An exploration of disclosure and psychological outcomes in individuals with Turner Syndrome.

Mhairi Nisbet, MA (Hons) Psychology

Submitted in partial fulfilment of the requirements for the degree of

Doctorate in Clinical Psychology

Institute of Health and Wellbeing

College of Medical, Veterinary and Life Sciences

University of Glasgow

July 2020

Acknowledgments

Firstly, I would like to thank the five families who took part in this study, for kindly giving up their time and sharing their experiences with me. This project would not have been possible without your thoughtful contributions and I feel truly humbled to have had the privilege of hearing your stories.

I would also like to thank the supervisors involved in the project, for your advice and guidance throughout; Prof Rory O'Connor, Dr Avril Mason, Dr Marie Freel and Dr Elizabeth Hunter. A special thanks to Dr Avril Mason, for providing me with so much practical support, knowledge, and insight around working with individuals with Turner Syndrome, and to Prof Rory O'Connor for providing me with invaluable supervision.

Thank you to all the friends I have made during clinical training, for the many coffees, dinners, laughs and support, which have made the experience so enjoyable. To my school and university friends, thank you for keeping me grounded over the last three years, I am so grateful to have such great friends.

Finally, thank you to my amazing partner Rory, and my wonderful family. Thanks for all of the endless support, encouragement, cooked dinners, prosecco, and cups of tea. You have taught me the importance of working hard, whilst remembering what is most important to me – friends and family.

Table of Contents

Chapter 1: Systematic Review

Is growth hormone treatment associated with psychological outcomes in girls with Turner Syndrome? A systematic review.

Prepared in accordance with authors' guidelines from the British Journal of Health Psychology (Appendix 1.1).

Abstract

Purpose

Growth hormone treatment (GHT) is a widely accepted intervention to increase adult height in girls with Turner Syndrome (TS). However, the impact of GHT on psychological outcomes in girls with TS remains unclear. This review aimed to systematically evaluate the research literature on TS girls treated with GH, to explore whether there are any associations with psychological outcomes.

Methods

A systematic search of five electronic databases was conducted to identify relevant studies. Following this, 2,823 studies were screened and fourteen met the inclusion criteria for this review. A narrative synthesis of the findings was conducted.

Results

To date, literature exploring whether there are any associations between GHT and psychological outcomes in girls with TS has predominantly focused on Quality of Life/Health-Related Quality of Life or Psychosocial Functioning. The results indicate there could be a small positive association between GHT and some psychological outcomes, however findings were inconsistent and variable across studies. Several factors such as the study design and various methodological limitations and biases may explain some of the variability within the results.

Conclusions

There does not appear to be any definitive association between GHT and psychological outcomes in girls with TS. Therefore, height enhancement alone should be used as the primary measure to determine whether girls with TS receive GHT.

Keywords: *Turner Syndrome, growth hormone therapy, psychological outcomes, systematic review*

Introduction

Turner Syndrome

Turner Syndrome (TS) is a relatively common genetic condition which affects between approximately 1/2000 and 1/2500 live female births (Stochholm *et al.*, 2006; Apperley *et al.*, 2018). The condition is caused by the absence of all or part of the second sex chromosome. Women with TS typically present with shorter stature, cardiovascular, reproductive, renal, endocrine, vision and/or hearing abnormalities (Morgan, 2007; Bondy, 2014).

Individuals with TS may develop severe medical conditions such as epilepsy and have increased mortality rates (Power, Langlois and Byard, 2014). Moreover, females with TS appear to demonstrate a unique cognitive profile, characterised by weaknesses in executive functioning and visual-spatial areas and relative strengths in verbal domains (Hong, Scaletta Kent and Kesler, 2009). Due to the variability in clinical manifestations, the age at which girls receive a diagnosis is widely variable, from the second trimester of pregnancy, through to adulthood (Apperley *et al.*, 2018).

Short Stature and Growth Hormone Therapy

Short Stature (SS), one of the most prevalent and salient features of TS, is statistically defined in the current literature as height more than 2 standard deviations below the mean for gender and age specific norms (Tanner and Whitehouse, 1976). Individuals with SS are treated by supplementing or replacing a missing or insufficient hormone, to allow for expected growth and to improve general health. The Food and Drug Administration in the USA approved recombinant human growth hormone (rhGH) in 1985 to accelerate growth and increase height in conditions not typically associated with growth hormone deficiency, including TS (Gault and Donaldson, 2001). A systematic review assessing the effects on children and adolescents with TS concluded that rhGH increased short-term growth by approximately three to six cm compared to untreated control groups (Baxter *et al.*, 2007). However, the final height of the participants was still below normal range.

The rationale for growth hormone treatment (GHT) traditionally rests on the belief that SS constitutes a psychosocial or psychoeducational vulnerability, or burden for the individual (Gardner *et al.*, 2016). As well as accelerated growth and increased adult height, an underlying assumption was that GHT would lead to improved psychosocial adaptation and quality of life (Siegel, Clopper and Stabler, 1998). An increased growth velocity may therefore reduce the “at-risk” status of these individuals for developing psychosocial adjustment difficulties in adulthood (Meyer-Bahlburg, 1990).

Psychological outcomes in females with TS

Alongside the physical health problems and cognitive deficits previously described, several studies suggest girls with TS may experience difficulties with mood, relationships and psychosocial functioning (Cardoso *et al.*, 2004; Rolstad *et al.*, 2007; Reimann *et al.*, 2018). Liedmeier *et al.* (2020) found women with TS aged 16-73 years reported impairments across a number of psychosocial variables in comparison to healthy controls, including QoL, depression, anxiety, self-esteem, social participation and romantic relationships. A systematic review similarly found that QoL appears to be compromised in women with TS (Reis *et al.*, 2018). The researchers suggest the reduction in QoL could be related to factors such as height, however the results were inconclusive.

Consistent with previous research, it could thus be assumed that GHT and a subsequent increase in height may be positively associated with psychological outcomes in girls with TS. However, the evidence base appears somewhat variable. After 18 months, TS girls randomised to GHT reported significantly better social relationships and self-concept in comparison to an untreated control group (Rovet and Holland, 1993). However, after six years of GHT, the researchers found no global differences across all psychosocial functioning domains measured (Rovet *et al.*, 2019). Moreover, a systematic review which examined the effects of GHT on psychological outcomes in individuals with SS concluded there is a high risk of bias present in the majority of the literature (Gardner *et al.*, 2016). This review focused on individuals with a range of conditions resulting in SS, rather than focusing on females with TS exclusively. It is therefore unclear whether there are any positive or negative associations between GHT and psychological outcomes in girls with TS, and whether the current literature is similarly at a high risk of bias.

Aims

To our knowledge, no systematic review has been conducted to specifically examine whether GHT is associated with psychological outcomes in girls with TS. The aim of this review, therefore, is to systematically evaluate the research literature on TS girls treated with GH, to explore whether there are any associations with psychological outcomes.

Methods

Search strategy

Psychological outcomes have been defined as quality of life, psychological adjustment/adaptation, psychosocial functioning, mood, well-being and emotional/behavioural outcomes. There does not appear to be a standardised definition of 'psychological outcomes' within current literature, and so our definition is based on previous analogous research (Broadstock, Michie and Marteau, 2000; Gardner *et al.*, 2016).

Prior to conducting the search, the search strategy was discussed and agreed with the author's academic supervisor and a University librarian. Full details of the search strategy can be found in Appendix 1.2. Variations of the following terms were used:

1. Turner Syndrome
   AND
2. Growth Hormone Therapy
   AND
3. Psychological outcome or psychosocial outcome or adaptation, psychological or emotional adjustment or social adjustment or quality of life or mental disorder or affective symptoms or mental health or anxiety or depression or well-being

The following electronic databases were searched on 23/04/20: CINAHL (1982-Present), Ovid Embase (1947-Present), Ovid MEDLINE (1946-Present), PsycINFO (1806-Present) and Web of Science (1864-Present). Citations that appeared potentially relevant from the reference list of full texts screened were also considered for inclusion. The search strategy used both text words and relevant indexing, and search terms were adapted to map onto subject headings where relevant. The results were exported to EndNote. The study was also registered on PROSPERO (registration no: CRD42019159559)

Inclusion/exclusion criteria

Inclusion:

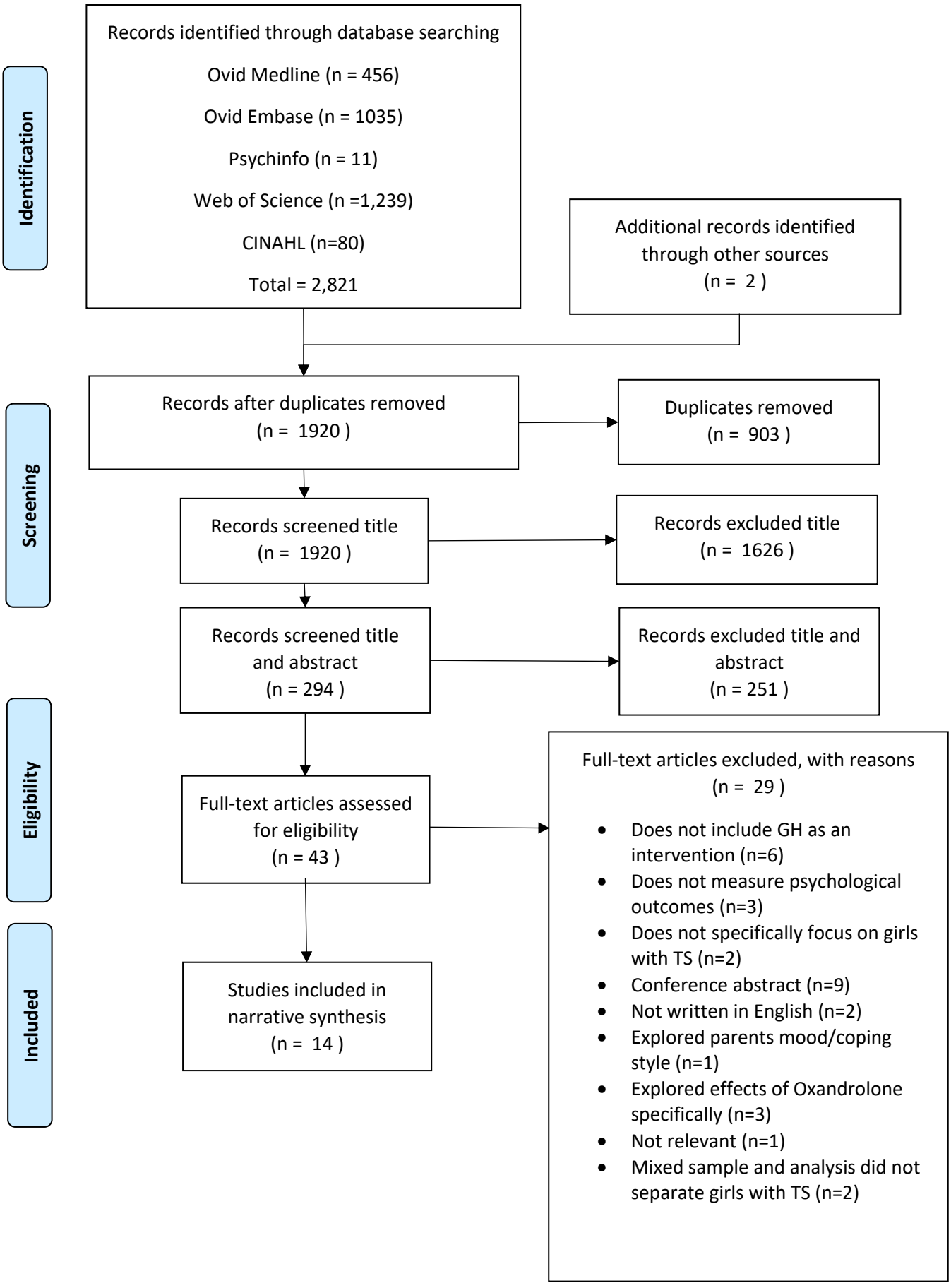
- Quantitative studies (both randomised and non-randomised trials) or qualitative studies
- Studies which include females diagnosed with TS AND;
- Participants have been prescribed GHT
- Studies which examined the association between GHT and psychological outcomes, as defined above
- Children, adolescent and adult females with a diagnosis of TS

Exclusion:

- Reviews or case studies
- Studies that are not written in English

Following the removal of duplicates, titles and abstracts were screened by the author to identify studies that did not meet the inclusion criteria. Full text versions of the remaining articles were reviewed for eligibility and included if all criteria were met. A PRISMA four-phase diagram was produced (Figure 1).

