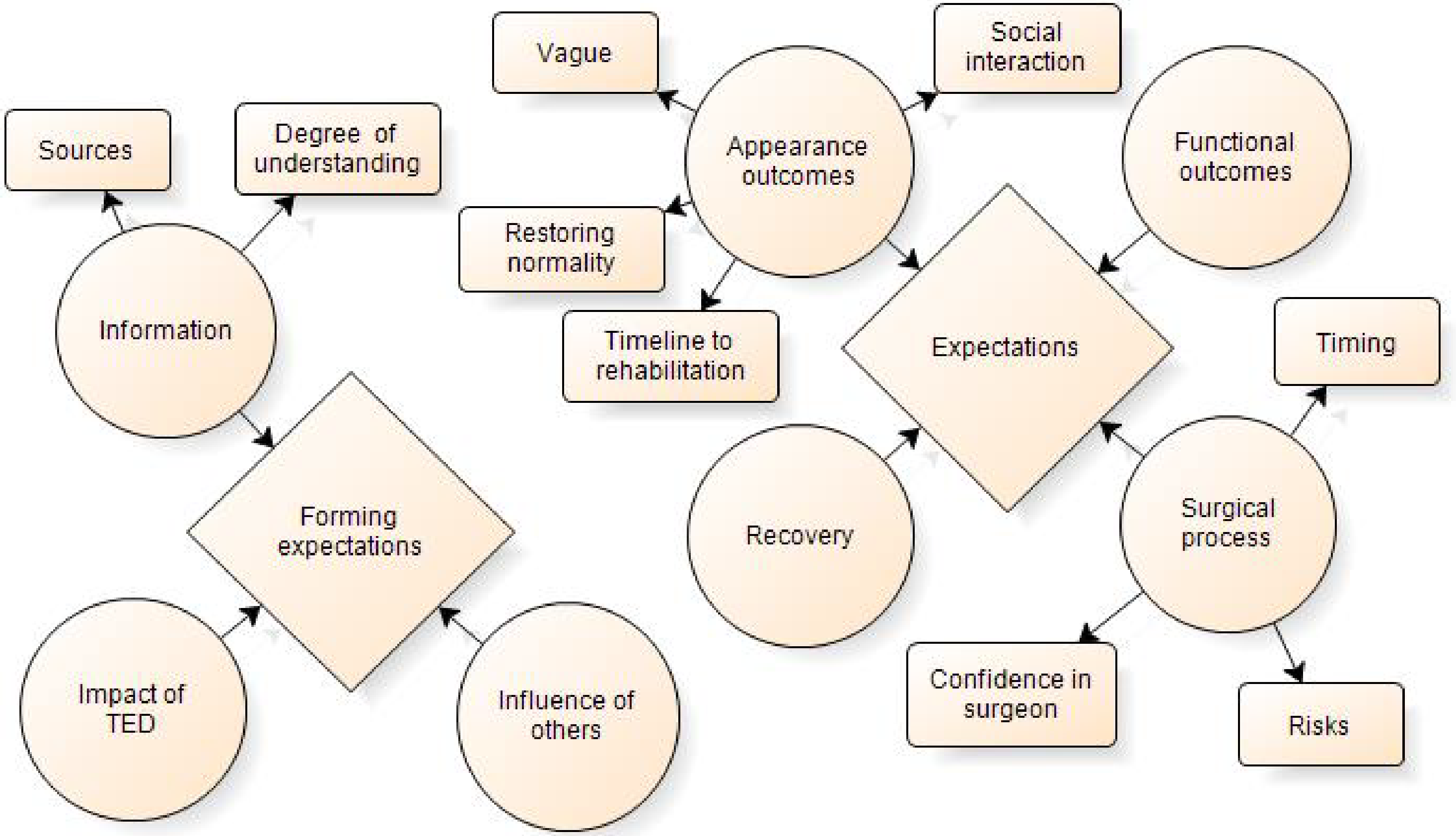


Figure 16. The developed thematic map, showing the two overarching processes (forming expectations, and expectations themselves) and the seven main themes within these processes

7.3.4.1 The consequences of living with TED

A majority of participants recounted their decision to have surgery, and what factors influenced this decision. Many participants described being motivated to have the surgery because of the impact TED had had on their lives, in terms of both appearance and unpleasant eye symptoms. For many participants the decision wasn't a difficult one: surgery was seen as inevitable. They described the surgery as the "next step along" having tried other treatments surgery was their "last option" and for some even the "cure" to restoring appearance.

> *"We had no choice, we tried everything. Different medications, radiotherapy, that didn't work. Everything was just taking it so far and not curing it, surgery was the last resort. Well surgery's got to cure it anyway. In the end you've got to have surgery to straighten it up and put it back"* – 16

> *"The last time we went [the consultant] said "we've talked about surgery before as a possibility, I think that might be the next stage along." And I said… OK, if that's what we have to do then so be it"* – 17

Participants spoke about their expectations of what surgery would help them to achieve in their lives, emphasising the influence these expectations had on their decision to have surgery. A common narrative running through participants' dialogue was the desire to achieve a sense of "normality", primarily referring to this in relation to their life before developing their TED. These participants talked about "hope" and now being "the right time" to have surgery.

> *"I've been on the prednisolone now for nearly two years and I can't see that much difference from then to now… so my hope is that this will almost speed the process up of getting back to normality and being able to do the things that I want to do and get off all the tablets and, you know, get back to being a normal me"* – 18

> *"The big thing for me is obviously when you're getting married, being the bride everybody's looking at you… and they say that I'm young and can get married in a few years but then there's other things, you want to spend time together and then have kids so the longer I'm leaving it it's just prolonging it, it's just taking too long. So if there's a chance with the operation that they can actually go back to the way they were then yeah, I would like to do that"* – 21

> *"My eyes were sore, they were running. My vision wasn't perhaps as good as it could have been. But more the sore eyes, and the swelling I suppose as well my age, it was time to - that probably played a part - to get it sorted"* – 02

7.3.4.2 Influence of others

A number of participants described the influence of significant others and family members on their decision to have surgery. Some participants described actively involving others in their decision, including family, who were found to be supportive but for one participant, sometimes unsupportive.

> *"My brother is a doctor in Hong Kong… he personally thinks that I shouldn't have the operation. He thinks that the prominence is not very big and because of the risk he thinks I shouldn't have it…it's because it's so uncommon in Hong Kong, that's why [my brother] doesn't think that I should have it"* – 06

> *"I talked to my family…and they've been supportive. I was told about the side effects, or risks, but I'd like another appointment to make sure that I'm making the right decision with the surgery. My brother's a doctor and he said he'd come with me to my next appointment to make sure I understand everything and I know fully what decision I'm making"* – 21

One participant described being heavily influenced by a friend who had undergone orbital decompression with the same surgeon, and was very positive about their experience. This had a direct impact on their feelings about the surgery, which included excitement, as well as forming positive expectations about surgical outcomes.

> *"I'd say a big influence really has been from what [my friend] said about [my surgeon] doing the surgery…the outcome, she said, it's been fantastic. And I said to my husband, I can't wait"* – 20

For other participants it was discussing the surgery with healthcare professionals that aided their decision. Three participants took time to decide to have surgery over a number of consultations with their surgeon. However, two others described believing it had been more their surgeon's choice than their own to have surgery.

> *"I don't think they hide anything, not because it's not worth it. I think they give you a full and frank picture of everything so you can make that conscious decision. If you don't want to make it there and then you don't have to. You can come away and you can go back. It's all been like a big family, if you want to call it that. Where you can ask as many questions as you like and they don't hold anything back"* – 17

> *"I'm kind of having second thoughts about the surgery and whether I should go through with it. The doctors told me that in time the eyes could go down… And like I said my right eye has gradually got better on its own so I'm not sure that I should go through with it now, or wait to see if they both go back…I'd like another appointment to make sure that I'm making the right decision with the surgery"*- 21

> *"Well it was [the consultant] really he said the last two or three visits we had, he said have you thought any more about it? And in the end I just decided well…we'll come and have a chat and go from there"*- 02

> *"No I didn't have a choice. It was: you're going for surgery"* – 16

> *"[The consultant] said about six months ago, just mentioned that the other thing they could do was a decompression. But I didn't feel it was really my choice, it was whether I needed it or not. I said, well, if that's what you think will help"* – 18

7.3.4.3 Impact of information

All participants reported being given information about orbital decompression by healthcare professionals on the day of being listed for surgery. However, as described later in this chapter (section 7.3.4.3.2) the degree of understanding about what the surgery would involve varied between participants. The majority of participants found that searching for information from additional sources was necessary, and these sources are described in the section below. Participants generally found that the type of information from these searches had a direct impact on the development of their expectations of the surgery. This will be described in the following sub-themes.

7.3.4.3.1 Sources of information

Participants identified a number of sources of information about orbital decompression including Consultant Ophthalmologists, Nurses, others who had undergone the surgery, the surgeon's website, online blogs and forums, and online videos of the surgery. Participants described the impact that this information had on both their emotions, and on their expectations of the surgery. Some participants described fear of the surgery increasing after hearing specific details about the surgery, particularly when it was described as "brutal" or "uncomfortable"

> *"[The consultant] did describe the decompression, he said if we can sort this all out with other treatment, he said, because you don't want to go down those lines because it can be quite brutal… and that put the fear of God into me"* – 01

> *"[The consultant] mentioned the numbing of the face. And I think my friend said that was something that wasn't very comfortable, the face numbness she had. And what that lady on the Internet said was the same.*

> *The numbness of the face, she couldn't eat, she couldn't drink. And I'm thinking, oh gosh"* – 20

Some participants avoided watching online videos of the surgery, as they felt these were too graphic. Some suggested this was because it was no longer something "happening to somebody else" and this made watching it too "real".

> *"No way, anything visual I couldn't look at. I'm happy doing research but I don't want to do too much. Just knowing what they do is enough, I couldn't look at it. It's too much for me"*- 21

> *"Don't type it into YouTube and look at it because it's horrible and it scares the hell out of you. Definitely don't sit there with your mother going, right, this is what I'm having, and watch it, because it's not the nicest thing in the world"* – 05

> *"Now I know I'm on the waiting list it's a little bit of a different ball game. I went a little bit hot and cold and thought, that is going to be me on the other end. I think the realisation of it's not just something happening to somebody else it's going to happen to me"* – 01

Three participants described being satisfied with the information they were given by healthcare professionals. Two of these expressed not wanting to know further details about the surgery and limited the amount of information from sources other than the professionals involved in their care

> *"They explain it in detail I think, so you fully understand what you're signing for. And they explained it really well, you know, to nip your bone here and up here and down here and what they actually do"* – 17

> *"I don't really want to know more. No I'm happy, just happy for it to go ahead"* – 03

> *"I haven't gone online. I know it can be dangerous to go online, you don't know what you might see…I did go on [the surgeon]'s website and he has a video of the surgery. I haven't watched it yet though"* – 04

A number of participants described a process of engaging in self-directed research leading up to the surgery. Using words such as "inquisitive", "informative" and "knowledge", these participants felt that the research they did online gave a clearer picture of what to expect in terms of the procedure, as well as outcomes. A number of these participants also suggested that the information they found online complimented what doctors had said.

> *"I look things up on YouTube, and so I'd already gone on to YouTube and looked at what they do… I'm inquisitive like that. And look, if you're going to put a knife to my face I want to know what you're doing. So I did look it up first, so it wasn't such a big impact when he told me… They haven't said what to expect from it. It's only been because I've looked online, and I've looked at things myself, that I've seen"* – 08

> *"Having done a bit of research into it and found out the facts I was more than confident to go ahead with the operations… being one of those pesky people that in this day and age as soon as they find something wrong with them they go on Google. You do, you Google it, it's just one of those things"* – 05

> *"I think in the hospital they've given me informative information, what I need to know, but I do get the impression that they know everybody will go and try and find out a little bit more about it. And in some ways it helps because I think you see it and you know exactly what you're in for… I think the more you understand about something I think the more informed you are, the more you can anticipate and expect what's going to happen"* – 01

> *"And explaining what they actually do, I found that a bit cringe worthy, but it's just part and parcel of having it done… But I think the fact that if*

> *as a person you can't listen to that, you can still come home and you can Google it. I think that's a brilliant idea"* – 17

A few participants spoke about strategies they used to find relevant information online in order to gain insight into the surgery, which they felt would help them form realistic expectations. However, some participants in particular avoided online blogs about the surgery from overseas patients, describing these as unhelpful, because of perceived cultural differences and differences in healthcare systems.

> *"I went on the Internet and it's quite difficult because you have to be quite picky about which bit of information you read. A lot of it that you pick up is American, and I don't look at American sites because I think a lot of stuff they do is unnecessary and is all about getting money out of their patients. So I was quite particular about making sure it was British sites and that it was sites more medically orientated, rather than just what other people's experiences are"* – 18

> *"I just Google searched it, some people said how upset they were, but fortunately those were in America"* – 06

> *"I generally went for a bit of a scattergun approach. I searched for the condition and then took bits from each different website really, to gain an overall impression… I think I'd expected to have the treatments closer together, the left and right eye. Because from the information I'd found from this woman in America's blog, she had her one eye done one… in one month, then ten days later she had the other eye done"* – 05

A number of participants described comparing themselves to other patients with TED they encountered online. A number found "before-and-after" photos on the surgeon's own website and on blogs, and others found forums, which seemed to influence their expectations of their own surgical outcomes. For some, this was done through a process of "downward comparison" whereby seeing patients who they perceived to have more severe TED than them have good surgical outcomes encouraged them to have high expectations for their own outcomes.

> *[A doctor] told me, go on to [the surgeon]'s website and if you go on there you'll see before and after pictures and of what you can expect…I looked at this one and his eyes was just horrendous…and the before and after results from his was good considering what they was like to begin with. So I look at mine and I think, no they're not as bad. I haven't got as much thyroid fat and everything where they're really out, so I'm hoping just to look like, normal."* – 08

> *"[My partner] showed me the before and after picture when he Googled it all, and you can see the woman's face. Yes her one side looks normal and, yes the other side looks slightly different but you can see the benefit of it. And I think that's where I'm aiming for, to be more myself… that's got to be a fantastic feeling."* – 17

> *"I have read online a lot of people's comments. I go on to a lot of forums and see what people had to say about recovery time and stuff like that. And there's good and bad recovery I think across the board really. Some people might recover quicker than others. Hopefully I'm one of those that recover quicker"* –08

Many participants who did further research into the surgery also found out more about the doctors involved in their surgery and described finding this information reassuring, which helped build their confidence about the surgery

> *"I did my research into…the treatments and a bit on the people who were treating me. I found out as much information as I could about the surgeons and the doctors who were in charge of what I was doing and found nothing but positive information about the people who were treating me. Which was a real reassurance"*- 05

> *I have Googled [the surgeon] and he has got a good reputation. And I think the fact that you can go on the Internet and see his surgery, if you choose to, is a really really good thing to do"*- 17

> *"I was speaking to an old colleague who knows [the surgeon]…she said of all the doctors, you're in very safe hands. So I thought the surgery would be something that I could look forward to, you know?"* – 04

> *"When I found out I was going to be under [my consultant] and again the feedback I've had off a friend, it was more, made it more promising. I thought, well, I've got a top surgeon"* – 20

7.3.4.3.2 Degree of understanding

Information given by healthcare professionals tended to be repeated in the participants' own words, with some confusion for a few participants about what the actual procedure would involve

> *"They said they make an incision under the eye, and somehow break the bone to make space for the muscles"* – 21

> *"He said that the eye's completely out of its socket now, so they'll have to remove the muscle and the bone, because before that they could push it back, just take the muscle out and just push it back, but they said 'cause it's come out of its socket they would have to remove the bone and the muscles…and the eye nerves"* – 13

> *"I understand that there's a small incision across the eye. And that there is a window taken from the orbital skull part there. What I'm not sure about is whether it just drops back or whether it gets stitched back into position"* – 01

> *"They explained to me that it's a cut and then they will try to open a space inside so there will be space for the pressure of the eyes"* – 19

Many participants described undertaking additional research to enhance their understanding of the information they had been given by healthcare professionals in hospital. Particularly given that initial pre-surgical consultations, where the surgery is first offered to patients, tended to be emotionally charged and thus specific details were not well recalled after the appointment.

> *“Information is knowledge, and if you don’t fully understand what’s being explained to you, probably 50% of the people don’t fully listen to what a doctor’s telling you because you’re trying to digest the first part. OK, you don’t do this, you’re going to have no eyesight. OK my brain’s trying to sort that out, and they’re trying to explain to you everything else; you only digest a small amount of that information. You do not fully take it in”* – 17

> *“It was just basic really. I don’t think [my consultant] actually went into loads of detail. I just can’t, I can’t really remember what he said to me about it, I think I was in shock”* – 20

A few participants described seeking, or coming across, additional information online that had not been mentioned by healthcare professionals. When they came across this information it was often confusing and participants described wanting to find out more from their own healthcare professionals.

> *“What I’ve been reading, I don’t know what stage…I don’t what’s, because I’ve been reading is it, one wall, two wall, left? I don’t know. I don’t know all that. I don’t know what extent I’m having done”* – 20

> *“That was the sort of information I was looking for: what were the major complications? What were the risks of those major complications? The only thing I found difficult to find was what were the risks if you didn’t have it done. That was the one thing that was difficult, it was if you don’t have this done what are the risks then?”* – 18

7.3.4.4 The surgical process

Patients' expectations of the surgical process reflected three key issues: perception of the risks associated with orbital decompression, confidence in the surgeon and in the healthcare system and the impact of the timing of surgery. Timing of surgery was described both in terms of the emotional impact of having to wait for surgery, and in terms of how the surgery fitted in with other life plans, including work and family commitments.

7.3.4.4.1 Risk of surgical complications

The majority of participants talked about the risks associated with orbital decompression surgery that had been described to them by surgeons, including "bleeding" and "blindness" and damage to facial nerves causing "numbness".

> *"They said in rare cases you could lose your eyesight, and said something about bleeding at the back. If the bone restructure doesn't work, they said they do something with the eyelids"* – 21

Participants who felt that consultants discussed risk as more of a formality, tended to perceive the risk of these complications happening to them as low.

> *"I was told that you can get some facial paralysis if it goes too low in the orbit… But that may very well get better and in most cases it does within a three month time period. There is a small risk that I could lose vision if they get a lot of bleeding I believe… but it's a very low risk but I have to be warned about it"* – 01

Many participants described what they expected the benefits of surgery to be and felt that these tended to outweigh any risk of complication, despite some of the potential complications being severe, for example blindness.

> *"I just want to move forward, and if that means taking a risk with one of my eyes, and I'm pretty sure that they wouldn't recommend it if they didn't have such a good success rate, and I think that's a massive thing"* - 17

> *"I know there's risks with the operation as well. And it's like, to me, the risks if I don't have it done are definite…If I have the op done, it's, yes there can be complications, but it's not certain that you'll get them. But if you don't have this done it's probably certain that you're going to have … some sight damage, even if you don't lose the whole sight, you're going to have some sight damage"* – 18

Several participants did however perceive the surgery as "risky", not just in terms of the risk of complications, but also in terms of the risk of their expectations not being met in regards to their appearance. A number of participants likened these risks to gambling, and described the weighing up of the risks and benefits.

> *"They do say there could be some damage to your sight…I know there is risk of losing my sight if something goes wrong. Fingers crossed that isn't going to happen. I am scared if anything happened to my right eye…I would manage but if I lost the vision in my right eye, I wouldn't need a white stick or anything, but I probably would need a guide dog. I just hope nothing happens to my right eye"* – 04

> *"I mean you have the operation it might go exactly the way you want it to… my eyes might go back to the way they were and I'd be over the moon if that happened, but then you've got to not think about the worst case scenario, kind of think OK, if that doesn't happen could I live with it?"* – 21

> *"Best case scenario I'd like my old eyes back. However, I'm completely at terms with the fact that I might not get them back ever and that after the operations there might be the option for cosmetic surgery …depending on the feasibility and the availability of those operations, it may be a case that I'd prefer to live with the eyes that I have afterwards rather than potentially risk causing further trauma to them to gamble for the eyes that I started with, which is something that I have to make a decision on at a later stage"* – 05

7.3.4.4.2 Confidence in surgeons and the healthcare system

A number of participants described their unquestioning belief in their surgeon and in the healthcare process, describing feeling "confident" and in "safe hands". Many participants described feelings of trust in their surgeon and other healthcare professionals involved in the process. Such beliefs enabled participants to feel positive in the time leading up to surgery.

> *"Well there are varying degrees of things that could go wrong or in the worst case I could lose an eye, but I'm in [the surgeon]'s hands…so I'm quite happy. I'm quite happy to have this job done"* – 03

> *"I'm very confident in [the surgeon] as a surgeon, and he's sort of been truthful with me all the way through, and I've got no reason to believe that he would tell me anything that wasn't the best for me. So I said well OK, if that's what it needs then that's what it needs"* – 18

> *"I have every confidence in [the surgeon], for him to do it otherwise I would never have agreed to it, never in a million years I wouldn't. It's too precious, isn't it? It's your eyes"* – 17

> *"I'd go in with an open mind….you've just got to put your trust in them, you know?"*– 04

7.3.4.4.3 Timing of surgery

Many participants described the timing of their surgery as an issue that was impacting on them emotionally. The majority of participants were still waiting for the date of their surgery to be confirmed and frequently described this time as "frustrating" and "annoying". One participant's surgery had been cancelled twice previously and this resulted in anger and low mood. Particularly as this group of patients were having surgery on one eye at a time and were facing an even longer journey towards rehabilitation.

> *"I think when my first operation was cancelled, obviously through no fault of anyone, it's broken equipment… but to me I worked myself up to that*

> *first surgery. And obviously they rang the night before, and that was it. I must have been absolutely a living hell to live with, because I was crying all the time… it was my starting point to getting things sorted, because if they do that one they've got to do the second one and then I can try and get my life back on track"* – 08

> *"I'm looking forward to it, I really want it done. It's so annoying that I can't be in the stream as it were because of this heart attack"* – 03

> *"They told me it's one day…I was suggesting that why don't they do it once so that there's no further pain and they told me now they are doing one eye at a time. The operation, I can't wait for it. Even my sister she was asking me "oh is it soon?" I just want to know when this operation is because we can't live like this"* – 19

An underlying narrative within many of the interviews was that the surgery couldn't come quick enough. Participants were prepared to take cancellations and had already notified colleagues at work in case their surgery date came soon. Many expressed the desire to "get it out the way" and wanting to "move on", but not having a date was making them feel held back.

> *"I think it really does depend on how long the list is…But I'm quite happy to do cancellations and things like that, which I have expressed so…. I mean I'd have had it done yesterday if I could"* – 01

> *"We were at one stage asked if we'd take a cancellation and I obviously said yes, because we were asked about holidays and one thing and another and I said to the lady that did my pre op, oh yes I will. And I thought we've got to get this done pretty quick, and it went on and on and on"* – 02

> *"I actually rung the hospital last week, because I think I need to get it done, move on, get it out the way. And I rung the hospital last week and I spoke to the receptionist there, and she said "oh I'll give you the number". Anyway, they give you a different number for the admin part who book*

> *surgeries, and it was constantly engaged and I was getting really frustrated. I was like, all I said to them was I just want a date now. Because then I can think "OK I've got a date now""* – 17

A number of participants had expected the surgical process to be much quicker because they had read information online that suggested it had been for other patients. This led to feelings of disappointment and surprise when patients had to wait longer than they'd hoped to have surgery on each eye individually.

> *"I think I'd expected to have the treatments closer together, the left and right eye close together. Because from the information I'd found from this woman in America's blog, she had her one eye done… in one month, then ten days later she had the other eye done. So I was expecting a quick turnaround, which I didn't get"* – 05

7.3.4.5 Recovery

For the majority of participants, recovery time was an important theme. Many participants were concerned about how long they would be off work, and others were concerned about when bruising would subside and when they would see a change in their appearance. These participants were left with a number of questions even after their pre-surgical consultations, suggesting a lack of clarity regarding what to expect in terms of hospital stay, return to work, bruising and post-surgical follow-up appointments. Participants were mixed in their expectations of the recovery process, which may reflect the varied level of information they feel they received prior to surgery.

> *"An overnight stay I think and a dressing for… I don't know, some days… I don't know. And follow up visits to the clinic and then I'm passed onto another specialist…I don't know what that's to do with? Perhaps an optical specialist, I don't know"* – 03

> *"The last [consultant] that I saw, you know, she said "we can never say… either a surgery can go very well and somebody gets massive swelling and*

> *massive bruising… or somebody that has a really brutal one has hardly anything." So I don't hold out that mine will be good"* – 01

> *"I was more concerned I think when they said it was bilateral rather than unilateral, I thought oh blimey, that's a bigger op then. And then of course after that you think oh, well what's going to be the healing time on that then? And how long will I be out of action?"*- 18

> *"One of the first questions I asked [the consultant] was how long am I going to be off work? Because the summer time is my busy time, very busy time… and he said "well from my point of view you'll be off for a week, but a fortnight ideally you ought to be able to go back to work". But…we decided against that"* – 02

> *"I'm hoping it might just be a small incision or something so it's not that big that you can actually see it. I think after the operation the main thing will be the bruising. And I think I would wait until it goes down before I go back to work"*- 21

7.3.4.6 Appearance outcomes

Participants generally struggled to articulate exactly how they expected the surgery to change their appearance, tending to use "normal", "better" and referring to their eyes as "going back in" rather than a concrete idea about how much they expected proptosis to reduce, or whether they would be left with any scarring. For some, specific reference was made to going back to how they looked before they had TED, which in turn would improve their social interactions and enable social reintegration. Despite expectations about physical appearance post-surgery not being fully formed for many, a number of participants spoke about how they expected their appearance-related cognitions and behaviours to change after surgery, including use of make-up, a change in general concern about appearance, a reduction in how noticeable they would perceive their eyes to be, and that they would evaluate their own appearance more positively after surgery.

7.3.4.6.1 Vague expectations

The majority of participants showed difficulty in expressing what they expected from their post-surgical appearance, with many disclosing that they didn't know exactly what to expect.

> *"I won't have the bulge… the eyeball won't be bulging out so much and I won't have like the swollen eyelids and stuff like that"* – 13
>
> *"I'm hoping my eye will go back in"* – 18
>
> *"Hopefully the redness will go. And they will just go back to a more normal position"* – 08
>
> *"I don't… to be honest I don't really know what to expect. Other than my eyes are going to look better for people looking at me"* – 02
>
> *"The only thing I was expecting was the prominence will be less, that's what I expect, but I don't know to what extent. Will I look exactly like what I was before?"* – 06

Four participants described having low expectations about what the surgery could do for their appearance, suggesting they would look much the same, except that their eyes would be in a slightly less prominent position. Of note, three of these were male participants. These participants appeared to be unbothered by what the surgery would do in terms of changing their appearance, which may have been associated with a lack of concern about appearance more broadly.

> *"It shouldn't change my appearance at all. It'll just push the eye back in…I don't expect nothing until it's over"* – 16
>
> *"I'm no beauty, I never was, so I'm not expecting too much…but if they can do something then that's good"* – 04

> *"No… it shouldn't change much. I expect there'll be a scar. But it doesn't…I don't care. I'm too old to worry about what I look like"* – 03

For a number of patients, not knowing how much their eyes were likely to improve their appearance was a cause for much anxiety and concern. Some participants had put plans on hold until they knew the outcome of the surgery. A few participants suggested their inability to fully imagine what their eyes would look like after the surgery was because they hadn't had enough information from surgeons about what exactly to expect, and that this lack of information was worrying.

> *"I do worry about how much it's going to go back. Because nobody's actually said, we take it back to this millimetres… so there's no like reassurances or telling me how much it's going to go back and how much physically it's going to look different"*- 01

> *"That's why I can't make really any plans because I don't know how the surgery's going to go"* – 13

> *"When I was due to have it done in December I was looking towards the summer, this year, thinking, oh it will all be done by then. Because they told me within six months you'd have that one done, that one done, your eyelids done, everything will be fine. So then I was thinking what I'll be doing in the summer. But obviously now that has gone by"*- 08

> *"Actually I think I don't really know what to expect after the surgery. I know that it should get better but compared to my old self, will I look completely… well exactly the same or is still a bit different? In terms of that I don't think it's very clear and I think it would be very helpful if before the surgery the doctor could tell the patients, well, or maybe give them some photos to show them"* – 06

7.3.4.6.2 Restoring normality

A number of references were made to expecting to look "more normal". In the absence of specific measurement guidelines from surgeons, for many this meant looking like they did before they had TED.

> *"I would like my eyes to go back to the way they were. I think that out of everything that's what I would like, I mean, looking at the way I was previously it was, you know, there wasn't anything that I would've changed in terms of my eyes or anything like that. So me personally I would love for them to go back to the way they were"* – 21

> *"Normal. How they were before I had the eye disease…No swelling, just normal"* – 20

> *"The first thing is the physical side of it, the look of them. I don't want people to look at my eyes and see them as any different to anybody else's"*- 01

The process of surgery for many was like a 'gateway' to achieving the goals they have for their appearance. For some their expectations generalised to every aspect of their lives, from the ability to carry out their normal job, to spending more time with their families. Many participants suggested that looking "normal" would result in regaining a sense of "normality" in their lives

> *"I just want to live a normal life and just take my grandson to the safari park and just… and those are exciting things. And so having this surgery it's, I would, do you know what I would go as far as to say my whole life depends on this surgery, it's having this surgery. And the outcome of it is to how I will lead my life in the future"* – 08

> *"I know when I'm serving somebody or I'm dealing with a complaint or whatever, they've stopped talking to my face because they're looking at my eyes. And I have to push that to the back of my head and think, OK, it's my*

> *job, get on with it. You know they're not looking at you any more because you look different. I don't want to look different any more. I just want to get up, go to work, deal with general public and go out and be… normal"* –17

> *"My quality of life, you know what I mean? Spend more time with my children, take them out and go on day trips, take them to the park, that's what I'm hoping for"* – 20

A number of female participants talked about expecting a change in their appearance after surgery to enable them to enhance their eyes in the ways they had before TED, such as wearing make-up. Some of these participants described attempting to use make-up to conceal their TED, but found this not to work, only drawing more attention to their eyes. Some participants described hoping not to "stand out" amongst others after their surgery. This reflected their desires to go back to who they used to be before they had TED. Participants talked about how they looked forward to no longer having to conceal their eyes after surgery.

> *"If I go out somewhere, just to be able to put that bit of make up on that doesn't look odd because if you've got different shaped eyelids, it's really difficult to get them to look right. It's a silly thing I know, but it means quite a bit…if you're going out somewhere nice, you want to make the best of your appearance. Just silly things like that, putting on a bit of make-up, getting rid of my fringe that's pulled over that eye more"* – 18

> *"I have got a goal. It's to go on holiday and lie on that beach in my bikini without my glasses, looking normal"* – 17

> *"Well hopefully I'll be able to wear make-up again and not…look strange. I think it looks strange, because obviously when you put mascara on and you put eyeliner on, I just think it enhances your eyes, that's what it's meant to do. But when your eyes are already protruding it just makes them look as if you're looking through the end of a milk bottle. So it's just to look normal"* – 08

7.3.4.6.3 Social interaction

Furthermore, the majority of participants talked about how difficult they found social interactions with TED, including facing members of the public, attending family occasions, and socialising with friends. Some participants described experiencing negative evaluations from others and had since withdrawn socially because of fear of this happening again. They often described expectations about their appearance post-surgery in terms of how others would react to them after their appearance had been "restored". Participants also discussed how they expected an increase in social reintegration once they'd had surgery, using terms such as "confidence" and "looking at the whole of me" and again making references to "not looking different anymore".

> *"If it's like big scars I won't really go out, I don't go out much now. Hopefully it'll be a lot better. I don't mind them calling me Scarface or whatever … it's just the Popeye thing. Hopefully it will improve, what people say"*- 13

> *"I'm hoping soon I will start going out with my friends again"*- 19

> *"Hopefully I can hold my head up, look at someone in the eye and have a conversation with them, rather than look at the floor, look at the table, or have a conversation with my daughter because she knows what my eyes looks like…I'll probably be looking forward just to socialising more, instead of having to miss out on things"* – 08

> *"I have a lot of face to face contact with people so I'm hoping that I won't look any different to the person sitting at the side of me, they'll just see me for who I am and not someone that stands out"* – 01

7.3.4.6.4 Timeline to rehabilitation

Some participants described a realistic insight into what the surgery could and could not do for their appearance and the potential need for further surgery after decompression to help restore their appearance further. An underlying narrative for many participants was an understanding that their appearance was not going to be restored overnight and having a realistic expectation for the process of operations to be a long one.