Figure 1. PRISMA flow-chart diagram



Data Extraction and Quality rating

A data extraction sheet was constructed (Appendix 1.3) in line with PRISMA guidelines on data extraction (Liberati *et al.*, 2009). The Crowe Critical Appraisal Tool (CCAT) (Crowe and Sheppard, 2011) was used to assess the quality of the included full texts as the author anticipated that the data and results would be heterogeneous in nature (Appendix 1.4). Therefore, the CCAT was chosen as it can be used across a variety of research designs. Four (35%) of the full texts identified were reviewed by a second, independent rater (trainee clinical psychologist), to ensure consistency in quality rating. One discrepancy was discussed until an agreement was reached.

Results

Study characteristics

Details of the sampling and methods for each of the fourteen included studies can be found in Table 1. Four of the studies are randomised-controlled trials (RCTs) and the remaining ten are non-randomised. All participants with TS in the included studies were treated with GHT in accordance with standardised guidelines (Bondy, 2009).

With regards to the psychological outcomes measured, seven studies explored Quality of Life (QoL) or Health-Related Quality of Life (HRQoL) (Study no. 4,5,6,7,8,9,12), six studies measured Psychosocial Functioning (Study no. 1,2,3,10,11,14) and one study examined 'Psychological profile' defined as intelligence, social competence and behaviour problems (Study no. 13). Several studies included secondary outcome measures including body image, self-concept, perception of stature and height. Three RCTs included an untreated TS group as the control condition, whilst six of the non-randomised studies used population control groups. Three studies had no control group and two included a population-based control group and control groups of participants with other conditions resulting in short stature e.g. idiopathic GH deficiency.

Quality of the studies

The maximum score a study could achieve is 40; quality appraisal scores ranged from 19 (48%) to 33 (83%). The quality of the papers was generally moderate; studies often failed to detail their sample size calculations or control for confounding variables.

Table 1. Study Characteristics and Key Findings

Study No.	Author, Year, Country	Design	Sample characteristics	Intervention	Psychological outcome	Measures used	Key Findings	Quality rating score
1	Rovet et al., 1993 Canada	RCT	N=48 28 treated TS girls (mean age 10.8) 20 untreated TS girls (mean age 10.7)	GHT for 18 months. All participants given oestrogen therapy at 13 years old.	Self-Concept Family functioning Behaviour, social abilities and school functioning	Piers-Harris Children's Self-Concept Scale (PHCSCS) (Piers, 1969) Youth Self-report (YSR) (Achenbach, 1991b) Child Behaviour Checklist (CBC) (Achenbach, 1991a) Olson's FACES III (Olson, 1986)	Prospectively, GH treated girls self-reported themselves as significantly more intelligent, attractive, having better self-concept, more friends, greater popularity and less teasing in comparison to untreated controls. No differences in behaviour other than hyperactivity which showed a greater decrease with time in untreated group.	28 (70%)
2	Rovet et al., 2019 Canada	RCT	N=131 70 treated TS girls 61 untreated TS girls (Session 1 mean age 10.4 - Session 4 mean age 16.3)	GHT for 6 years. Majority of patients received oestrogen therapy.	Psychosocial functioning	PHCSCS YSR CBC	No global group differences between treated and untreated girls were found on any scales or subscales across the four psychosocial functioning domains.	33 (83%)
3	Huisman et al., 1993 Netherlands	RCT	N=38 girls with TS (mean age at entry 12.2. At T3 mean age 14.6)	Participants were randomly assigned to one of two dose regimens: GH, 8 HJ/m2 body surface 3 times/week and GH. 4 HJ/m2 6 times/week. Participants over 12 years old received ethinyl oestradiol.	Psychosocial functioning	PHCSCS CBC The Social Anxiety Scale for children (La Greca *et al.*, 1988) The Silhouette Apperception Technique (Child and Parent Version) (Grew *et al.*, 1983) The Therapy Evaluation Scale (Child and Parent Version) Parental Interview Teacher rating form (Keith Conners *et al.*, 1998)	Post GHT girls and their parents reported increased independence, happiness and more involvement in social interactions. No significant changes in self-concept, social anxiety, or behavioural problems were found.	20 (50%)
4	Taback et al., 2011 Canada	RCT	N=33 From the Canadian RCT. 21 treated TS girls (mean age 20.0)	GHT for 6 years. Majority of patients received oestrogen therapy.	Health related quality of life	Short Form-36 Health Survey (SF-36) (Ware and Sherbourne, 1992)	No differences between treated and untreated controls or the general population, indicating neither benefits nor adverse effect of GHT on HRQoL in females with TS.	29 (73%)

			12 TS girls from the untreated group, however only 10 had never had GHT (mean age 20.2)					
5	Amundson et al., 2010 Sweden	Cross-sectional, case controlled	N=222 111 TS women (age range 18–59) 111 randomly selected, age matched women (25–54)	GH and Oxandrolone treatment were given to 45(40%) GH only to 13(12%) Oxandrolone only to 19(17%) Neither GH nor oxandrolone had been given to 35 (31%) TS women.	Quality of Life	The Psychological General Well-being Index (PGWBI) (Dupuy, 1984) The Nottingham Health Profile (NHP) (McEwen, 1993)	TS women reported more social isolation than population controls. Untreated TS women reported more sleeping problems and social isolation in comparison to GH treated women. After adjustment for age, pain remained the only variable significant and attributable to GHT.	23 (58%)
6	Bannick et al., 2006 Holland	Cross-sectional case controlled	N = 165 49 girls with TS 116 general population controls (Mean age 19.4)	34 had GHT once daily at a dose of 1.3, 2, or 2.7 mg/m2 body surface area/day (∼0.045, 0.067, or 0.09 mg/kg/day). 15 had GHT once or twice daily in a dose of 2 mg/m2 body surface area/day (∼0.067 mg/kg/day). Participants also received ethinyl oestradiol.	Health-related Quality of Life	SF-36 TNO/AZL Adult Quality of Life (TAAQOL) (Kamphuis *et al.*, 2004)	Women with TS reported significantly better social functioning, role limitations–emotional, bodily pain, daily activities, sexuality, and aggressive emotions in comparison to population controls. No other differences were observed.	23 (58%)
7	Butler et al., 2019 UK	Prospective one year controlled	73 = IGHD 45 = AGHD 22 = TS 49 = controls with non GHD short stature (aged 6-16)	GHT	Health Related Quality of Life	Paediatric Quality of Life Inventory (Upton *et al.*, 2005) Strengths and Difficulties Questionnaire (Goodman, 1997) The Youth Life Orientation Test Revised (Ey *et al.*, 2005)	All measures evaluated showed an equal improvement over the year of GHT, across all groups. After 12 months, the untreated SS controls and TS group scored higher than UK norms.	30 (75%)
8	Carel et al., 2005 France	Population-Based cohort study	N=568 treated TS girls (Mean age 22.6)	GHT	Quality of life and its determinants	SF-36 General Health Questionnaire 12 (GHQ-12) (Goldberg, 1972)	QoL scores were similar between GH treated women with TS and the general population.	27 (68%)

9	Krantz et al., 2019 Sweden	Longitudinal cohort study	N=228 treated TS girls N=317 controls (randomly selected population-based sample) (aged 16-78)	GHT	Health-related Quality of Life	PGWBI NHP	No associations were found between HRQoL and GHT in women with TS and there were no differences between participants and the general population.	30 (75%)
10	Lagrou et al., 1998 Belgium	Descriptive non-randomised	N=31 girls with TS A: 3-6 years B: 7-12 years C: 13-16 years	GHT 6 engaged with oestrogen treatment after 1 year of therapy.	Perception of stature Psychosocial functioning	CBC YSR Self-esteem Inventory (Coopersmith, 1984) Observation of play and semi-structured interviews with both girl and parents	Following GHT girls reported no changes in psychosocial functioning other than improvements in social self-esteem and social competence. The researchers found some differences in perception of height and acceptance of GHT between age groups.	22 (55%)
11	Lagrou et al., 2006 Belgium	Cross-sectional case controlled	N=74 30 treated TS girls (mean age 22.1) 44 aged matched controls (mean age 20.5)	GHT Some participants received oestrogen therapy.	Psychosocial functioning (behavioural and emotional problems) Self-concept Body image	Young Adult Self Report (Achenbach, 1997) Self-Perception Profile for College Students (Harter and Neemann, 1986) Bodily Attitude Scale (BAS) (Simis, Verhulst and Koot, 2001)	Following GHT, in comparison to population controls, women with TS reported no significant differences other than more attentional difficulties and perceiving themselves as less socially competent. The TS group reported fewer problems in some subscales including fewer delinquent behaviours and somatic complaints.	23 (58%)
12	Lasaite, Lasiene and Lasas, 2010 Lithuania	Cross-sectional, case-controlled	N=57 18 = treated TS girls (mean age 21.5) 39 = age/sex matched controls	GHT for at least five years. Some participants received hormone replacement therapy.	Cognition, Emotions and Quality of Life	Profile of mood states (POMS) (McNair, Lorr and Droppleman, 1992) Quality of Life Assessment of GH Deficient Adults (Holmes *et al.*, 1995)	After GHT discontinuation, women with TS reported significantly higher Tension-anxiety, depression-dejection and cognitive functioning (suggesting worse psychometric speed) than controls. Vigour-activity and QoL were significantly lower compared to controls.	19 (48%)
13	Siegel, Clopper & Stabler, 1998 US	Longitudinal cohort	N=429 146 = children of normal stature matched for age, sex and socioeconomic status (control) 37 = girls with TS	GHT for three years	Psychological profile: Intelligence Social competence and behaviour problems	CBC The Wide Range Achievement Test The Slosson Intelligence Test (Hammill, 1968)	Over three years of GHT girls with TS reported significant decreases in attention, social problems, and withdrawal. No differences in IQ or achievement scores.	24 (60%)

			27 = girls with isolated growth hormone deficiency 24 = girls with idiopathic short stature					
14	Van Pareren et al., 2005 Holland	Cross-sectional case-controlled	N=50 36 = treated TS girls from dose response study (mean age 18.2) 14 = treated TS girls from frequency response study (mean age 20.4) 359 = normal population control (mean age 17.1)	GHT Hormone replacement therapy.	Psychosocial functioning (behavioural problems, self-perception, depression, body image, family functioning, coping)	YASR Harter Self-Perception Profile (Harter, 1985) Child Depression Inventory (Kovacs, 1992) BAS Family Assessment Device (Byles *et al.*, 1988) Utrecht Coping List (Bijstra, Jackson and Bosma, 1994)	After reaching final height following GHT, women with TS reported no significant differences in behavioural problems or depression in comparison to controls. Self-perception and bodily attitude were significantly lower than the normal population, however family functioning was rated higher.	24 (60%)

Narrative Synthesis

This review provides a narrative synthesis of findings from included studies, structured around the psychological outcome explored and study design.

Quality of Life/Health Related Quality of Life

Randomised-Controlled Trials

Taback and Van Vliet (2011) measured HRQoL post GHT in a group of untreated and treated participants; the researchers found no differences in scores between the treatment groups and similar scores to norms of females within the general population.

Non-randomised Studies

Carel *et al.* (2005) evaluated the determinants of QoL in GH treated young women with TS; there were no significant differences in scores between participants and the general female population. A 20-year longitudinal study comparing HRQoL in TS females to that of the general population indicated HRQoL was not significantly associated with GHT, despite a mean 5.7cm increase in height (Krantz *et al.*, 2019). There were no significant differences between the groups at baseline and follow-up.

A cross-sectional case-controlled study compared QoL in females with TS to randomly selected, age-matched controls (Amundson *et al.*, 2010). After adjustment for age in a logistic regression analysis, with GHT as the dependent variable, only less physical pain remained significant and attributable to GHT. TS women without GHT reported more social isolation compared with controls. The Bannink *et al.* (2006) study compared HRQoL in GH treated young women with TS to a general population control group, post intervention. There were no statistically significant differences between scores, other than a small number of domains including social functioning and bodily pain, where the TS group reported significantly higher scores.

Following a prospective one year controlled study, girls with TS reported an improvement in HRQoL across all measures, and higher scores than UK norms (Butler *et al.*, 2019). However, there were no statistically significant differences in scores between TS and SS controls. Lastly, Lašaite, Lašiene and Lašas (2010) reported significantly higher tension-anxiety and depression-dejection scores and significantly lower QoL scores following GHT discontinuation in a TS group compared to age/sex matched controls.