> *"I know it's not a quick fix. I know that, and I've always said I know it's not a quick fix. And I know that it's going to take time. Obviously whether it be swelling, bruising, and how long that might take. So I'm not, I know it's not going to be immediate, but having it done I know that it is going to happen"* – 08

> *"Once I've got the surgery done that's another milestone and there's just different things for me to sort of aim for to try and get me back to where I was. But I don't expect it to happen overnight, I don't expect that. I know it's going to be a long process"*- 01

> *"Well I have to have the surgery to push it back in and then once that's healed I presume go and see the squint surgeon, then once that's healed I've got to have cosmetic surgery…because all my skin's stretched here, over the eyelid"*- 16

There was a sense that participants would rather it was a quicker process, but were patiently accepting of what needed to be done.

> *"Not look at [my eyes] but look at the whole of me and think, yes, that's what I look like… So I think that gives you the confidence to say yes to having the next lot of surgery done and the next one after that because you know in here and up here you are going to get a goal, and that's your goal, to think, OK, I haven't got to ask anybody to take me anywhere … I'll just walk in a crowd with everybody else and not "oh, God, do you see her eyes?""*- 17

> *"I'm hoping in a year's time I would have had both eyes done then, and my eyes will be perfectly perfect basically. That's what I'm hoping. But again, with it being such a long drawn process, I'll probably end up having my*

> *right eye done first, wait a few months have my left eye done. And knowing me I'll end up having more surgery"*- 20

> *"I'd like to think I've sort of, got past it and been done with it. I like to think I'm a very confident person and like I need to be, especially with the work, you need to have confidence and assured of what you're doing in your abilities. So I think I've taken it in my stride and just dealt with it as, yeah, it's one of those things I've got and it's there for now but…it's being dealt with"*- 05

7.3.4.7 Functional outcomes

Participants appeared to be mixed in their understanding of what orbital decompression surgery could do for their visual function. Their understanding impacted on their expectations of surgical outcomes. For instance, a number of participants were clear that decompression would not necessarily improve double vision and that further surgery would be required, whilst others described an expectation that orbital decompression would cure their double vision.

> *"So my eyesight itself, I'm not expecting anything to be different because that's a different surgery. That's the next one along. Mine, so I understand, is more getting them back into position before they can do anything else. It's no good doing the double vision surgery because there's still too much going on at the back of my eyes"* – 17

> *"I have to have the surgery to push it back in and then I go… once that's healed I presume go and see the squint surgeon"*- 16

> *"I was quite looking forward to having this done, to having the eye put back so that I haven't got double vision"*- 03

> *"I'm hoping that it is going to help with the vision as well, though I do understand that there may be other surgery afterwards that may be needed to help with the vision… but I do know that that could be a little bit further*

> *down the line even after that, I do understand that, I know it's going to be a slow process"*- 01

Participants had desires to be able to return to work and their usual hobbies. A common narrative was that improvements in visual function would increase confidence in abilities such as sewing and driving. Some participants spoke about the surgery enabling them to not have to rely on others so much, for instance to be driven somewhere, and gain back some independence and control in their lives. Again, participants spoke about reaching a level of "normality" closer to their lives before TED.

> *"Just to give me a bit of my confidence back … to go to work and stuff. To get my confidence back. To be more like independent…because I have to depend on the family a lot now because I can't see properly some days"*- 13

> *"I just want to get back to normal reading and I notice when I'm in a theatre and I'm sitting at one side I've still got double vision…because of the angle I'm looking, I'm not looking straight at the stage. So I really do want to get back to being able to see properly"* – 04

> *"I just want to improve my way of life. I'm just hoping it will make me better. My vision, you know, it's not* poor *poor, but with the prisms in this just controls double vision… So I'm just hoping all round when I have the surgery, it just improves… well, I am hoping everything"* – 20

Of note, all four male participants spoke more about concerns regarding post-operative functional outcomes, specifically in terms of return to work and hobbies, than about their post-surgical appearance

> *"As long as I can still drive and I can still, you know, enjoy life, enjoy doing things, that'll suit me. You know, I'm not expecting miracles"* - 02

> *"When I was told that I'd be listed for the second one and that it might be a matter of months and I was initially thinking, well hang on, I'm going to have one eye that's in focus and one eye that's not in focus because of the difference in the pressure I thought I'm not going to be able to see properly"* – 05

> *"I really do want to get back to being able to see properly"* - 03

7.4 DISCUSSION

The aim of this study was to explore the expectations of patients with TED listed for orbital decompression surgery and to understand what may influence the formation of these expectations. The overall narrative was that participants lacked clarity on exactly what to expect from the surgical procedure, recovery, and their post-operative appearance. This caused concern for many participants. However, participants were generally confident in their surgeon's abilities, perceiving the risks of surgery as low. Despite not knowing exactly what to expect from their post-surgical appearance, participants had high expectations for the surgery to enable them to regain "normality" in their lives including appearance, independent living and social reintegration. Each of these themes will now be discussed in relation to previous research, and a discussion of the strengths and weaknesses of this study will be provided in section 7.4.8. The implications of these findings in relation to research and clinical practice will be discussed in Chapter 10. The findings from this study in combination with the quantitative results from the cross-sectional study described in Chapter 6 will be discussed in Chapter 8.

7.4.1 Consequences of living with TED

All participants spoke about the impact TED had had on their lives, and the influence this had on their decision to have surgery. The consequences of TED ultimately formed their expectations of what surgery would help them to achieve. Participants generally felt that surgery was the next step and the "last resort" in their treatment, following a range of drug treatments that failed to improve appearance, vision, or both. Surgery was generally considered necessary in enabling participants to achieve their goals and to return to some level of “normality”. Understandably, many patients with disfiguring conditions opt to have rehabilitative surgery to help restore their appearance to “normal” (Denford et al., 2011; Bramwell, Morland & Garden, 2007; Bhty, 1999; Harcourt & Rumsey, 2001).

7.4.2 Influence of others

Participants spoke about the impact of shared-decision making with healthcare professionals, or lack thereof, in forming their expectations and decisions to have surgery. For some, consultations did not involve as much shared decision-making, but rather patients felt that they didn’t have a choice about having the surgery. Similar findings have been reported in the context of reconstructive surgery following breast mastectomy, with patients reporting that surgeons *expected* them to have breast reconstruction rather than giving them the option and were shocked when patients were inclined not to have surgery (Noone et al., 1982; Harcourt & Rumsey, 2004). In contrast, many participants felt they had been given time to make an informed choice and could return to the hospital for further consultations if they needed them. This division in response to the consultation supports findings from a previous qualitative study where patients with TED felt disengaged from their care if they had difficult encounters with healthcare professionals, but felt empowered in their treatment process if they felt actively involved in consultations (Estcourt et al., 2008).

Participants generally felt that family and friends had been supportive of them having surgery. For one, a friend who recommended the surgery had a big impact on their decision to go ahead with the procedure and ultimately this influenced their expectations for positive surgical outcomes. However, another participant recounted that her medically trained brother disagreed with the necessity of her operation. This is particularly important given that a recent literature review found a lack of support from significant others about having surgery can predict poor psychological outcomes after surgery (Honigman, Phillips & Castle, 2004). Whilst having others who are able to support a decision to undergo surgery enhances feelings of confidence about the decision, going against the advice of someone close to you could impact on psychological well-being following surgery.

7.4.3 Impact of information

The information needs of the majority of participants appeared to be high. Many participants described themselves as "inquisitive" and exploring additional sources of information following information given by healthcare professionals. Participants described a number of sources of information in addition to healthcare professionals, including other patients who had had the surgery, and the Internet, which was the source for forums, blogs, medical websites, and videos of the surgery.

Participants expressed confusion in relation to the information given by healthcare professionals and often struggled to articulate exactly what they had been told about the surgery. This has previously been found after patients are given information about surgery, particularly when this consists of medical jargon and technical terms that they find hard to understand (Newell et al., 2004). Information accessed online has also tended to raise further questions, particularly if patients found it difficult to understand new information that healthcare professionals hadn't mentioned before. In a recent study by Edmunds et al. (2013), online information about TED was identified using a Google search and assessed for readability using the Flesch-Kincaid Readability Score and the Gunning-Fog Index. Edmunds et al. (2013) found information to be written for comprehension levels higher than is recommended by published guidelines, with no significant differences between countries of origin of the web page. This is an important issue because if information is difficult to understand, patients misinterpret health guidelines (Walsh & Volsko, 2008). It is therefore unsurprising that this group of patients were left with further questions about the surgery, and there is a risk that misinterpreting health guidelines may give rise to unrealistic expectations.

A number of participants, however, found that using the Internet for additional information complimented what surgeons had told them in prior consultations, as well as giving them questions to ask in future consultations to further their understanding. Online information about the surgery therefore has the potential to assist with understanding and managing patients' expectations. However, due to the uncontrolled nature of the Internet, there is a need for healthcare professionals to understand what information patients have accessed and where possible provide additional comprehensible information.

Some participants described difficulty recalling information given by their surgeon, as the pre-surgical consultations tended to be emotionally charged, where patients felt overwhelmed and unable to “take it all in”. Difficulty in absorbing information has been found to be related to consultations that are emotive and packed with information about diagnoses and treatment, particularly in appearance changing conditions including head and neck cancer (Newell et al., 2004) and breast reconstructive surgery (Harcourt & Rumsey, 2001). This is an important issue that healthcare professionals need to be aware of. Checking understanding after each piece of information is given to the patients, and being compassionate when patients become emotional are skills that have been found to be effective at increasing information retention and compliance with medical treatment after healthcare consultations (Ong et al., 1995; Girgis & Sanson-Fisher, 1995). These skills could therefore be useful in the management of patient expectations of surgery.

Participants who did consult the Internet found that “before-and-after” photos on online blogs and positive information about the surgeon increased expectations, tended to reduce fear, and increase excitement about potential surgical appearance outcomes. One participant described how seeing another patient who they perceived as “worse off” prior to surgery who then had a good aesthetic surgical outcome increased expectancy that their own outcome could only be good. A rise in demand for, and accessibility of, “real life” information about surgical procedures including online videos and “reality TV”, have led researchers to begin to explore the impact of such information on patient expectations. In studies of women who had undergone breast enlargement, accessing the media has been found to play a significant role in women’s conceptualisation of surgical outcomes, with women reporting that television programmes influenced them to pursue cosmetic surgery (Byram et al., 2001; Crockett, Pruzinsky & Persing, 2007).

In contrast, videos of the surgery accessed online increased fears about the surgery in some patients, as it made surgery feel "too real". The influence of videos in patients' decisions to have surgery has been highlighted by one study that found subsequently lower surgery rates for back problems in patients who watched an interactive video compared to those who only read a booklet (Deyo et al., 2000). However, quality of life did not reduce in patients who did not have surgery compared to those who did (Deyo et al., 2000), suggesting the importance of ensuring patients are fully informed before making a decision to have surgery. In particular, this suggests that deciding not to have surgery will not necessarily result in poorer quality of life outcomes. Additionally, Zvara et al. (1996) found that using surgical videos as a teaching tool in patients awaiting surgery did not increase knowledge or patient well-being. This further highlights the importance (but difficulty) for healthcare professionals to help manage patient expectations by providing accurate information. This also demonstrates the various sources of information about surgery that may be accessed by patients and the variation in knowledge attainment and influence on decision to have surgery from these sources.

For many, accessing information about the surgery online helped to enhance understanding in future consultations with surgeons. With more perceived knowledge came a less anxious patient with more concrete expectations of the procedure. Women who regularly watch "reality TV" shows about cosmetic surgery have been found to report higher degrees of self-perceived knowledge about the surgery after consultations with surgeons than women who watched at lower-intensities (Crockett, Pruzinsky & Persing, 2007). "Real life" accounts of surgical outcomes can be helpful for some patients in terms of reducing anxieties and increasing expectations; however if such accounts are only ever examples of "best case scenarios" and tend to consistently be in favour of such procedures, this might generate unrealistic expectations. Furthermore, whilst surgical videos might increase perceived knowledge, they do not always increase factual knowledge (Zvara et al., 1996). This highlights the importance for healthcare professionals to attempt to ensure that expectations of orbital decompression are realistic, particularly if patients are relying heavily on "before-and-after" photos to present them with a realistic idea of what to expect from their surgery.

7.4.4 The surgical process

All but one of the participants was waiting for a date for their surgery and many found themselves to be waiting far longer than they had expected. This resulted in feelings of frustration, anger and disappointment. Many described putting various plans on hold until they knew when their surgery would be, such as holidays, and even weddings. Patients with TED often face a delay in their treatment and the rehabilitative process is commonly a long one (Estcourt et al., 2009). On the basis of the finding s in this study, it would seem valuable therefore, for patients to be made aware of potential delays to the surgery at the earliest time possible.

Participants in this study appeared to be aware of the risks involved in orbital decompression surgery, which ranged from the more rare risk of blindness, to more common complications including facial numbness and double vision. Participants tended to perceive these to be low and many were happy to go ahead with the surgery regardless. One or two patients however were anxious about the risks and had thus booked additional appointments with healthcare professionals prior to surgery to discuss these further. The tendency to anticipate many problems ("vigilant coping") versus the tendency to anticipate few problems ("avoidant coping") is a common finding in studies investigating expectations prior to major surgery (Kiyak et al., 1988; Cohen & Lazarus, 1973). Interestingly, avoidant coping prior to surgery has been found to be associated with better post-surgical outcomes, including fewer problems with recovery and better mood, than vigilant coping (Kiyak et al., 1988).

Low perceptions of risk were often associated with having great trust in surgeons and the surgical process. Patients in this study often described themselves as being in "safe hands". This contradicts previous research in TED that has suggested that patients find it hard to develop trust and confidence in healthcare professionals (Estcourt et al., 2011; Estcourt et al., 2008). Studies in women who have undergone breast surgery found that patients perceiving their surgeon to be caring, reassuring, and available to answer their questions enabled them to trust their surgeon, feel confident about their surgery, and form realistic expectations about what the procedure can achieve (Klassen et al., 2009; Snell et al., 2010).

7.4.5 Recovery

Expectations about recovery after the surgery were a source of anxiety for many. The majority were uncertain about how their recovery would go, and many continued to ask questions even after their consultations. Participants did however seem to have clear expectations with regards to recovery and talked about anticipating bruising, pain, and for recovery to take a long time and to require at least two weeks off work. Many anticipated having to take more time off work than the two weeks the surgeon had suggested, particularly if their jobs involved a potential risk to further damage to their eyes, such as working on a construction site, or working at a computer for long hours. This is particularly important given that accurate expectations for recovery prior to surgery and a sense of perceived control have been found to lead to fewer postoperative difficulties (Johnston, 1986). However, postoperative recovery has been found to be slower, and distress greater, in patients who are highly anxious prior to surgery (Johnston, 1986). This highlights the importance for surgeons to identify patients that go beyond a realistic insight of what post-operative symptoms and side effects to expect into anxiously anticipating the worst, in order to enhance post-operative outcomes.

7.4.6 Appearance outcomes

This study found that some participants did not know what to expect in regards to their post-surgical appearance. Many participants were used phrases like "less prominence", and indicated the desire to know exactly what they would look like. Similar findings have been reported in a study of women awaiting breast reconstructive surgery, where patients often described vague expectations (Mazza, 2014). One reason for participants being tentative about their expectations regarding their post-surgical appearance might be because having high expectations could lead to disappointment if surgery didn't meet their expectations. This hypothesis is supported by a study that found women were unable to articulate their expectations for their outcomes from surgery for gynaecological cancer, for fear of having too high expectations (Bhty, 1999). For many, the post-surgical change in appearance would mean their lives would be "back on track". The majority of participants reflected on their expectations for surgery to enable them to look how they did before they had TED. It has been found in a number of studies on outcomes after reconstructive surgery that expectations for surgeons to "recreate lost looks" (Partridge, 2006, p. 956) can cause disappointment, dissatisfaction, and even distress with the outcome (Partridge, 2006; Snell et al., 2010; Harcourt & Rumsey, 2001). Patients with TED might therefore face similar disappointment if surgery does not meet their high expectations.

Some people in this study felt that their whole lives depended on having orbital decompression surgery. Orbital decompression was described in terms of it being a 'gateway' to achieving goals in appearance and re-gain a "normal" appearance. This is particularly important as patients who expressed disappointment after surgery for TED in a previous study had unrealistic expectations that the surgery would enable them to go back to the life they had before TED (Estcourt et al., 2008).

Patients with TED consistently report that the change in appearance of their eyes causes problems in social interaction, including feeling others avoid them, or misinterpret their facial expressions (Jensen & Harder, 2010; Terwee et al. 1998). It is therefore unsurprising that participants in this study had high hopes for being able to reintegrate socially after surgery. Participants in this study reported high levels of social avoidance and withdrawal due to TED, and were expecting this to change after their surgery in a number of ways. They expressed hopes not to stand out, or look different from others after surgery. A number of female participants had a desire to stop concealing their eyes in public and were expecting surgery to enable them to do so. Participants generally felt surgery would bring back their confidence to make eye contact with others, face the public, socialise with friends and family, and be accepted by others. How quickly this is likely to happen has been raised by Partridge (1990) who suggests that social reintegration following a disfiguring condition or injury requires a process of learning new communication skills, which is unlikely to happen overnight. For participants who expect to look exactly as they did before TED it might be a shock to find they might still need to adjust to slight differences in their appearance even after surgery by making efforts to manage the occasional comment from others.

7.4.7 Functional outcomes

A number of participants described expecting many aspects of their lives to improve after the surgery, including work, family life, hobbies, and re-gaining independence. This was not only from a change in appearance but also from improvements in visual function. More than half the sample had double vision and some expressed expecting orbital decompression to improve their vision, despite the fact that this surgery often does not resolve double vision and may even make it worse (EUGOGO et al., 2009). Research on expectations of cataract surgery has found similarly high preoperative expectations about postoperative function, with 60% expecting to achieve near perfect vision. Post-surgical realities however failed to meet expectations with only around 60% achieving expected outcomes (Pager, 2004; Tielsch et al., 1995). This further highlights that discrepancies often exist between pre-surgical expectations for improvements in function and post-surgical outcomes.

The finding that male participants appeared to be more concerned about their functional outcomes than appearance outcomes is in line with previous studies that have found for men the biggest impact of having a disfiguring disease are physical limitations rather than changes in appearance (Andreasen & Norris, 1972; Brown et al., 1988). Estcourt et al. (2008) found men with TED did not report feeling socially inhibited because of changes in their appearance. This supports the notion that men with disfiguring conditions are more concerned with functional limitations as their appearance changes do not appear to inhibit them socially. It is also possible that in TED, where men are often found to have more severe clinical symptoms than women, express more concern about these issues.

This qualitative study has highlighted the complexity of the expectations of patients with TED prior to rehabilitative surgery. As with all studies, findings need to be interpreted in light of limitations of the methods used. The next section of this chapter will therefore describe the strengths and weaknesses of the methodology used.

7.4.8 Strengths and weaknesses of the study

As semi-structured interviews depend on participants' willingness to guide the interview and describe their experiences in depth, they may vary in their quality and length. Interviews also rely on participants' understanding of the topics and concepts initiated by the researcher. However, complex psychological concepts, such as issues of expectations and quality of life are important to explore using qualitative methodology but could pose a problem for participants with poor education or for whom English is not a first language.

As the researcher had prior experience collecting data about quality of life and other psychosocial issues in TED, they may have formed pre-conceptions about what participants would talk about in interviews. It is possible that the researcher's preconceived notions of what the data would reveal might have influenced the content of the interview guide and the way questions were asked during interviews. To a certain extent this would have been overcome by the asking the supervisory team to review the topic guide before interviews commenced, and again when it was amended after the pilot interview. This is also commonly overcome by keeping a reflective diary after each interview (Shauver & Chung, 2010), which was done for this study and can be found in Appendix Q.

A sample size of 14 patients was interviewed for this study, which might be considered too small to be generalizable to a wider population of patients with TED. The sample was, however, diverse in their age (which ranged from 23 to 76), disease duration, and their treatment history reflected the typical history of a patient with TED being offered orbital decompression surgery. The gender distribution of the sample reflected a ratio typically found in samples of patients with TED and in the wider population of patients with TED. In addition saturation was achieved with the number available.

Three of the participants included in this study had had orbital decompression on one eye prior to their interview and were awaiting decompression on their other eye. This was unavoidable due to time restrictions to recruit the desired number of patients for this study and as BMEC perform around 10 to 15 decompression surgeries each year (Perros et al., 2012). The experiences of these patients of prior decompression are likely to have influenced their expectations of surgery. For example, their expectations may have been better formed than patients at other stages of their treatment trajectory. However, this sub-sample were also considered too small a group to analyse their data separately. Furthermore their prior experience did not affect the quality of their answers in interviews about their expectations and the data they provided was still considered relevant and valuable for this study.

One criticism of qualitative research is that "anything goes" (Braun & Clarke, 2006, p95). However, the phases of thematic analysis have been clearly outlined in recent years and the analysis methods were rigorously applied. Validity checks were undertaken, including applying the COREQ checklist (Tong, Sainsbury & Craig, 2007), for example that a variety of participant quotations were presented to illustrate themes/ findings and to add transparency to the data and interpretations. In addition, a second researcher independently coded 20% of the interviews to ensure accuracy of the coding process and that nothing was missed by the researcher. In addition the researcher kept a reflective diary during interviews and the analysis in an attempt to understand the influence they might have had on the data collected and the analysis of the results.

The present study did not deal with patient experiences after surgery, so it is uncertain whether patient expectations of orbital decompression for TED were met, had an impact on mood and quality of life after surgery, or changed over time. As a result no definitive conclusions can be made about whether expectations were unrealistic, or resulted in dissatisfaction with post-surgical outcomes.

7.4.9 Summary

The aim of this study was to explore patients' expectations of orbital decompression surgery for TED. This was the first qualitative study in TED to explore patients' expectations of their upcoming surgery. The overall narrative was that participants perceived surgery to be inevitable, and the gateway to restoring their appearance and enabling them to get back to the life they had before TED. Participants lacked clarity over exactly what to expect of the procedure, and of post-surgical appearance outcomes, remaining tentative and hopeful for "best case" scenarios they had viewed online. Participants commonly referred to a desire to re-gain a sense of "normality" in all aspects of their lives. Participant felt frustrated at having to wait so long for surgery, but remained trusting of the healthcare process and confident in their surgeon's abilities to help them achieve their goals in terms of both functional and appearance-related quality of life.

The ability of healthcare professionals to manage patient expectations of surgery for TED depends on their understanding of patients' beliefs, concerns, and the impact on patients of accessing certain information about the surgery online, or hearing from others. Only with such knowledge can they give clear, relevant, information about the surgery that patients need, given in terms they can comprehend. In the context of this study it appears it is important that patients feel able to return for consultations prior to surgery in order to ask questions, and talk about their fears about the surgery so healthcare professionals can dispel any myths or correct any misinterpreted information. The results of this study could help to inform shared decision making between patients with TED and their surgeons in future consultations.

7.5 REFLEXIVE ACCOUNT

The researcher has prior experience interviewing participants for qualitative health psychology projects. The researcher is female and is educated to postgraduate level. The researcher had spoken to each of the participants on the phone to arrange the interviews; no further relationship was established prior to the interviews. The aims of the study and instructions for interviews were explained clearly before each interview, and understanding checked, to ensure that participants weren’t surprised by any questions or unclear about the study. The researcher introduced herself as a PhD student at City University London and made it clear to participants that she did not have medical training. On any occasion where participants asked medical questions during the interviews, the researcher urged participants to speak to the healthcare professionals involved in their care.

As the researcher had prior experience recruiting patients with TED for quantitative studies, she understood that TED can cause significant anxiety, depression and appearance concern for many patients and was aware of the need to approach topics sensitively and compassionately. During three of the interviews, participants became upset when they recalled particular experiences with their disease. The researcher gave these participants the opportunity to have a break from the interview, or indeed to terminate the interview if the participant felt this was necessary. On all such occasions, participants wanted to continue with the interview after a short break. The researcher approached this study with the understanding that qualitative data is rich in detail and felt it inappropriate to interrupt participants during interviews even if they were going slightly off-topic. This may explain the length of some of the interviews. Similarly, the researcher felt uncomfortable pushing participants into giving great detail where they clearly found it difficult to articulate their views. This may explain the short length of some of the interviews.

At the end of each interview, the researcher ensured that participants were not left in a distressed or emotional state. The researcher offered participants the contact details of two TED charities, which offer information, advice and support to patients.

Reflective notes that were taken during the thematic analysis, which position the researcher within the analytic process, can be viewed in Appendix Q.

Chapter 8 will now bring together the findings from this qualitative study, along with the results of the cross-sectional study reported in Chapter 6, to discuss the areas of new knowledge and the implications for research, theory and practice.

8. SYNTHESIS OF THE QUANTITATIVE AND QUALITATIVE FINDINGS IN PATIENTS WITH TED PRESENTING FOR ORBITAL DECOMPRESSION SURGERY

8.1 PROLOGUE

The following chapter will present the key similarities and differences between the results of the cross-sectional quantitative and qualitative studies investigating demographic, clinical and psychosocial factors in patients with TED presenting for orbital decompression surgery. Embedding a qualitative study within the quantitative investigation of patients prior to surgery provided valuable insight into participants' beliefs and expectations about their upcoming surgery, which have provided additional detail to the research findings. Interpreting these embedded results in relation to the results from the main quantitative study is a key stage of good quality mixed methods research in health sciences (O'Cathain, Murphy & Nicholl, 2008).

8.2 DEMOGRAPHICS

The quantitative study found that being female was associated with poorer appearance-related quality of life. The findings from the qualitative study supported this, with female participants talking extensively about their hopes for their appearance outcomes after surgery. Gender was not found to be associated with vision-related quality of life in the quantitative study, despite male participants in the qualitative study referring more to their expectations for their visual function after surgery. The findings from the qualitative study support previous research in the field of visible differences, where men have been found to be more concerned about the functional limitations of their visible disfigurement compared to women, whom it is suggested were more concerned about appearance-related issues (Andreasen & Norris; 1972; Brown et al., 1988). However, with only four male participants in the qualitative study, it is difficult to confirm these findings.

Interestingly, despite men appearing to be less concerned about appearance outcomes post-surgery in the qualitative study, the quantitative study found no significant difference between men and women in their levels of appearance-related distress and social avoidance, as measured by the DAS24 (Carr, Harris & Moss, 2005). This discrepancy may be due to the bias associated with these different methodologies. It might be that during interviews, men felt more socially inclined to minimise the impact of their condition on their perceptions of their appearance, as men are commonly expected to be less concerned about their appearance. Whereas questionnaires completed anonymously at home might allow for more honest responses.

8.3 CLINICAL FACTORS

The only clinical factor prior to surgery found to be associated with quality of life in the quantitative study was having asymmetrical TED. This finding was unsurprising as having asymmetrical TED can impact on visual function (Terwee et al., 1999). No other clinical characteristic provided a unique contribution to explaining variance in quality of life in the quantitative study. Participants in the qualitative study rarely referred to clinical characteristics when discussing the formation of expectations, or even their expectations of surgery. The only exceptions were when they referred to not knowing exact millimetres to expect orbital decompression to reduce their proptosis by and double vision:

> *"I do worry about how much it's going to go back. Because nobody's actually said, we take it back to this millimetres… so there's no like reassurances or telling me how much it's going to go back and how much physically it's going to look different"*

Participants expressed a desire to know more about how their eyes would look after surgery, to enable them to form expectations about their objective appearance post-surgery. Additionally, participants in the qualitative study spoke about hoping that their vision would improve after the surgery. However, they related these hopes to activities of daily living that had been affected by their double vision due to having TED rather than having specific clinical expectations, such as expecting double vision to change from "constant" to "intermittent" or "inconstant", which is one potential clinical outcome from orbital decompression (Terwee et al., 2001; EUGOGO et al., 2009).

8.4 INTERVENING COGNITIVE PROCESSES

8.4.1 Appearance related social anxiety and avoidance

Both studies have offered insight into the psychosocial consequences of living with TED. The quantitative study found that appearance-related social anxiety and avoidance were associated with quality of life. Similarly, the majority of participants in the qualitative study raised the issue about the consequences of living with TED, in particular that a change in their appearance had affected their ability to interact with others as normal and had resulted in a number of patients withdrawing from social participation. The findings from both these studies are consistent with other studies in TED (Estcourt et al., 2008) and other types of facial disfigurements (Rumsey et al., 2004). They also support Newell's (1999) fear avoidance model in that anticipated unpleasant encounters with others have led to social withdrawal in TED. The qualitative study also found that many patients expected orbital decompression to enable them to engage in social activities as they had before they developed TED. This was in all aspects of their life, including facing the public, attending family occasions and socialising with friends.

8.4.2 Salience and valence of appearance

Evaluating their appearance more negatively was found to be associated with poorer appearance-related quality of life in the quantitative study. This was supported by the qualitative study where many participants gave reasons for having surgery that included wanting their appearance to improve.

8.4.3 Perceived noticeability

Perceived visibility of TED was found to be associated with appearance-related quality of life in the quantitative study. Furthermore, many participants in the qualitative study discussed the issue of feeling that their TED was highly noticeable to others, fearing negative evaluations because of this, and placing great hope on the surgery reducing the noticeability of their TED. The basis for reconstructive surgery for a disfiguring condition is founded on the belief that an improvement in appearance and noticeability of a disfigurement will lead to a better quality of life (Ong et al., 2007). It has, however, been previously suggested that patient satisfaction with the outcome and reduced levels of distress will only follow if surgery reduces subjective noticeability of the condition regardless of the objectively successful result (Moss, 2005).

8.4.4 Mood

Previous studies in TED have reported low mood in patients, with around a quarter found to have possible clinical levels of depression (Kahaly et al., 2005), a finding consistent in the current quantitative study. Depression was found to be strongly associated of the variance in both visual- and appearance-related quality of life in the quantitative study. Participants in the qualitative study indicated that levels of low mood were associated with the frustration of having to wait longer than expected for surgery, as well as the impact of their visual function and change in appearance. This could be one explanation for the high levels of depression found in the quantitative study where patients were awaiting surgery.

8.4.5 Expectations of surgery

No study to date has explored in detail patient expectations of orbital decompression surgery. The quantitative study aimed to investigate what demographic, clinical and psychosocial factors are associated with quality of life in this patient group. It has been suggested in previous studies that expectations are complex psychological processes and expectations of treatment outcomes might impact on patients' perceptions of the success of treatment. It was therefore deemed important to explore whether expectations were potential intervening cognitive process that might be associated with variation of quality of life in TED prior to surgery.

The E-TEDS was developed for this purpose as no other questionnaire existed that measured expectations of surgery for TED. However, expectations measured using the E-TEDS were not significantly associated with quality of life. There appeared to be differences in the importance of some concepts associated with expectations of surgery between the two studies. For instance, the item regarding expectations of the relationship with eye doctors was removed from the E-TEDS as it did not correlate well with the other items in each subscale (appearance concern, visual function and intimacy and social relationship). However, the results of the qualitative study gives some indication that their relationship with healthcare professionals was more closely related to information provision and confidence in their care; concepts that were not captured by the E-TEDS. Furthermore, patient's interactions with healthcare professionals have been found to influence their perceptions of and satisfaction with their care in TED (Estcourt et al., 2008). It could be argued that the 23-item expectations questionnaire did not capture the full scope of patients' expectations of orbital decompression surgery. As argued by Dawn and Lee (2004) in a recent literature review of patient expectations in ophthalmology, "patients' expectations are complex and require further inquiry" (p.519) and this seems to have been supported by the qualitative study in this thesis.

8.4.5.1 Information about orbital decompression

The impact of information about orbital decompression patients had sought, or received, was found to heavily influence the formation of patient expectations of surgery in the qualitative study. A number of recent studies have found that patients place high priority on communication with healthcare professionals and explanation of medical information when undergoing surgery (Dawn & Lee, 2004; Newell et al., 2004). When participants did not find out everything they wanted to know from healthcare professionals, they accessed other sources of information, including the Internet. For some, this helped clarify what had been said in previous consultations but for many these raised further questions and fears about the surgery. Information patients had received about surgery was not something that was measured in the quantitative study so it is unclear how different levels and understanding of treatment information might predict psychological adjustment. This would be an important area of further enquiry, particularly as detailed and comprehensive information about surgery can help to manage patient expectations (Newell et al., 2004; Houtman, 2000).

8.4.5.2 Managing expectations

Because ophthalmologists are involved in both medical and surgical management of TED, it has been argued that knowledge and management of patients' expectations are even more important in ophthalmology than other specialities (Dawn & Lee, 2004). Whilst the quantitative study suggested that expectations of the outcome of surgery in terms of appearance, function and intimacy and social relationships, were not associated with quality of life in patients presenting for surgery. The qualitative study found that expectations are either under-developed, or optimistic and bordering on unrealistic, leading to the potential for unmet expectations to impact on quality of life post-surgery. The qualitative study highlights the value that patients place on healthcare professionals in the formation of their expectations and as the “gateway” to enabling them to go back to the “normality” of life before TED, and in whom they have great confidence to help them reach these goals. The need for healthcare professionals to manage patient expectations prior to surgery for TED has been highlighted by the qualitative study. Initial research has found that interventions that manage patients’ expectations are effective at increasing postoperative satisfaction with the outcome (Dawn & Lee, 2004). This study implies the need for healthcare professionals to understand patients’ beliefs, concerns, and the impact on of accessing information about TED surgery on the Internet, and to give clear, relevant information about the surgery in terms they can comprehend.

8.5 STRENGTHS AND WEAKNESSES OF USING MIXED METHODS

The concurrent embedded approach used within this thesis is characterised by one approach being more dominant (Curry et al., 2013); in this case the qualitative study was embedded within the quantitative design, which was the dominant method. However this is one method of many within mixed methods research: the synthesis of quantitative and qualitative methods is a rapidly growing area of research methodology and new techniques are likely to arise in the future (Pope, Mays & Popay, 2007).

One limitation of the current study was the ordering of the quantitative and qualitative elements. The research program might have benefited from conducting the quantitative study after the qualitative study, as the results of the qualitative study could have informed the development of a more comprehensive expectations questionnaire. However, due to the need to complete this research in a specified time frame so as to accommodate the constraints in the data collection period it was necessary for the two studies to run concurrently. Despite this, the results of the qualitative study largely confirmed what had been measured in the quantitative study and the results are unlikely to have been drastically different.

The experiences of people with TED are complex and involve limitations in visual functioning as well as the psychological impact of a changed appearance. This is further complicated by the need for a range of drug treatments and radiotherapy which, if ineffective, can lead to the requirement for major and multiple surgeries to rehabilitate appearance and improve visual outcomes. Due to the complexity of the condition and its treatment a mixed methods approach enabled the researcher to gain insight into variable individual experiences and to assess patterns and similarities across patients, perhaps beyond what would have been achieved through the use of only one method or the other.

This section of the thesis has explored cross-sectionally the quality of life and expectations of patients presenting for orbital decompression surgery. The next Chapter describes the results of a longitudinal follow-up study that examined whether clinical and psychosocial factors change after orbital decompression surgery, and what factors might predict quality of life outcomes after surgery.

9. THE PSYCHOSOCIAL AND CLINICAL IMPACT OF ORBITAL DECOMPRESSION SURGERY FOR TED

9.1 PROLOGUE

This chapter presents the results of the study that has investigated the following research questions:

(3) Does quality of life change from pre- to post- decompression surgery?

(4) Which clinical and psychosocial factors change from pre- to post-decompression surgery?

(5) What demographic, clinical and psychosocial patient characteristics at baseline predict change in quality of life from pre- to post-decompression surgery?

(6) Which changes in clinical and psychosocial factors from pre- to post decompression surgery predict change in quality of life from pre- to post-surgery?

Chapter 4 described how the basis for reconstructive surgery for a disfiguring condition is founded on the belief that an improvement in appearance and noticeability of the disfigurement will lead to a better quality of life (Ong et al. 2007). It has, however, been previously suggested that patient satisfaction with the outcome and reduced levels of distress will only follow if surgery reduces subjective noticeability of the condition regardless of an objectively successful result (Moss, 2005). The systematic review in this thesis (Chapter 3) reported that past studies evaluating orbital decompression in terms of clinical and quality of life outcomes have failed to capture other psychosocial variables that might impact on quality of life and help to explain the variability in quality of life outcomes (EUGOGO et al., 2009; Tehrani et al., 2004; Terwee et al., 2001; Kashkouli et al., 2011b; Fichter, Krentz & Guthoff, 2013). This study, therefore, aimed to evaluate the effects of orbital decompression surgery on clinical and psychosocial outcomes using the framework of adjustment to disfiguring conditions (ARC, 2008) to guide the analytical model (Figure 9, page 117).

Data for this study was collected at three time points: prior to surgery, 6 weeks post-surgery and 6 months post-surgery. The analysis described in the following 3 sections of this chapter focuses on change over time from pre- to post-surgery. Research questions (3) and (4) have been addressed by analysing change across all three time points (see section 5.10.4.2 for a detailed summary of the methods used). Research questions (5) and (6) have been addressed by evaluating change from pre- to 6 months post-surgery (see sections 5.10.4.3 and 5.10.4.4 for a detailed summary of the methods used).

9.2 DATA ASSUMPTIONS

9.2.1 Scale reliability

All scales were found to be highly reliable at each time point (i.e. $\alpha > 0.7$, Table 16)

Table 16. Internal reliability of psychosocial scale variables at all 3 study time points

	Baseline		6 weeks		6 months	
Scale & subscale	**No. of items**	**Cronbach's α**	**No. of items**	**Cronbach's α**	**No. of items**	**Cronbach's α**
HADS Anxiety	7	.874	7	.865	7	.880
HADS Depression	7	.851	7	.863	7	.838
DAS24	24	.943	24	.927	24	.936
GOQOL Visual function	9	.917	9	.920	9	.952
GOQOL Appearance	8	.870	8	.886	8	.912
CARSAL	5	.898	5	.850	5	.876
CARVAL	8	.890	8	.865	8	.934
MSPSS Friends	4	.935	4	.951	4	.932
MSPSS Family	4	.915	4	.941	4	.939
MSPSS Significant other	4	.967	4	.971	4	.965
BFNE	12	.855	12	.864	12	.895
INCOM	11	.865	11	.801	11	.860
E-TEDS VF	11	.968	-	-	-	-
E-TEDS AC	7	.965	-	-	-	-
E-TEDS ISR	5	.915	-	-	-	-

9.2.2 Normality

The Shapiro-Wilk statistic was significant ($p<0.05$) for all scales and subscales, apart from the E-TEDS visual function subscale and DAS24 at baseline and BFNE and INCOM at all time points, which were normally distributed (Table 17). However, as this test can be sensitive to small deviations in normality (Field, 2009), histograms and normal probability plots were also assessed. Normal distributions were observed for the majority of the variables in histograms and normal probability plots. However, histograms indicated that data for the HADS depression subscale was skewed to the left at 6 week and 6 month follow-ups. Salience (CARSAL), valence (CARVAL), GO-QOL visual function and the three MSPSS subscales were skewed to the right at all time points.

Table 17. Results of Shapiro-Wilk test of normality for each psychosocial variable at the 3 time points

	Baseline			**6 week**			**6 month**		
Scale & Time point	**Statistic**	**df**	***p***	**Statistic**	**df**	***p***	**Statistic**	**df**	***p***
E-TEDS AC	**.869**	**96**	**.000****	-	-	-	-	-	-
E-TEDS VF	.983	82	.350	-	-	-	-	-	-
E-TEDS ISR	**.933**	**85**	**.000****	-	-	-	-	-	-
CARSAL	**.808**	**77**	**.000****	**.913**	**54**	**.001***	**.890**	**63**	**.000****
CARVAL	**.803**	**55**	**.000****	**.951**	**61**	**.016***	**.948**	**71**	**.005***
HADS Anxiety	**.975**	**106**	**.043***	**.966**	**77**	**.039***	**.958**	**86**	**.007***
HADS Depression	**.960**	**106**	**.003***	**.939**	**81**	**.001***	**.931**	**84**	**.000****
DAS24	.953	45	.065	**.936**	**50**	**.009***	**.929**	**64**	**.001***
GOQOL Visual function	**.934**	**109**	**.000****	**.911**	**83**	**.000****	**.841**	**85**	**.000****
GOQOL Appearance	**.950**	**109**	**.000****	**.969**	**84**	**.039***	**.948**	**85**	**.002***
Perceived visibility	**.804**	**106**	**.000****	**.922**	**77**	**.000****	**.918**	**77**	**.000****
MSPSS Family	**.890**	**109**	**.000****	**.863**	**81**	**.000****	**.891**	**84**	**.000****
MSPSS Friends	**.908**	**108**	**.000****	**.905**	**81**	**.000****	**.919**	**84**	**.000****
MSPSS Significant other	**.800**	**107**	**.000****	**.779**	**80**	**.000****	**.785**	**85**	**.000****
BFNE	.989	100	.607	.978	80	.186	.980	78	.274
INCOM	.989	102	.576	.975	80	.114	.992	83	.893

9.3 CHARACTERISTICS OF THE STUDY SAMPLE

Participants from the cross-sectional study described in Chapter 6 were followed up after their surgery at two time points: 6 weeks and 6 months post-surgery.

9.3.1 Dropouts & loss to follow-up

Dropouts at follow-up are a common problem in longitudinal healthcare studies. Of the 121 participants in the cross-sectional study, a proportion did not respond to one of the follow-up questionnaire packs, and a small number did not respond to either follow-up (Figure 17). Orbital decompression was cancelled for 11 participants after the pre-surgical assessment and one participant failed to complete more than 50% of the data in their follow-up questionnaires. Seventy-three (60.1%) participants completed questionnaires at all three time points. Eleven participants filled in only baseline and 6 week follow-up questionnaires (9.8%) meaning that 84 participants were followed up at 6 weeks after surgery. Thirteen participants filled in only baseline and 6 month follow-up questionnaires (10.6%), meaning that 86 participants in total were followed up 6 months after surgery.

The one participant with over 50% data missing was removed from the follow-up analysis. Multiple imputations were not performed for the analyses described in this chapter as MLM, the analytical method used to investigate research questions (3) and (4), is able to handle missing data. MLM uses all available information for the analysis and can be performed on unbalanced sample sizes at each time point, or for each scale (Quené & van den Bergh, 2004). This is in contrast to pairwise or listwise deletions, which retain cases but do not analyse missing variables (pairwise) or remove entire cases with at least one variable missing (listwise). For consistency with all follow-up analyses investigating changes over time, the same dataset was used to answer research question (5), i.e. the investigation of what baseline factors predict change in quality of life from pre- to post-surgery, and research question (6), i.e. the investigation of what changes over time in clinical and psychosocial factors predict change in quality of life over time, from pre- to post-surgery. Pairwise deletion was used in these analyses in order to retain valuable data.

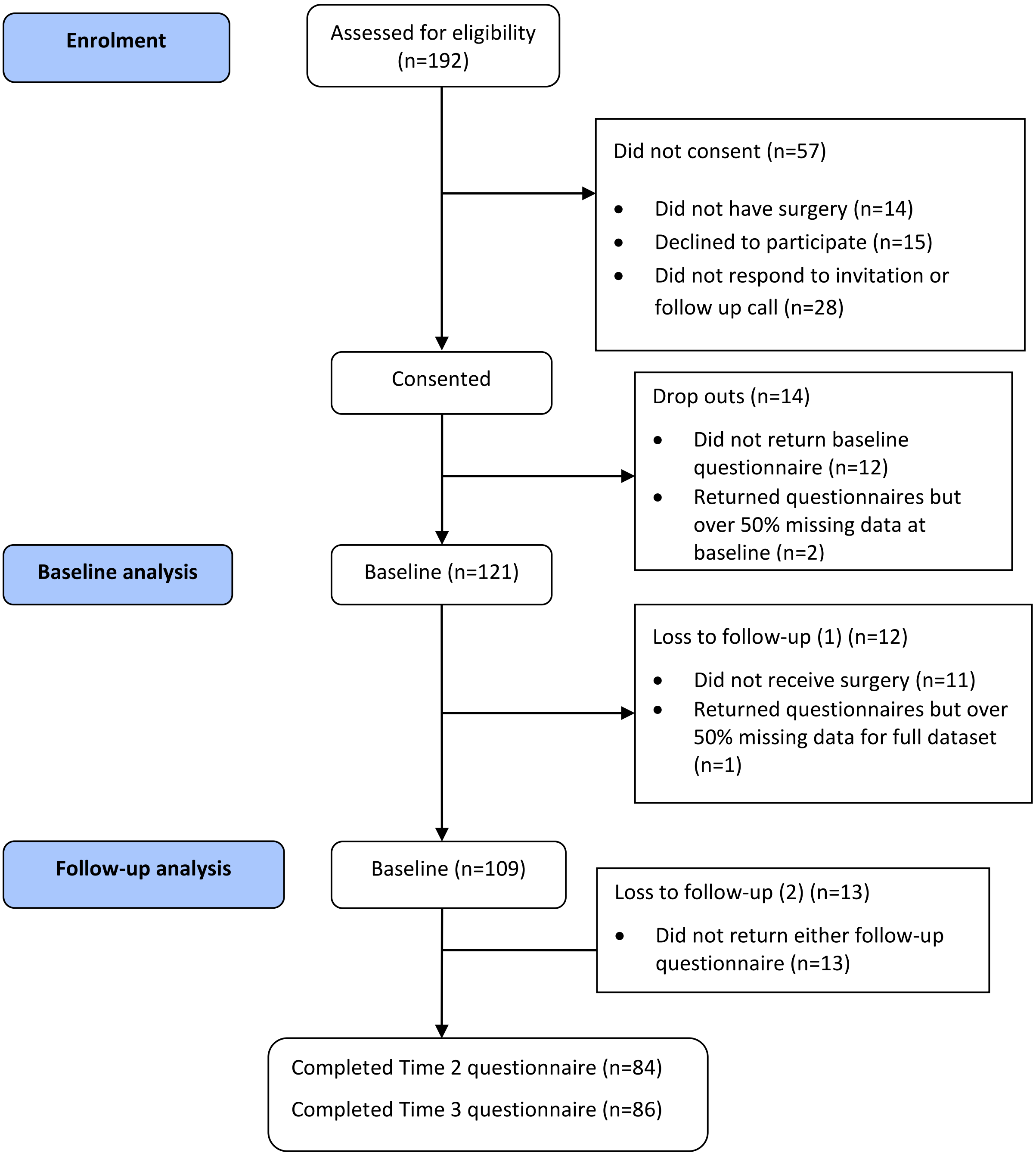


Figure 17. A flow diagram showing participation rates and losses to follow-up based on CONSORT guidelines (Schultz et al., 2010)

9.3.1.1 Differences between responders & non-responders

A sensitivity analysis was conducted to assess whether there were any differences between patients that responded to follow-up questionnaires and those who did not. T-tests and Pearson's chi square tests were performed to compare patients who had only completed a baseline questionnaire with patients who completed a baseline questionnaire and at least one follow-up questionnaire on clinical and psychosocial variables. Odds ratios were calculated, which are a common useful measure of effect size for categorical data (Field, 2009). White patients were found to be more likely to respond to follow-up than other ethnic groups χ^2 (1) = 4.79, $p<0.05$, with the odds being 2.9 more likely if the patient was White. Non-smokers were more likely to complete follow-up questionnaires χ^2 (3) = 11.43, $p<0.05$, with the odds being 2.8 more likely if patients did not smoke.

9.3.2 Side effects from surgery

Patients' subjective experiences of side effects (pain, swelling, scarring and redness) were measured 6 months post-surgery on a scale of 0 to 10 (a full description of this measure is provided in section 5.8.1.4.2, page 108). Eighty-four participants responded to this item (missing n=2). The majority of patients experienced either no side effects, or very low level of severity in each of the four side effects measured (Figure 18). Of the four side effects, a higher proportion of patients reported scarring to be a mild to moderate problem 6 months after surgery than any other side effect.

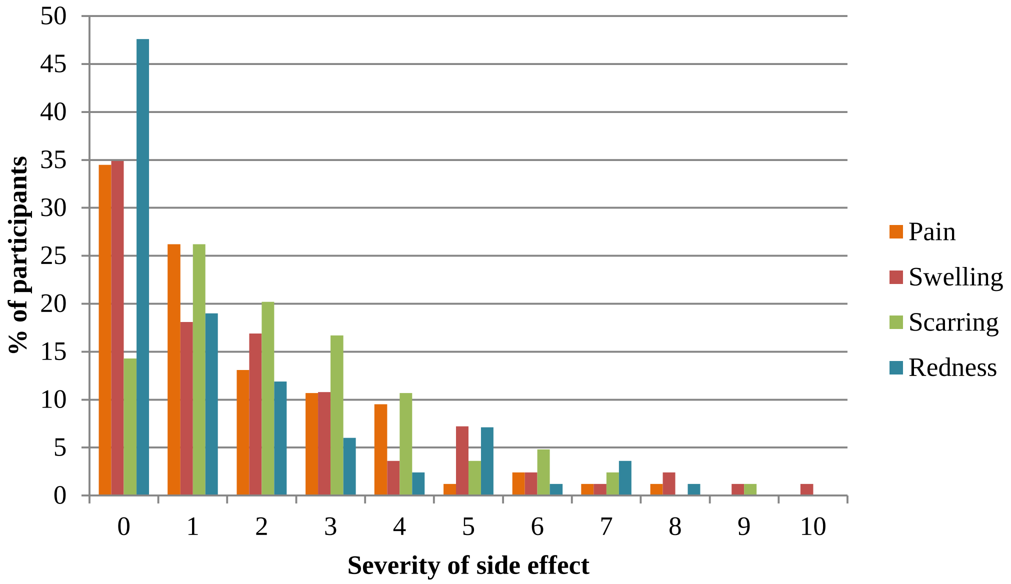


Figure 18. Severity of side effects from surgery including pain, swelling, scarring and redness (n =84)

Participants were also asked to rate how their experience of these symptoms compared to their expectations prior to surgery. A high proportion of patients experienced much less pain than they had expected (43%), with only 3% finding that pain was much worse than expected. Many patients found redness to be the same as they had expected (33%) and scarring was generally found to be less than expected (35%). Of the four side effects, participants most frequently reported swelling to be "much worse than expected" and 25% of patients found it to be "worse than expected".

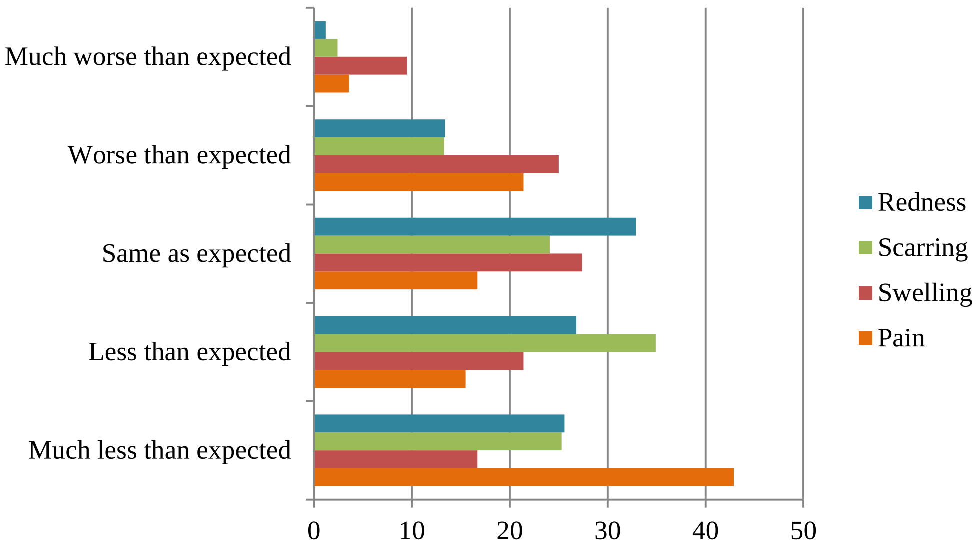


Figure 19. Percentage of each response to item asking patients to compare the experience of their symptoms to what was expected prior to surgery (n=84)

9.3.3 Patient satisfaction with surgery

Patient satisfaction with surgery was assessed using 3 single item measures at 6 months post-surgery. Generally, patients reported high levels of satisfaction with orbital decompression, with the majority reporting that they did not regret having the surgery (Figure 20), would be willing to go through the operation again (Figure 21) and would be willing to recommend the surgery to others who might need it in the future (Figure 22). The majority of participants were satisfied with the information given to them prior to surgery (85.5%) and the remaining felt they were given too little information (Figure 23).

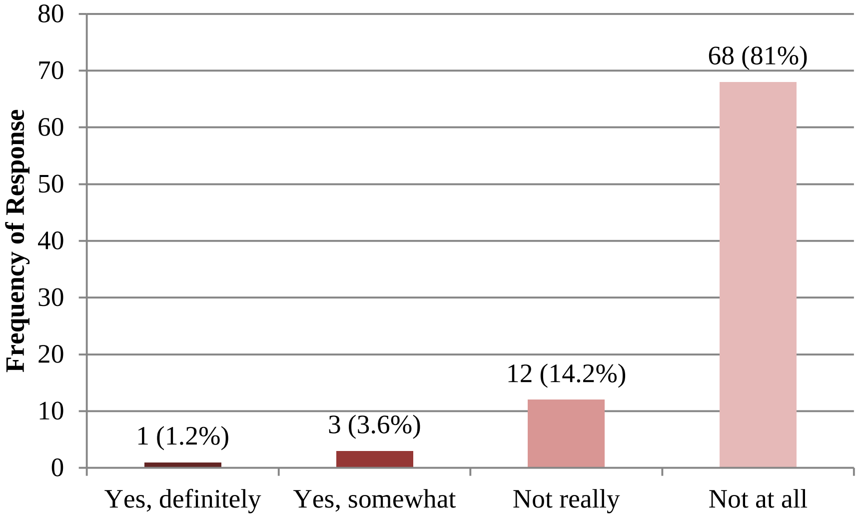


Figure 20. Frequency and percentage of responses to the question "Do you regret having surgery?" at 6 months post-surgery (n=84)

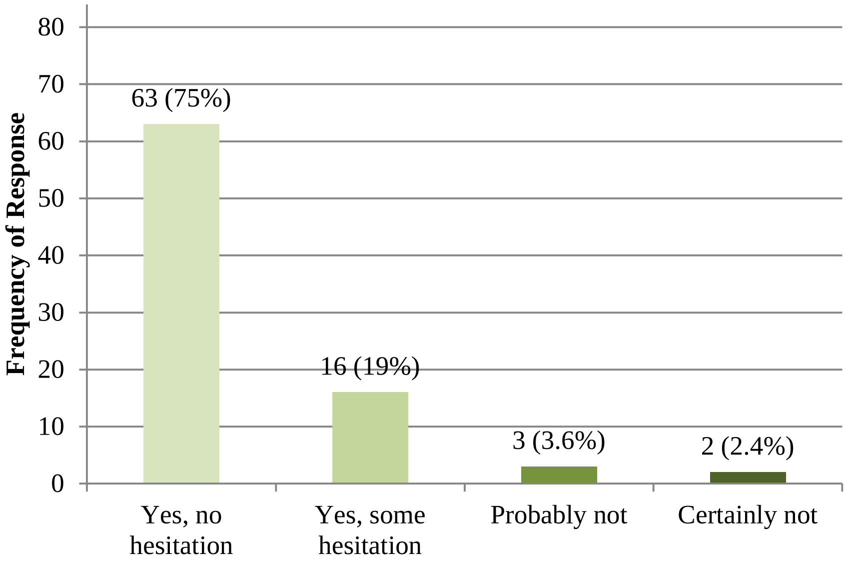


Figure 21. Frequency and percentage of responses to the item "Would you go through the operation again?" at 6 months post-surgery (n=84)

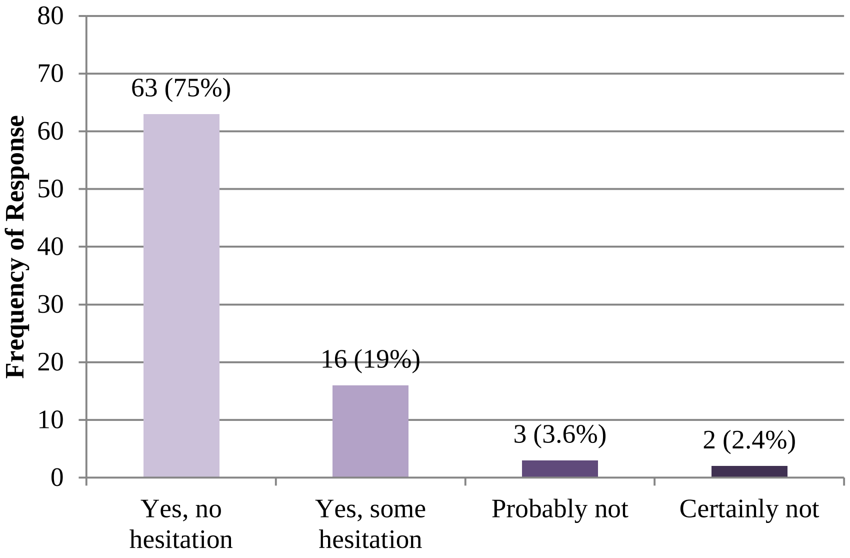


Figure 22. Frequency and percentage of responses to the item "Would you recommend the operation to others?" at 6 months post-surgery (n=84)

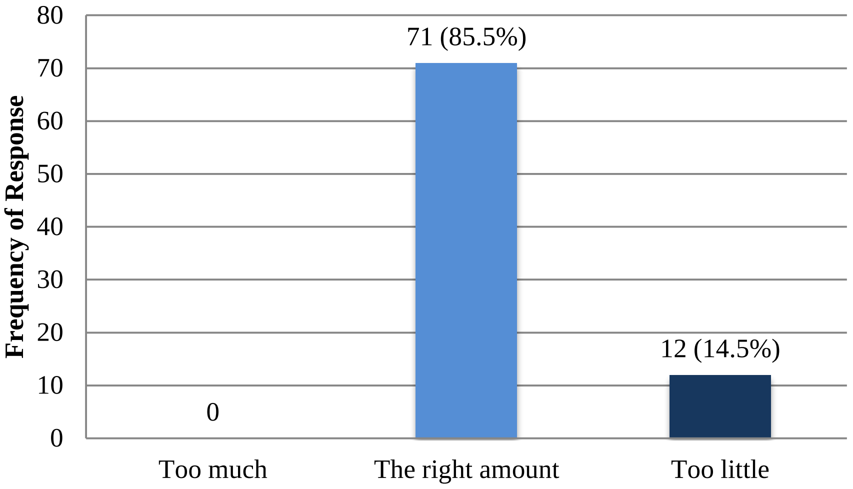


Figure 23. Frequency and percentage of responses to the item "Were you given the right amount of information preoperatively?" at 6 months post-surgery (n=83)

9.3.4 Further surgery

A total of 37 patients required further surgery after orbital decompression, which included eyelid lengthening, strabismus surgery and a small number of patients were due to have a second orbital decompression (n=3) on the opposite eye.

9.4 WHICH CLINICAL AND PSYCHOSOCIAL FACTORS CHANGE AFTER SURGERY?

To examine the effects of orbital decompression surgery on clinical and psychosocial factors, as well as quality of life outcomes, multilevel modelling (MLM) was performed. ICCs were all found to be above 0.05 and therefore MLM was deemed suitable to examine change over time for all the variables measured in the study (Stride, 2009).

9.4.1 Clinical outcomes

Table 18 presents adjusted means and standard deviations (SDs) for continuous clinical variables at each time point. As SPSS generated standard errors, these were converted into standard deviations as described in section 5.10.4.2, page 144. F-test results for the analyses present the effects of time, from pre- to post-surgery. Partial eta squared (ŋ$^{2}_{p}$) was calculated to establish each effect size as described in section 5.10.4.2 (page 144) and these results have also been provided in the tables presented. Differences in change scores between baseline and each post-surgical follow up, and differences in scores between the two follow ups, were examined using pairwise comparisons, which are also presented in Table 18.

Table 19 presents proportions and predicted probabilities for categorical clinical predictor variables. MLM analysis for categorical variables was implemented, which involved examining whether patients changed from ‘present’ to ‘not present’. In Table 19 β represents the log odds coefficients and Exp(β) represents effect sizes as described in section 5.10.4.2, page 145.

9.4.2 Intervening psychosocial processes

Table 20 presents adjusted mean scores and SDs for the psychosocial process variables, F-test results for the effects of time analyses, effect sizes (ŋ$^{2}_{p}$), differences in change scores between baseline and each post-surgical follow-up and differences in scores between the two follow-ups.

Statistical tests for which results were significant are presented in bold.