Overall, 3/7 studies found no associations between GHT and QoL/HRQoL in girls with TS (Carel *et al.*, 2005; Taback and Van Vliet, 2011; Krantz *et al.*, 2019). Two studies reported no significant differences aside from a small number of subscales including pain and social functioning, in which TS girls reported significantly better scores compared to population controls (Bannink *et al.*, 2006; Amundson *et al.*,

2010). One study reported improvements across all HRQoL measures following one year of GHT (Butler *et al.*, 2019), whilst Lašaite, Lašiene and Lašas (2010) reported significantly lower QoL in GH treated girls in comparison to controls.

Psychosocial functioning

Randomised-Controlled Trials

Rovet and Holland (1993) compared psychological functioning in girls with TS randomised to either a GHT group or an untreated control group. After 18 months, girls in the treated group reported significantly higher scores in self-concept and social relationships. Rovet *et al.* (2019) completed a longitudinal sub-study of the original RCT; after 6 years of GHT the researchers found no global differences across the four domains measured.

A third RCT measured psychosocial functioning in girls with TS randomised to one of two dose regimes, before and after two years of GHT (Huismen, 1993). The results showed no significant changes in social anxiety, self-concept or behavioural problems. Both girls and their parents self-reported an improvement in independence, happiness and social interaction.

Non-randomised Studies

In a group of girls with TS, over two years of GHT, researchers found no significant changes in scores, other than an improvement in social competence for 7-12 and 13-16 year olds, and general/social self-esteem scores in 13-16 year olds (Lagrou *et al.*, 1998). Lagrou *et al.* (2006) found no significant differences between GH treated girls with TS and age matched controls, other than the TS group reporting more attentional difficulties, fewer delinquent behaviours and perceiving themselves as less socially competent.

Van Pareren *et al.* (2005) compared psychosocial functioning in girls with TS after GHT had been discontinued for six months, to a normal population control group. The results showed self-perception and bodily attitude were significantly lower in the TS group, however there were no significant differences in behavioural problem or depression scores. Lastly, Siegel, Clopper and Stabler (1998) explored the 'psychological profile' of GH treated girls with TS and noted significant decreases in specific subscales such as social problems, attention and withdrawal over three years.

With regards to psychosocial functioning, the results are mixed and reveal some paradoxical findings. A number of improvements were reported by treated girls in comparison to untreated girls and between pre/post GHT trials, for example improvements in self-concept, social relationships, interaction and attention (Huismen 1993; Rovet and Holland, 1993; Siegel, Clopper and Stabler, 1998). However, in comparison to a normal population group, girls with TS treated with GHT reported significantly lower

self-perception scores (Van Pareren *et al.*, 2005) and an RCT found no global differences between treated and untreated girls (Rovet *et al.*, 2019).

The one 'high quality' study measuring psychosocial functioning found no global differences between treated and untreated girls (Rovet *et al.*, 2019). The two 'high quality' studies measuring QoL/HRQoL similarly indicate no association with GHT (Butler *et al.*, 2019; Krantz *et al.*, 2019); although participants reported an improvement in HRQoL following one year of GHT in the Butler *et al.* (2019) study, the authors suggest the changes are more likely due to factors such as the test re-test phenomenon and conclude there was no independent effect of GHT.

Discussion

This review systematically evaluated the available literature on TS girls treated with GH, to explore whether there are any associations with psychological outcomes. To date, the research has mainly focused on examining GHT in relation to QoL/HRQoL or psychosocial functioning in girls with TS.

Initially, the results indicate there could be a small positive association between GHT and both QoL/HRQoL and psychosocial functioning in girls with TS. A number of improvements were reported following GHT across a variety of outcome measures (Huismen, 1993; Rovet and Holland, 1993; Lagrou *et al.*, 1998; Siegel, Clopper and Stabler, 1998; Butler *et al.*, 2019). However, the majority of high quality studies found no differences between treated and untreated girls or pre/post GHT (Krantz *et al.*, 2019; Rovet *et al.*, 2019).

There are several factors which could explain the variations within the results. Firstly, differences in psychological outcomes could be assumed to reflect differences in treatment success and subsequent increased final adult height. A number of studies found positive associations between greater height gain or taller adult height and improved QoL (Bannink *et al.*, 2006) or psychosocial functioning (Rovet and Holland, 1993; Rovet *et al.*, 2019). However, 6/7 studies examining QoL/HRQoL found no association between final adult height and GHT and three non-randomised studies found no correlation between height and any individual differences in scores or psychosocial functioning parameters (Lagrou *et al.*, 1998, 2006; Van Pareren *et al.*, 2005). These results indicate it is unlikely any positive associations between QoL/HRQoL and GHT are mediated by an increase in height and further questions the premise that reduced QoL in females with TS may be related to short stature (Reis *et al.*, 2018). It is not possible to confirm whether height mediates the relationship between GHT and psychosocial functioning in girls with TS.

Contradictory results highlighted by studies comparing girls with TS to general population samples could be indicative of limitations within study designs. Several studies did not compare outcomes pre/post treatment; as the researchers did not collect any baseline scores, it is therefore not possible to infer whether there were any changes in psychological outcomes in relation to GHT (Van Pareren *et al.*, 2005; Bannink *et al.*, 2006; Lagrou *et al.*, 2006; Lašaite, Lašiene and Lašas, 2010). Longitudinal studies found no global difference in psychosocial functioning or HRQoL between treated and untreated women (Krantz *et al.*, 2019; Rovet *et al.*, 2019) Therefore, it could be argued that any observed positive effects may diminish over time.

Diminished effects could be indicative of an initial bias from both parents and their children to respond positively following GHT, given the greater time they have invested, alongside the hope that treatment shall result in improved outcomes. Once girls have reached final adult height and on average continue to remain shorter than their peers, it could be the case participants' expectations are more realistic and therefore less biased in their reporting. Alternatively, research indicates infertility can negatively impact upon psychosocial functioning (Greil, Schmidt and Peterson, 2016) and QoL (Chachamovich *et al.*, 2010); it may be the case that as girls progress through adulthood, the impact of infertility becomes more apparent and/or meaningful.

Interestingly, in accordance with recent qualitative research in which TS girls viewed themselves as more socially competent than parental reports (Wolstencroft, Mandy and Skuse, 2020), two studies found parents perceived their daughters social functioning as much lower than girls themselves (Bannink *et al.*, 2006; Butler *et al.*, 2019). These discrepancies could reflect a social desirability bias, similar to that described in young females with ASD (Bauminger and Kasari, 2000). Differences in findings may therefore reflect a lack of multi-informant data.

Moreover, there were several methodological limitations and biases within the included studies. Only two studies excluded girls that had received Oestrogen therapy to induce puberty and/or Oxandrolone which is an anabolic steroid also used for height gain (Rovet and Holland, 1993; Butler *et al.*, 2019). It is therefore not possible to determine whether any changes in psychological outcomes are associated with GHT, one of these additional treatments or an interaction between co-interventions. Historically, paediatric management of TS focused primarily on height gain, and thereby delayed pubertal development to allow more time for growth to improve final height (Turner and Hozjan, 2019). This is no longer considered best practice as it fails to recognise the importance of age-appropriate development for psychosocial adjustment and general health. Carel *et al.* (2006) found delayed puberty induction in girls with TS could have a long-lasting, negative impact on self-esteem and self-adjustment; any positive or negative effects on the psychological outcomes observed may therefore be associated with pubertal development and the induction/lack of induction of puberty, rather than GHT.

Furthermore, within the RCTs, neither the participants nor the researchers were blinded to which treatment group girls had been allocated to i.e. there were no placebo control groups. This is understandable given the unethical implications around injecting children daily with a placebo for several years (White, 1993). However, a systematic review of trials that randomised patients to blinded and nonblinded studies highlighted nonblinded patients exaggerated the effect size by 0.56 SD on average (Hróbjartsson *et al.*, 2014).

Additionally, although the majority of studies used standardised measures, these measures were self-report questionnaires not specifically designed for TS, and so it is unclear how valid and/or reliable they are within this population. Lastly, the studies varied significantly in sample size, with 12/14 failing to report whether they had conducted sample size calculations.

Limitations

The decision was made to exclude articles in which the effects of Oxandrolone were specifically examined in relation to psychological outcomes as this is an adjuvant therapy to GHT. However, future research to widen the inclusion criteria to include these studies may highlight additional findings. Moreover, one researcher conducted the database searching, screening of articles and data extraction. To increase the reliability of the results, the addition of a second researcher at these stages would be of benefit. Furthermore, due to time constraints, inter-rater reliability was achieved for 4 of the included studies. Two raters independently assessing each of the studies included would have further reduced any biases and increased the reliability of the results. While the search strategy was comprehensive and the search terms were reviewed by a member of the University library team, literature outside of searched databases may exist, in languages other than English.

Clinical and Research Implications

Although improvements were reported across several psychological domains following GHT in girls with TS, the lack of consistency across findings alongside several methodological limitations and biases found within the included studies, limit any conclusions that can be drawn. Moreover, several high-quality longitudinal studies indicate no association between GHT and psychological outcomes. QoL/HRQoL and/or psychosocial functioning should therefore not be used as a primary measure to determine whether girls with TS should receive GHT; it could be argued that height enhancement alone should be considered the main rationale for providing GHT to girls with TS.

It is therefore important clinicians do not over-emphasise the benefits of GHT on psychological outcomes and manage both parents and girls' expectations. Given the expense, considerable commitment required by girls and their families, and substantial variation in treatment response, both clinicians and families should carefully consider whether to pursue GHT. It should also be noted several studies found

alternative variables such as ontological involvement, cardiac involvement, BMI and age at diagnosis were negatively associated with QoL/HRQoL and/or psychosocial functioning. The management of TS in relation to psychological outcomes should thus be person-centred, tailored to the individual and consider how a range of TS associated health problems may impact upon psychological well-being.

Ideally, future research exploring the association between GHT and psychological outcomes would utilise double-blinded trials in which girls with TS are randomly allocated to either GHT or a placebo, including both multi-informant and multi-method outcome measures. However, the ethical implications of such a trial render this as unfeasible. It could be helpful to conduct further follow-up studies of the Canadian RCT to determine whether there are any associations between GHT and psychological outcomes as women progress through adulthood. Lastly, whether or not short stature does result in psychological disadvantages continues to be a topic of debate within the literature. Earlier studies suggest short stature individuals experience poorer quality of life and problems with psychosocial adaptation due to chronic psychosocial stress (teasing and stigmatisation) and/or height-related physical limitations (Wheeler et al., 2004, Voss, 2001). However, a recent review concluded teasing alone is not associated with dysfunction and height as an isolated characteristic, does not impair positive psychosocial adaptation (Sandberg and Gardner, 2015). A clearer theoretical framework may help determine more sensitive and focussed measurement of the impact of increased growth on psychological wellbeing. Although there are a small number of outcome measures which assess HRQoL/QoL in children and adolescents (Bullinger et al., 2013) and adults (Holmes et al., 1995) with SS, these questionnaires have been developed for individuals with GH deficiency. Therefore, a TS-specific instrument may beneficial.

Conclusion

The current literature exploring whether there are any associations between GHT and psychological outcomes in girls with TS, primarily investigates QoL/HRQoL or psychosocial functioning. Although the results indicate there could be positive associations within a number of psychological outcomes, it is unlikely GHT leads to global, long lasting improvements. Several methodological biases such as failing to control for co-interventions and lack of participant and researcher blinding were found throughout the literature and may explain some of the variability within the results. These limitations are consistent with those noted by Gardner *et al.* (2016) in a systematic review examining the risk of bias in the literature around the effects of GHT on psychological outcomes in children with general SS. When managing treatment, clinicians should avoid over-emphasising the benefits of GHT and use a person-centred, holistic approach to consider how the wide variety of possible TS-related health problems may impact upon psychological outcomes in girls with TS.

References

Achenbach, T. . (1991a) *Manual for the Child Behaviour Checklist/4–18 and 1991 Profile*. University of Vermont, Department of Psychiatry, Burlington, VT.

Achenbach, T. . (1991b) *Manual for the Youth Self-report and 1991 Profile.* University of Vermont, Department of Psychiatry, Burlington, VT.

Achenbach, T. . (1997) *Manual for the Cross-Informant Program for the Young Adult Self Report and Young Adult Behavior Checklist.* Burlington: University of Vermont, Department of Psychiatry.

Amundson, E. *et al.* (2010) 'Impact of growth hormone therapy on quality of life in adults with turner syndrome', *Journal of Clinical Endocrinology and Metabolism*, 95(3), pp. 1355–1359. doi: 10.1210/jc.2009-1754.