Table 18.Adjusted means for continuous clinical outcomes at baseline and follow-up and F-test results for the effect of time

Measures	Baseline (M±SD)	6 weeks (M±SD)	6 months (M±SD)	Effect of Time	Effect size (η^2_p)	Baseline to 6 weeks	Baseline to 6 months
Exophthalmometry	23.69±2.45	19.28±2.41	19.11±2.39	$F_{2, 149.80}$= 252.33, p<0.001**	0.77	4.41, p<0.001**	4.58, p<0.001**
Asymmetry	1.84±1.48	0.83±1.48	0.75±1.47	$F_{2, 161.90}$= 20.18, p<0.001**	0.20	1.02, p<0.001**	1.09, p<0.001**
LogMAR	0.08±0.25	-0.00±0.25	-0.01±0.24	$F_{2, 160.40}$= 4.53, p<0.05*	0.05	0.08, p=0.029*	0.09, p=0.031*
MRD1	6.00±1.82	5.29±1.78	5.29±1.79	$F_{2,145.94}$= 8.26, p<0.001**	0.10	0.71, p=0.001*	0.71, p=0.004*
MRD2	6.77±1.25	5.46±1.25	5.47±1.25	$F_{2,156.65}$= 46.45, p<0.001**	0.37	1.31, p<0.001**	1.30, p<0.001**
CAS	1.17±1.44	0.64±1.42	0.40±1.43	$F_{2,155.20}$= 9.41, p<0.001**	0.11	0.53, p=0.007*	0.77, p<0.001**

Estimated marginal means
** p<.05, ** p<.001*

Table 19.Frequencies of categorical clinical outcomes at baseline and follow-up and probabilities of presence over time

Model parameter	Baseline n(%)	6 weeks n(%)	6 months n(%)	β	SE	Wald χ^2	*p*	Exp(β)	95%CI for Exp(β)
Optic neuropathy	12(11.2)	4(3.7)	2(1.9)						
Intercept				-2.07	0.31	45.67	**<0.001****	0.13	0.069, .230
6 weeks vs baseline				-1.13	0.50	5.08	**0.024***	0.32	0.121, .863
6 months vs baseline				-1.55	0.61	6.33	**0.012***	0.21	0.064, .711
Corneal SPK	33(72)	27(25.2)	13(12.1)						
Intercept				-0.77	0.21	13.77	**<0.001****	0.46	0.307, .695
6 weeks vs baseline				-0.22	0.27	0.66	0.418	0.80	0.469, 1.369
6 months vs baseline				-1.02	0.34	8.91	**0.003***	0.36	0.185, .705
Diplopia	56(52.3)	51(47.7)	38(35.5)						
Intercept				0.08	0.19	0.15	0.696	1.08	0.74, 1.571
6 weeks vs baseline				-0.03	0.22	0.02	0.891	0.97	0.637, 1.481
6 months vs baseline				-0.50	0.23	4.58	**0.032***	0.61	0.383, .959
Hydraulic orbit	20(18.7)	3(2.8)	5(4.7)						
Intercept				-1.43	0.25	33.27	**<0.001****	0.24	0.146, .388
6 weeks vs baseline				-2.03	0.65	9.61	**0.002***	0.13	0.037, .474
6 months vs baseline				-1.43	0.52	7.57	**0.006***	0.24	0.086, .662

** $p<.05$, ** $p<.001$*

Table 20. Adjusted means for continuous psychosocial outcomes at baseline and follow-up and F-test results for the effect of time

Measures	**Baseline (M±SD)**	**6 weeks (M±SD)**	**6 months (M±SD)**	**Effect of Time**	**Effect size (η^2_p)**	**Baseline to 6 weeks**	**Baseline to 6 months**
GOQOL Visual function	63.42±29.32	65.02±27.42	71.43±27.78	**$F_{2, 130.52}$=5.30, p=0.006***	**0.08**	-1.60, p=0.873	**-8.02, p=0.008***
GOQOL Appearance	35.42±26.19	48.66±24.70	54.89±25.08	**$F_{2, 131.55}$=31.02, p<0.001****	**0.32**	**-13.23, p<0.001****	**-19.46, p<0.001****
HADS Anxiety	9.43±4.52	7.23±4.20	7.04±4.29	**$F_{2, 156.80}$= 27.05, p<0.001****	**0.26**	**2.21, p<0.001****	**2.40, p<0.001****
HADS Depression	7.87±4.52	6.09±4.21	5.81±4.32	**$F_{2,120.04}$= 14.92, p<0.001****	**0.20**	**1.77, p<0.001****	**2.06, p<0.001****
DAS24	52.19±14.15	44.08±14.34	41.15±15.35	**$F_{2, 68.01}$= 17.18, p<0.001****	**0.34**	**8.11, p<0.001****	**11.04, p<0.001****
CARSAL	25.35±5.41	23.40±4.92	23.18±5.28	**$F_{2, 102.71}$= 5.96, p=0.004***	**0.10**	**1.95, p=0.006***	**2.17, p=0.013***
CARVAL	41.26±9.66	34.02±9.65	31.76±9.88	**$F_{2, 90.99}$= 21.94, p<0.001****	**0.33**	**7.24, p<0.001****	**9.50, p<0.001****
Visibility	5.76±1.68	4.01±1.62	3.75±1.63	**$F_{2, 157.24}$= 58.62, p<0.001****	**0.43**	**1.76, p<0.001****	**2.01, p<0.001****
MSPSS Friends	15.32±3.86	15.31±3.56	15.52±3.66	$F_{2, 110.52}$= 0.23, p=0.794	0.01	0.01, p=1.000	-0.20, p=0.935
MSPSS Family	15.50±4.12	16.14±3.84	15.60±3.91	$F_{2, 131.88}$= 1.95, p=0.147	0.03	-0.64, p=0.195	-0.10, p=0.991
MSPSS Significant other	15.94±4.69	16.03±4.26	16.23±4.43	$F_{2, 161.38}$= 0.27, p=0.766	0.01	-0.29, p=0.987	-0.29, p= 0.858
BFNE	38.13±8.95	36.68±8.28	36.11±8.39	**$F_{2,102.80}$= 3.93, p=0.023***	**0.07**	1.46, p=0.054	**2.02, p=0.033***
INCOM	35.91±6.80	35.14±6.46	35.56±6.54	$F_{2,133.57}$= 0.73, p=0.485	0.01	0.77, p=0.545	0.35, p=0.936

Estimated marginal means
** p<.05, ** p<.001*

As shown in Table 18 and Table 19 all clinical variables changed significantly pre- to post-surgery, suggesting that in this sample orbital decompression led to improvements in all clinical outcomes. Improvements in all continuous clinical variables were observed from baseline to 6 weeks post-surgery and baseline to 6 months post-surgery but there were no statistically significant changes from 6 weeks to 6 months indicating that the bulk of improvements occurred in the first 6 weeks after surgery. Of the categorical clinical variables, this effect was observed for optic neuropathy and hydraulic orbit. However for corneal SPK and diplopia, changes in the probability of reducing from ‘present’ to ‘absent’ were not observed until 6 months after surgery. Of note, a number of outliers were observed for these clinical variables (Appendix R) and the analysis was repeated with and without these participants by means of a sensitivity analysis. As the results were consistent, these participants were retained to avoid reducing the sample size and losing important data. The effect sizes for the effect of time in the clinical variables were small to large (0.05 to 0.77),

Improvements were observed in all psychosocial variables apart from the MSPSS subscales (friends, family and significant other) and social comparison (INCOM) (Appendix S). For HADS anxiety, HADS depression, DAS24, CARSAL, CARVAL and perceived visibility improvements were observed as early as 6 weeks after surgery. This improvement was maintained at 6 months post-surgery with no statistically significant additional improvement observed between 6 week and 6 month follow-ups. BFNE and GO-QOL visual function scores did not improve significantly until 6 months post-surgery. Significant differences were found between 6 week and 6 month follow-ups for the GO-QOL visual function (mean difference -6.41, $p<0.05$); however the improvement in this score did not reach the MCID for the GO-QOL (Terwee et al., 2001). The GO-QOL appearance subscale however improved as early as 6 weeks after surgery and continued to significantly improve up to 6 months after surgery (mean difference -6.23, $p<0.05$). The MCID was observed in the GO-QOL appearance subscale at the 6 week follow-up. The effect sizes for the effect of time in the psychosocial variables ranged from small to moderate (0.07 to 0.43).

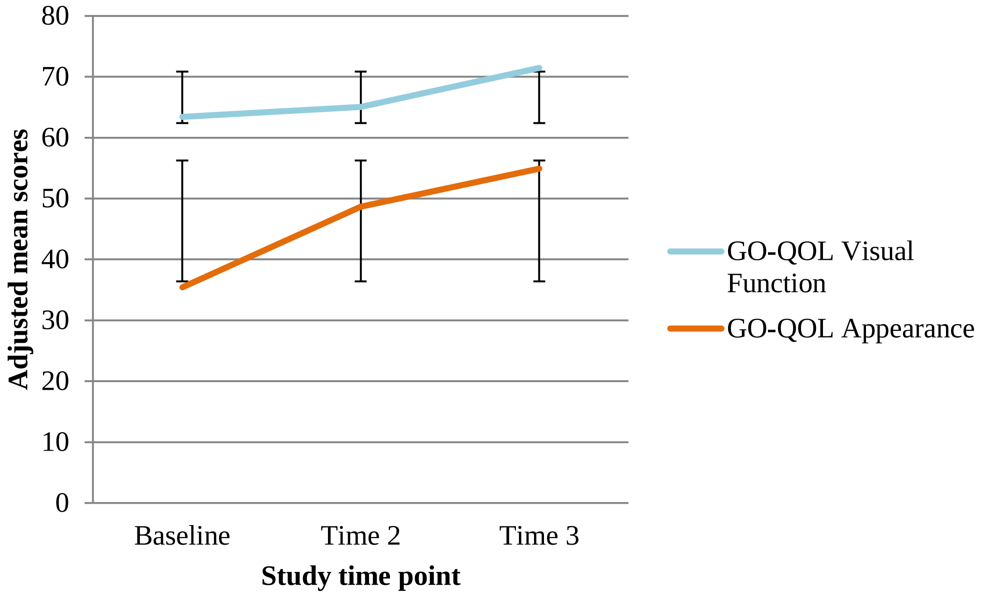


Figure 24. Graphical representation of change over time in GO-QOL subscale scores with error bars

9.5 BASELINE PREDICTORS OF CHANGE IN QUALITY OF LIFE FROM PRE- TO POST-SURGERY

To investigate which factors at baseline predict change in quality of life from pre- to post-surgery, residualised change scores were calculated for the GO-QOL subscales. These were calculated to capture the change from pre- to 6 months post-surgery, as the most amount of change was found at this postoperative time point. Two hierarchical multiple regressions were performed using baseline factors as the predictor variables (IVs) and the residualised change scores for the GO-QOL subscales as the DVs. A full description of the methods used has been provided in Chapter 5, section 5.10.4.3 page 120.

As before, the number of predictors for the regression model was reduced by performing initial univariate linear regressions to examine the association between each baseline predictor variable and each DV. Only significant predictors were entered into the regression models.

9.5.1 GO-QOL visual function change

Residualised change scores for the GO-QOL visual function subscale were calculated for the 85 participants who provided this data at both baseline and 6 month follow-up. Univariate linear regressions indicated that four variables significantly predicted the improvement in GO-QOL visual function from pre- to post-surgery. The variables were: ethnicity ($F_{(1,83)}$=5.11, p<0.05, f^2 =0.06), hydraulic orbit ($F_{(1,81)}$ =6.24, p<0.05, f^2 =0.08), diplopia ($F_{(1,82)}$=4.74, p<0.05, f^2 =0.06), and CAS ($F_{(1,83)}$ =11.13, p<0.05, f^2 =0.10). No other variables significantly predicted change in GO-QOL visual function.

Entry of variables into the regression was based on Figure 9. As only demographic and clinical variables were found to significantly predict GO-QOL visual function scores, all variables were entered into the regression at the same time. This model explained 16% of the observed variance in the change in GO-QOL visual function (adjusted R^2=0.12, $F_{(4,78)}$=3.74, p<0.05, f^2 = 0.19). Beta coefficients indicated that whilst the overall model was significant, there were no significant unique predictors of GO-QOL visual function change (Table 21). Therefore improvements in GO-QOL visual function after surgery were predicted by a combination of demographic and clinical factors, including being of non-White ethnicity, having a lower CAS score, not having hydraulic orbit and not having double vision. However none of these variables were unique predictors that explained a significant amount of variance over the other variables.

Table 21. Results for the hierarchical multiple regression used to analyse baseline predictors of change in GO-QOL visual function scores

	B	SE B	*t*	*p*
Step 1				
Constant	**0.49**	**0.24**	**2.01**	**.048***
Ethnicity	**-0.60**	**0.27**	**-2.23**	**.028***
Step 2				
Constant	**0.69**	**0.25**	**2.75**	**.007***
Ethnicity	-0.48	0.27	-1.82	.073
CAS	-0.11	0.07	-1.68	.097
Hydraulic orbit	-0.18	0.33	-0.54	.592
Diplopia	-0.26	0.22	-1.19	.237

Note: $R^2 = .06$ for Step 1 ($p < 0.05$), $R^2 = .16$ for Step 2 ($p < 0.05$)

9.5.2 GO-QOL appearance change

Univariate linear regressions indicated that five variables significantly predicted change in GO-QOL appearance from baseline to 6 months post-surgery. The variables were: ethnicity ($F_{(1,83)}=4.75$, $p<0.05$, $f^2 = 0.06$), previous radiotherapy, ($F_{(1,74)}=4.19$, $p<0.05$, $f^2 = 0.06$), hydraulic orbit ($F_{(1,81)} =4.72$, $p<0.05$, $f^2 = 0.06$), diplopia ($F_{(1,82)}=8.46$, $p<0.05$, $f^2 = 0.10$), and CAS ($F_{(1,83)} =7.88$, $p<0.05$, $f^2 = 0.09$). No other variables were significant predictors of GO-QOL appearance change.

As before, as only demographic and clinical variables significantly predicted GO-QOL appearance scores, variables were entered into the regression at the same time. This model accounted for 20% of the observed sample variation in the change in GO-QOL appearance (adjusted $R^2=0.14$, $F_{(4,70)}=3.17$, $p<0.05$, $f^2 = 0.25$). As found for GO-QOL visual function change, beta coefficients indicated that whilst the overall model was significant, there were no significant unique predictors of GO-QOL appearance change (Table 22). Hence the significant improvement in GO-QOL appearance was predicted by a combination of demographic and clinical factors including being of ethnic origin other than white, not having had previous radiotherapy, absence of hydraulic orbit and diplopia and lower CAS score, with no unique predictors.

Table 22. Results for the hierarchical multiple regression used to analyse baseline predictors of change in GO-QOL appearance scores

	B	SE B	*t*	*p*
Step 1				
Constant	0.47	0.26	1.85	.068
Ethnicity	**-0.58**	**0.28**	**-2.06**	**.043***
Step 2				
Constant	**0.80**	**0.26**	**2.94**	**.004***
Ethnicity	-0.50	0.28	-1.80	.077
Previous radiotherapy	-0.60	0.40	-1.41	.164
Hydraulic orbit	-0.01	0.34	-0.02	.987
Diplopia	-0.37	0.23	-1.59	.118
CAS	-0.10	0.07	-1.54	.127

Note: $R^2 = .05$ for Step 1 ($p < 0.05$), $R^2 = .20$ for Step 2 ($p < 0.05$)

9.5.3 Regression assumptions

The VIF and tolerance statistics were analysed for each multiple regression analysis described in this section to ensure tolerance values were above 0.2 and VIF values were well below 10. This was found to be the case for both regressions. Therefore it can be concluded that there was no collinearity within the data for any model used.

9.6 CHANGES IN CLINICAL AND PSYCHOSOCIAL FACTORS AS PREDICTORS OF CHANGE IN QUALITY OF LIFE FROM PRE- TO POST-SURGERY

To investigate whether the change in clinical and psychosocial factors from pre- to 6 month post-surgery could predict improvement in quality of life from pre- to 6 month post-surgery, residualised change scores were calculated for each clinical and intervening cognitive process variable in addition to the previously calculated change scores for the quality of life variables. Two further hierarchical multiple regressions were performed with the GO-QOL subscale residualised change scores as the dependent variables and the residualised change scores on the intervening psychosocial variables as IVs. As before, univariate linear regressions were performed for each IV and the DV to assess whether any were significant predictors that could be included in the regression analysis.

9.6.1 Change predictors of GO-QOL visual function change

To control for significant baseline predictors of GO-QOL visual function change, ethnicity was entered into this model. Further univariate linear regressions indicated that nine variables in total significantly predicted the improvement in GO-QOL visual function from baseline to 6 months post-surgery. The variables were: ethnicity ($F_{(1,83)}$=5.11, $p<0.05$, $f^2 = 0.06$), change in diplopia ($F_{(1,72)}$=5.88, $p<0.05$, $f^2 = 0.08$), support from significant others ($F_{(1,81)}$ =5.51, $p<0.05$, $f^2 = 0.07$), change in fear of negative evaluation ($F_{(1,71)}$=5.30, $p<0.05$, $f^2 = 0.07$), change in social comparison ($F_{(1,77)}$=4.36, $p<0.05$, $f^2 = 0.06$), change in social anxiety and social avoidance ($F_{(1,28)}$=6.26, $p<0.05$, $f^2 = 0.22$), change in valence of appearance ($F_{(1,39)}$=6.86, $p<0.05$, $f^2 = 0.18$), change in anxious mood ($F_{(1,82)}$=10.56, $p<0.05$, $f^2 = 0.13$), and change in depressed mood ($F_{(1,79)}$=20.51, $p<0.001$, $f^2 = 0.26$). These variables were entered into the hierarchical multiple regression model in the order as stipulated by the ARC framework (Figure 9). This involved entering demographic variables in block 1, clinical variables in block 2, socio-cognitive variables in block 3, appearance cognitions in block 4 and mood in block 5.

The regression model for change in GO-QOL visual function was not significant (adjusted R^2=-0.01, $F_{(9,15)}$=0.97, p=0.50, $f^2 = 0.59$). Although the univariate regressions between each of the IVs and DV were statistically significant, the clinical and psychosocial variables did not contribute significantly to the regression model. Apparently improvements in GO-QOL visual function 6 months after surgery were not well predicted by change in the clinical or psychosocial variables from pre- to post-surgery (Table 23).

Table 23. Results of the hierarchical multiple regression used to analyse change predictors of change in GO-QOL visual function

	B	SE B	*t*	*p*
Step 1				
Constant	0.49	0.46	1.07	.295
Ethnicity	-0.60	0.51	-1.19	.246
Step 2				
Constant	0.44	0.45	0.98	.338
Ethnicity	-0.55	0.50	-1.09	.289
Diplopia	-0.26	0.20	-1.27	.217
Step 3				
Constant	0.35	0.47	.75	.462
Ethnicity	-0.43	0.52	-0.83	.419
Diplopia	-0.28	0.21	-1.33	.200
MSPSS Significant other	0.17	0.20	0.84	.411
BFNE	-0.19	0.24	-0.80	.433
INCOM	-0.13	0.25	-0.53	.603
Step 4				
Constant	0.19	0.48	0.40	.696
Ethnicity	-0.23	0.54	-0.44	.669
Diplopia	-0.29	0.24	-1.20	.246
MSPSS Significant other	0.11	0.21	0.55	.589
BFNE	-0.05	0.25	-0.19	.855
INCOM	-0.22	0.27	-0.80	.435
CARVAL	0.00	0.29	0.01	.991
DAS24	-0.36	0.27	-1.31	.207
Step 5				
Constant	0.19	0.50	0.39	.705
Ethnicity	-0.24	0.56	-0.42	.680
Diplopia	-0.27	0.26	-1.02	.324
MSPSS Significant other	0.09	0.22	0.43	.676
BFNE	-0.02	0.27	-0.07	.948
INCOM	-0.19	0.29	-0.65	.524
CARVAL	0.01	0.31	0.03	.978
DAS24	-0.26	0.31	-0.84	.414
HADS Anxiety	-0.06	0.28	-0.23	.824
HADS Depression	-0.15	0.29	-0.54	.598

Note: R^2 = .06 for Step 1 (p =0.246), R^2 = .12 for Step 2 (p =0.217), R^2 = .24 for Step 3 (p =0.416), R^2 = .34 for Step 4 (p =0.292), R^2 = .37 for Step 5 (p =0.764)

9.6.2 Change predictors of GO-QOL appearance change

As before, ethnicity was entered into this model to control for its predictive value of change in GO-QOL appearance. Further univariate linear regressions indicated that in total, thirteen variables significantly predicted improvement in GO-QOL appearance from baseline to 6 months post-surgery. The variables were: ethnicity ($F_{(1,83)}=4.75$, $p<0.05$, $f^2=0.06$), previous radiotherapy ($F_{(1,74)}=4.19$, $p<0.05$, $f^2=0.06$), change in upper eyelid retraction ($F_{(1,69)}=4.54$, $p<0.05$, $f^2=0.07$), change in hydraulic orbit ($F_{(1,73)}=4.94$, $p<0.05$, $f^2=0.07$), significant others support ($F_{(1,81)}=7.22$, $p<0.05$, $f^2=0.09$), family support ($F_{(1,82)}=5.72$, $p<0.05$, $f^2=0.07$), change in fear of negative evaluation ($F_{(1,71)}=9.88$, $p<0.05$, $f^2=0.14$), change in valence of appearance ($F_{(1,39)}=51.86$, $p<0.001$, $f^2=1.3$), change in social anxiety and social avoidance ($F_{(1,28)}=19.67$, $p<0.001$, $f^2=0.70$), change in perceived visibility ($F_{(1,75)}=17.08$, $p<0.001$, $f^2= 0.23$), change in anxious mood ($F_{(1,82)}=11.71$, $p=0.001$, $f^2=0.14$), and change in depressed mood ($F_{(1,79)}=29.57$, $p<0.001$, $f^2=0.37$). These variables were entered into the hierarchical multiple regression as previously outlined (Figure 9).

This model accounted for 81% of the observed sample variation in the change in GO-QOL appearance from baseline to 6 months (adjusted $R^2=0.58$, $F_{(13,11)}=3.52$, $p<0.05$, $f^2 = 4.3$). Beta coefficients indicated that an improvement in a person’s subjective evaluation of their own appearance uniquely predicted the improvement in GO-QOL appearance from pre- to 6 months post-surgery (Table 24).

Table 24. Results of the hierarchical multiple regression used to analyse change predictors of change in GO-QOL appearance

	B	SE B	*t*	*p*
Step 1				
Constant	0.47	0.46	1.03	.312
Ethnicity	-0.58	0.51	-1.15	.263
Step 2				
Ethnicity	0.46	0.47	1.00	.334
Previous radiotherapy	-0.50	0.51	-0.98	.340
MRD1	-0.68	0.74	-0.92	.367
Hydraulic orbit	-0.19	0.21	-0.95	.355
Step 3				
Constant	0.28	0.44	0.64	.529
Ethnicity	-0.26	0.49	-0.53	.605
Previous radiotherapy	-0.88	0.69	-1.27	.221
MRD1	-0.33	0.20	-1.65	.119
Hydraulic orbit	-0.21	0.19	-1.09	.292
INCOM	-0.30	0.24	-1.23	.235
BFNE	-0.11	0.24	-0.47	.648
MSPSS Significant other	0.15	0.22	0.65	.523
MSPSS Family	0.27	0.24	1.10	.288
Step 4				
Constant	0.14	0.33	0.43	.676
Ethnicity	-0.21	0.36	-0.57	.576
Previous radiotherapy	0.34	0.59	0.58	.571
MRD1	-0.21	0.17	-1.28	.222
Hydraulic orbit	0.06	0.16	0.36	.726
INCOM	-0.08	0.19	-0.40	.697
BFNE	-0.15	0.18	-0.84	.414
MSPSS Significant other	0.12	0.17	0.75	.470
MSPSS Family	-0.11	0.20	-0.52	.610
CARVAL	**-0.64**	**0.21**	**-3.01**	**.010***
DAS24	-0.26	0.20	-1.28	.223
Perceived visibility	0.00	0.17	0.01	.991
Step 5				
Constant	0.10	0.32	0.30	.767
Ethnicity	-0.16	0.36	-0.46	.657
Previous radiotherapy	0.41	0.60	0.70	.501
MRD1	-0.24	0.16	-1.47	.169
Hydraulic orbit	0.07	0.17	0.43	.678
INCOM	-0.05	0.19	-0.25	.809
BFNE	-0.20	0.18	-1.11	.292
MSPSS Significant other	0.10	0.17	0.59	.565
MSPSS Family	-0.15	0.20	-0.73	.479

CARVAL	**-0.71**	**0.22**	**-3.26**	**.008***
DAS24	-0.27	0.23	-1.21	.251
Perceived visibility	0.05	0.18	0.29	.779
HADS Anxiety	0.26	0.19	1.42	.183
HADS Depression	-0.21	0.19	-1.09	.301

Note: R^2 = .05 for Step 1 (p = 0.263), R^2 = .19 for Step 2 (p=0.373), R^2=.45 for Step 3 (p=0.153), R^2 = .76 for Step 4 (p <0.05), R^2 = .81 for Step 5 (p = 0.339)

9.6.3 Regression assumptions

Analysis of the distribution of the residualised change scores showed a normal distribution for all the scales apart from MSPSS subscales, BFNE and CARSAL (Table 25). The VIF and tolerance statistics were analysed for each multiple regression analysis to ensure tolerance values were above 0.2 and VIF values were well below 10, which was found to be the case. Therefore it can be concluded that there was no collinearity within the data for any model used.

Table 25. The normality (Shapiro-Wilk) of the residualised change scores used to answer research questions (5) and (6)

Scale	**Statistic**	**df**	***p***
CARSAL	**.884**	**39**	**.001***
CARVAL	.950	41	.073
HADS Anxiety	.982	85	.268
HADS Depression	.984	82	.392
DAS24	.969	30	.517
GOQOL Visual function	.971	85	.052
GOQOL Appearance	.989	85	.715
Perceived visibility	**.964**	**77**	**.027***
MSPSS Family	**.921**	**84**	**.000****
MSPSS Friends	**.914**	**83**	**.000****
MSPSS Significant Other	**.902**	**83**	**.000****
BFNE	**.950**	**73**	**.006***
INCOM	.976	79	.153

9.7 DISCUSSION

This study aimed to establish which clinical and psychosocial factors changed after surgery. Another aim was to investigate whether any demographic, clinical or psychosocial variables at baseline predicted the change in GO-QOL subscale scores between baseline and 6 months post-surgery. Finally, the study also aimed to examine whether the changes in clinical and psychosocial factors from baseline to 6 months post-surgery explained variance in the change in GO-QOL subscale scores.

This section of the thesis will discuss the results of the analyses presented in this chapter within the context of these aims. It will then discuss the strengths and weaknesses of the study. Comparisons of the findings of this study in relation to previous literature will also be made.

9.7.1 Demographic variables

Ethnicity was the only demographic factor found to predict change in visual function and appearance-related quality of life from before to after surgery. Non-white patients experienced greater improvements in quality of life in both these areas in comparison to White patients. People from non-White backgrounds have been found to report more worry about their appearance and an increase in perceived noticeability when they have a visible difference, compared to White individuals (Rumsey et al., 2004). Research into the perceptions of individuals belonging to South Asian communities has reported that beliefs about the causes of disfigurements are sometimes founded within religious or cultural myth and superstition and that having a facial disfigurement can cause shame and burden on families (Hughes et al., 2009). This suggests that improvements in appearance might have additional implications for an individual who belongs to a particular cultural or ethnic group. Taking this previous research into account it is therefore unsurprising that particular ethnic groups might benefit more than others psychologically from their surgery. However, when entered into the regression model with other predictors, ethnicity was not found to significantly explain any of the variance in change in quality of life above other predictors, suggesting that other factors might be more important in explaining changes in quality of life after surgery.

Contrary to pre-surgery findings, where age predicted quality of life related to visual function and gender predicted quality of life related to appearance, these demographic variables did not predict the change in quality of life scores from baseline to 6 months post-surgery. This supports findings in strabismus (Jackson, Morris & Gleeson, 2013), where age and gender were not found to be associated with a change in postoperative quality of life, highlighting the limitations in such factors in predicting which patients might improve in quality of life after eye surgery.

9.7.2 Clinical variables

A number of clinical factors patients present with prior to surgery appeared to predict some of the variation in change in quality of life from pre- to post-surgery. Specifically, a lower CAS score and an absence of hydraulic orbit and diplopia predicted better vision-related quality of life outcomes after surgery. Not having had previous radiotherapy, absence of hydraulic orbit and diplopia and a lower CAS score predicted better appearance-related quality of life. However, none of these variables provided a significant unique contribution to each model. Only 16% of the variance in GO-QOL visual function change and 20% of the variance in GO-QOL appearance change were explained by these factors. It appears that there are other factors not measured at baseline in this study that might better explain change in quality of life. It is therefore not possible to predict which patients might benefit the most from rehabilitative surgery for TED from the clinical or psychosocial factors assessed in this study prior to surgery. This finding has been supported to an extent by studies that have investigated quality of life outcomes following surgery for aesthetic improvement. These authors have argued the difficulty in defining who will adjust positively after surgery from the factors that people present with prior to surgery (Pruzinsky, 2004; Castle, Honigman & Phillips, 2002). No other TED study has explored the factors that patients present with prior to surgery that might predict adjustment after surgery.

All clinical factors improved after orbital decompression surgery. A number of the clinical factors were found to significantly improve as early as 6 weeks after surgery. These included proptosis, eyelid retraction, asymmetry between the eyes, clinical activity, optic neuropathy, visual acuity, and hydraulic orbit, although with these variables, there was no significant further improvement between 6 week and 6 month follow-ups. Some other variables appear to take longer to demonstrate any improvement, including corneal SPK and diplopia suggesting that orbital decompression does not immediately resolve these factors. These findings are in line with previous TED studies evaluating clinical and quality of life outcomes of orbital decompression 6 months post-surgery (EUGOGO et al., 2009; Fichter et al., 2013). Terwee et al., (2001) found no significant difference in diplopia 3 months after orbital decompression surgery and a significant difference emerged only after eye muscle (strabismus) surgery was performed to correct this.

Vision-related quality of life did not significantly change until 6 months after surgery. Although it may be considered that this may in part be due to corneal SPK and double vision not improving until this time, the model was not found to significantly explain any variance in change in vision-related quality of life. Thus indicating that no changes in clinical variables from pre- to post-surgery predicted change in visual related quality of life. Furthermore, improvements in eyelid retraction and hydraulic orbit no longer predicted change in appearance-related quality of life when entered into the model with intervening cognitive process variables. These findings reflect those of previous studies in TED that have evaluated the relationship between clinical and quality of life outcomes after surgery. For instance, Jellema et al. (2014) found a weak correlation between double vision and GO-QOL visual function scores after strabismus surgery for TED, however no relationship was found to exist between double vision and appearance-related quality of life. Terwee et al. (2001) found weak correlations between postoperative clinical characteristics and changes in visual function-related quality of life including double vision and visual acuity and between changes in appearance-related quality of life and eyelid retraction, proptosis and orbital inflammation. However, the authors have not reported whether these relationships were found to be statistically significant, nor which type of surgery is associated with each specific characteristic. Other studies that have evaluated clinical and quality of life outcomes of orbital decompression surgery have failed to examine the relationship between changes in clinical variables and change in quality of life pre- to post-surgery (Fichter et al., 2013). A study that investigated the relationship between clinical and psychological outcomes following treatment for facial lipoatrophy also failed to find any a relationship (Ong et al., 2007).

9.7.3 Intervening psychosocial outcomes

The majority of intervening psychosocial factors improved after surgery. Appearance-related social anxiety and avoidance, importance of appearance, personal evaluation of appearance, perceived visibility of TED, anxiety and depression were all found to improve as early as 6 weeks after surgery but did not significantly improve beyond this time point. These findings are consistent with other studies investigating psychosocial outcomes following elective cosmetic surgery (Moss & Harris, 2009) and surgery for strabismus (Jackson, Morris & Gleeson, 2013) where improvements in anxiety, depression, appearance-related social anxiety and avoidance and quality of life were found not to improve significantly beyond 3 months post-surgery.

Fear of negative evaluation was found not to improve until 6 months after surgery. This suggests that the emotions associated with social factors take some time to evolve after surgery. This is in line with previous research that has found patients often need to adjust to changes in facial appearance and might still feel unsure about the reactions of others following orthognathic surgery (Cadogen & Bennun, 2011). It is therefore likely that it takes time for people to gain confidence and reduce their fear that others may react to their appearance. This may relate to their early experiences after surgery.

Perceptions of social support from friends, family and significant other remained the same over time. This is the first study to have evaluated these psychological constructs in patients with TED prior to and after surgery. This implies that for the group as a whole family and friends did not provide significantly more, or less, support post-surgery. The tendency to make social comparisons was also found not to change significantly after surgery. It is possible that this is a more stable trait and therefore may not be expected to change significantly over time. Some research has linked the tendency to make social comparisons with personality styles (Gibbons & Buunk, 1999; VanderZee, Buunk & Sanderman, 1996), including in patients with multiple sclerosis (Hemphill & Lehman, 1991), providing some support for this hypothesis.

A change for GO-QOL visual function was only observed 6 months post-surgery and did not reach a MCID. A number of variables were found to independently predict the change in GO-QOL visual function including significant other support, fear of negative evaluation, social comparisons, appearance-related social anxiety and avoidance, evaluation of appearance, and mood. However, when these variables were entered into the regression, the model was found not to be significant and thus did not adequately predict change in visual function quality of life. Terwee et al. (2001) found GO-QOL visual function scores not to change significantly after surgery when orbital decompression was performed to improve appearance. However they did find a significant improvement in these scores when decompression was performed to restore sight. Kashkouli et al. (2011b) also failed to find a significant improvement in GO-QOL visual function scores in their sample 6 months after surgery. As the current study only included 15 patients with optic neuropathy, patients having orbital decompression to correct appearance probably dominated the sample. However, as patients with optic neuropathy also often have symptoms that cause a change in their appearance it would be unreasonable to assume these patients are not also adjusting to a change in their appearance. This makes it difficult to distinguish between patients having orbital decompression for proptosis and orbital decompression only for sight loss, when orbital decompression for sight loss also leads to improvements in appearance.

Appearance-related quality of life improved significantly at 6 weeks and continued to significantly improve 6 months post-surgery, reaching a large MCID. Significant improvements in appearance-related quality of life have been observed after orbital decompression surgery in previous studies (Terwee et al., 2001; Fichter et al., 2013), although vision-related quality of life was found to show more improvement in previous studies (Fichter et al., 2013; Kashkouli et al., 2011b; EUGOGO et al., 2009). However, sample sizes for these studies were notably small. There does appear to be a need for studies with larger samples when investigating TED surgery.

A large amount of variance in GO-QOL appearance change was explained by the analytical model in the current study, which included a range of demographic, clinical, socio-cognitive, appearance cognitions, and mood. However, an improvement in personal evaluation of appearance was the only unique predictor of improvements in appearance-related quality of life from baseline to 6 months post-surgery. Personal evaluation of appearance has been found to be an important factor in predicting adjustment above other clinical factors associated with strabismus (McBain et al., 2014). Personal evaluation of appearance following cosmetic surgeries including breast enlargement, breast reduction, liposuction, abdominoplasties and eyelid surgery has been found to improve to levels of a non-clinical sample 5 years after surgery (von Soest et al., 2011). However, the study in this thesis appears to be the first to have evaluated changes in evaluation of appearance (as measured by the validated CARVAL; Moss & Rosser, 2012) in terms of the ability to predict changes in quality of life following surgery for TED. This suggests that changes in appearance-related quality of life are not well predicted by demographic or changes in clinical factors, but rather intervening psychosocial processes and in particular, significant changes in appearance evaluation. This supports the outcome of the cross-sectional study presented in this thesis that found pre-surgical quality of life was more often associated with psychosocial rather than clinical factors.

9.7.4 Strengths and weaknesses of the study

A number of factors contributed to the strengths and weaknesses of this study.

A common problem in longitudinal research is drop out over time and this study was no exception with a 60% response rate for all three time points. However, the follow-up response rate for this study was similar to other studies following patients up after cosmetic surgery and treatments for TED (e.g. von Soest et al., 2011; Terwee et al., 2002) and the sample size at follow-up was still more than adequate when compared to studies that have investigated quality of life outcomes following orbital decompression for TED (EUGOGO et al., 2009; Terwee et al., 2001; Fichter et al., 2013; Kashkouli et al., 2011b).

As different levels of orbital decompression were performed on patients, from one-wall to 3-wall approaches for more severe TED, these might have impacted on quality of life scores. As suggested by EUGOGO et al. (2009), it is possible that different types of orbital decompression could have led to varying changes in quality of life in the current study. However, the approaches to decompression were not greatly different in the current study with one of three approaches used depending on the number of bony walls removed, and no surgeon used the coronal approach. Furthermore, by reducing patients into sub-groups this would have reduced the sample size and ignored potential similarities and overlaps between 1, 2 and 3-wall approaches.

Orbital decompression surgery is part of a treatment sequence and a number of patients continued to have further surgery after this surgery. A 6 month follow-up might not have allowed the study to gain insight into the longer term benefits of orbital decompression, or whether quality of life continued to improve after further surgery, such as eyelid lengthening and/or strabismus surgery. Terwee et al. (2001) suggest that minor invasive surgeries such as strabismus and eyelid lengthening do not change quality of life outcomes significantly. If this is the case then it raises questions as to the necessity of such surgery from the patients’ perspective. Pruzinsky (2004) argues that it is not at all clear to what extent multiple rehabilitative surgeries for disfiguring conditions could facilitate change in body image perceptions. It would be useful to establish the longer-term benefits of such surgery so that patients can be fully informed of how much they can expect a combination of these rehabilitative surgeries to improve their perceptions of their own appearance and, ultimately, quality of life.

Expectations of orbital decompression were measured prior to surgery, with some promising results. However, follow-up interviews were not conducted to explore whether expectations of orbital decompression are met and if this is linked with post-surgical outcomes. A follow-up interview study might have further established the mechanisms that predict and explain variance in post-surgical quality of life outcomes. Preoperative beliefs and assumptions related to expectations of rehabilitative surgery for an acquired disfigurement will influence adaptation to a changed body image (Pruzinsky, 2004). In support of this hypothesis pre-operative expectations have been found to influence and predict psychological outcomes after breast reconstruction surgery following mastectomy for breast cancer (Snell et al., 2010; Klassen et al., 2009; Mazza, 2014). In addition, a recent literature review found that unrealistic expectations predicted poor psychosocial outcomes after cosmetic surgery (Honigman, Phillips & Castle, 2004).

The prevalence of co-morbid psychiatric disorders were not formally measured in this study. Body dysmorphic disorder (BDD) is characterised by a preoccupation with particular body features that are objectively absent or minimal and has been found to be one of few factors to predict poor subjective satisfaction with cosmetic surgery outcomes (Castle, Honigman & Phillips, 2002; Honigman, Phillips & Castle, 2004). Psychiatric morbidities prior to surgery have been linked with poor postoperative psychological outcomes, including historical depression and anxiety disorders and personality disorder (Honigman, Phillips & Castle, 2004). These may have accounted for some of the variance in change in quality of life in the current sample.

This is one of few studies to evaluate quality of life after orbital decompression and the first to systematically examine predictors of change in psychological outcomes following orbital decompression. The findings from this study have a number of implications for clinical practice, which are described in more detail in Chapter 10, section 10.3.

10. OVERALL DISCUSSION

The results of each study have been discussed separately in this thesis. In this chapter the main findings from the literature reviews and systematic review reported in Chapters 2 to 4 and the quantitative and qualitative studies reported in Chapters 6 to 9, are highlighted in order to integrate the results of the thesis. The aims of the thesis will be discussed in relation to the studies novel contribution to both the TED and the visible differences bodies of literature. This chapter will also describe the implications these findings have for practice, describe the overall strengths and weaknesses of the thesis and make recommendations for future research.

10.1 THESIS AIMS

This thesis aimed to establish not only the quality of life of patients with TED presenting for orbital decompression surgery but also the demographic, clinical and psychosocial factors that might be associated with quality of life in this population at presentation. It also set out to examine changes in quality of life after surgery. The specific aims of the thesis were:

- To investigate what demographic, clinical and psychosocial factors are associated with quality of life in patients presenting for orbital decompression surgery.
- To explore patients’ expectations of orbital decompression surgery, and what influences these expectations.
- To investigate which clinical and psychosocial factors improve after surgery.
- To establish whether any demographic, clinical and psychosocial characteristics patients present with prior to surgery can predict the variability in patients’ improvement in quality of life after surgery.
- To identify any factors that change after surgery that might predict the variability in patients’ improvement in quality of life after surgery.

10.2 NOVEL CONTRIBUTIONS TO THE LITERATURE

10.2.1 Factors associated with quality of life in TED

This is the first study to apply the ARC (2008) framework in attempting to further understand the psychosocial factors that might vary between patients with TED, and how these might account for the variability of quality of life in TED. To the researcher’s knowledge only one study has looked at multiple psychological factors associated with quality of life in TED. Kahaly et al. (2005) found that physical quality of life was related to depression, blurred vision, diplopia, depressive coping and age, whereas mental quality of life was associated with depression, anxiety, depressive coping, hyperthyroidism, blurred vision, age and stressful life events. However Kahaly et al’s (2005) study did not use the TED-specific GO-QOL, which has advantages over generic HRQL measures as described in Chapter 2, section 2.3.2 of this thesis. Furthermore, the study in this thesis has investigated additional intervening psychosocial factors to account for the variability adjustment to TED, and how these factors change over time after treatment.

There has been debate within the literature about whether demographic or clinical characteristics are associated with adjustment in people living with a visible difference. Whilst some studies in TED have failed to find a relationship (e.g. Kulig et al., 2009; Kashkouli et al., 2011b), a number of other studies have suggested a relationship between clinical severity including proptosis, diplopia and disease activity, and quality of life (e.g. Terwee et al., 2001; Yeatts, 2005; Park et al., 2005; Choi et al, 2012). Appearance researchers generally argue that levels of psychosocial distress related to having a disfigurement are not well associated with severity of the condition (Rumsey, Clarke & White, 2003; Rumsey et al, 2004; Thompson & Kent, 2001). Although some research suggests that location of the disfiguring condition may play a role in adjustment for some. In particular, conditions that affect the eyes have been found to complicate social interaction and increase perceived visibility (Rumsey et al, 2000; McBain et al, 2014), leading to high levels of social anxiety and social avoidance in these patient groups (Clarke & Wyn-Williams, 2000). This appears to be the case in the current study, with both men and women with TED reporting higher levels of appearance-related distress than the general population.

This study found that prior to surgery, predominantly intervening psychosocial factors are associated with quality of life in TED including appearance-related social anxiety and avoidance, salience of appearance-related information, personal evaluation of appearance, perceived visibility of TED and depression. Only one clinical factor was associated with vision-related quality of life, thus highlighting the importance of the intervening psychosocial factors first suggested by the ARC

(2008) in predicting how well, or poorly, patients adjust to having TED. Demographic factors including being female and older age were associated with poorer appearance-related and vision-related quality of life, respectively, prior to surgery. Women have consistently been found to adjust poorly to changes in their appearance due to disfiguring conditions (Rumsey et al., 2003; James et al., 2011; ARC, 2008). Where the work in this thesis differed from other studies on eyes was on the finding for age. Previous studies in strabismus found that older people were less concerned about appearance and demonstrated less appearance-related distress and social anxiety (James et al, 2011; Nelson et al, 2008). This study, however, found that being older was associated with poorer vision-related quality of life.

However as this study was cross-sectional, it is not possible to infer causal direction of the effects. A postoperative follow-up study was required to investigate the predictors of quality of life over time. This would be difficult to perform without an intervention as these patients were recruited prior to their surgery. The following section deals with the novel findings from the thesis regarding predictors of quality of life over time with surgery occurring between assessments, thus enabling an analysis of the effects of surgery.

10.2.2 Expectations of surgery

By the time patients have made a decision to undergo rehabilitative surgery for TED they have gone through a range of processes that appear quite variable. Patients' expectations of their surgery are influenced by a desire to return to the life they had before TED, healthcare professionals who felt they should have surgery, other patients who have had the surgery, and forums, blogs, and websites found on the Internet that recommended the surgery. Thus expectations appeared to be high in this group of patients.

The studies in this thesis found that patients expect recovery to take longer than healthcare professionals suggest and expect the time of recovery to affect their working lives. Some discrepancy was found between certain side effects being expected prior to surgery and those experienced after surgery. Participants in the qualitative study spoke about their expectations for scars and bruising but did not mention swelling. The quantitative follow-up study indicated that around a quarter of patients experienced post-operative swelling that was worse than they had expected, indicating this may be a particular side effect that is not well addressed by sources of information prior to surgery.

This study also highlighted patients' awareness that further surgery after orbital decompression could be necessary to further rehabilitate their appearance and participants described their treatment journey as a long and frustrating process. The majority of patients expected to look exactly as they did before TED, often referring to returning to "normality", which would enable them to reintegrate socially and increase their subjective evaluation of their own appearance, supporting the findings of Estcourt et al. (2008). However, Rumsey and Harcourt (2004) stress the importance of consultations between healthcare professionals and patients prior to multiple surgeries as these may conflict with "the patient's need to accept a less than perfect outcome" (p.92).

10.2.3 Impact of treatment for TED on psychosocial factors

The systematic review in Chapter 3 suggested that orbital decompression is associated with large improvements in both visual function and appearance-related quality of life. However it also found that long-term benefits in quality of life were found after treatment using selenium. Although this raises questions for the necessity of major surgery to improve quality of life when non-invasive natural remedies can lead to similar improvements, the quality of the evidence is generally poor. The poor reporting of methods and results of the studies included in the systematic review made it impossible to make definite conclusions about which treatments were most effective for improving quality of life outcomes. The systematic review highlighted the lack of studies that have evaluated clinical and psychosocial outcomes after orbital decompression surgery using validated measures. Furthermore, the need to attempt to identify predictors of quality of life in the longer term to consider how these may be influenced to improve outcomes in TED was emphasised by the review.

This was the first study to conduct a multilevel analysis of change over time in factors from pre- to post-surgery for TED. Previous studies have failed to take into account the fact that measures are taken from the same participant at different time points, thus data from adjacent time points are likely to be correlated. MLM analyses account for the within-participant variation and correlation in scores over time (Cartwright, Traviss & Blance, 2012; Heck, Thomas & Tabata, 2014).

The results of the follow-up study described in Chapter 9 suggested significant improvements in all clinical characteristics following orbital decompression. However, not all psychosocial factors improved after surgery. Perceptions of social support and a tendency to make social comparisons with others remained the same over time, and fear of negative evaluations from others did not improve until 6 months after surgery. The ‘delay’ in change in fear of negative evaluation is perhaps not surprising considering that patients with TED have reported high levels of fear of negative evaluation in the cross-sectional study of this thesis, comparable to samples of patients with panic disorder (Collins et al., 2004). Prior to surgery, patients also reported the tendency to make social comparisons that were comparable to a group of patients with a range of ophthalmic conditions in a previous study (James et al., 2011). Some research has linked the tendency to make social comparisons with personality styles (Gibbons & Buunk, 1999; VanderZee, Buunk & Sanderman, 1996; Hemphill & Lehman, 1991). Such studies suggest social comparison might be a more stable trait that cannot be resolved through surgery.

Despite appearance-related social anxiety and avoidance (measured by the DAS24) improving immediately after surgery, it appears that more general social anxieties take some time to evolve after surgery. Participants in the qualitative study described high expectations to feel accepted by others and returning to the social activities they enjoyed before TED to happen after surgery, although they did not indicate how quickly they expected this to happen. Whilst there was some indication that fear of being evaluated negatively by others began to diminish 6 months after surgery, it is likely that the tendency to make social comparisons could take longer to reduce.

The results of this thesis suggest that intervening psychosocial processes better explain variability in quality of life, both prior to and 6 months after surgery, than clinical or demographic factors. In particular, it is improvement in subjective evaluation of own appearance that predicts improvement in appearance-related quality of life after surgery. Having a negative evaluation of one’s own appearance was significantly associated with quality of life prior to surgery and improvements in this factor have strongly predicted improvements in quality of life. This supports appearance research that has found significant improvements in appearance evaluation after cosmetic surgery, and appearance satisfaction being the most common reason people state for undergoing cosmetic surgery (von Soest et al., 2011). This is the first study to identify the importance of this factor in patients with TED.

10.2.4 Information needs of patients with TED

Previous studies have indicated that the information needs of patients with TED are high (Estcourt et al., 2008; Edmunds et al., 2013). This was supported in the follow-up study in this thesis that found no participants reported receiving “too much” information prior to surgery and 14% reported not receiving enough. Furthermore, the qualitative study in this thesis described the information-seeking practices that patients engage in prior to surgery form their expectations, which often lead to confusion and misunderstanding of what surgery could achieve.

Accessing comprehensible information appears to be a problem for patients with TED. One previous study has evaluated the readability of web pages related to TED and has found them to be aimed at reading levels higher than the average patient (Edmunds et al, 2013), raising concerns for possible misinterpretation if information is not well understood. Patients were found to place particular value on websites that provide “before-and-after” photos of other patients who have had orbital decompression surgery as they were perceived to give a good sense of what to expect from changes in their appearance. However, when such websites only include examples of ideal case scenarios, this can raise expectations that might be unrealistic.

10.3 RECOMMENDATIONS FOR PRACTICE

The systematic review raised questions for clinical practice over optimal treatments to improve quality of life. In particular, IV methylprednisolone appeared to lead to better quality of life outcomes than oral methylprednisolone and lower doses of the steroid than those used in clinical management of TED could be more affective at improving appearance-related quality of life than higher doses, which are more costly and lead to more adverse effects. However limitations of some of the studies reviewed make it impossible to draw clear conclusions about the most effective TED treatments for improving quality of life and this question was not the focus of this systematic review.

Surprisingly few studies evaluating treatment for TED to date have used the GO-QOL or other available tools to measure other psychosocial constructs. The GO-QOL has been recommended as a primary outcome measure in RCTs evaluating treatments for TED (Wiersinga, 2012) and its authors have emphasised the importance of assessing the impact of treatments on the quality of life of patients. However, with the growing recognition that quality of life outcomes are an essential component of the outcome set for clinical trials, more data on quality of life changes is likely to become available. The findings of the systematic review and the follow-up study described in Chapter 9 suggest that clinicians need to be aware when planning rehabilitative treatments such as surgery that there is variability in the effects they have on quality of life. Considering the discrepancy between ophthalmologist-evaluated and patient-evaluated severity of TED (Terwee et al, 2003b), it is important that assumptions are not made about the impact TED might have on a patients’ perceptions of their appearance. Patients need to be fully informed that whilst the aim of treatment is to improve clinical symptoms, not all treatments will improve their quality of life, particularly with regards to their concerns about their appearance.

The findings of the cross-sectional study prior to surgery suggest that healthcare professionals could identify patients with TED who are likely to adjust poorly to the change in their appearance and limitations in vision resulting from their condition by evaluating their levels of appearance-related distress and mood at the time of diagnosis. This could be done by routinely administering psychosocial measures including the HADS (Zigmond & Snaith, 1983), DAS24 (Carr, Moss & Harris, 2005), CARSAL and CARVAL (Moss & Rosser, 2012).

Overall however, the results from the study that assessed the impact of surgery, suggest that it is difficult to predict which patients will adjust well after surgery for TED from the factors they present with at baseline. Whilst a combination of ethnicity and clinical factors including low clinical activity scores, absence of hydraulic orbit and diplopia and, for appearance-related quality of life an addition of not having had prior radiotherapy, significantly predicted variation in quality of life, the proportion of variance explained by these factors was strikingly small (16% for visual function and 20% for appearance-related quality of life).

The results of the qualitative study could help to inform shared decision making between patients with TED and their surgeons in future consultations prior to surgery. This study highlighted the importance of healthcare professionals managing expectations by giving comprehensible, relevant information tailored to each patient. It would be valuable to patients for healthcare professionals to understand their beliefs, concerns, and the impact of accessing certain information about the surgery online. Healthcare professionals could therefore dispel any myths or correct any misinterpreted information in consultations prior to surgery, thus enabling patients to have realistic expectations of what surgery may or may not do for their appearance, vision, or both. This recommendation has been made before for clinicians working with patients with TED (Lane, 2006).

10.4RECOMMENDATIONS FOR FUTURE RESEARCH

Some initial research has suggested that adjustment to having a visible difference fluctuates over time (ARC, 2008; Harcourt & Rumsey, 2012). This is particularly pertinent when the visible difference fluctuates over time as it does when there are interventions such as surgery. Whilst this was one of few studies that have evaluated quality of life in TED for as long as 6 months after surgery, this is still a relatively short time after surgery and longer-term follow-ups might provide some useful insight into how quality of life might change over time, and whether different factors predict quality of life when assessed over a longer time period.

The follow-up study in the present thesis found that none of the measures of changes in clinical or psychosocial outcomes predicted change in vision-related quality of life. This suggests that other variables not measured in this study could explain the variation in change in vision-related quality of life. One possible area that could explain change in quality of life is the change in expectations over time, i.e. whether pre-surgical expectations were met. Unmet post-surgical expectations have been widely explored in the contexts of appearance and living with a disfigurement and have consistently been found to be associated with post-surgical dissatisfaction and impaired quality of life (Snell et al., 2010; Klassen et al., 2009; Honigman, Phillips & Castle, 2004; Dawn & Lee, 2004; Finlay, Atkinson, & Moos, 1995; Finlay et al., 1995; Pager, 2004; Bhty, 1999). In patients who were bitterly disappointed in the outcome of orbital decompression for appearance it would be likely to find little or no improvement in quality of life at 6 months post-surgery. Particularly as the qualitative study in this thesis found expectations for visual function to be unrealistically high, and considering that orbital decompression often does not cure double vision, and in some cases making it worse (EUGOGO et al., 2009).

Therefore a useful area of future research would be to examine whether expectations after surgery were met. As this was the first study to examine expectations of patients with TED about their surgery, it was useful to explore this new area using both quantitative and qualitative methods. For instance, confidence in healthcare professionals and expectations for recovery were important areas for participants in the qualitative study, which were not included in the E-TEDS developed for the quantitative study. It might be useful to take a similar methodological approach to investigating whether expectations are met after surgery, or indeed whether they change over time.

The qualitative study in this current thesis found expectations were heavily influenced by the type and source of information patients received, or sought, before surgery. Estcourt et al. (2011) have suggested that patients often have difficulty interacting with healthcare professionals and in an earlier study (Estcourt et al. 2009) found that only around half of patients were satisfied with their treatment for TED. Furthermore this study found that patients were often influenced to have orbital decompression by others, including other patients who had had the surgery and a positive result, family, and surgeons themselves, with some patients feeling they were expected to have orbital decompression by others. Others influence on patients' decisions to have cosmetic surgery has been found to have negative effects on patients' personal evaluation of surgical outcomes (von Soest et al., 2011). Patients' interactions with healthcare professionals and their satisfaction with information received *after* surgery were not measured in the present study and might have had an impact on post-surgical quality of life. Therefore another useful factor to explore in future studies would be the influence of others in the decision-making process to have surgery and their influence on post-surgical psychological outcomes.

Moss and Rosser (2012) urge researchers to move on to the integration of findings about theory to produce testable interventions with practical application. Appearance researchers have begun to deliver therapeutic interventions to improve outcomes in people with disfiguring conditions. Therapeutic interventions for people with visible differences aim to reduce distress and increase social skills and psychological well-being (Jenkinson, 2012). Such interventions have taken the forms of social interaction skills training (SIST), cognitive behavioural therapy (CBT), acceptance commitment therapy (ACT), and support groups, amongst others. In particular, social skills training and cognitive behavioural therapies have shown promising early results (Jenkinson, 2012; Thompson & Kent, 2001). This is perhaps partly explained by the difficulties people with visible differences encounter often being related to social interactions (Rumsey et al., 2004). Social skills training involves preparing someone with a visible difference to deal with staring, comments, and questions from others, and to be assertive and outgoing in social situations (Clarke, 1998; Borwick & Khanche, 2012). These skills have shown to be effective at increasing mood and reducing social avoidance and distress in people with facial disfigurements (Robinson, Rumsey & Partridge, 1996).

CBT in the context of visible difference involves encouraging people to re-evaluate the importance of appearance and gradual exposure to social situations (Jenkinson, 2012; Rumsey & Harcourt, 2004). CBT in this form has been provided in face-to-face individual and group-based sessions (Bessell & Moss, 2007), and more recently online (Bessell et al, 2012). Both face-to-face and online modes of delivery have been found to effectively reduce anxiety and appearance-related distress for people with facial disfigurements (Bessell et al, 2012). However, interventions often fail to identify the specific behaviour change techniques that make the different approaches effective and studies need to be clear about what constructs the intervention is targeting and the specific strategies used (Thompson & Kent, 2001).

Only 27% of patients with TED in the UK feel that they’ve been helped to deal with the psychosocial impact of their condition (Estcourt et al., 2009). Many patients have expressed wanting to talk to a professional about their psychological issues, however whilst patients are routinely offered support after the loss of an eye, patients with TED are not commonly offered support following their diagnosis of TED (Clarke et al., 2003). Considering that some of the highest levels of appearance-related distress and social avoidance are seen amongst patients with disfiguring eye conditions (Clarke et al., 2003; Richards et al., 2014), a finding that this study has supported, it is likely that patients with TED would benefit from psychological support designed specifically for these patients. At a recent patient and public involvement (PPI) event for TED in the UK, patients identified improving psychological support as a key priority for future research (Smith et al., 2014). The next logical step for the research programme would therefore be to use the results of this thesis to guide the development of a psychosocial intervention specifically targeted towards patients with TED.

10.1 OVERALL STRENGTHS AND WEAKNESSES OF THE THESIS

As with all studies there were variables that were not included in the study. Socioeconomic status wasn’t measured in the quantitative study and this might have highlighted some potential differences in quality of life in patients with TED. However, socioeconomic status has not been found to affect appearance concern in the general population (Harris & Carr, 2001) and there was not a sufficient rationale for measuring it in TED, particularly as studies evaluating treatment for TED have in the past failed to report socioeconomic status (e.g. Kahaly et al., 2005; Terwee et al., 2001, Fichter et al., 2013; Kashkouli et al., 2011b). Level of education was recorded for the qualitative study but not for the quantitative study, making it difficult to comment on whether the findings from each sample were representative of one another. Furthermore, the sample in the quantitative study appeared to be overrepresented by participants of White British backgrounds and did not match the ethnic diversity of patients with TED that attend MEH each year.

Due to the number of patients having orbital decompression surgery each year at MEH, time constraints on recruitment, and not wanting participants being interviewed to be influenced by their answers on questionnaires, or vice versa, it was necessary to recruit patients from an additional site. However, recruiting patients for the quantitative and qualitative studies from two different centres has its limitations.

As the patients were not recruited from the same population it is difficult to be certain that any inferences about the two studies is not due to cultural factors. It is however uncommon to suggest cultural differences between cities but the socioeconomic status of patients from Birmingham and its surrounding areas may be different to patients living in London and its surrounding counties.

Asking patients to fill in a questionnaire pack that takes up to 40 minutes to complete on three different occasions might have caused participant burden, which is one potential reason for drop-outs at follow-up time points. However, the researcher attempted to avoid this where possible by using any available validated short form versions of patient-reported psychosocial measures, including the Brief Fear of Negative Evaluation scale (BFNE; Leary, 1983), and single item measures of perceived visibility and patient satisfaction.

It is possible that some of the psychosocial measures touched on patients' emotional reactions to their disease, for example the DAS24 and GO-QOL included items on the topic of feeling distressed by their appearance and rejected by others. For any participants particularly distressed by the change in their appearance the contact numbers for a variety of support and information charities available to patients, including Changing Faces, The Healing Foundation, and the Thyroid Eye Disease Charitable Trust (TEDcT) were provided at the end of every questionnaire pack (Appendix G). In addition, the ordering of the questionnaires in the questionnaire pack might have influenced patients' answers on subsequent measures and ordering effects were not controlled for in this study. However, as far as the researcher is aware this did not cause any extreme emotional responses.

Notably, a small number of participants in the quantitative studies were still suffering from unstable thyroid function when they were listed for orbital decompression. Thyroid hormone state has been linked to a number of psychological issues as described in Chapter 2, section 2.4. Whilst potentially unstable thyroid function was controlled for in the regression analyses that assessed predictors of variation in quality of life, it is possible that this might have accounted for some of the mood disturbance in participants included in the study, as measured by the HADS.

A total of 11 participants did not have surgery, which, it could be argued, might have been followed up as a control group to assess change in quality of life in patients who did not receive orbital decompression surgery. However, this sample would not have been big enough to assess as a suitable comparison group and it would make a better study to have a large control sample. Furthermore, the aim of the current study was to evaluate predictors of quality of life specifically in patients undergoing orbital decompression surgery where a gap in the literature was identified.

Psychological co-morbidities other than anxiety and depression were not formally assessed when recruiting patients for this study. It is possible that unidentified co-morbid or historical severe psychiatric disorders might have influenced the high prevalence of anxious and depressed mood in the current sample, as found in Wong & Yu’s (2013) study. Additional psychiatric morbidities prior to surgery have been linked with postoperative satisfaction with outcomes and quality of life (Honigman, Phillips & Castle, 2004) and might have accounted for some of the variance in change in quality of life in the current sample. Furthermore, the prevalence of BDD was not measured in the current study. Studies investigating psychological outcomes following elective cosmetic surgery have highlighted the prevalence of BDD in these samples, and that it has been found to predict poor subjective satisfaction with cosmetic surgery outcomes (Castle, Honigman & Phillips, 2002). However, the present thesis focused on rehabilitative surgery for TED rather than cosmetic surgery on features of minimal or non-existent abnormality.

Finally, this study was not able to control for levels of appearance-related distress prior to developing TED as it was not possible to assess patients prior to them presenting for surgery. It would also have been unreliable to retrospectively capture appearance-related distress and social anxiety prior to developing TED. It is therefore unclear whether high levels of appearance-related distress had manifested in patients who had previously had low levels of distress, or whether patients with low levels of distress had always been relatively unconcerned about their appearance. Available data from the general population was used as a possible comparison. This is a common approach in assessing levels of appearance concern in different patient groups (Harris & Carr, 2001; Rumsey et al., 2004; Clarke et al., 2003; James et al., 2011).

10.2 OVERALL CONCLUSIONS

This thesis has made a number of novel contributions to the literature, in particular the application of a framework of adjustment to living with a disfiguring condition to patients with TED. The cross-sectional study demonstrated that predominantly intervening psychosocial processes explain variation in quality of life in patients with TED. Ethnicity and a group of clinical variables patients present with prior to surgery were found to predict a small proportion of the variability in change in quality of life from pre- to post-surgery. Changes in subjective evaluation of appearance predicted a large proportion of the variability in change in appearance-related quality of life from pre-to post-surgery, however no factors measured by the study significantly predicted change in visual functioning. This study added to our understanding of patient’s expectations of surgery; however further research is required to establish whether expectations are met after surgery, and whether this predicts quality of life outcomes in relation to both appearance and visual functioning. Implications for clinical practice need to be considered in light of the limitations of this thesis. This thesis does however highlight potential intervening cognitive processes amenable to change that can be targeted in future psychological interventions for patients with TED.

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Appendix A. Systematic Review Search Strategy: Ovid MEDLINE Example

Ovid MEDLINE
thyroid eye disease.af OR
thyroid-associated ophthalmopathy.af OR
graves ophthalmopathy.af OR
graves orbitopathy.af OR
dysthyroid orbitopathy.af OR
dysthyroid ophthalmopathy.af.

AND

psychosocial.af OR
psychological.af OR
psych*.af OR
"quality of life".af OR
depression.af OR
anxiety.af OR
social.af OR
adjustment.af.

AND

surgery.af OR
decompression.af OR
"orbital decompression".af OR
radiotherapy.af OR
radiation.af OR
surgical intervention.af or
steroid*.af or
rituximab.af or
azathioprine.af or
octreotide.af.

Appendix C. Data Extraction Form

Introduction

Author(s)	
Year	
Title	
Peer-reviewed journal	
Country	
Objectives/ aims	

Study design

Retrospective	
Cross-sectional	
Prospective observational	
Cross sectional observational	
RCT	
Qualitative	
Case control	

Study characteristics

Study population.	
Sample size	
Power calculation reported?	
Recruitment strategy (recruitment bias?)	
Definition of treatment groups	
If control group used, number of people & characteristics	
Eligibility criteria	
Exclusion criteria	

Participants

Age range	
Gender	
Occupation	
Duration of TED	
Severity of TED at baseline reported? Measure(s) used?	
Activity of disease at baseline reported? Measure(s) used?	
How was TED diagnosed?	
Previous treatments	
Smoking status	

Co-morbidities reported?	

Materials & Methods

Psychosocial outcome measure(s) used	
Additional variables measured & measures used	
Assessment methods	
Reliability & validity of each measure discussed?	
Reliability & validity reported in this sample?	
If RCT, method of randomisation? Was it blind?	
Length of follow-up, number of follow-up measurements	
Consideration of confounding variables, control variables used	

Analysis

Type and appropriateness of data analysis – are they measuring differences over time?	
Analysis of differences at baseline?	
Any missing data? How did the authors deal with this?	

Results

Participants: numbers at each stage (potentially eligible, included in study, completing follow-up, analysed)	
Number of withdrawals	
Reasons for withdrawal	
Number of exclusions	
Characteristics of those excluded from analysis	
Results from analysis at baseline – if reported	
Key Findings (i.e. relationships between psychosocial factors, clinical variables and	

outcome)	
Other important findings (e.g. effects of treatment on clinical factors)	
Effect size (means, *r*, etc)	
Was power/ adequate sampling achieved?	

Conclusions

Conclusions made by authors	
Generalisability of findings	
Implications for clinical practice or for future research	

Notes

Appendix D. Results of the Quality Assessment (Downs & Black, 1998) for the studies included in the review

Source	**Abraham-Nordling et al (2010)**	**Aktaran et al (2007)**	**Bartalena et al (2012)**	**Dickinson et al (2004)**	**Elberling et al (2004)**	**EUGOGO et al (2009)**	**Kahaly et al (2005)**	**Kashkouli et al (2009)**	**Kashkouli et al (2011)**	**Kulig et al (2009)**	**Marcocci et al (2011)**	**Prummel et al (2004)**	**Terwee et al (2001)**	**Terwee et al (2002)**	**Wémeau et al (2005)**	**Jellema et al (2014)**	**Beleslin et al (2014)**	**Fichter et al (2013)**
Aims and objectives clearly described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Main outcomes clearly described in the Introduction or Methods section	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Patient characteristics clearly described (i.e. Inclusion and exclusion criteria are given)	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	-
Interventions clearly described	✓	✓	✓	✓	✓	-	✓	-	-	✓	✓	✓	-	-	✓	✓	✓	✓

Distributions of principal confounders in each group clearly described	✓	✓	✓	✓	✓/ -	-	✓	✓	✓	✓	✓	✓	-	✓/ -	✓	✓/ -	✓/ -	✓/ -
Main findings clearly described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Estimates of random variability in the data provided	-	-	✓	-	✓	✓	-	-	✓	✓	✓	✓	✓	✓	-	✓	✓	✓
Adverse events have been reported	-	✓	✓	✓	✓	✓	✓	-	-	-	✓	-	-	-	✓	-	✓	✓
Characteristics of patients lost to follow-up have been described	✓	✓	✓	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	-	-
Actual probability values have been reported except where p< 0.001	✓	✓	✓	-	-	-	✓	✓	✓	✓	✓	-	✓	-	✓	✓	-	✓

The subjects approached for the study were representative	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
The subjects who were prepared to participate were representative	-	-	✓	✓	✓	-	-	-	-	-	✓	-	-	-	-	-	-	-
The staff, places, and facilities where the patients were treated were representative	✓	✓	✓	✓	-	✓	✓	-	-	✓	-	✓	✓	✓	-	✓	✓	-
Subjects were blinded	-	✓	✓	✓	-	-	-	-	-	-	✓	✓	-	-	✓	-	-	-
Those measuring the main outcomes were blinded	-	✓	✓	✓	-	-	✓	-	-	-	✓	✓	-	-	✓	-	-	-
Any unplanned analyses were reported (if done)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
The analyses adjust for different lengths of follow-up of patients	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	✓	-	✓	✓

Statistical tests were appropriate	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	✓	✓	✓
Compliance with the interventions was reliable	-	✓	-	✓	-	✓	✓	✓	✓	✓	-	✓	-	-	-	✓	✓	✓
Outcome measures were valid and reliable	✓	✓	✓	✓	✓	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓
Subjects in different intervention groups were recruited from the same population	✓	✓	✓	-	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	-	✓	✓	✓
Subjects in different intervention groups were recruited over the same period of time	✓	✓	✓	-	-	✓	✓	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓
Subjects were randomised	✓	✓	✓	✓	-	-	✓	-	-	-	✓	✓	-	-	✓	-	-	-
Randomisation was concealed from both patients and health care staff	-	✓	✓	✓	-	-	-	-	-	-	✓	✓	-	-	✓	-	-	-

Adequate adjustment for confounding in the analyses	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓	✓	-	✓	✓	-	-	-
Losses of patients to follow-up were taken into account	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
The study had sufficient power	-	-	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total score /32	**18**	**25**	**31**	**23**	**16**	**15**	**22**	**17**	**17**	**21**	**25**	**23**	**14**	**14**	**21**	**18**	**18**	**16**

Appendix E. Patient Information Sheet for the Quantitative Study

Project ID number: 11- H0724- 6
Date: 06.01.12

PATIENT INFORMATION SHEET

Study title: Psychosocial and clinical outcomes of surgery for Thyroid Eye Disease (TED)

Investigators: Prof S Newman Tel. [redacted]
Dr Daniel Ezra, Tel. [redacted]
Mrs Hayley McBain, Tel. [redacted]
Ms Sadie Wickwar, Tel [redacted]

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Part 1

1. **Why is the research taking place?**

Thyroid Eye Disease (TED) can impact upon not only a person's appearance and vision, but the way they feel. Orbital decompression surgery is often performed to improve vision and/or cosmetic appearance.