Apperley, L. *et al.* (2018) 'Mode of clinical presentation and delayed diagnosis of Turner syndrome: a single Centre UK study', *International Journal of Pediatric Endocrinology*, 2018(1), p. 4. doi: 10.1186/s13633-018-0058-1.

Bannink, E. M. N. *et al.* (2006) 'Quality of Life after Growth Hormone Therapy and Induced Puberty in Women with Turner Syndrome', *The Journal of Pediatrics*, 148(1), pp. 95–101. doi: 10.1016/J.JPEDS.2005.08.043.

Bauminger, N. and Kasari, C. (2000) 'Loneliness and Friendship in High-Functioning Children with Autism', *Child Development*, 71(2), pp. 447–456. doi: 10.1111/1467-8624.00156.

Baxter, L. *et al.* (2007) 'Recombinant growth hormone for children and adolescents with Turner syndrome', *Cochrane Database of Systematic Reviews*, (1), p. CD003887. doi: 10.1002/14651858.CD003887.pub2.

Bijstra, J. O., Jackson, S. and Bosma, H. A. (1994) 'De Utrechtse Coping Lijst voor Adolescenten', *Kind en adolescent*, 15(2), pp. 67–74. doi: 10.1007/BF03060546.

Bondy, C. (2014) 'Recent Developments in Diagnosis and Care for Girls in Turner Syndrome', *Advances in Endocrinology*, 2014. doi: http://dx.doi.org/10.1155/2014/231089.

Bondy, C. A. (2009) 'Turner Syndrome 2008', *Hormone Research in Paediatrics*, 71(1), pp. 52–56. doi: 10.1159/000178039.

Broadstock, M., Michie, S. and Marteau, T. (2000) 'Psychological consequences of predictive genetic testing: a systematic review', *European Journal of Human Genetics*, 8, pp. 731–738. Available at: www.nature.com/ejhg (Accessed: 5 June 2020).

Bullinger, M. *et al.* (2013) ' Assessing the quality of life of health-referred children and adolescents with short stature: development and psychometric testing of the QoLISSY instrument', *Health and Quality of Life Outcomes*, 11(76). doi: 10.1186/1477-7525-11-76.

Butler, G. *et al.* (2019) 'Growth hormone treatment and health-related quality of life in children and adolescents: A national, prospective, one-year controlled study', *Clinical Endocrinology*, 91(2), pp. 304–313. doi: 10.1111/cen.14011.

Byles, J. *et al.* (1988) 'Ontario Child Health Study: Reliability and Validity of the General Functioning Subscale of the McMaster Family Assessment Device', *Family Process*, 27(1), pp. 97–104. doi: 10.1111/j.1545-5300.1988.00097.x.

Cardoso, G. *et al.* (2004) 'Current and lifetime psychiatric illness in women with Turner syndrome', *Gynecological Endocrinology*, 19(6), pp. 313–319. doi: 10.1080/09513590400021227.

Carel, J.-C. *et al.* (2005) 'Quality of Life Determinants in Young Women with Turner's Syndrome after Growth Hormone Treatment: Results of the StaTur Population-Based Cohort Study', *The Journal of Clinical Endocrinology & Metabolism*, 90(4), pp. 1992–1997. doi: 10.1210/jc.2004-1395.

Carel, J. C. *et al.* (2005) 'Quality of life determinants in young women with Turner's syndrome after growth hormone treatment: Results of the StaTur population-based cohort study', *Journal of Clinical Endocrinology and Metabolism*, 90(4), pp. 1992–1997. doi: 10.1210/jc.2004-1395.

Carel, J. C. *et al.* (2006) 'Self-esteem and social adjustment in young women with Turner syndrome - Influence of pubertal management and sexuality: Population-based cohort study', *Journal of Clinical Endocrinology and Metabolism*, 91(8), pp. 2972–2979. doi: 10.1210/jc.2005-2652.

Chachamovich, J. R. *et al.* (2010) 'Investigating quality of life and health-related quality of life in infertility: A systematic review', *Journal of Psychosomatic Obstetrics and Gynecology*, pp. 101–110. doi: 10.3109/0167482X.2010.481337.

Coopersmith, S. (1984) *Self-esteem inventory.* Edited by du C. de P. Applique´e. Paris.

Crowe, M. and Sheppard, L. (2011) 'A review of critical appraisal tools show they lack rigor: Alternative tool structure is proposed', *Journal of Clinical Epidemiology*, 64(1), pp. 79–89. doi: 10.1016/j.jclinepi.2010.02.008.

Dupuy, H. (1984) 'The Psychological General Well-being (PGWB) Index.', in Wenger, N. et al. (eds) *Assessment of Quality of Life in Clinical Trials of Cardiovascular Therapies.* New York.: Le Jacq Publishing, pp. 170–83.

Ey, S. *et al.* (2005) 'A new measure of children's optimism and pessimism: The youth life orientation

test', *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 46(5), pp. 548–558. doi: 10.1111/j.1469-7610.2004.00372.x.

Gardner, M. *et al.* (2016) 'Coming Up Short: Risks of Bias in Assessing Psychological Outcomes in Growth Hormone Therapy for Short Stature', *The Journal of Clinical Endocrinology & Metabolism*, 101(1), pp. 23–30. doi: 10.1210/jc.2015-3256.

Gault, E. and Donaldson, M. (2001) *Efficacy of growth hormone therapy in Turner's Syndrome*. Available at: http://bspe.shef.ac.uk/XONICE.html YR:2001 (Accessed: 4 June 2019).

Goldberg, D. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

Goodman, R. (1997) 'The strengths and difficulties questionnaire: A research note', *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 38(5), pp. 581–586. doi: 10.1111/j.1469-7610.1997.tb01545.x.

La Greca, A. M. *et al.* (1988) 'Development of the Social Anxiety Scale for Children: Reliability and Concurrent Validity', *Journal of Clinical Child Psychology*, 17(1), pp. 84–91. doi: 10.1207/s15374424jccp1701_11.

Greil, A. L. ., Schmidt, L. . and Peterson, B. . (2016) 'Understanding and treating the psychosocial consequences of infertility. - PsycNET', in *The Oxford handbook of perinatal psychology*. Oxford University Press, pp. 524–547. Available at: https://psycnet.apa.org/record/2016-21623-040 (Accessed: 7 May 2020).

Grew, R. S. *et al.* (1983) 'Facilitating patient understanding in the treatment of growth delay.', *Clinical pediatrics*, 22(10), pp. 685–90. doi: 10.1177/000992288302201003.

Hammill, D. (1968) 'The Slosson intelligence test as a quick estimate of mental ability', *Journal of School Psychology*, 7(4), pp. 33–37. doi: 10.1016/0022-4405(68)90052-6.

Harter, S. (1985) *Manual of the Self-Perception Profile for Children.* Denver.

Harter, S. and Neemann, J. (1986) *Manual for the Self- Perception Profile for College Students.* Denver: University of Denver.

Holmes, S. *et al.* (1995) 'Development of a questionnaire to assess the quality of life of adults with growth hormone deficiency', *Endocrinology and metabolism*, 1(2(1)), pp. 63–69. Available at: https://www.rtihs.org/publications/development-questionnaire-assess-quality-life-adults-growth-hormone-deficiency (Accessed: 10 June 2020).

Hong, D., Scaletta Kent, J. and Kesler, S. (2009) 'Cognitive profile of Turner syndrome.', *Developmental*

disabilities research reviews, 15(4), pp. 270–8. doi: 10.1002/ddrr.79.

Hróbjartsson, A. *et al.* (2014) 'Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies', *International Journal of Epidemiology*, 43(4), pp. 1272–1283. doi: 10.1093/ije/dyu115.

Huisman, J. *et al.* (1993) 'Psychosocial Effects of Two Years of Human Growth Hormone Treatment in Turner Syndrome', *Hormone Research*, 39, pp. 56–59.

Kamphuis, M. *et al.* (2004) 'A cardiac-specific health-related quality of life module for young adults with congenital heart disease: development and validation.', *Quality of Life Research*, 13(4), pp. 735–745.

Keith Conners, C. *et al.* (1998) 'Revision and restandardization of the Conners Teacher Rating Scale (CTRS-R): Factor structure, reliability, and criterion validity', *Journal of Abnormal Child Psychology*, 26(4), pp. 279–291. doi: 10.1023/A:1022606501530.

Kovacs, M. (1992) *Children's Depression Inventory.* New York.

Krantz, E. *et al.* (2019) 'Health-Related Quality of Life in Turner Syndrome and the Influence of Growth Hormone Therapy: A 20-Year Follow-Up', *The Journal of clinical endocrinology and metabolism*, 104(11), pp. 5073–5083. doi: 10.1210/jc.2019-00340.

Lagrou, K. *et al.* (1998) 'Age-related perception of stature, acceptance of therapy, and psychosocial functioning in human growth hormone-treated girls with Turner's syndrome', *Journal of Clinical Endocrinology and Metabolism*, 83(5), pp. 1494–1501. doi: 10.1210/jc.83.5.1494.

Lagrou, K. *et al.* (2006) 'Psychosocial Functioning, Self-Perception and Body Image and Their Auxologic Correlates in Growth Hormone and Oestrogen-Treated Young Adult Women with Turner Syndrome', *Hormone Research in Paediatrics*, 66(6), pp. 277–284. doi: 10.1159/000095547.

Lašaite, L., Lašiene, D. and Lašas, L. (2010) 'Cognition, emotions and quality of life in Lithuanian girls with Turner syndrome after growth hormone therapy discontinuation', *Journal of Pediatric Endocrinology and Metabolism*, 23(5), pp. 443–450. doi: 10.1515/jpem.2010.075.

Liberati, A. *et al.* (2009) 'The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration', *PLoS Medicine*, 6(7), p. e1000100. doi: 10.1371/journal.pmed.1000100.

Liedmeier, A. *et al.* (2020) 'Psychosocial well-being and quality of life in women with Turner syndrome', *Psychoneuroendocrinology*, 113. doi: 10.1016/j.psyneuen.2019.104548.

McEwen, J. (1993) 'The Nottingham Health Profile', in *Quality of Life Assessment: Key Issues in the 1990s*. Springer Netherlands, pp. 111–130. doi: 10.1007/978-94-011-2988-6_5.

McNair, O., Lorr, M. and Droppleman, L. (1992) *Edits Manual: Profile of mood state.* SanDiego (Calif.).

Meyer-Bahlburg, H. (1990) 'Short stature: Psychological issues', *Pediatric Endocrinology*, pp. 173–196.

Morgan, T. (2007) *Turner Syndrome: Diagnosis and Management*. Available at: www.aafp.org/afp. (Accessed: 24 September 2018).

Olson, D. H. (1986) 'Circumplex Model VII: Validation Studies and FACES III', *Family Process*, 25(3), pp. 337–351. doi: 10.1111/j.1545-5300.1986.00337.x.

Van Pareren, Y. K. *et al.* (2005) 'Psychosocial functioning after discontinuation of long-term growth hormone treatment in girls with turner syndrome', *Hormone Research*, 63(5), pp. 238–244. doi: 10.1159/000085841.

Piers, E. . (1969) *Manual for the Piers-Harris Children's Self-concept Scale.* Nashville, Tenn.: Counselor Recordings & Tests.

Power, T., Langlois, N. E. I. and Byard, R. W. (2014) 'The Forensic Implications of Turner's Syndrome', *Journal of Forensic Sciences*, (10.1111), 59(3), pp. 671–675. doi: 10.1111/1556-4029.12365.

Reimann, G. E. *et al.* (2018) 'Psychosocial Characteristics of Women with a Delayed Diagnosis of Turner Syndrome', *The Journal of Pediatrics*, 199, pp. 206–211. doi: 10.1016/j.jpeds.2018.03.058.

Reis, C. T. *et al.* (2018) 'Systematic review of quality of life in Turner syndrome', *Quality of Life Research*, 27(8), pp. 1985–2006. doi: 10.1007/s11136-018-1810-y.

Rolstad, S. G. *et al.* (2007) 'Sexual Functioning and Partner Relationships in Women with Turner Syndrome: Some Empirical Data and Theoretical Considerations Regarding Sexual Desire', *Journal of Sex & Marital Therapy*, 33(3), pp. 231–247. doi: 10.1080/00926230701267886.

Rovet, J. F. *et al.* (2019) 'Growth hormone supplementation and psychosocial functioning to adult height in Turner syndrome: A questionnaire study of participants in the Canadian randomized trial', *Frontiers in Endocrinology*, 10(MAR), pp. 1–14. doi: 10.3389/fendo.2019.00125.