There has, however, been very little research looking at how people feel before and after surgery so this research aims to investigate how surgery impacts upon a person in the long term.

We hope that this research will help us to provide better care for people who come for surgical decompression in the future, by helping to develop appropriate means of support for those affected. The research will be conducted over 3 years by healthcare professionals at Moorfields Eye Hospital and researchers from City University London.

2. **Why have I been invited?**

You are being invited to participate because you are a patient attending for orbital decompression surgery at Moorfields Eye Hospital. We are seeking a total of 172 people over the age of 18 to take part in this study.

3. **Do I have to take part?**

No, taking part is voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, please keep this information sheet. You are still free to withdraw at any time and without giving a reason. Nobody will be upset if you do decide not to take part. Please be reassured that deciding to withdraw at any time or choosing not to take part at all will not affect the standard of care you receive at any time, either now or in the future.

4. **What will happen to me if I take part?**

On the day of your surgical pre-assessment appointment, a researcher will be present in the clinic to discuss the study with you. If you agree to take part, they will give you a questionnaire to complete. This will include various questions about how you feel with regards to your Thyroid Eye Disease and the surgery you are about to receive. We do not anticipate that this will take you more than 40 minutes to complete. You can choose to complete the questionnaire whilst you are at the clinic or take the questionnaire home, along with a stamped addressed envelope for you to return it to us. You will then be asked to complete another questionnaire a few weeks after surgery and then again 6 months later; this is to see how you feel over time.

5. **What will I have to do?**

If you consent to taking part in the study, you will be asked to complete a series of 3 questionnaires: one before your surgery, then again after surgery, and again 6 months later. The researchers may contact you at home, by telephone, if they have not received your questionnaire.

6. **What are the possible disadvantages and risks of taking part?**

We are always required to tell you about any risks to you, should you agree to take part in research. However, in this instance we are not aware of there being any such risks to you. It does not involve any additional medical treatment. It consists only of completing a series of questionnaires.

7. **What are the possible benefits of taking part?**

We do not expect there to be any personal benefits for you in taking part, but we expect that the information we get from this study will help us to provide more appropriate support to people who are to have this surgery in the future.

8. **What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

9. **Will my taking part in this study be kept confidential?**

All information which is collected from you during the course of the research will be kept strictly confidential and will only be used for research purposes.

If you agree, we would like to inform your GP that you are taking part. This is as a matter of courtesy, but rest assured that they will not know what information you have given to us.

This completes part 1.

If the information in Part 1 has interested you and you are considering taking part, please read the additional information in Part 2 before making any decision.

Part 2

1. What will happen if I don’t want to carry on with the study?

If you decide at any point during your participation in the study that you wish to withdraw from the study, you can contact the research or clinical team to discuss this. It would be useful for us to use the information you have given us up until that point in the study; however, if you wish for us to destroy this data, this can also be arranged.

2. What if there is a problem?

If you have a concern about any aspect of this study, you should speak to the researchers who will do their best to answer your questions. You can do so either at your next appointment or contact them at [redacted] or by email at [redacted]. If you remain unhappy and wish to complain formally, you can do this through the Complaints Manager, Moorfields Eye Hospital NHS Foundation Trust, 162 City Road, London EC1V 2PD, Telephone: [redacted]. Please quote the project number at the top of this information sheet.

3. Will my taking part in this study be kept confidential?

We need permission to access your medical records which relate directly to this study. All the information collected during the study will be held securely in the strictest confidence and will only be used for research purposes.

If you agree, we would like to inform your GP that you are taking part. This is as a matter of courtesy, but rest assured that they will not know what information you have given to us.

The data that we collect will be kept anonymously on password-protected computers and in locked filing cabinets. Only members of the research team will see this anonymous information, and the researcher will be the only person who will have access to identifiable data.

4. What will happen to the results of the research study?

The findings of this research will be reported in professional publications or at meetings, but you will not be identified in any report or publication. If at any point during the study you lose capacity to take part, the data you have provided up until that point will remain within the study, but only with the permission of your next of kin.

5. Who is organising the research?

This research is being organised by researchers at City University London, along with surgeons at Moorfields Eye Hospital.

6. Who has reviewed the study?

This study has been reviewed and approved by the North London Research Ethics Committee REC2.

7. Further Information and contact details

If you want some general information about taking part in research please contact the Patient Advice Liaison Service (PALS) on [redacted] or [redacted], or by email on [redacted]
.
If you have any questions about this study and what you are being asked to consider, please contact one of the research team.

If you would like any further information about this research or if you have any queries at any time in the future, please contact Sadie Wickwar in Health Services Research, City University London on [redacted] or via email at [redacted]

Thank you for reading this information sheet.

Appendix F. Consent Form for the Quantitative Study

Project ID number: 11-H0724-6

Patient Identification Number for this study:

CONSENT FORM

Title of Project: The psychosocial and clinical outcomes of surgery for thyroid eye disease (TED)

Name of Principal Investigator: Professor Stanton Newman

1. I confirm that I have read and understood the information sheet dated 06.01.12 (version 4) for the above study and have had the opportunity to ask questions. ☐
2. I confirm that I have had sufficient time to consider whether or not want to be included in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I agree to take part in the above study. ☐
6. I give my permission for my GP to be informed that I am taking part in this research. ☐
7. I understand that taking part in this research project will involve completing a questionnaire on one or more occasions. ☐
8. I would like to receive feedback about the findings of the study. ☐

Name of patient	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Researcher (to be contacted if there are any problems)	Date	Signature

Comments or concerns during the study
If you have any comments or concerns you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager at Moorfields Eye Hospital, details for which can be found on the information sheet. Please quote the project number at the top this consent form.

1 form for Patient
1 to be kept with hospital notes
1 to be kept as part of the study documentation

Appendix G. Pre-surgery Questionnaire Pack

Project ID number: 11- H0724- 6
Participant ID number:
Date completed:
Baseline

PSYCHOSOCIAL AND CLINICAL OUTCOMES OF SURGERY FOR THYROID EYE DISEASE (TED)

Research Study

We are a team of researchers from City University London and Moorfields Eye Hospital, conducting a study investigating the impact of orbital decompression surgery. We hope that this research will help us to provide better care for people who come for this type of surgery in the future by developing appropriate means of support for those affected.

If at any point during completing this questionnaire you feel any distress, details of support groups are provided at the end of the questionnaire. Similarly, if you wish to discuss any aspect of the project, contact details for the research team are also provided at the end of the questionnaire.

If you are happy to complete the questionnaire then please turn over and work through the booklet, completing all questions. This shouldn't take more than 40 minutes. If you are unable to complete this on your own, please contact the research team to assist you.

Please respond to EACH statement by circling the response that best reflects how you feel.

Circle only ONE response for each statement.

Thank you again for your participation.

[1] **What is your gender?** *(please circle)*

Male Female

[2] **What is your age?** *(please write in)* _______________

[3] **How would you describe your ethnic background?** *(please circle one)*

1	Bangladeshi	2	Indian
3	Pakistani	4	Other Asian background
5	White British	6	White Irish
7	Other White background	8	Black Caribbean
9	Black African	10	Other Black background
11	Chinese	12	Other ethnic group

[4] **How would you describe your relationship status?** *(please circle one number)*

1 Married
2 Divorced
3 Widowed
4 Single
5 Living with partner
6 Other

[5] **How long have you lived with your Thyroid Eye Disease?**

…………………………………………………………………………………………

[6] **Have you ever had surgical treatment for your Thyroid Eye Disease? *(please circle)***

Yes No

If yes how many? ....

Date/Year of your first ....

Date/Year of your last ....

The following questions are about your general mood in the past week. Please read each item below and then place a tick in the box next to the reply which comes closest to how you have been feeling in the past week. Try to give your first reaction. This will probably be more accurate than spending a long time thinking about an answer

1) *I feel tense or wound up*
Most of the time [ ]
A lot of the time [ ]
Time to time, occasionally [ ]
Not at all [ ]

2) *I feel as if I am slowed down*
Nearly all the time [ ]
Very often [ ]
Sometimes [ ]
Not at all [ ]

3) *I still enjoy the things I used to enjoy*
Definitely as much [ ]
Not quite so much [ ]
Only a little [ ]
Hardly at all [ ]

4) *I get a sort of frightened feeling like "butterflies" in my stomach*
Not at all [ ]
Occasionally [ ]
Quite often [ ]
Very often [ ]

5) *I get a sort of frightened feeling as if something awful is about to happen*
Very definitely & quite badly [ ]
Yes, but not too badly [ ]
A little, but it doesn't worry me [ ]
Not at all [ ]

6) *I have lost interest in my appearance*
Definitely [ ]
I don't take as much care as I should [ ]
I may not take quite as much care [ ]
I take just as much care as ever [ ]

7) *I can laugh and see the funny side of things*
As much as I always could [ ]
Not quite so much now [ ]
Definitely not so much [ ]
Not at all [ ]

8) *I feel restless as if I have to be on the move*
Very much indeed [ ]
Quite a lot [ ]
Not very much [ ]
Not at all [ ]

9) *Worrying thoughts go through my mind*
A great deal of the time [ ]
A lot of the time [ ]
From time to time but not often [ ]
Only occasionally [ ]

10) *I look forward with enjoyment to things*
As much as I ever did [ ]
Rather less than I used to [ ]
Definitely less than I used to [ ]
Hardly at all [ ]

11) *I feel cheerful*
Not at all [ ]
Not often [ ]
Sometimes [ ]
Most of the time [ ]

12) *I get sudden feelings of panic*
Very often indeed [ ]
Quite often [ ]
Not very often [ ]
Not at all [ ]

13) *I can sit at ease & feel relaxed*
Definitely [ ]
Usually [ ]
Not often [ ]
Not at all [ ]

14) *I can enjoy a good book or TV programme*
Often [ ]
Sometimes [ ]
Not often [ ]
Very seldom [ ]

The following questions are concerned with the way you feel or act. They are all simple. Please circle the answer that applies to you. **If the item does not apply to you at all, circle the N/A (not applicable option)**. Don't spend long on any one question.

a. **How confident do you feel?**

Not at all	Slightly	Moderately	Extremely

b. **How distressed do you get when you see yourself in the mirror/window?**

Extremely	Moderately	A Little	Not at all Distressed

c. **My self-consciousness makes me irritable at home:**

N/A	Never/Almost never	Sometimes	Often	Almost always

d. **How hurt do you feel?**

Extremely	Moderately	Slightly	Not at all	N/A

e. **At present my self-consciousness has an adverse effect on my work:**

Almost always	Often	Sometimes	Never/almost never	N/A

f. **How distressed do you get when you go to the beach?**

N/A	Not at all	A little	Moderately	Extremely

g. **Other people misjudge me because of my feature:**

Almost always	Often	Sometimes	Never/almost never	N/A

h. **How feminine/masculine do you feel?**

Not at all	Slightly	Moderately	Extremely

i. **I am self-conscious about my feature:**

N/A	Never/Almost never	Sometimes	Often	Almost always

j. **How irritable do you feel?**

Not at all	Slightly	Moderately	Extremely

k. **I adopt certain gestures (e.g. folding my arms in front of other people, covering my mouth with my hand):**

Never/almost never Sometimes Often Almost always

l. I avoid communal changing rooms:

Almost always Often Sometimes Never/almost never N/A

m. How distressed do you get by shopping in department stores/supermarkets?

N/A Not at all Slightly Moderately Extremely

n. How rejected do you feel?

Not at all Slightly Moderately Extremely

o. I avoid undressing in front of my partner:

N/A Never/Almost never Sometimes Often Almost always

p. How distressed do you get while playing sports/games?

Extremely Moderately Slightly Not at all N/A

q. I close into my shell:

Almost always Often Sometimes Never/Almost never

r. How distressed are you by being unable to wear your favourite clothes?

Extremely Moderately Slightly Not at all N/A

s. How distressed do you get when going to social events?

N/A Not at all Moderately A fair amount Extremely

t. How normal do you feel?

Not at all Slightly Moderately Extremely

u. At present my self-consciousness has an adverse effect on my sex life:

Almost always Often Sometimes Never/almost never N/A

v. I avoid going out of the house:

Almost always Often Sometimes Never/Almost never

w. How distressed do you get when other people make remarks about your feature?

N/A	Not at all	Moderately	A fair amount	Extremely

x. I avoid going to pubs/restaurants:

Almost always	Often	Sometimes	Never/almost never	N/A

y. My feature causes me physical pain/discomfort:

Never/almost never	Sometimes	Often	Almost always

z. My feature limits my physical ability to do the things I want to do:

Almost always	Often	Sometimes	Never/Almost never

The GO-QOL is a short questionnaire with statements about how your Thyroid Eye Disease may affect you in your everyday life.

Please focus on the **past week** while answering these questions. During the past week, to what extent were you limited in carrying out the following activities, because of your Thyroid Eye Disease?

Please circle only one answer for each question.

	Yes, seriously limited	**Yes, a little limited**	**No, not at all limited**
Driving (no driver's licence ☐)	1	2	3
At work (usual job)	1	2	3
Performing domestic duties (e.g. cooking and cleaning)	1	2	3
Moving around the house	1	2	3
Walking outdoors	1	2	3
Reading	1	2	3
Watching TV	1	2	3
Hobby or pastime, **i.e. _____________**	1	2	3

	Yes, severely hindered	**Yes, a little hindered**	**No, not at all hindered**
During the past week, did you feel hindered from something that you wanted to do because of your Thyroid Eye Disease?	1	2	3

The following questions deal with your thyroid eye disease **in general**

	Yes, very much so	**Yes, a little**	**No, not at all**
Do you feel that your appearance has changed because of your thyroid eye disease?	1	2	3
Do you feel that you are stared at in the streets because of your thyroid eye disease?	1	2	3
Do you feel that people react unpleasantly because of your thyroid eye disease?	1	2	3
Do you feel that your thyroid eye disease has an influence on your self confidence?	1	2	3
Do you feel socially isolated because of your thyroid eye disease?	1	2	3
Do you feel that your thyroid eye disease has an influence on making friends?	1	2	3
Do you feel that you appear less often on photos than before you had thyroid eye disease?	1	2	3
Do you try to mask changes in appearance caused by your thyroid eye disease?	1	2	3

These questions are trying to examine how aware you are of your physical appearance. Please indicate how much you agree with each statement below by circling a number.

	Strongly disagree	**Moderately disagree**	**Slightly disagree**	**Slightly agree**	**Moderately agree**	**Strongly agree**
Sometimes, the way I look is the furthest thing from my thoughts	1	2	3	4	5	6
It is not often that I think about how the way I look comes over to people	1	2	3	4	5	6
For me, my appearance is an important part of who I am.	1	2	3	4	5	6
I am often aware of the way that I look to other people.	1	2	3	4	5	6
In most situations, I find myself aware of the way my face and body look.	1	2	3	4	5	6
I often think about the impression that the appearance of my face and body make.	1	2	3	4	5	6
The look of my face and body is not something that often comes to mind for me.	1	2	3	4	5	6
I am usually conscious of my appearance.	1	2	3	4	5	6
I don’t usually give much thought to my appearance.	1	2	3	4	5	6

These questions assess how you feel about your appearance. Please indicate how much you agree with each statement below. (***Please circle one response for each question***)

	Strongly disagree	**Moderately disagree**	**Slightly disagree**	**Slightly agree**	**Moderately agree**	**Strongly agree**
I am satisfied with my physical appearance	1	2	3	4	5	6
I don't like the way I look	1	2	3	4	5	6
The way I look makes me feel good about myself	1	2	3	4	5	6
The way I look makes me unattractive	1	2	3	4	5	6
My body and face look pretty much the way I would like	1	2	3	4	5	6
I feel bad about my body and my appearance	1	2	3	4	5	6
I like the way I look	1	2	3	4	5	6
My appearance makes me feel attractive	1	2	3	4	5	6

How visible do you feel your proptosis (bulging eyes) is to other people?

Not at all visible			Moderately visible			Extremely visible
1	2	3	4	5	6	7

We are interested in how much you feel you are supported by your friends, family, and a special person in your life. Please **circle** one of the five numbers to indicate how much you agree with each statement.

	Strongly disagree	**Disagree**	**Neither disagree nor agree**	**Agree**	**Strongly agree**
There is a special person who is around when I am in need	1	2	3	4	5
There is a special person with whom I share my joys and sorrows	1	2	3	4	5
My family really tries to help me	1	2	3	4	5
I get the emotional help and support I need from my family	1	2	3	4	5
I have a special person who is a real source of comfort to me	1	2	3	4	5
My friends really try to help me	1	2	3	4	5
I can count on my friends when things go wrong	1	2	3	4	5
I can talk about my problems with my family	1	2	3	4	5
I have friends with whom I can share my joys and sorrows	1	2	3	4	5
There is a special person in my life who cares about my feelings	1	2	3	4	5
My family is willing to help me make decisions	1	2	3	4	5
I can talk about my problems with my friends	1	2	3	4	5

Using the five point scale below please rate how you expect surgery to change various aspects of your life.

	Made considerably worse	**Made worse**	**Remained the same**	**Improve**	**Considerably Improve**
My vision	1	2	3	4	5
The appearance of my eyes	1	2	3	4	5
The appearance of my face	1	2	3	4	5
My ability to drive	1	2	3	4	5
My ability to move around the house	1	2	3	4	5
My ability to perform domestic duties (e.g. cooking and cleaning)	1	2	3	4	5
My ability to engage in my hobby or pastime	1	2	3	4	5
My ability to read	1	2	3	4	5
My ability to watch TV	1	2	3	4	5
My ability to use the computer	1	2	3	4	5
My ability to work (usual job)	1	2	3	4	5
My ability to walk outdoors	1	2	3	4	5
My double vision	1	2	3	4	5
My dry eyes	1	2	3	4	5
My headaches/ eye pain	1	2	3	4	5

	Made considerably worse	Made worse	Remained the same	Improve	Considerably Improve
My ability to obtain a job	1	2	3	4	5
My self confidence	1	2	3	4	5

My ability to make new friends	1	2	3	4	5
My ability to form new intimate relationships	1	2	3	4	5
The relationship with my family	1	2	3	4	5
The relationship with my current friends	1	2	3	4	5
The relationship with my current partner/wife/husband	1	2	3	4	5
The relationship with my eye doctor	1	2	3	4	5
Other people's reactions to my TED	1	2	3	4	5
My willingness to appear in photographs because of my TED	1	2	3	4	5
My desire to mask the changes in my appearance as a result of my TED	1	2	3	4	5

Please indicate how much you agree with each statement below by circling a number.

	Not at all characteristic of me	**Very uncharacteristic of me**	**Moderately characteristic of me**	**Very characteristic of me**	**Extremely characteristic of me**
I worry about what other people will think of me even when I know it doesn't make any difference	1	2	3	4	5
I am unconcerned even if I know people are forming an unfavourable impression of me	1	2	3	4	5
I am frequently afraid of other people noticing my shortcomings	1	2	3	4	5
I rarely worry about what kind of impression I am making on someone	1	2	3	4	5
I am afraid that others will not approve of me	1	2	3	4	5
I am afraid that other people will find fault with me	1	2	3	4	5
Other people's opinions of me do not bother me	1	2	3	4	5
When I am talking to someone, I worry about what they may be thinking of me	1	2	3	4	5
I am usually worried about what kind of impression I make	1	2	3	4	5
If I know someone is judging me, it has little effect on me	1	2	3	4	5
Sometimes I think I am too concerned with what other people think of me	1	2	3	4	5
I often worry that I will say or do the wrong things	1	2	3	4	5

It is natural at times to compare yourselves with others. For example, you may compare the way you feel, your opinions, your abilities, and/or your situation with those of other people. There is nothing particularly 'good' or 'bad' about this type of comparison, and some people do it more than others. I would like to find out how often you compare yourself with other people in relation to your appearance.

Please indicate how much you agree with each statement below. (***please circle one response for each question***)

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
I often compare how my loved ones (boy or girlfriend, family members) are doing with how others are doing.	1	2	3	4	5
I always pay a lot of attention to how I do things compared with how others do things.	1	2	3	4	5
If I want to find out how well I have done something, I compare what I have done with how others have done.	1	2	3	4	5
I am not the type of person who compares often with others.	1	2	3	4	5
I often compare how I am doing socially (e.g., social skills, popularity) with other people.	1	2	3	4	5
I often compare myself with others with respect to what I have accomplished in life.	1	2	3	4	5
I often like to talk with others about mutual opinions and experiences.	1	2	3	4	5
I often try to find out what others think who face similar problems as I face.	1	2	3	4	5
I always like to know what others in a similar situation would do.	1	2	3	4	5
If I want to learn more about something, I try to find out what others think about it.	1	2	3	4	5

I never consider my situation in life relative to that of other people.	1	2	3	4	5

Thank you very much for completing this questionnaire. Please return the questionnaire to us using the freepost envelope provided, once you feel happy to do so.

By taking part in this research you have contributed to a study that we anticipate will benefit many people. The findings from this research will help guide and develop new treatment techniques that will aid people with Thyroid Eye Disease (TED) to deal with appearance-related issues. The research findings will also increase our knowledge of the experiences people face when dealing with TED.

If at any point you wish to discuss the project or any other issues around the subject of appearance, please do not hesitate to contact the research team on the number provided below. Similarly, if you have more general concerns about appearance related issues, the charities ***Changing Faces*** and ***The Healing Foundation*** provide specialist advice and resources about differences in appearance. Contact details for these organisations are also provided below.

If you wish to talk to someone regarding this project, please do not hesitate to call **Ms Sadie Wickwar** in the department of Health Services Research at City University, Tel [redacted] or e-mail [redacted]

If you have concerns relating to an appearance-related condition or have experienced any distress completing this questionnaire then you can contact either of the following organisations for expert and confidential advice:

Changing Faces on **Tel: 0845 4500 275** or email: **info@changingfaces.org.uk**

The Healing Foundation on **Tel. 020 7869 6920** or email: **info@thehealingfoundation.org**

The Royal National Institute for the Blind (RNIB) on **Tel: 0303 123 9999** or email: **helpline@rnib.org.uk**

Appendix H. Letter Sent to Participant's GP

City Road
London
EC1V 2PD

Tel: 020 7253 3411
www.moorfields.nhs.uk

Project ID number: 11- H0724- 6
Dear

RE: [PATIENT NAME], D.O.B: [PATIENT D.O.B]

Research title: Psychosocial and clinical outcomes of surgery for Thyroid Eye Disease (TED)

6. Your patient has agreed to take part in some research that aims to investigate the psychosocial and clinical factors which contribute to successful adaptation after surgical decompression. The study has been approved by the Research Ethics Committee and is open to all patients over the age of 18 who have opted for surgical decompression at Moorfields Eye Hospital, London.

7. Your patient will be completing a series of questionnaires over a 6 month period. Any information provided will be treated as strictly confidential. Be assured that your patient will always receive the best possible treatment available. The research is being conducted in collaboration with the department of Health Services Research, City University London.

8. The study does not involve any additional treatment and your patient is free to withdraw from the study at any time. They are able to contact the researcher with any questions or concerns about the research at any time during or after the study. Similarly, if you have any questions about the research please contact Sadie Wickwar at City University on Tel [redacted] or via email [redacted]

Thank you for reading this. If you have any questions or require further information then please contact me.

Yours Sincerely

Sadie Wickwar
PhD Student in Health Psychology
City University

Appendix I. Patient Information Sheet for the Qualitative Study

Project ID number: 11- H0724- 6

PATIENT INFORMATION SHEET

9.

Study title: Patient expectations of surgery for Thyroid Eye Disease (TED)

Investigators: Prof S Newman Tel. [redacted]
Mr Omar Durrani, Tel. [redacted]
Ms Sadie Wickwar, Tel. [redacted]
Mr Matthew Edmunds, Tel. [redacted]

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Part 1

1. Why is the research taking place?

Thyroid Eye Disease (TED) can impact upon not only a person’s appearance and vision, but the way they feel. Orbital decompression surgery is often performed to improve vision and/or cosmetic appearance.

There has, however, been very little research looking at how people feel before and after surgery so this research aims to investigate how surgery impacts upon a person in the long term.

We hope that this research will help us to provide better care for people who come for surgical decompression in the future, by helping to develop appropriate means of support for those affected. The research will be conducted over 3 years by healthcare professionals at Moorfields Eye Hospital, Birmingham and Midland Eye Centre and researchers from City University London.

2. Why have I been invited?

You are being invited to participate because you are a patient attending for orbital decompression surgery at Birmingham and Midland Eye

Centre. We are seeking up to 25 people over the age of 18 to take part in this study.

3. Do I have to take part?

No, taking part is voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, please keep this information sheet. You are still free to withdraw at any time and without giving a reason. Nobody will be upset if you do decide not to take part. Please be reassured that deciding to withdraw at any time or choosing not to take part at all will not affect the standard of care you receive at any time, either now or in the future.

4. What will happen to me if I take part?

On the day of your surgical pre-assessment appointment, a researcher will be present in the clinic to discuss the study with you. If you agree to take part, you will be asked to meet with the researcher for an interview within the next two weeks, and again 5-6 months after your surgery. Both interviews will be arranged at a time that is convenient for you. Each interview should last no longer than one hour.

10. What will I have to do?

If you consent to taking part in the study, you will be asked to take part in two interviews that will last no longer than one hour each. You will be asked a series of questions about your thyroid eye disease and scheduled surgery. We will ask you if we can tape record each interview, however you do not have to agree to this and the researcher can take notes instead. Any tape recorded interviews will be kept secure and any data from the interviews will be made anonymous so that it cannot be linked to you.

6. What are the possible disadvantages and risks of taking part?

We are always required to tell you about any risks to you, should you agree to take part in research. However, in this instance we are not aware of there being any such risks to you. It does not involve any additional medical treatment. It consists only of taking part in two interviews.

7. What are the possible benefits of taking part?

We do not expect there to be any personal benefits for you in taking part, but we expect that the information we get from this study will help us to provide more appropriate support to people who are to have this surgery in the future.

9. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

9. Will my taking part in this study be kept confidential?

All information which is collected from you during the course of the research will be kept strictly confidential and will only be used for research purposes.

This completes part 1.

If the information in Part 1 has interested you and you are considering taking part, please read the additional information in Part 2 before making any decision.

Part 2

8. What will happen if I don't want to carry on with the study?

If you decide at any point during your participation in the study that you wish to withdraw from the study, you can contact the research or clinical team to discuss this. It would be useful for us to use the information you have given us up until that point in the study; however, if you wish for us to destroy this data, this can also be arranged.

9. What if there is a problem?

If you have a concern about any aspect of this study, you should speak to the researchers who will do their best to answer your questions. You can do so either at your next appointment or contact them at 0207 040 0876 or by email at sadie.wickwar.1@city.ac.uk. If you remain unhappy and wish to complain formally, you can do this through the Complaints Department, Sandwell & West Birmingham Hospital NHS Trust, City Hospital, Dudley Road, Birmingham B18 7QH, telephone: [redacted]; e-mail [redacted]. Please quote the project number at the top of this information sheet.

10. Will my taking part in this study be kept confidential?

We need permission to access your medical records which relate directly to this study. All the information collected during the study will be held securely in the strictest confidence and will only be used for research purposes.

The data that we collect will be kept anonymously on password-protected computers and in locked filing cabinets. Only members of the research team will see this anonymous information, and the researcher will be the only person who will have access to identifiable data.

11. What will happen to the results of the research study?

The findings of this research will be reported in professional publications or at meetings, but you will not be identified in any report or publication. If at any point during the study you lose capacity to take part, the data you have provided up until that point will remain within the study, but only with the permission of your next of kin.

12. Who is organising the research?

This research is being organised by researchers at City University London, along with surgeons at Moorfields Eye Hospital and Birmingham and Midland Eye Centre

13. Who has reviewed the study?

This study has been reviewed and approved by the North London Research Ethics Committee REC2.

14. Further Information and contact details

If you want some general information about taking part in research please contact the Patient Advice Liaison Service (PALS) on [redacted], or by email on [redacted]

If you have any questions about this study and what you are being asked to consider, please contact one of the research team.

If you would like any further information about this research or if you have any queries at any time in the future, please contact Sadie Wickwar in Health Services Research, City University London on [redacted] or via email at [redacted]

Thank you for reading this information sheet.

Appendix J. Consent Form for the Qualitative Study

Project ID number: 11-H0724-6
Patient Identification Number for this study:

CONSENT FORM

Title of Project: Patient expectations of surgery for thyroid eye disease (TED)

1.

Name of Principal Investigator: Professor Stanton Newman

1. I confirm that I have read and understood the information sheet dated 07.11.11 (version 4) for the above study and have had the opportunity to ask questions. ☐
2. I confirm that I have had sufficient time to consider whether or not want to be included in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I agree to take part in the above study. ☐
6. I understand that taking part in this research project may involve taking part in two interviews; one before my surgery, and another 5-6 months after my surgery. I am happy for the researcher to contact me to arrange a further interview at a time that is suitable for me. ☐

Continued on next page…

7. I would like to receive feedback about the findings from the study ☐

Name of patient	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Researcher (to be contacted if there are any problems)	Date	Signature

Comments or concerns during the study
If you have any comments or concerns you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager at Birmingham and Midland Eye Centre, details for which can be found on the information sheet. Please quote the project number at the top this consent form.

1 form for Patient
1 to be kept with hospital notes
1 to be kept as part of the study documentation

Appendix K. Clinical Data Form for the Quantitative Study

PSYCHOSOCIAL AND CLINICAL OUTCOMES OF SURGERY FOR THYROID EYE DISEASE (TED)

Clinical Data Collection Form
Preoperative assessment

Patient number: .... Date of assessment: .../..../.....

Date of Birth: .../..../..... Date of planned Surgery: .../..../.....

Thyroid function stable? Y/N

Duration of eye symptoms: Years: …… Months: ……

Quiescent? Active?

Previous treatments: Steroids/ Radiotherapy/ Immunomodulation/ Surgery/ None

Previous decompression surgery? Y/N If yes, date of previous……..

Is patient currently taking steroids? Y/N

Is patient currently smoking? Y/N

Laterality of TED: ☐ Left
☐ Right
☐ Both

Laterality of surgery: ☐ Left
☐ Right
☐ Both

Right		**Left**
....	Best Corrected Visual Acuity (Snellen)	....
Y/N	Optic Nerve Dysfunction (Ishihara, Red Desat, RAPD)	Y/N
	Exophthalmometry	
	Palpebral Aperture	
	MRD1	
	MRD2	
	Scleral show 1	
	Scleral show 2	
Y/N	Lagophthalmos	Y/N
Y/N	Corneal SPK	Y/N
Y/N	Hydraulic orbit	Y/N

Diplopia present?   Y/N

CAS SCORE – PLEASE CIRCLE EACH YES OR NO:

Pain:	Y/N Painful oppressive feeling behind globe during last 4 weeks
	Y/N Pain on eye movements in last 4 weeks
Redness:	Y/N Redness of eyelid
	Y/N Diffuse redness of conjunctiva, covering at least 1 quadrant
Swelling:	Y/N Swelling of the eyelid
	Y/N Chemosis
	Y/N Swollen caruncle
	Y/N Increase of proptosis > 2mm during a period of 1-3 months
Impaired function	Y/N Decrease of eye movements in any direction in the last 3 months
	Y/N Decrease of visual acuity >1 line in last 3 months

CAS SCORE = Number of items present = ………..

Appendix L. Pilot Interview Schedule for Qualitative Study

Pre-Surgery Interview

Topics to cover– current impact of illness on daily activities; current feelings about appearance; treatment options; personal reasons for having surgery; goals for surgery/ outcomes; motivation for going forward with corrective surgery; what has influenced decision to go for surgery; what preparations might they have made for surgery; expectations of results; expectations about the recovery process; expectations for appearance; expectations about social encounters; expectations for daily activities

Example questions *(to use as a general guideline)*:

A. Introduction

14) Can you tell me about the impact your thyroid eye disease (TED) might have had on your daily activities?
15) Can you tell me how you feel about the impact that your TED might have had on your appearance?
16) Can you tell me how you feel about the impact that your TED might have had on how you feel about yourself?

B. Motivation(s) for having surgery

17) When did you first start thinking about having surgery?
18) Did you consider alternative treatment options? If so, reasons for choosing surgery over others
19) What do you feel your reasons might be for having surgery?
20) Could you tell me what is motivating you to have this surgery?
21) Are there any particular goals you hope to achieve by having surgery?
22) Can you tell me what you think might have influenced your decision to have surgery? Who in your life has influenced your decision to have surgery?
23) Could you tell me about what you might have done to prepare for your surgery, or that you plan on doing to before your surgery?

C. Expectations of surgery

24) Can you tell me what you might be expecting from your surgery?
25) Do you think surgery might change your appearance? If so, in what ways?
26) Do you think surgery might change your daily life? If so, in what ways?
27) Can you tell me about the recovery process you might be expecting after your surgery?

Appendix M. Demographic Data Form for Qualitative Study

Project ID number: 11-H0724-6
REC Approved: 29.10.12

Patient Identification Number for this study:

Demographic Details Questionnaire

[1] **What is your gender?** *(please circle)*

Male Female

[2] **What is your age?** *(please write in)* _______________

[3] **How would you describe your ethnic background?** *(please circle one)*

1 Bangladeshi
2 Indian
3 Pakistani
4 Other Asian background
5 British
6 Irish
7 Other White background
8 Caribbean
9 African
10 Other Black background
11 Chinese
12 Other ethnic group

[4] **How would you describe your relationship status?** *(please circle one number)*

7 Married
8 Divorced
9 Widowed
10 Single
11 Living with partner
12 Other _______________________

[5] **How would you describe your employment status?** *(please circle one number)*

1 Full time work
2 Part time work
3 Full time homemaker
4 Unemployed
5 Other ______________________

Job Title (where applicable) _______________________

[6] **What is your highest qualification?** *(please circle one number)*

1 None
2 GCSE / O Level / equivalent
3 A Level / equivalent
4 HNC / HND / equivalent
5 Degree / equivalent
6 Post graduate

[7] **How long have you lived with your Thyroid Eye Disease?**

……………………………………………………………………………………………

[8] **Have you ever had surgical treatment for your Thyroid Eye Disease before this planned surgery?** *(please circle)*

Yes No

If yes how many? ....

Type of previous surgery ....

Date/Year of your first ....

Date/Year of your last ....

Appendix N. Thematic Coding Framework

Thematic Coding Framework - table developed using elements of a good thematic code described by Boyatzis (1998):

1) A label (i.e. a name), 2) A definition of what the theme concerns (i.e. the characteristic or issue constituting the theme), 3) A description of how to know when the theme occurs (i.e. indicators on how to "flag" the theme), 4) A description of any qualifications or exclusions to the identification of the theme, and 5) Examples, both positive and negative, to eliminate possible confusion when looking for the theme.

CODE NAME	DESCRIPTION	QUALIFICATIONS OR EXCLUSIONS	EXAMPLES
Social comparisons	Talk about feelings towards others with TED, including those with more severe TED, other conditions, and others who look 'more normal'	*See description*	*Well when I went on there, there was… I looked at this one and he… his eye… his eyes was just horrendous. I think if my eyes looked like that, well, I don't know what I'd do. But, so I know my eyes aren't as bad as a lot of other peoples'*
Confidence & self-esteem	Impact of having TED on confidence and self-esteem before surgery	*Excludes talk about expectations in improvements in confidence after surgery – see 'expectations – post op confidence & appearance concern'*	*I lost my self-esteem, my confidence, everything*
Confidence – surgery & healthcare processes	Feelings of confidence in HCPs or the healthcare system or surgery	*See description*	*I do find them very approachable, all of them, and I think that gives you the confidence…to be able to say, yes, OK, they're offering me this and they're explaining it fully and they wouldn't be doing it if they didn't think it was beneficial*
Coping strategies - negative	Talk about dealing with TED by avoiding social situations, may stay in the house for example	*Including withdrawing within a social situation by for example covering the eyes and avoiding social situations e.g. by 'not going out'*	*I just go down to my local supermarket. If obviously when I got to go to Birmingham I go there. But if I don't have to go out, if it's a choice, then I'm not going, I'd rather stay in*
Coping strategies -	Coping/ adjusting positively to having	*All talk about coping positively, including*	*But there again I think myself lucky, there are a*

positive	TED and change in appearance	*stoicism 'got to get on with it', and how others may have helped them cope positively*	*lot more things worse out there so that's how I tend to counterbalance myself, it's not life threatening, it's just something I've just got to deal with*
Disagreement between patient's and others' perceptions of their TED	Any talk about a discrepancy between what doctor/ HCP/ others thinks about eyes e.g. measurements, which eye is worse, and patient's own perception	*Includes comments from others and talk that suggests patient doesn't agree with others' evaluation of their appearance*	*I'm having my right one done first because apparently that one's more protruding than my left, which is strange because when I look in the mirror I don't agree*
Expectations - further surgery after decompression	Talk about further surgery after decompression and what patient expects in terms of the outcome from this. Will it be necessary? Will it be successful? How much surgery are they expecting to have?	*Includes all surgery after decompression*	*…if it was something that, well OK I can cope with this then I may not go down the lines of having other surgery and I may just revert to having distance glasses and reading glasses rather than trying to have something*
Expectations - surgery, HCPs and healthcare process	What patients are expecting from the NHS, the process of surgery, care from HCPs and so on.	*Includes talk about feelings of confidence in HCPs or the healthcare system or surgery*	*I think it's great that the NHS offer it to be honest because I honestly would have thought that it would have been well, you know, there's nothing wrong with you now, your eyes are OK*
Expectations - functional problems	What patient expects from surgery in terms of improvements or worsening of functional problems including double vision, dry eyes, and so on	*See description*	*I'm hoping that when…when that's… when the double vision's gone, or when I'm finished with the eye hospital I can then have the treatment for the thyroid*
Expectations - post op change in appearance	Talk about what patient expects in terms of a change in their appearance after the operation	*See description*	*I'd like to go back to the way I was*
Expectations - post op daily life	Expectations about the change in daily life after the surgery, such as work	*Includes expectations about any changes in mood expected after surgery*	*I didn't really have any expectations that it would affect any other aspects of my… of my career and my daily life, as you say*
Expectations - post op social interactions	Patients' expectations of how social interactions, including with members of the public, family and so on, will be after surgery	*See description*	*Well again I have a lot of face to face contact with people so I'm hoping that I won't look any different to the person sitting at the side of me*
Expectations -	Expectations about a	*See description*	*I'm sure after I've had the*

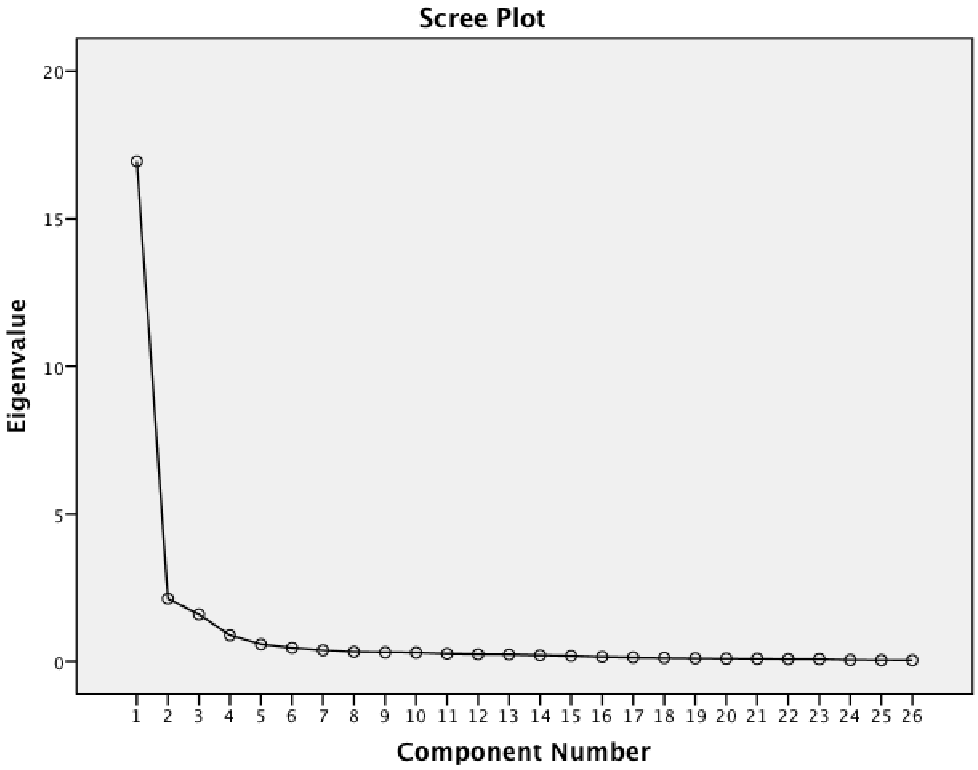
post op confidence & appearance concern	change in socio-cognitive processes after surgery, including self-esteem, confidence, comparisons with others, appearance concern etc		*second done it'll be even more progression in my…sort of, self confidence*
Expectations – of disease & other treatments before surgery	Talk about what was expected from TED and the impact it might have on daily life (before having orbital decompression), as well as about what patient expected other treatments to do before surgery	*Excludes any talk about what impact they expect TED to have after surgery – see above codes for those areas*	*So then I was thinking, well how much worse can it get?! You know expecting, is it going to get a lot worse than this?*
Expectations - recovery process	What patient is expecting from the recovery process after orbital decompression	*See description*	*A couple of weeks apparently off work, an overnight stay*
Fear of operation	Talk about being scared or fearful of having surgery, or what might happen on the day	*Includes fear of any operation discussed*	*I think I always think the worst. For me, the worst, before I wake up would be not waking up.*
Impact - change in appearance	Impact that a change in appearance caused by TED has had, including talk about inability to wear make-up etc.	*Includes psychological impact – changes in evaluation of appearance, social encounters and so on. Physical impact of TED, such as functional problems as a result os eyes being pushed forward, is covered by other codes*	*I do wish it hadn't happened to me. I don't look the way I used to look. I get sad when I look at old photographs*
Impact - change in appearance - loss of identity	Talk about losing aspects of self that make up identity due to having TED, such as not being able to wear make-up that they would've worn every day previously	*See description*	*I always used to wear makeup, always. That was first and foremost I'd get up in the morning, makeup, hair… that was my first thing I used to do. But obviously where my eyes are protruding, when you put mascara on or eye makeup it just makes them even more like, in your face sort of thing*
Impact - diagnosis	Talk about being diagnosed with TED, including emotions or feelings around this, adjustments that had to be made etc.	*Includes talk about being referred from doctor to doctor in order to be diagnosed*	*I just expected to come and have some more eye drops and to be kept here all day and given that sort of news was quite disturbing*
Impact - employment	Ways that having TED or Graves' disease has affected employment, such as	*Includes ways that colleagues at work have reacted to change in appearance caused by TED*	*it's my appearance, because of what, the qualifications, that I can do care work but I want to*

	getting a job, changes in responsibilities at work		*work with kids in a nursery but I know they would say, you know, “scary eyes”*
Impact - mood	Talk about feelings of depression or anxiety due to having TED	*Excludes talk about confidence or self-esteem*	*I don’t like the way my…my face now… the appearance of my face is and stuff. It’s just depressing really.*
Impact - reactions from others - friends & family	Any talk about comments or reactions from friends and family about changes in appearance or TED in general.	*See description*	*No, I mean talking to my husband… he’s very supportive. But he has in a sort of a sideways… well you are going to have the surgery aren’t you?*
Impact - reactions from others - public	Talk about reactions or comments about appearance or TED whilst out in the general public, such as comments or staring	*Excludes comments from colleagues at work, can include comments from the public whilst in a public facing role*	*I notice if we do go out on occasions I do feel people are looking.*
Impact - reactions from others - work	Staring or comments from colleagues at work (whether joking or otherwise), or difficulties experienced in public-facing roles	*Includes reactions from public when in public facing role, as this is related to reactions whilst at work*	*And working in the NHS sector, people looking at you, I don’t like it.*
Impact - steroids	Impact of taking steroids on daily life, including weight gain and facial appearance, difficulties in physical activity	*Excludes impact of other treatments – see ‘other treatments’*	*…the physical changes with the eyes and also with my face because of being on the steroids so I’ve become very sort of ‘moon-faced’ for want of a better word*
Impact – vision & other symptoms	Impact of double vision and other unpleasant symptoms on daily life	*See description*	*It’s a strain to read. I can read for short periods and then I have to you know, stop, and then go back to it you know, after a rest*
Information - HCPs	Talk about information given by HCPs and the process of obtaining or receiving information. This includes talk about doctor patient communication and the quality of information from HCPs	*Talk about any information from HCPs about any aspect of disease or surgery. Also includes all talk about process of receiving information from HCPs*	*When it was offered to me really, I didn’t even realise they could do that. My specialist sent a letter to my GP. It was…my GP didn’t respond though*
Information - HCPs - orbital decompression	Talk about the information received from healthcare professionals, including GP or hospital staff,	*Includes talk about information about surgeries following OD and treatments given after OD*	*…he started talking about, you know, he’d got a model of the eye and he was very good, he explained it all to me*

	surgeons themselves, etc		
Information - HCPs - post op change in appearance	Talk about what information was given by HCPs about what change patient should expect, including being unsure exactly how much to expect proptosis to reduce	*See description*	*And I do worry about how much it's gonna go back. Because nobody's actually said, we take it back to this millimetres…*
Information – TED & orbital decompression - online	Talk about finding out about orbital decompression online, including Googling, surgeon's websites, online forums etc	*Includes talk about anything patient found out about TED or Graves.*	*on YouTube I found the video of the actual surgery taking place and that was a very… a graphic videoing of actually what happened during the operation*
Information - orbital decompression - risks	Risks of surgery discussed, including weighing up pros and cons of having the surgery. Includes finding information online or that received from HCPs	*See description*	*I was told that um you can get some facial paralysis if it goes too low in the orbit*
Information - significant others	Talk about information sought out or obtained from friends, relatives or others about orbital decompression	*See description*	*…for my mother's sake I'd say because she did some research on it and found that everyone, oh yeah, homeopathic Arnica, oh it's brilliant*
Personal goals and life plans	Patient's goals or plans for their lives and how surgery or the process of going for the surgery fits into these goals and plans	*See description*	*once I've got the surgery done that's another milestone and there's just different things for me to sort of aim for to try and get me back to where I was*
Personal reasons for having orbital decompression	Talk about why patient feels they need surgery, their reasons for going for the surgery	*See description*	*from an eyesight point of view and from a physical point of view I just, I just want to change*
Self-directed research	Patient looks up further information about TED, Graves' disease or surgery to enhance understanding of conditions etc	*Patient might not specify where they 'read up on it', or they might describe the process of searching for more information, not necessarily online or about OD. If they specifically describe looking up information about OD online, also code as "information – OD – online"*	*I've never sort of realised you could have it on one eye and then obviously since I've read up about it, then yeah, it's not that uncommon*
Significance of 'eyes'	Talk about how important eyes are, or being 'funny' about having an operation	*Evaluating eyes as best feature – this is evaluation of appearance*	*I'm very funny about my eyes. I know you're dead when you're dead but I want my eyes for the*

	on the eyes		*afterlife.*
Support from others	Talk about friends and family being supportive	*Can include both positive and negative aspects of support – such as family members being overly worried about surgery*	*I've got a very supportive family, a very supportive husband and I am a strong person*
Timing of surgery	Impact of when surgery is booked, how this fits into daily life (e.g. plans changing), how this fits with their appearance cognitions and plan for change in appearance (e.g. being desperate to change appearance and operation can't come soon enough), impact of waiting for surgery	*Includes any references to having OD one eye at a time and any impact this might have had*	*We were at one stage asked if we'd take a cancellation… and… I obviously said yes, because we were asked about holidays and one thing*
Patient understanding of TED & orbital decompression surgery	Descriptions of TED and orbital decompression/ other surgery from patient's perspective	*Includes any talk that involves misconceptions about TED as well as talk that appears well informed*	*I'm hoping that it is going to help with the vision as well, though I do understand that there may be other surgery afterwards that may be needed to help with the vision*
Making decision to have surgery	Talk about the process of deciding whether to go for surgery, weighing up pros and cons, what makes patients decide to go through with it?		*If I was offered the surgery, what are the chances that it'll a) be better, be back to normal or b) could it make it worse?...I think that's something I was assessing as and when I needed to really on my own…through my own decisions really*

Appendix O. Screeplot Generated from the Principle Components Analysis (PCA) for the Original 26-item E-TEDS Questionnaire



Appendix P. Pattern and Structure Matrix of the Original 26-item E-TEDS following PCA with Oblimin Rotation

Item	Pattern Coefficients			Structure Coefficients		
	Factor 1	**Factor 2**	**Factor 3**	**Factor 1**	**Factor 2**	**Factor 3**
5. Move around the house		-.971		.429	-.894	.548
6. Perform domestic duties		-.981		.461	-.913	.533
9. Watch TV T1				.660	-.911	.438
4. Drive		-.858		.602	-.888	.410
10. Use the computer		-.789		.711	-.916	.459
8. Read				.714	-.923	.472
12. Walk outdoors		-.741		.656	-.872	.508
1. Vision		-.747		.661	-.848	.381
7. Engage in my hobby or pastime		-.586		.731	-.843	.594
13. Double vision	.351	-.639		.690	-.799	.366
11. Work at my usual job		-.648		.697	-.859	.590
23. Mask the changes in my appearance	.912			.904	-.550	.475
22. Willingness to appear in photographs	.896			.936	-.592	.550

15. Self confidence	.823		.948	-.673	.596
2. Appearance of my eyes	.858		.939	-.673	.485
21. Other people's reactions to my TED	.797		.915	-.606	.656
3. Appearance of my face	.722		.900	-.709	.558
14. Ability to obtain a job	.426		.683	-.596	.569
16. Ability to make new friends	.499	.479	.776	-.605	.758
18. Relationship with my family		.875	.467	-.475	.896
19. Relationship with my current friends		.920	.366	-.387	.911
20. Relationship with my current partner/wife/husband		.824	.528	-.527	.896
17. Ability to form new intimate relationships	.309	.484	.678	-.630	.737
24. Headaches/ eye pain	.709		.852	-.656	.504
25. Dry eyes	.697		.896	-.747	.522
26. Relationship with my eye doctor		.522	.351	-.362	.580

INITIAL IDEAS AND POTENTIAL CODES NOTED DURING TRANSCRIBING AND FAMILIARISATION WITH THE DATA

Initial idea: patient is unsure exactly how much to expect proptosis to reduce/ appearance to change. Potential code: information (or lack of) about what physical change in appearance to expect. (ID 1 line 632-636 & ID 6 line 310-15)

Initial idea/ potential code: positive coping styles/ cognitions (ID 1, line 704-5)
(the same? ID 5, line 563-66 initial idea: resilience? Positive coping styles for dealing with upcoming surgery ; ID 17 line 309-312)

Initial idea: Quality of information given by HCPs. Importance of doctor ensuring patient understands information prior to surgery (ID 1, line 715-18 & line 727-31)

Initial idea: patient unsure what level of decompression they are having (ID 20 line 122-125)

Initial idea: self-research into the surgery – equipping self to be ready to ask doctors specific question to get a deeper understanding of the surgery (ID 5, line 237-240, 259-60, 290-93; ID 8 line 167-9)

Initial idea: differentiating between a ‘good’ eye and ‘bad’ eye in terms of visual problems – and appearance concerns (ID 2; ID 4; ID 5 line 407-11)

Initial idea: realistic understanding of what the decompression surgery can do (ID 5, line 467-9)

Initial idea: understanding of further surgery post-decompression; the possibility of having this and what this can do (ID 5, line 470-73)

Initial idea: the risk to appearance of going for further post-decompression surgery being like ‘gambling’ (ID 5 line 500-03, ID 6 line 183-90)

Initial idea: contradiction/ conflict between understanding that appearance won’t go back to exactly how it was before, and still ‘desiring’ to look as before (ID 5, line 591-94; ID 6 line 136; ID 8 line 279-81; ID 21 line 209-11)

Initial idea: expecting appearance to go back to how it was before TED (ID 20 line 539-40)

Initial idea: stereotypical imagery attached to having eye disfigurements and eye surgery (ID 5, line 650-51)

initial idea: comparing own severity to other patients’ and seeing self as less severe (ID 6, line 79-81; ID 8 line 250-52; ID 17 line 313-316)

initial idea: patient’s perception that eyes are more severe than others without TED think (ID 17 line 376-80, line 794-5; ID 20 line 576-9) initial idea: patient’s own understanding of decompression surgery (ID 6 line 208-9; ID 8 line 184-87; ID 13 line 20-22)

Initial idea: patients (mis)understanding of medical information about what the surgeons can do – double vision can be successful treated with strabismus surgery after decompression (ID 13 line 109-112 & line 238-39)

Initial idea: decompression surgery as ‘safe’ (ID 6 line 214-6)

potential code: seeking information online about the surgery (ID 6 line 254-5; ID 8 line 163-66)

Initial idea: patient expectation of success based on subjective cultural ideas (ID 6 line 254-5)

Initial idea: conflicting information about risks. UK doctors vs family member doctor overseas (ID 6, line272-3)

Potential code: weighing up risks (ID 6 line 279-81)

Initial idea: this supports previous research that finds others react to patient’s appearance in social situations – negative connotations of being on drugs when you’re not (ID 8 line 13-15)

Initial idea: this supports previous quali research that has found patients report feeling uncoordinated because of limited eye movements or vision (ID 8 line 17-20; ID 13 line 84-87)

Initial idea: strategies to hide appearance don’t always work – shift in wellbeing when they cease to work (ID 8 line 27-30; ID 13 line 49-52)

Initial idea: extreme situation: social avoidance due to previous negative social interactions (ID 8 line 44-9)

initial idea: losing previous identity due to TED (make up) (ID 8 line 63-66; ID 20)

Potential code: effect of TED on mood/ depression (ID 8 like 93-4)

Initial idea: COGNITIONS about negative consequences of social situations (ID 8 line 130-34)

initial idea: doctors relying on website to form realistic expectations (ID 8 line 239-41)

initial ideas: high expectations when others with more severe disease have greatly improved in appearance – on surgeon’s website! (ID 8 line 267-70)

initial idea: COGNITIONS. Perceptions of negative social situations that haven’t happened yet (ID 8 line 370-74) initial idea: expectations for life to go back to how it was before TED, including 'silly little things' like wearing make up (ID 8 line 513-15)

initial idea: online forums of TED patients influencing expectations (ID 8 line 538-40)

initial idea: expecting recovery time/ time to notice a difference in appearance to be short (ID 8 line 551-54)

initial idea: this supports research that suggests clinical measurements do not correlate with patient's perceptions of appearance. Damaging to patients who feel their proptosis is less than measurements suggest (ID 8 line 563-68)

initial idea: for social interactions to improve after surgery. Reduce social withdrawal & avoidance (ID 8 line 633-35)

Potential code: social withdrawal avoidance. Initial idea: even avoiding family gatherings (ID 13 line 67-70)

initial idea: As a parent feeling like your condition also affects your children (ID 17 line 116-18)

initial idea: involving family in pre-surgery consultations to increase understanding of medical information (ID 17 line 140-42)

initial idea: using humour to cope with visual problems at work (ID 17 line 195-200)

intial idea: wanting to avoid family occasions but feeling a duty to go; keeping head down to hide eyes (ID 8; ID 17 line 272-277)

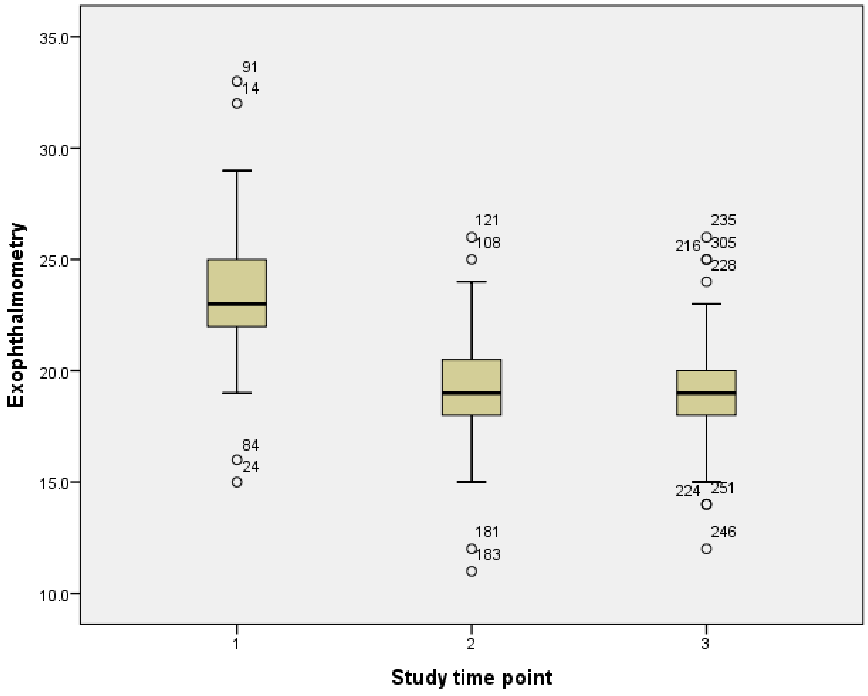
initial idea: this supports research that suggests patients only take in information from the beginning of medical consultations (ID 17 line 407-12; ID 20 line 132-35 particularly when news is shocking)

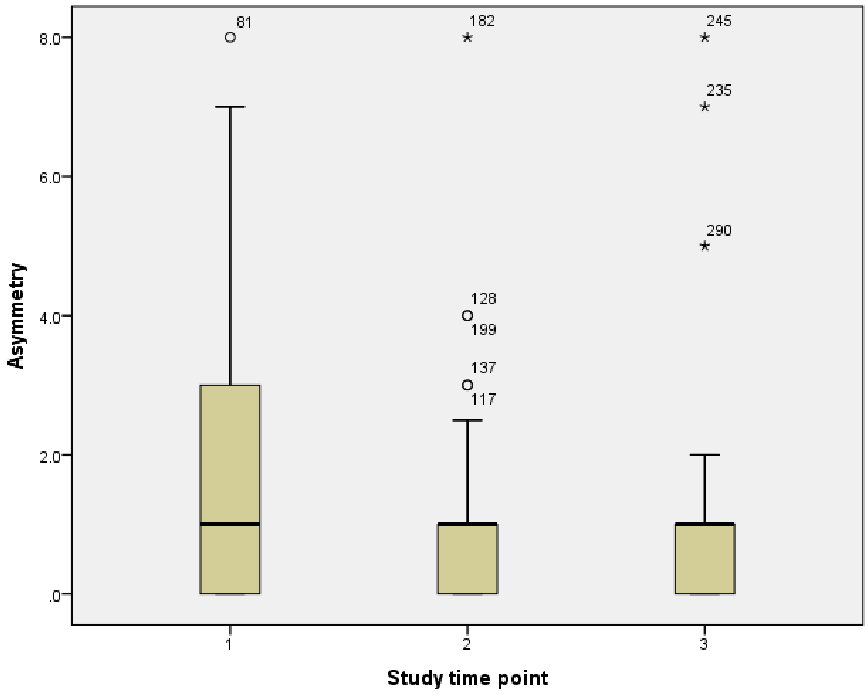
initial idea: TED affecting independence when problems with vision. Desire to be able to carry out simple everyday activities again – independence (ID 17 line 466-67)

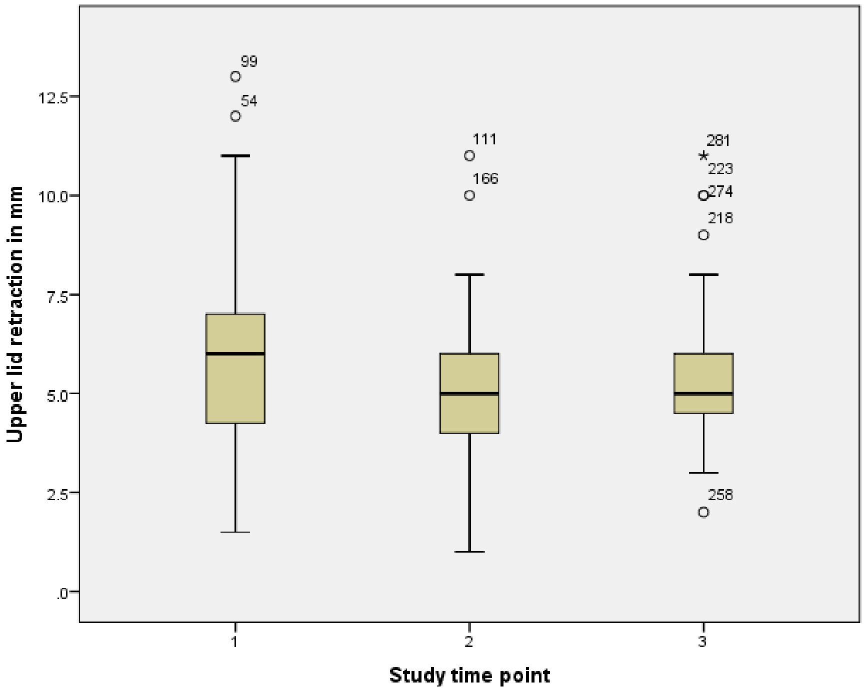
initial idea: pain as a symptom of TED. This supports research (ID 17 line 630-33)

initial idea: feeling more anxious about surgery on eyes because of important function and risk of losing sight (ID 20 line 192-96 & line 269-70)

Appendix R. Boxplots with Error Bars Showing Changes Over Time on Continuous Clinical Variables and Outliers