Rovet, J. and Holland, J. (1993) 'Psychological Aspects of the Canadian Randomized Controlled Trial of Human Growth Hormone and Low-Dose Ethinyl Oestradiol in Children with Turner Syndrome', *Hormone Research*, 39(2), pp. 60–64. doi: 10.1159/000182772.

Sandberg, D.E. and Gardner, M. (2015) 'Short Stature: Is it a Psychosocial problem and does changing height matter?', *Pediatric Clinics of North America*, 62(4), pp. 963–982. doi: 10.1016/j.pcl.2015.04.009

Siegel, P. T., Clopper, R. and Stabler, B. (1998) 'The psychological consequences of Turner syndrome and review of the National Cooperative Growth Study psychological substudy.', *Pediatrics*, 102(2 Pt 3),

pp. 488–91. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9685450 (Accessed: 7 June 2019).

Simis, K. J., Verhulst, F. C. and Koot, H. M. (2001) 'Body Image, Psychosocial Functioning, and Personality: How Different Are Adolescents and Young Adults Applying for Plastic Surgery?', *Journal of Child Psychology and Psychiatry*, 42(5), pp. 669–678. doi: 10.1111/1469-7610.00762.

Stochholm, K. *et al.* (2006) 'Prevalence, Incidence, Diagnostic Delay, and Mortality in Turner Syndrome', *The Journal of Clinical Endocrinology & Metabolism*, 91(10), pp. 3897–3902. doi: 10.1210/jc.2006-0558.

Taback, S. P. and Van Vliet, G. (2011) 'Health-related quality of life of young adults with Turner syndrome following a long-term randomized controlled trial of recombinant human growth hormone', *BMC Pediatrics*, 11(1), p. 49. doi: 10.1186/1471-2431-11-49.

Tanner, J. M. and Whitehouse, R. H. (1976) 'Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty.', *Archives of disease in childhood*, 51(3), pp. 170–9. doi: 10.1136/adc.51.3.170.

Turner, H. E. and Hozjan, I. R. (2019) 'Diagnosis and Management of Turner Syndrome in Children and Adults', in *Advanced Practice in Endocrinology Nursing*, pp. 771–801. doi: 10.1007/978-3-319-99817-6_40.

Upton, P. *et al.* (2005) 'Measurement properties of the UK-English version of the Pediatric Quality of Life Inventory™ 4.0 (PedsQL™) generic core scales', *Health and Quality of Life Outcomes*, 3. doi: 10.1186/1477-7525-3-22.

Voss, L.D. (2001) 'Short normal stature and psychosocial disadvantage: a critical review of the evidence.', *Journal of Pediatric Endocrinology and Metabolism*, 14, pp. 701–711.

Ware, J. E. and Sherbourne, C. D. (1992) 'The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and Item Selection', *Medical Care*, pp. 473–483. doi: 10.2307/3765916.

Wheeler, P.G., Bresnahan, K., Shephard, B.A., Lau. J., and Balk, E.M (2004) 'Short stature and functional impairment: a systematic review.', *Archives of Pediatric Adolescents Medicine*, 158, pp. 236–243. doi: 10.1001/archpedi.158.3.236

White, G. B. (1993) 'Human growth hormone: the dilemma of expanded use in children.', *Kennedy Institute of Ethics journal*, 3(4), pp. 401–409. doi: 10.1353/ken.0.0170.

Wolstencroft, J., Mandy, W. and Skuse, D. (2020) 'Experiences of social interaction in young women with Turner syndrome: A qualitative study', *Child: Care, Health and Development*, 46(1), pp. 46–55. doi: 10.1111/cch.12710.

Chapter 2: Major research project

A qualitative study exploring disclosure in girls with Turner Syndrome: their experience of diagnostic disclosure and disclosing their condition to others.

Prepared in accordance with authors' guidelines from the British Journal of Health Psychology (Appendix 1.1).

Plain English summary

Title

A qualitative study exploring disclosure in girls with Turner Syndrome: their experience of diagnostic disclosure and disclosing their condition to others.

Background

Historically, clinicians tended not to share a diagnosis of illness with children to protect them from distress. However, more recently, doctors have been encouraged to adopt a much more open approach. Although there is a lot of research around how to tell a child about illnesses such as HIV or cancer, there is far less around how to tell a child about a genetic condition. Turner Syndrome (TS) is a genetic condition which affects females, causing difficulties such as short stature and infertility. Preliminary research suggested that in the past, some girls with TS had not been told they have the condition (Gravholt *et al.*, 2003) or not been told TS affects fertility (Sutton *et al.*, 2006). To date, there has not been any research exploring how girls with TS feel disclosing their condition to others, or how TS affects families as a unit. Research conducted from the joint perspectives of girls with TS and their parents is also limited.

Aims

The main aim of this study was to explore the experiences of diagnostic disclosure and disclosure to others in adolescent girls with TS and their parents/guardians. A further aim was to examine the impact of TS on girls and their family's lives.

Method

This research used a qualitative design. Five girls with TS aged between 12-25 and at least one of their parent/guardians were recruited from two local TS clinics in Scotland. Participants completed semi-structured interviews together and then individually, which were audio recorded and later transcribed. Interpretative Phenomenological Analysis (IPA) was used to analyse the results. IPA focuses on the way people make sense of their experiences and beliefs, which are interpreted by the researcher. This leads to a very in-depth understanding of a particular phenomenon. Interviews were coded and the researcher identified themes occurring across the five interviews.

Results

Three main themes were identified: Communication and Support, Stigmatisation of TS and Psychological Consequences. These main themes included eleven subthemes, which are discussed alongside relevant quotes from the participants.

Conclusions

This study adds to the limited research around disclosure in girls with TS, indicating that although families feel they are very open discussing TS with each other, both girls and their parents avoid telling others about the condition. The results highlight variations in the way TS can affect families, from the unique, joint perspectives of girls and their parents. These insights provide recommendations for parents and clinicians, and suggest more research is required to explore factors which may help enable girls to disclose TS to others.

References

Gravholt, C. H. *et al.* (2003) 'Increased fracture rates in Turner's syndrome: a nationwide questionnaire survey', *Clinical Endocrinology*, 59(1), pp. 89–96. doi: 10.1046/j.1365-2265.2003.01807.x.

Sutton, E. J. *et al.* (2006) 'Truth-telling and Turner Syndrome: The Importance of Diagnostic Disclosure', *The Journal of Pediatrics*, 148(1), pp. 102–107. doi: 10.1016/J.JPEDS.2005.08.022.

Word count: 496 (including references)

Abstract

Objectives

Previous literature exploring diagnostic disclosure in girls with Turner Syndrome (TS) is limited and has not yet examined how girls feel about disclosing their condition to others. Moreover, research conducted from the joint perspectives of girls and their parents is lacking. The primary aim of this study was to explore the experiences of diagnostic disclosure and disclosure to others in adolescent girls with TS and their parents/guardians. The secondary aim was to examine the impact of TS on girls and on their family's lives.

Design

A qualitative method utilising Interpretative Phenomenological Analysis (IPA) was employed within this study.

Methods

Five girls with TS and one parent/guardian of each girl completed dyadic and individual semi-structured interviews. Interviews were audio recorded and analysed verbatim. Data were analysed in accordance with IPA guidelines, with a focus on the dynamic interactions within dyads.

Results

Analysis identified three superordinate themes across the ten participants' accounts: (i) Communication and Support, (ii) Stigmatisation of TS and (iii) Psychological Consequences. Eleven related sub-themes are described alongside relevant quotations.

Conclusions

The present findings provide insight into the lived experience of receiving a diagnosis of TS, highlighting a desire from both girls and their parents to conceal TS from others and demonstrating the varying impact TS can have within families. These insights provide potential recommendations for both clinicians and parents, such as ensuring direct conversations about infertility occur within treatment and facilitating open, honest communication. Future research exploring barriers around disclosure to others may enable girls and their families to facilitate this conversation.

Introduction

Diagnostic disclosure in children

Historically, clinicians took a 'protective approach' when communicating a diagnosis of an illness or condition to children, the rationale being that children should be shielded from distress (Sisk *et al.*, 2016). However in recent years, a more open approach has been recommended, taking hope and prognosis (Mack *et al.*, 2006), individual differences (e.g., developmental stage; Bluebond-Langner, Belasco and DeMesquita Wander, 2010) and family culture (Bluebond-Langner *et al.*, 2007) into consideration.

Poor communication or insensitive care from health professionals during diagnostic disclosure appears to result in negative consequences for both children and their families (Davies, Davis and Sibert, 2003; Stein *et al.*, 2019). Research exploring children with a diagnosis of cancer found that poor communication between clinicians, parents and children can increase the suffering of patients and their families (Sisk *et al.*, 2016). Gaff and Bylund (2010) note that if a diagnosis is withheld it could evolve into a family secret, resulting in an environment of distrust and strain affecting family interpersonal relationships.

Moreover, research exploring adolescents' views and experiences of disclosing conditions such as autism and HIV highlighted teenagers are often reluctant to tell others about their diagnosis, for fear of being treated differently or experiencing stigma (Humphrey, Neil and Lewis, 2008; Michaud *et al.*, 2009). Metcalfe *et al.* (2008) found children with genetic conditions rarely discussed the condition or its risks with their siblings. Most communication took place between the child and parent(s). In addition, it has been recognised that when a child is unwell, the whole family is affected (Stein *et al.*, 2019). Therefore, clinicians are encouraged to adopt family-centred models of paediatric care, which include the potential impact of the illness on parents/carers (Watts *et al.*, 2014). Prior studies have identified considerable variety with regards to the level of impact a child's chronic condition can have on family functioning and quality of life (Barlow and Ellard, 2006).

While most diagnostic disclosure studies focus on children with intellectual disabilities, HIV or cancer, there is less research exploring disclosure in children with genetic conditions. Turner Syndrome (TS) is a genetic condition which occurs in between 1:2000 and 1:2500 live born females (Stochholm *et al.*, 2006; Apperley *et al.*, 2018) The condition is caused by the complete or partial absence of the second X chromosome. TS is characterised by short stature and infertility, alongside a broad range of other phenotypical characteristics such as an increased risk of renal and heart defects (Hall and Gilchrist, 1990). The age at which girls are diagnosed can therefore vary, from the antenatal period through to adolescence, depending on which features are evident (Apperley *et al.*, 2018).

Diagnostic disclosure in girls with TS

Preliminary research suggests that in the past, individuals with TS may not have always been informed of their diagnosis or may have had some aspects of the condition withheld from them. Gravholt *et al.* (2003) conducted a questionnaire study to explore the characteristics and risk factors for bone fractures in women with TS. Unexpectedly, they discovered 45/322 participants they surveyed were unaware of their TS diagnosis. Further qualitative research by Sutton *et al.* (2005) explored the challenges experienced by females with TS across the lifespan; many participants spontaneously reported that some aspect of the TS diagnosis had been kept secret from them. Secondary analysis examining the impact of secret-keeping on girls and women with TS suggested parents are the most likely individuals to withhold diagnostic information from their daughters, particularly around the infertility component (Sutton *et al.*, 2006). A recent cross-sectional study indicated age and emotional maturity were key factors in determining when parents would choose to discuss infertility with their daughters with TS (King *et al.*, 2016). Being afraid of negative emotion and struggling with the balance of educating plus protecting their daughters were two of the main barriers which affected parent's ability to have the conversation.

To date, most studies have explored the views of parents of a child with TS or adult women with TS. To our knowledge, there has been no prior research conducted which focuses on the joint perspectives of adolescent girls with TS and their parents. Given that a moderate percentage (26%) of girls receive their TS diagnosis within the first year of infancy (Apperley *et al.*, 2018), it is likely their parents or guardians will have been involved in the disclosure process, and therefore a joint account may provide a more in-depth understanding. Moreover, TS is likely to impact individual members of a family as well as families as a whole and so joint interviews will provide important insight into any similarities or differences in experiences. Analogous research exploring the experiences of parent-child dyads within families affected by Huntington's disease highlights the importance of co-constructed accounts within the process of meaning making (the dynamics and interactions between them) (Maxted, Simpson and Weatherhead, 2014). Advantages of dyadic interviews include the opportunity to bring interaction into the interview (Kitzinger, 1995) and expand the coverage of the research topic by participants sharing their point of view (Morgan, Eliot, Lowe, & Gorman, 2015). Therefore, this study interviewed girls and parents together.

Conversely, previous research also indicates family members may not talk openly in front of each other to an interviewer if they worry about criticising or raising sensitive topics which could hurt another's feelings or damage the relationship (Morris, 2001; Corbin and Morse, 2003). Girls and their parents/guardians were subsequently also interviewed separately.