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7.5
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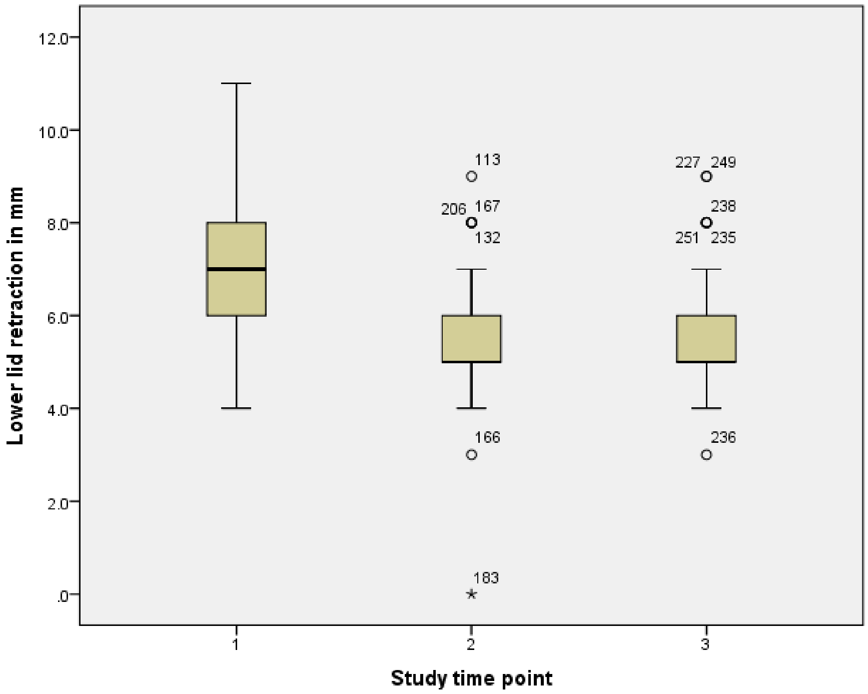
166
281
223
274
218
258
1
2
3
Study time point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4.0
2.0
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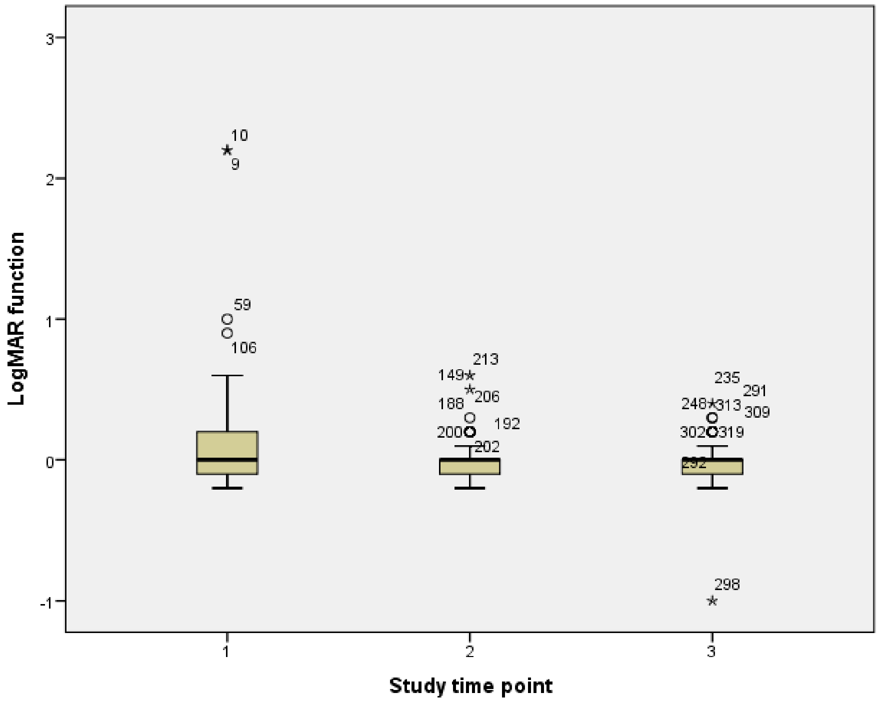
227
249
238
251
235
236
1
2
3
Study time point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2
1
0
-1
10
9
59
106
213
149
206
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192
200
202
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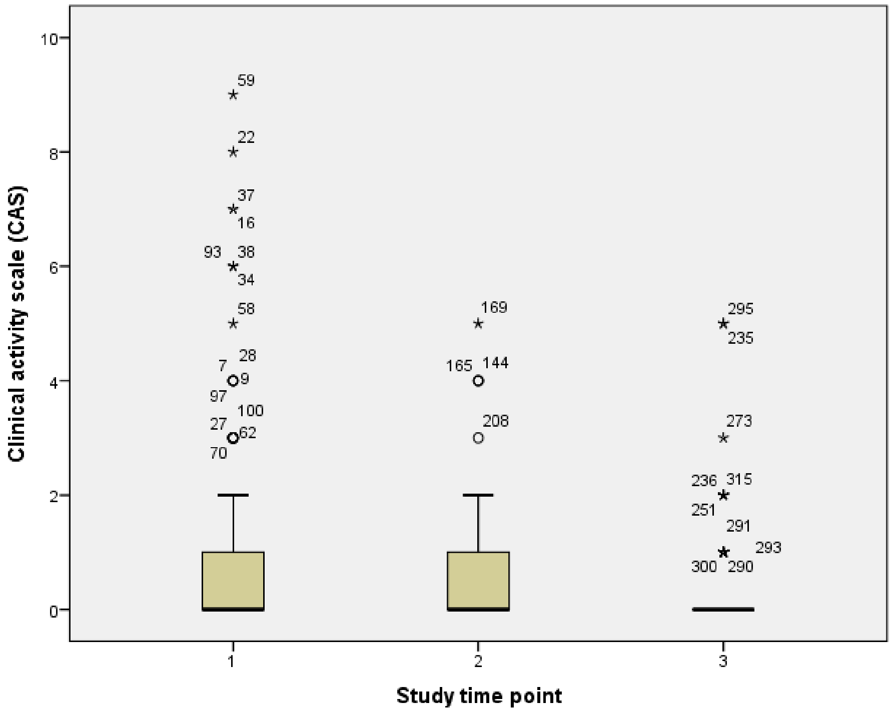
248
313
309
302
319
292
298
1
2
3
Study time point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93
38
34
58
28
7
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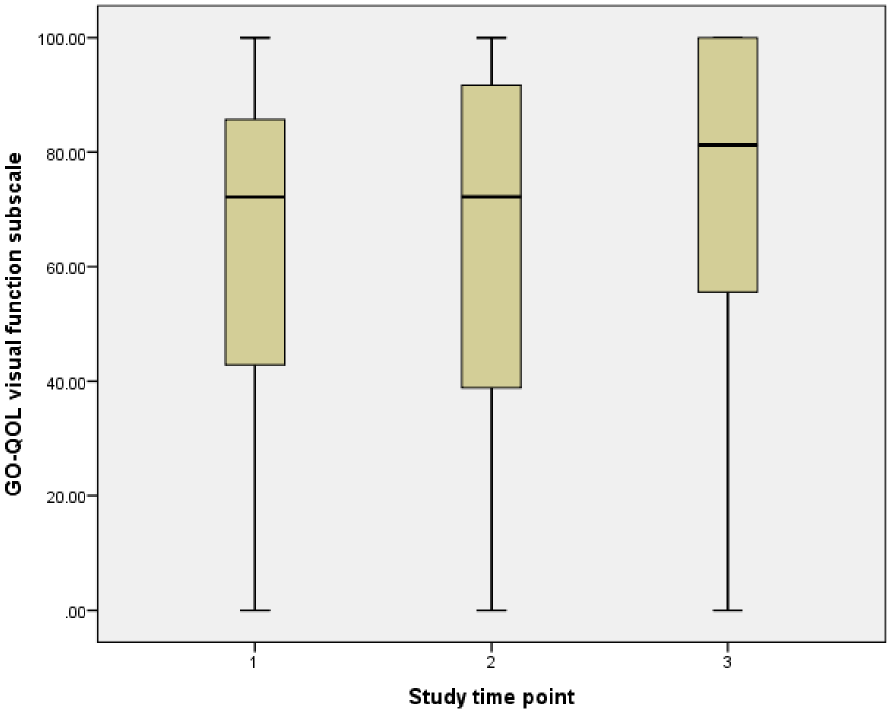
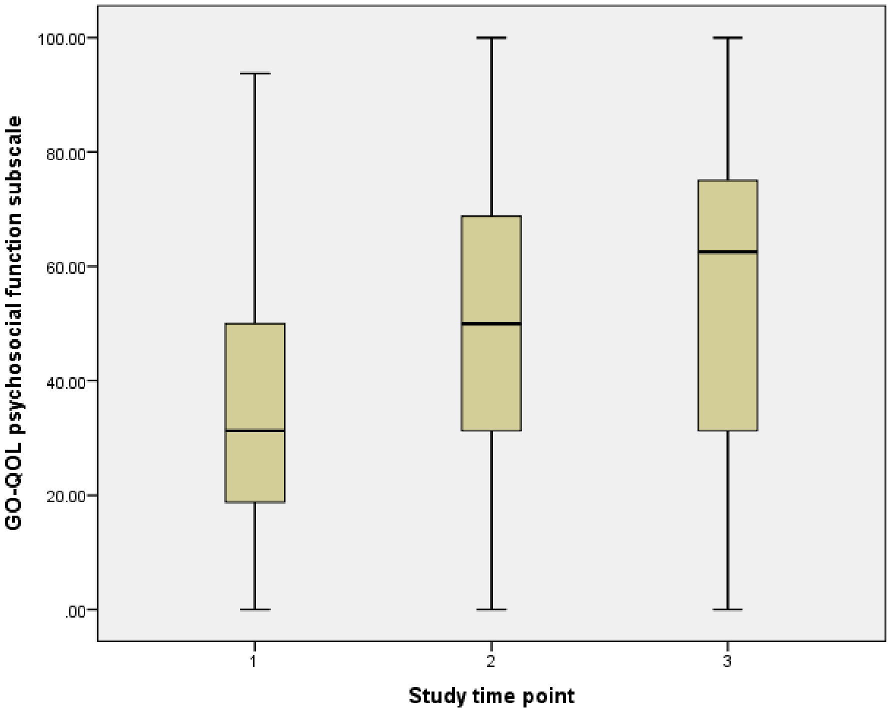
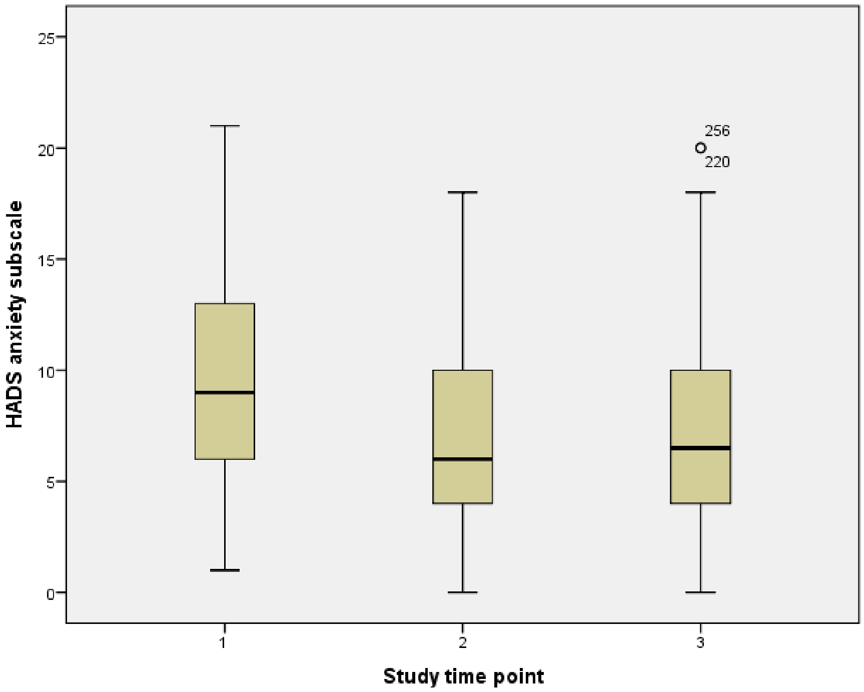
100
27
62
70
169
165
144
208
295
235
273
236
315
251
291
293
300
290
1
2
3
Study time point

Appendix S. Boxplots with Error Bars Showing Changes Over Time on Continuous Psychosocial Variables and Outliers



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15
10
5
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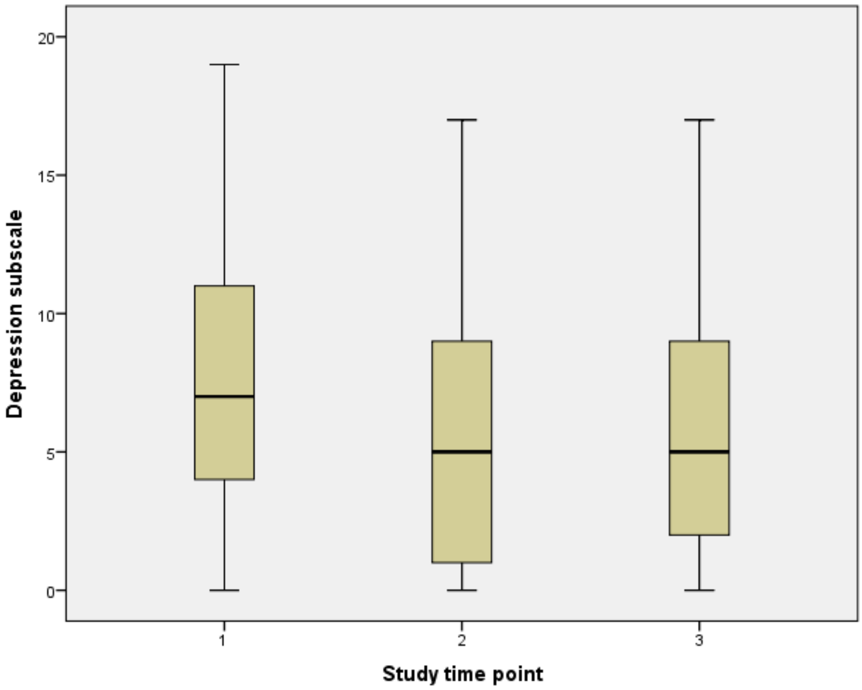
1
2
3
Study time point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1
2
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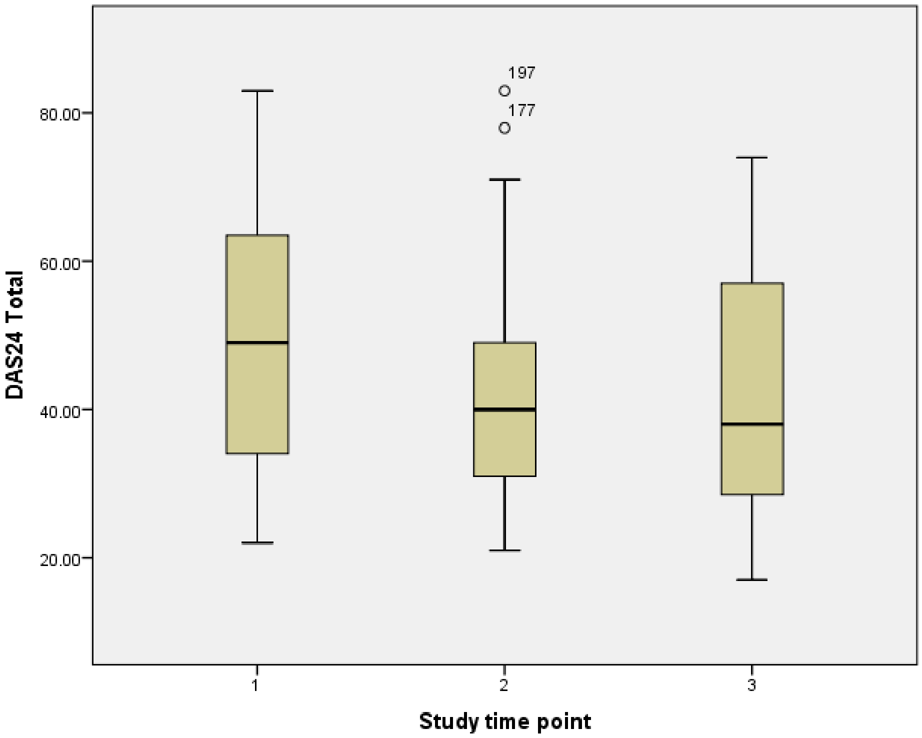
Study time point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20.00
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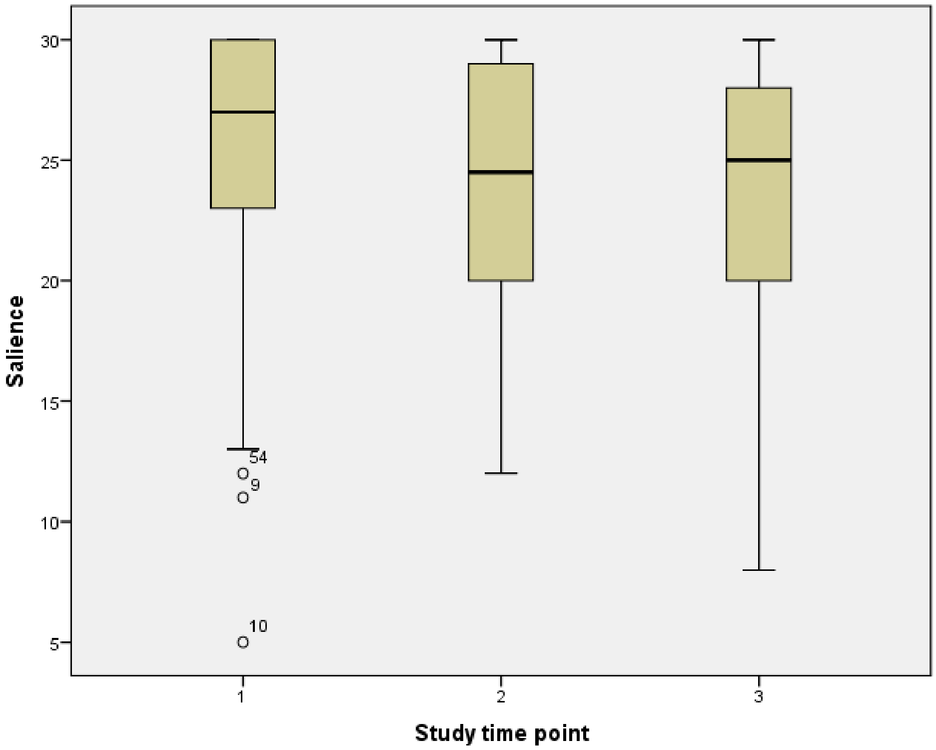
1
2
3
Study time point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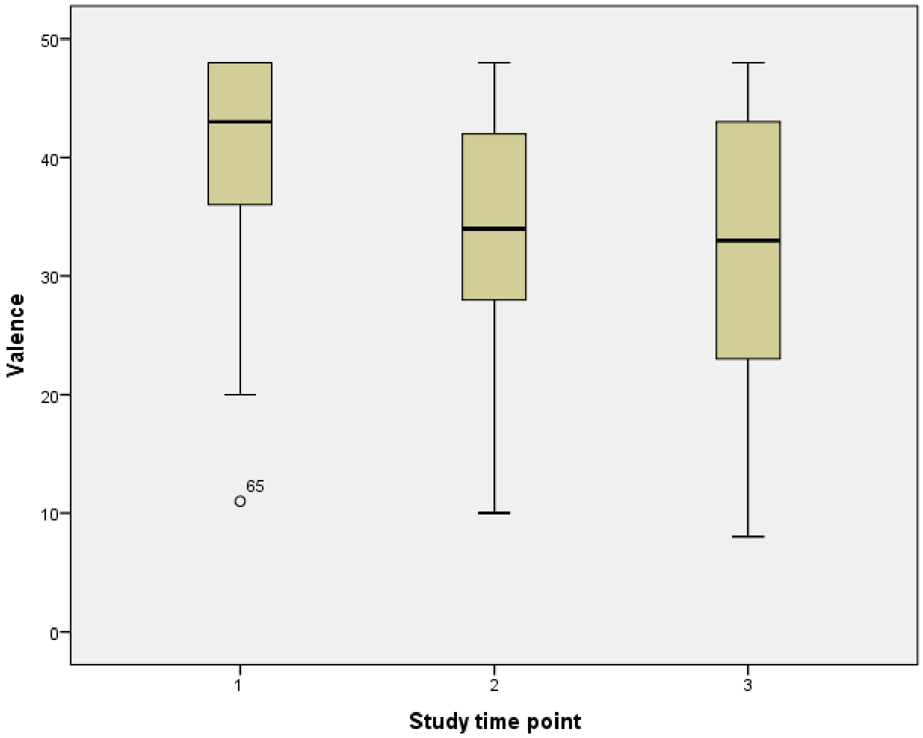
9
10
1
2
3
Study time point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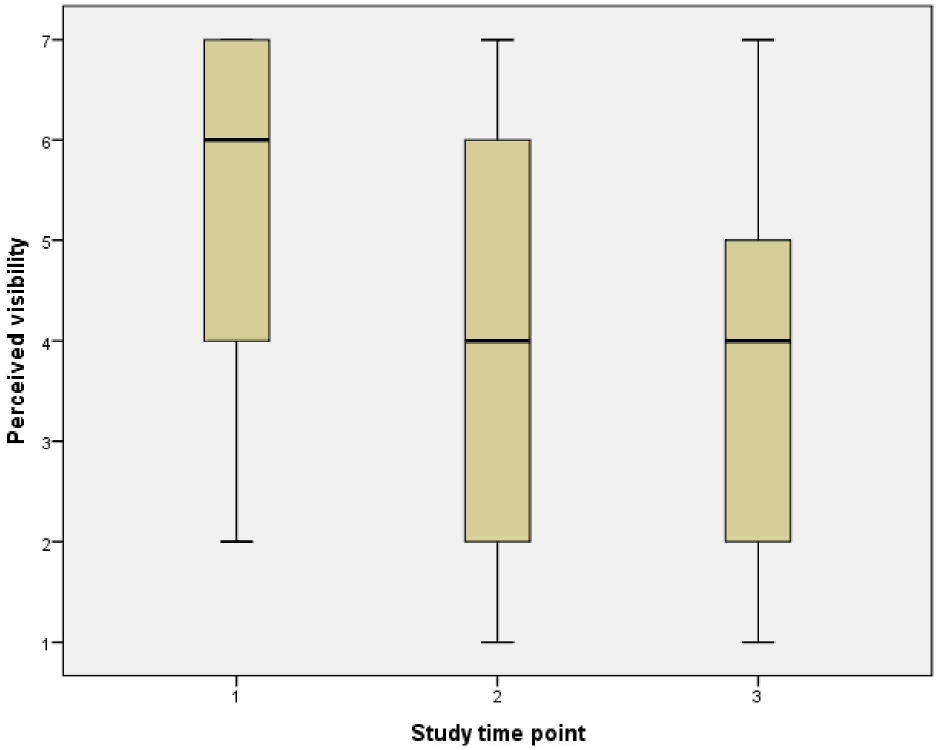
Study time point


Perceived visibility
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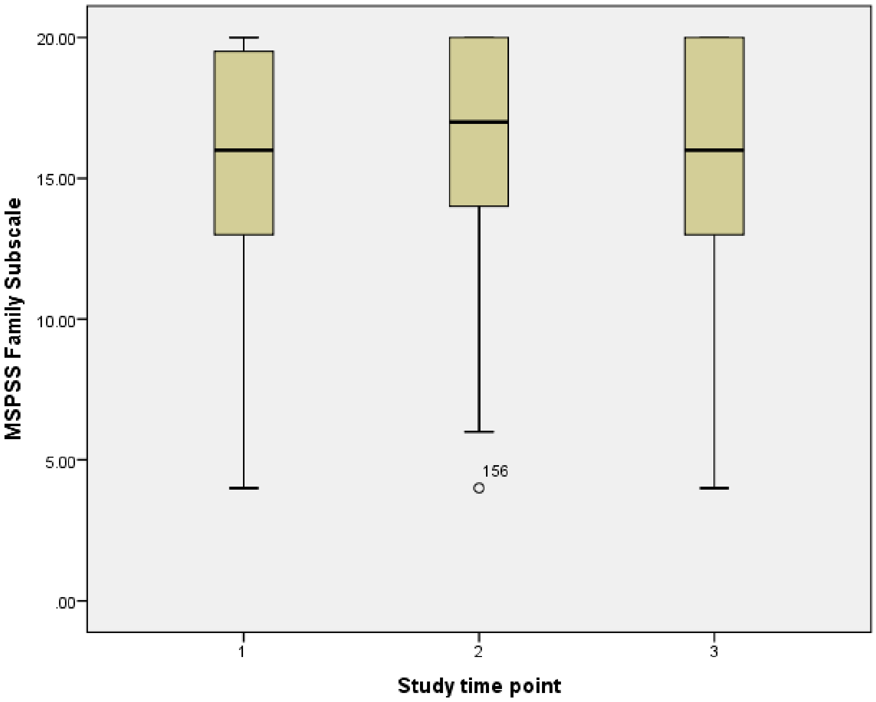
6
5
4
3
2
1
1
2
3
Study time point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10.00
5.00
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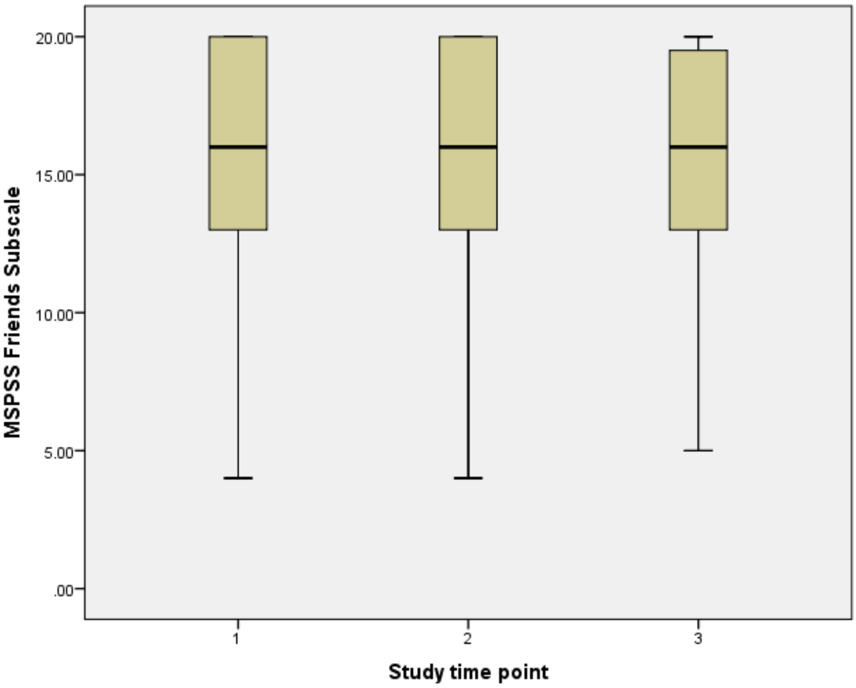
MSPSS Family Subscale
156
1
2
3
Study time point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MSPSS Friends Subscale
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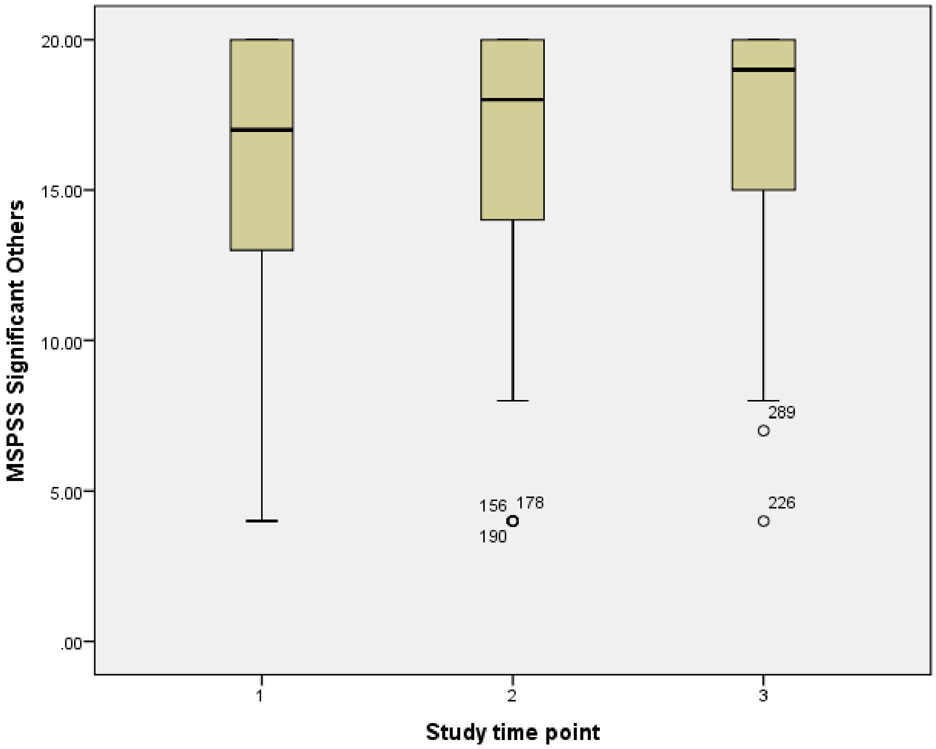
2
3
Study time point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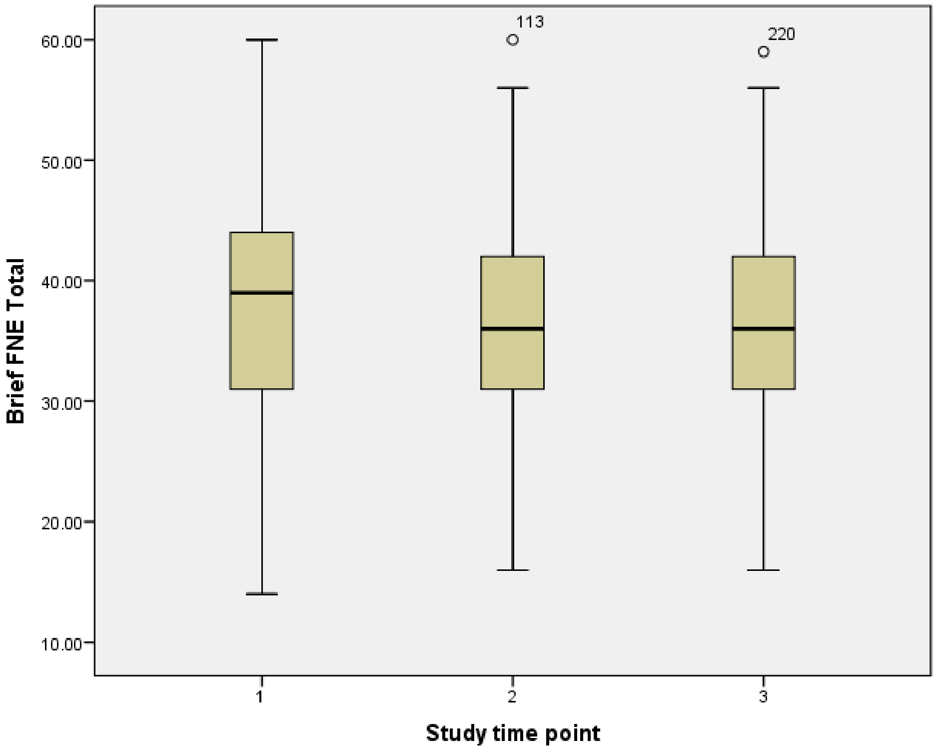
Study time point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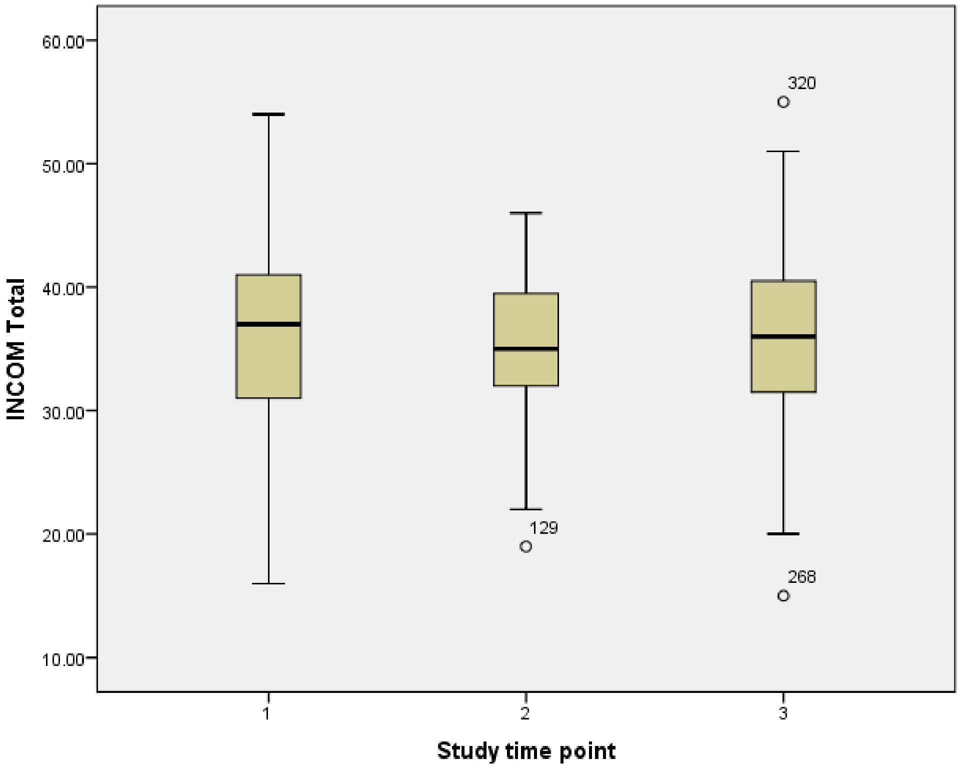
Study time point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INCOM Total
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2
3
Study time point