Overall, prior research exploring the nature of disclosure in girls with TS is limited. The issue of diagnostic disclosure was highlighted by chance, and subsequent research aimed to describe the perceived effects of secret-keeping on females with TS, rather than explore the nature of disclosure as a process

within the family (Sutton *et al.*, 2006). Although King *et al.* (2016) provides further insight into why infertility may be a difficult aspect of TS to discuss for parents, their study is quantitative in nature. Qualitative methods may arguably provide a more holistic view, and help to develop a richer understanding (Bogdan and Taylor, 1975). Lastly, as far as we are aware, no prior research has been conducted to explore how girls with TS feel about disclosing their condition to others, and the extent to which TS impacts upon families as a system has not yet been explored.

Aims

The primary aim of this study was to explore the nature of disclosure in adolescents with TS, including how girls learned they had TS, how they feel/felt disclosing their condition to others and parents' experience of discussing and potentially disclosing aspects of TS to their children. The secondary aim of this study was to explore whether TS has had an impact on girls and their family's lives.

Method

Design

A qualitative approach was employed, and Interpretative phenomenological analysis (IPA) was the method of analysis. The aim of IPA is to explore in detail the processes through which participants make sense of their own experiences, focusing on their own perceptions, understanding and views (Brocki and Wearden, 2006). As this study explores patients' lived experience of having a health condition, which naturally plays a significant part in their lives and concerns of those with the condition and their families, IPA was decided to be the most appropriate method of analysis. The aim of this study was to develop a rich insight into parents' and girls' experiences of disclosure and the impact of TS on their lives; one of the key benefits of IPA is that it offers an in-depth approach, detailing the processes of meaning making about a particular phenomenon. It was felt that IPA would therefore further add to the evidence base, by gaining a richer understanding from the participants. This method should not only provide insight into the experiences of each parent and child but also the points of divergence and convergence in their experiences and the dynamics between them. IPA also represents an accessible approach for a researcher without expertise in qualitative methods (Smith, Flowers and Larkin, 2009).

Participants

Participants were five girls who had been diagnosed with TS and one of each of their parents/guardians. Participants were recruited from two designated TS clinics within NHS Greater Glasgow and Clyde between October-December 2019: a children's clinic and an adult clinic. The participant inclusion and exclusion criteria are outlined below:

Participants with TS

Inclusion criteria:

- Aged between 12-25 years old.
- Received diagnosis of Turner Syndrome.
- Have at least one parent/guardian who also wishes to take part.

Exclusion criteria:

- Participants with a significant learning disability (LD). (Participants who do not or did not attend mainstream school were not included).
- Participants that do not speak English.

Parents/guardians

Inclusion criteria:

- Be the parent/guardian to a girl aged between 12-25 years old diagnosed with TS.

Exclusion criteria:

- Participants that do not speak English.

Sample size and data saturation

Due to the depth and detail of the analysis to understand a particular phenomenon, a small purposively selected sample was deemed appropriate (Smith, Flowers and Larkin, 2009). We therefore expected to reach saturation of themes by interviewing 6-8 girls and at least one of their parents/guardians. Similar qualitative studies interviewing dyads recruited around the same number of participants (Akeson, Worth and Sheikh, 2007; Maxted, Simpson and Weatherhead, 2014). However, Smith, Flowers and Larkin (2009) suggest between 3-6 participants can be a reasonable sample size for student studies using IPA.

Ethics

Ethical approval was obtained through the West of Scotland Ethics Committee (REC) (Appendix 2.1) (ref: 19/WS/0132) and the NHS Greater Glasgow and Clyde Research and Development Department (ref: GN19MG312).

With permission from participants, all interviews were recorded using a portable audio recording device and then uploaded to a secure server. The audio files were deleted from the device and each participant was assigned a unique code and pseudonym. Interviews were transcribed using only the identifier code and any identifiable information (e.g. hometown) was removed.

Recruitment and Procedure

The lead clinicians from the TS clinics invited the girls and their parents/guardians to take part via post. Participant information sheets (PIS)(Appendix 2.2) were posted alongside the invitations. Girls with TS aged over 18 years old, who may not live with their parents, were also sent the parent/guardian PIS sheet, and asked to distribute this to their parents/guardians.

There were two methods in which participants could indicate consent. Firstly, they could contact a member of the research team prior to their appointment if they wished to take part. Alternatively, the lead clinicians asked all potential participants if they would like to take part when they attended the clinic. If they indicated they would like to take part, the Principle Investigator (PI) contacted them to provide any further information required and arrange the interview. The PI also attended both clinics to provide further information about the study and answer any questions from potential participants.

Prior to each interview, the PIS was supplied for the participants' review and any questions answered. Written consent was then obtained (Appendix 2.3). One interviewer conducted semi-structured, face-to-face in person interviews, lasting between 53-92 minutes. Girls and their parents/guardians were initially interviewed together using a dyadic interview approach. Both parties were then interviewed individually unless they chose to decline. All interviews were transcribed verbatim.

Interview

The interview schedule was developed by the Trainee Clinical Psychology, in consultation with the lead clinician who facilitated the children's TS clinic and another researcher who is a Clinical Psychologist working within a Paediatric Clinical Psychology service (Appendix 2.4). The aim of the schedule was to facilitate a comfortable interaction with participants to help them feel at ease, thereby enabling them to provide an in-depth account of their experiences (Smith, Flowers and Larkin, 2009). Open-ended, expansive questions were prepared in accordance with the sequence described by Smith, Flowers and Larkin (2009); the range of topic areas and how to sequence these were considered alongside how to phrase each question and related prompts, before further discussion with members of the research team and re-drafting as appropriate. To explore participants experience of diagnostic disclosure, the girls were asked "Can you tell me a bit about how you found out you had Turner Syndrome?" and their parents/guardians were asked "Can you tell me how you found telling (participant) about the aspects of their condition?". To investigate the experience of disclosure to others, girls were asked "How do you feel talking about your condition to others?".

Data analysis

Data were analysed using IPA in accordance with the steps and procedures outlined by Smith, Flowers and Larkin (2009), before conducting an overarching analysis within each dyad, focusing on the

interactions between participants (Morgan *et al.*, 2015; Van Parys *et al.*, 2017). To ensure concepts and themes were constructed from participants individual perspectives, the transcripts were initially analysed individually. The transcripts were then read and re-read, whilst taking initial notes. Line by line coding was conducted to increase methodological rigour, the initial codes representing different levels of interpretation: descriptive, linguistic and conceptual. Emergent themes were developed, before moving on to the next member of the dyad. Emergent themes were organised into three categories; 'Individual with TS', 'Parent' and 'Both' to reflect whether the interpretations were experienced by individual members of the dyad or both members. Each dyad's emergent themes were finally integrated and analysed across all family units to produce overarching superordinate themes (Van Parys *et al.*, 2017).

We acknowledge the dyadic approach utilised is not typical of IPA, in that researchers would usually seek out a single and reasonably homogenous sample of participants. However, a number of studies have used IPA to explore complex, systemic experiences from multiple perspectives (Burton, Shaw and Gibson, 2015), and a recent article outlines a series of multiple perspective designs and analytic procedures using IPA, which can be adapted and used across diverse populations and settings (Larkin, Shaw and Flowers, 2019). The authors propose dyadic designs in particular are able to maintain a strong idiographic focus, because couples or family members provide us with a coherent and familiar unit of analysis.

Reflexivity

Reflexivity has been established as one of the methods researchers use to ensure rigor, trustworthiness and quality within qualitative research (Dodgson, 2019). The PI therefore maintained reflective notes throughout the data collection, transcription and analysis, with the aim of continually refining the thematic process. The PI was able to revise codes and themes to reflect the experiences and interactions between girls and their parents, until they were an accurate interpretation of the data as a whole. The PI is a female, trainee clinical psychologist and prior to contacting participants that had indicated they would like to take part, she had no relationship with them. She had no prior clinical or research experience of working with females with TS. Her background in clinical psychology training facilitated the interviews and data analysis, given her experience conducting assessments, building relationships with clients, and interpreting and analysing language within sessions.

Two of the five transcripts were separately coded by an independent investigator (trainee clinical psychologist) to reduce researcher bias and improve the quality of the study. We hope the inclusion of an additional investigator's viewpoint improves the credibility of the results, through the process of triangulation; the codes were compared and discussed to reach an agreement, arguably increasing the scope and deepening the understanding of the interpretation (Tracey, 2010).The PI acknowledges that prior to conducting the interviews she expected girls to report negative experiences regarding diagnostic

disclosure. The PI also recognises the influence her own life experiences and position as a clinical psychologist may have had on her interpretation of the data.

Results

Five girls and five parents/guardians completed semi-structured interviews with the PI. Each parent-child dyad was initially interviewed together and then separately, in accordance with the protocol. None of the participants declined the individual interview. Relevant participant characteristics are outlined below in Table 1. Their names are pseudonyms.

Table 1. Characteristics of participants

Participant	**Age (years)**	**Age at diagnosis (years)**	**Age at diagnostic disclosure (years)**	**Parent**
Sarah	16	Birth	There was no one defining moment of diagnostic disclosure; Jack estimated Sarah was around 5 as this was when she began receiving growth hormone injections.	Jack
Mary	17	13	13	Jim
June	21	Birth	Jane estimated around 4 or 5.	Jane
Lisa	17	8	8	Amy
Erin	14	Birth	There was no one defining moment disclosure; neither Erin nor Sue could recall a specific age.	Sue

Three Superordinate and eleven related subthemes were identified; the results are presented in Table 2 below. Each superordinate theme and associated sub-theme are outlined in detail, alongside relevant quotations to illustrate participants' lived experience. As stated, the data were analysed to capture both individual and shared experiences. Therefore, each sub-theme indicates whether it represents the experiences of girls, parents or both members of the dyad. The results have been presented in an integrated manner, in line with each superordinate theme as this was felt to be the most coherent, systematic narrative.

Table 2. Superordinate themes and related subthemes

Theme	**Subtheme**	**Participant (Individual with TS/Parent/Both)***
Communication and support	Disclosure as a process	Both
	The process of acceptance	Both
	Open communication within support systems	Both
Stigmatisation of TS	Avoid diagnostic disclosure	Both
	Infertility; the elephant in the room	Both
	I am not disabled	Individual with TS
	Separation between TS and the self	Both
Psychological consequences	Avoidant coping strategies	Both
	I'm not good enough	Both
	Anxiety and Uncertainty	Both
	Self-fulfilling prophecy	Parent

*Subthemes representing the experiences of individuals with TS, their parents or both members of the dyad.

COMMUNICATION AND SUPPORT

Disclosure as a process

Whilst the two girls diagnosed with TS aged 8 and 13 were informed by a health professional (HP), the parents of girls who were diagnosed at birth (3/5) reported being significantly involved in disclosing the condition to their daughter, and described disclosure as a gradual process over time:

"It was done subtly and naturally all throughout, all throughout her life." (Sue)

Progressively disclosing TS appeared to be a conscious decision, aimed at minimising potential distress, and increasing the likelihood of successful adaptation to the condition. Developmental age and stage were factored into the decision-making process, in relation to when to disclose certain aspects of TS:

"Some parts I suppose we told her at that age and some parts maybe a bit later. I mean with your children, you know infertility, you're not going to tell an eight-year-old everything" (Jack)

4 of the 5 girls could not recall many specific memories around diagnostic disclosure and tended to seek the information from their parents, who in turn, were able to provide much more detailed accounts. The lack of detail could signify that as children, the initial disclosure had minimal impact on their self-concept, whereas for parents, recalling the disclosure appeared to be a much more emotive topic, indicating greater significance. The girls appeared to develop an understanding and attach subsequent meaning to their condition gradually over time:

"[infertility] I think when I was younger it never really mattered, it never really….came to me what it was, em, until I kind of started high school and I realised this is kind of quite a big thing. This could have a big impact on my life." (Lisa)

The process of acceptance

Both the girls and their parents similarly describe coming to terms with the diagnosis as a gradual process over time:

"I'm slowly coming to terms with it." (Sarah)

"You need time to process it yourself…definitely over the years I have gotten into the swing of things." (Mary)

The process of acceptance appeared to be endless, continually challenged by changes in the manifestation of TS, alongside shifts in what the condition means. One parent spoke about the role that the acquisition of knowledge played in accepting her daughter's diagnosis, which could stem from a reduction in uncertainty:

"And then the more you learn about it the more you think, oh, oh right, oh I can deal with that." (Jane)

Lisa and Mary similarly discuss the way in which gathering information helped them understand and accept their diagnosis, which was interpreted as a method of feeling more in control. Lisa notes how the involvement of siblings in care can aid acceptance, possibly indicating a transition from perceiving illness as an individual experience to experiencing illness as a family:

"I think another thing that's really helped me in terms of like advice and the advice I've been given is having [sister] there at the appointments. And she knows so much about it…and like, so like I know I can go to her as well and I know that like…I can come to my mum and because they're just as knowledgeable about it as me whose living it." (Lisa)

Open communication within support systems

A systemic culture of openness within families was described by both girls and their parents, suggesting childhood illness may, at times, bring families closer together:

"I can talk about anything with them, with my turner's syndrome. My family is quite a close family and we all talk." (Sarah)

"We can have –" "Yeah dead kind of frank, honest conversations" "True, me and my mum are dead open with each other." (June and Jane)

Both girls and their parents reflected on their experiences with HP's and 4 out of 5 reported an overall positive experience of diagnostic disclosure and subsequent management TS. Both members of the dyad cited openness and honesty as factors which facilitated a positive experience, signifying the importance of trust within the patient-clinician relationship:

"[consultants] They've never sugar coated anything, em, they've always explained em eh like...if...like everything that was going on, like if my height wasn't going so well or if the injection needed upped or the tablets or if there was something else they wanted to try, the blood tests or everything like that they've been really open and as my mum said from the get go, em, people have been open and honest." (Lisa)

"[nurses name] was fabulous. She was just a very down to earth, caring and quite direct. There was never any kind of like oh shhh shhh or anything, she would have been there having conversations with June and stuff. Direct conversations." (Jane)

STIGMATISATION OF TS

Avoid diagnostic disclosure

Conversely, despite all participants reporting open communication within their immediate families and generally with HP's, both parents and girls described a desire to conceal their diagnosis from others. Girls appeared to be particularly avoidant in discussing their diagnosis with their peers, highlighting possible feelings of shame:

"if the situation arises and they need to know, I'll let them know. But otherwise I do kind of keep it to myself." (June)

The main barrier to diagnostic disclosure for girls was a fear of being treated or perceived differently, suggesting the girls had formed outward identities which could, in some sense, be tarnished by the disclosure of TS. A quote from June has been used to best demonstrate below:

"I'd be worried if once I'd let them know…they'd….they'd treat me in a different way, or something like that eh, [becomes tearful], I don't want people's perceptions of me to be….coloured by this." (June)

It's possible girls are modelling their parents' behaviours; most parents (3/5) subtly encouraged their daughter to hide their diagnosis from others and/or avoided disclosing to others out with the immediate family:

"All turner girls are different but if people are looking at you and just thinking oh you're small or as Lisa says you wear hearing aids or you wear glasses or whatever then just let them accept that, don't, don't give too much information I think to other people unless you know they specifically ask." (Amy)

"I mean, my dad, Erin's granddad doesnae know. We, we, we didn't, we haven't, we've shared it with just us." (Sue)

Infertility; the elephant in the room

Infertility was highlighted as a particularly difficult aspect of TS to disclose or discuss by both members of the dyad, possibly due to infertility being perceived as a more intimate, personal topic, combined with perceived stigma:

"[infertility] Everything else just kind of…leads into like an explanation or something that can be explained but then…I don't really want to talk about that and then….because that feels more personal to me than kind of, the height or the hearing. That kind of feels like…my, my thing almost like that's something that I'm going to need to deal with and like, find ways around so, I would struggle talking about that a wee bit more." (Lisa)

"I still feel uncomfortable….em…talking about things like, like periods and having babies." (Jack)

Infertility was often cited much later during the interviews, after height or other TS-specific difficulties, which could be indicative of subtle avoidance. Surprisingly, three dyads spontaneously reported HP's might also avoid discussing infertility with girls with TS and their families. Although infertility was never kept a secret, the topic was never thoroughly discussed which could similarly reflect underlying stigmatised beliefs:

"It was alluded to in the first appointment." (Jim)

"Nobody's actually ever sat down and had a conversation about it." (Amy)

I am not disabled:

All girls described a fear of being perceived as disabled by others due to TS. Mary discussed this in relation to the minimal impact she feels the diagnosis has had on her life overall:

"it's not something that you can catch, it's not contagious. Um…yeah I've lived with it for eh…my whole life and it never…impacted anything, I was never, you know, unable to do stuff." (Mary)

For Lisa and June, the belief that others may perceive them as disabled led them to overcompensate and strive to 'prove' to others they are able:

"I just kind of wanted to prove that I can….that I'm good at maths and I can do this and I can do that, all the things that I'm not supposed to be able to do." (Lisa)

"because….I wanted to be…the same as everybody else. And to be treated fairly, a level playing field, like I can do it….. because…I just practice and study, practice and practice". (June)

The worry that others may perceive TS as a disability acted as a barrier for Erin to disclose her diagnosis to others:

"[others] thinking I can't do things, because I've got turners syndrome when that's not really the case." (Erin)

Separation between TS and the self:

Both girls and their parents/guardians reported a strong feeling that TS did not define them as an individual, which could be understood as a fight against the diagnosis, or alternatively reflect the minimal impact of TS on the girls identity:

"Feel comfortable knowing that it's just a part of you, it's not kind of all of you, it's just a small, pardon the pun [all laugh] but, eh, it's just a wee bit of you, it's not….all of you." (Lisa)

Sarah relates this to the universality of being a human being:

"like I have turners syndrome but I'm just like….I'm just like them…in that I am a human." (Sarah)

All parents described viewing their daughter as 'more than a syndrome', and during the dyadic interviews this was interpreted as a way of providing reassurance and normalising TS. Jane's quote below best demonstrates this:

"they're not a turner syndrome, they're a girl who happens to have turner syndrome. They're a girl not a syndrome, they're just a girl. Just don't give them a, a something to make them feel they're odd or….you know." (Jane)

In conjunction, both girls and their parents described a sense of separation between the self and TS, possibly to externalise the condition:

"I don't know when it stops being me and kind of more about the condition…so I think with that like, it's trying to disassociate it, like people that I meet from being the condition." (Lisa)

"This is not Sarah; this is the Turner Syndrome." (Jack)

Alongside interpreting certain behaviours or traits as directly related to TS, some parents also described having difficulty differentiating or separating what was TS and what was their daughter's natural temperament:

"We don't, you know, is it turner syndrome? Is this how she would be naturally anyway other than being a bit tall, well nobody can answer that question because you wouldn't know." (Sue)

Interestingly, one parent reflected on the image that is portrayed of girls with TS e.g. on the internet. She talks about the change in society's perception of individuals with Down Syndrome and states she feels there needs to be a similar shift in the way others perceive TS. This could be interpreted as stepping away from a 'medical model' of illness towards an individual difference model of acceptance within society:

"So if you google that you think oh my god is that what's going to happen to my child? I mean what was obviously, that was how it was back then, whereas I just think it could be….yeah overhauled and modernised and….a fresher look because there's probably loads of girls that look like Erin you know… I just think…a wee overhaul and let's not hang on to it…like a badge." (Sue)

PSYCHOLOGICAL CONSEQUENCES

Avoidant coping strategies

A variety of individual coping strategies were discussed throughout the interviews, however using avoidance to cope with TS was a common subtheme across both the girls and parents' experiences. 4 out of the 5 dyads described feeling 'lucky'; either because they had developed few TS-related physical health difficulties or generally believing TS had not significantly impacted on everyday life:

"I think I'm lucky that I've no had any of the major health complications, you know, kidney problems or heart problems, all that stuff." (June)

"We feel very very lucky it's affected her so little." (Jim)

Perceiving themselves as 'lucky' appeared to reflect an underlying hierarchy of illness e.g. I have 'mild' TS in comparison to others, which could be a strategy to distance themselves and avoid feeling like they belonged to a TS group. 4 out of the 5 dyads tended to minimise any difficulties:

"It's not a big deal, it's just em…yeah something I've lived with my entire life and knowing hasn't really changed that much, so yeah." (Mary)

"Lisa has been very fortunate with it, it was a tiny tiny mosaic on you know once of her chromosomes, it wasn't as if it was like really bad." (Amy)

June describes a lack of romantic relationships and initially expresses worry that a potential partner may reject her because of her TS. However, she appears to then immediately downplay this by stating:

"like I said, maybe a wee bit bothered but not overly bothered. Because….if I meet someone, I meet someone, all good. If I don't, I don't. It doesn't really matter." (June)

Sue describes deliberately concealing her daughter's diagnosis from her teachers, to wait and see if they notice she has TS. Her teachers did not report any concerns which Sue appears to interpret as 'if you can't see it, it doesn't exist':

"as I say, I put that to the test to the school, for to them to tell me, you tell me there's something wrong, and that's again why I didn't tell my mum and dad at the time, and now just my dad obviously, em. You tell me, that's what I was always waiting on, you tell me. And nobody's ever told me. So." (Sue)

Jane similarly seemed to minimise June's difficulties during the dyadic interview, however when interviewed alone she wonders whether her daughter uses avoidance to protect her:

"Aye she appears to be content but June will…June will tell you what she thinks you want to hear a wee bit. And she'll say that everything's fine, she'll say that's fine, but she'll no want me to worry, she might be doing it to protect me." (Jane)

It is possible both girls and their parents minimise any difficulties to protect the other from distress, resulting in a cycle of avoidance.

I'm not good enough

Several psychological consequences were described in relation to TS. Four dyads reported TS has had a negative impact on the girl's confidence and self-esteem:

"Maybe I would have slightly more confidence. Some days I feel self-conscious and just generally….a bit rubbish about having turners syndrome." (Sarah)

"Sarah's very insecure. She lacks confidence." (Jack)

Low confidence and/or low self-esteem appeared to be exacerbated by the tendency to compare oneself to others:

"I think I would have had a slightly different outlook on like...the way I've grown up and stuff and the comparison that I make of myself to others." (Sarah)

"She compares herself to other folk, like I should be doing this or be the same as him or her or you know I should be at that level." (Jane)

Jack similarly agreed and noted how although comparing yourself to your peers may be typical of adolescents, feeling different from your peers due to TS may intensify negative comparisons:

"and how she feels, the difference between her and her peers, I can see how much more serious that would be than with another child who didn't have TS." (Jack)

Several parents (3/5) describe their daughter developing perfectionistic traits, perhaps to compensate for negative self-beliefs around not being good enough:

"June's dead cautious and likes to do everything right, doesn't like making mistakes and stuff." (Jane)

Anxiety and Uncertainty

Several girls (Mary, June and Lisa) spoke about experiencing anxiety and engaging in unhelpful thinking patterns such as rumination, in relation to TS and the associated health difficulties and generally across day to day life:

"Every time I went to one [appointment] before, especially endocrine, I just got myself into a big panic and that and…I just, it wasn't a nice feeling." (Lisa)

Their anxiety was observed and confirmed by their parents:

"I used to feel sorry for the wee soul because she used to get quite, quite upset going to clinics. She thought something you know bad was going to happen to her so you know, something sore or something, and eh, we would have this talk in the car coming on the day getting ready to go, because I used to no tell her like, until that day because I didn't want to worry her, because she worries, she's stressy." (Jane)

TS appeared to generate a great deal of uncertainty for families. The variety in clinical manifestations, the unpredictable nature of how the condition develops over time and uncertainty for the future lead to difficulties for both girls and their parents:

"It's kind of this…unknown kind of thing and nobody was kind of sure what was going to happen with it or what sort of things I would have with it." (Lisa)

"Again, it was the uncertainty of 'there might be' sort of thing, there might be a problem." (Jim)

Worries about their daughters' future were particularly evident in parents' experiences. These concerns became more apparent during the parent's individual interviews, further emphasising the desire to minimise difficulties or worries in front of their daughter, to shield them from distress:

"What we do think about is obviously will it…affect her more, in later life?" (Jim)

Self-fulfilling prophecy

As well as making comparisons to others, three parents (Jane, Amy and Sue) talked about the idea of a 'self-fulfilling prophecy' whereby their daughters have been informed girls with TS can have difficulties e.g. with math or co-ordination and these beliefs manifest in real-time problems. The quote below from Amy clearly illustrates this:

"I think the problem she did have at the beginning when Dr Smith said girls can have problems obviously with maths, with em, coordination, differences like that, pointed out she could have but I think she took it in her head that this is something that she is going to have problems with." (Amy)

Experiencing TS-related difficulties may further serve to maintain beliefs around not being good enough.

Discussion

The current study investigated the experience of having TS, specifically focusing on the nature of disclosure and the impact of the condition on girls and their families. It explored these experiences from the perspective of both adolescent girls and one of their parents/guardians. The analysis revealed three key themes; the findings are discussed below in relation to the current literature, considered in light of limitations as well as implications for clinical practice and future research.

Communication and Support

Consistent with previous qualitative research exploring disclosure in children with genetic conditions (Gallo, Angst and Knafl, 2009), parents described disclosing TS to their children as a gradual process, dependent on developmental age and stage. The present findings are consistent with cross-sectional research indicating in addition to emotional maturity, age acted as a key factor which influenced when parents would choose to discuss infertility with their daughters with TS (King *et al.*, 2016).

Conducting joint interviews appeared to be particularly important in developing an accurate, comprehensive narrative around diagnostic disclosure and revealed differences in the emotional impact of receiving the initial diagnosis. The girls recalled few memories around diagnostic disclosure, frequently turning to their parents for detail, and in turn parents were able to expand upon the topic, often reporting significant distress and feelings of shock following diagnostic disclosure.

Gradual disclosure appeared to be used as a strategy to facilitate acceptance of the diagnosis, alongside the acquisition of knowledge and a shift towards experiencing illness as a family rather than an individual. Overall, 3 out of the 5 dyads expressed the belief that TS did not currently significantly impact upon their day to day life. Due to the wide variability in clinical manifestations, it could be the case that these girls suffer from fewer TS-related health difficulties and families have therefore adapted well to living with a health condition. The culture of openness and honesty described within family and wider support systems may have also facilitated successful adjustment to TS; Robinson (2017) notes having an open support system and being able to 'share the experience' helps both individuals and their families

successfully manage chronic illness. There did not appear to be a finite end to the process of acceptance, which may reflect the way in which TS can continually change and develop across the lifespan.

In contrast to previous research (Sutton *et al.*, 2006), none of the girls reported perceived secret-keeping in relation to their diagnosis from either their parents or HP's; a culture of openness and closeness between parents and children was reported by all five dyads. Moreover, 4 out of the 5 dyads reported a positive disclosure experience, citing honesty and openness as key contributing characteristics. These findings may reflect positive changes in the way clinicians and parents have approached the disclosure of TS over the last two decades. The results are consistent with recent guidance produced for the successful lifelong management of females with TS, which emphasises the importance of open and truthful communication from HP's (Turner and Hozjan, 2019).

Stigmatisation of TS

Conversely, both girls and their parents expressed a desire to conceal the TS diagnosis from others, which could be indicative of perceived or experienced stigma in relation to TS. In conjunction with qualitative research exploring the experiences of adolescents with visible and invisible chronic illness (Kaushansky *et al.*, 2017), girls discussed the particular challenges around disclosure to peers. Kaushansky *et al.* (2017) identified perceived fear of rejection, pity and fear of being perceived as vulnerable or different as key barriers to disclosure; these results are strikingly similar to barriers to disclosure cited in the current study, consistent with the sub-theme 'I am not disabled'.

A distinction can be made between perceived or anticipated stigma and experienced or 'felt' stigma. Anticipated stigma refers to the degree to which individuals expect others will discriminate or reject them if they disclose a 'stigmatised identity', such as an illness or disability (Quinn and Chaudoir, 2009). This may be particularly relevant for individuals whose condition or illness is invisible, as unlike those with a visible illness they may not know how someone will react when they disclose. Although girls with TS are small in stature, many of the girls and parents referred to height as being the 'only' visible characteristic of TS and therefore, for some, TS could be defined as an invisible illness. It could be the case that perceived or anticipated stigma is more prevalent in girls with TS rather than actual experienced stigma; only one of the dyads reported experiencing discrimination or teasing as a result of having TS.

Consistent with previous literature (Sutton *et al.*, 2006), infertility was described as being particularly difficult to discuss/disclose. A subtle avoidance of infertility was also evident during the interviews. Surprisingly, 3 of the 5 dyads reported HP's showed signs of avoidance in relation to infertility. HP's hesitation around discussing infertility could reflect underlying beliefs that infertility is shameful or taboo, thereby acting as a predisposing factor for families to form stigmatised beliefs. These findings are consistent with literature describing the social stigma (Ergin *et al.*, 2018) and 'secret stigma' (Whiteford and Gonzalez, 1995) accompanying infertility.

A distinct sub-theme representing the experience of girls with TS demonstrated that they did not want to be perceived as having a disability, which could be linked to the perceived negative connotations around disability. Sociological research around disability stigma suggests historically, disability has been seen as a form of involuntary social deviance, signified by physical differences, which generates negative responses from others (Grue, 2016). It could be the case that although the girls do not perceive themselves as being disabled, they worry others will attach this label, should they disclose TS. The determination expressed by a few of the girls to 'prove' they are able or intelligent could also be interpreted as a desire for normalcy; previous research has suggested young people diagnosed with a chronic illness can feel different from their peers and therefore strive to present themselves as 'normal' to protect or reinforce a nondifferent identity (Benson *et al.*, 2015).

The stigmatisation of TS may coincide with both the girls' and parents' tendency to view the diagnosis as part of their self-identity but in no way the whole of oneself. Perceptions of stigma due to illness can significantly affect individuals identity and sense of self (Kleinman, 1988). The girls and their parents could be, in some sense, compartmentalising or externalising the diagnosis, as a way of protecting the girl's nondifference identity. The extent to which individuals felt TS was separate from their self-concept seemed to vary, reflecting differences in the perceived impact of the condition. Therefore, it could also be the case that girls who are not significantly impacted, view TS as less meaningful and less integral to their sense of self.

Psychological consequences

Although 3 out of the 5 families reported little impact of TS on their lives, the majority of dyads seemed to minimise TS-related difficulties, often through the perception they were 'lucky' in comparison to other girls with TS. Minimising their difficulties was initially interpreted as an avoidant method of coping. Avoidance has similarly been highlighted as a common coping strategy used by adolescents with a range of health conditions such as diabetes (Iturralde, Weissberg-Benchell and Hood, 2017), asthma and celiac disease (Oppenheimer *et al.*, 2018). Avoidant coping may relate to the previously described normalcy theory; minimising difficulties alongside concealment of the diagnosis could facilitate the compartmentalisation of TS as separate from the self, in the pursuit to feel 'normal'. However, the researcher recognises that the 'Avoidant coping strategies' subtheme could reflect an underlying bias, stemming from her own life experiences and experience as a trainee clinical psychologist. She acknowledges she has an awareness of the potential impact of physical health difficulties on well-being and therefore viewed participants as having existing underlying difficulties which were minimised during the interviews. These beliefs could reflect a 'medical model' of disability, and she noted she felt hesitant to include this subtheme, for fear of offending the participants. An alternative interpretation could suggest that both girls and their parents genuinely do not perceive TS significantly impacts their daily lives, either

due to having few TS-related health difficulties or having formed adaptive, 'strength-based' cultures within their family units.

Consistent with previous research (Liedmeier *et al.*, 2020), several girls reported anxiety and/or perceived a negative impact of TS on their confidence and self-esteem. Interviewing dyads jointly helped to provide a deeper level of understanding around this topic; when the girls described not feeling good enough, their parents often expanded the interpretation. For example, parents subsequently described their daughters developing perfectionistic traits to compensate for negative self-beliefs, alongside the idea of a self-fulfilling prophecy. If the girls have a belief or expectation they will struggle or fail e.g. at math and these beliefs manifest in real problems, this could further compound the idea they are not good enough.

In line with prior research around uncertainty due to illness (Mishel, 1988; Brown and de Graaf, 2013), the wide spectrum in disease severity and unpredictable nature of how TS develops over time appeared to generate a great deal of uncertainty for families. Uncertainty about their daughter's future and general concerns around TS became particularly apparent during parent's individual interviews. The inclusion of both individual and joint interviews highlighted a circular pattern of protection between dyads; however, this was particularly evident in parents. It could be the case parents felt if they expressed concerns about the future this would exacerbate their daughter's anxiety or fear of being different to others, and therefore they especially minimise difficulties in their daughters presence as a method of protection.

Limitations

We recognise this study included a wide age range of participants with TS; TS is a rare condition and therefore the sample population in which to recruit from was relatively small. Although this study aimed to recruit a homogeneous sample, the age at which girls had been diagnosed with TS varied amongst participants, which may have impacted upon their accounts. Differences in the experience of disclosure were highlighted between girls diagnosed at birth and girls diagnosed in later childhood/adolescence, and this may also impact upon other areas of life. Reimann *et al.* (2018) found receiving a TS diagnosis over the age of 13 could contribute to adverse outcomes relating to lack of perceived competence and depression.

Moreover, the families who volunteered to take part did so in the knowledge they would be asked to discuss the topic of disclosure together. The sample may therefore be biased towards families who have an existing culture of openness around the topic of disclosure. Individuals with poor or no relationships with their parents may also have been reluctant to take part. Lastly, we excluded participants with a significant LD; it is possible individuals with an LD and their parents may feel TS has had a much greater impact on their day to day lives.

Implications for clinical practice

The results indicate HP's should ensure they initiate explicit discussions around infertility with girls and their parents. HP's may wish to reflect upon their own beliefs around fertility and their role in relieving patients of perceived stigma in relation to infertility; some researchers suggest clinicians have a duty to protect and counteract harm done to patients due to infertility stigma (Cook and Dickens, 2014). A question arises around whose responsibility it is to inform girls of the fertility difficulties associated with TS, be that clinicians or parents. It could be helpful for clinicians to raise this topic with parents, to agree upon how to navigate the disclosure of infertility and encourage parents to utilise a 'drip feed' approach. A similarly gradual process of disclosing infertility to girls may facilitate successful adaptation.

Understanding the positive impact of open, honest communication within family systems and wider support systems highlights the importance of establishing this approach from initial diagnosis, to build an effective foundation for continued care and management of TS. Girls and their parents might minimise TS-related difficulties, which could arguably act as a barrier to help-seeking behaviours; if families wish to portray a 'normal' identity they may be less likely to engage with services or seek support. Consistent with current guidelines, this study recommends clinicians continually assess and monitor mood and psychosocial functioning and encourage girls and their parents to seek and utilise additional supports when necessary.

This study may also have wider implications around how society view's TS and difference, suggesting that stepping away from a 'medical model' to a 'strength-based model' or model of individual differences could benefit girls and their families. Perhaps viewing TS as a neutral difference rather than a negative abnormality which needs to be 'fixed', would also facilitate successful adjustment and minimise the impact of TS, as observed in the current study.

Implications for future research

When considering disclosure in future research, comparisons between girls diagnosed at birth and girls diagnosed in later childhood/adolescence may be helpful, as this likely impacts upon girls and their family's experiences. Further research around how to enable disclosure of TS to others may help to inform future care guidelines; the inclusion of advice around how to disclose TS to others could thus become a standard element of TS management. Moreover, future research exploring clinicians' perceived barriers to discussing infertility may provide further insights into infertility stigma and provide recommendations around how clinicians can manage this.

This study highlights acceptance of TS as a process and therefore additional research to specifically examine this process could provide insight into factors which facilitate or hinder successful acceptance and adaptation as a family. Considering the differences in how TS can impact upon individuals and families, further research exploring how clinicians can assess the level of adjustment in girls and their families may be of use. Although the current study provides useful insight into the impact of TS on girls'

identity and sense of self, future research to fully explore the effect of TS on identity in both adolescents and adult women with TS may be helpful.

Conclusions

This research has provided an in-depth account of the experience of diagnostic disclosure and the tendency to avoid disclosure to others, from the perspectives of girls with TS and their parents/guardians. The study has also highlighted variations in the level of impact of TS across families. Recommendations for clinical practice include explicitly discussing infertility with girls and their families and emphasising the importance of open, honest communication. Future research to further explore how to enable girls to disclose their diagnosis to others may be of use.

References

Akeson, N., Worth, A. and Sheikh, A. (2007) 'The psychosocial impact of anaphylaxis on young people and their parents', *Clinical & Experimental Allergy*, 37(8), pp. 1213–1220. doi: 10.1111/j.1365-2222.2007.02758.x.

Apperley, L. *et al.* (2018) 'Mode of clinical presentation and delayed diagnosis of Turner syndrome: a single Centre UK study', *International Journal of Pediatric Endocrinology*, 2018(1), p. 4. doi: 10.1186/s13633-018-0058-1.

Barlow, J. H. and Ellard, D. R. (2006) 'The psychosocial well-being of children with chronic disease, their parents and siblings: An overview of the research evidence base', *Child: Care, Health and Development*, pp. 19–31. doi: 10.1111/j.1365-2214.2006.00591.x.

Benson, A. *et al.* (2015) '"I don't want them to look at me and think of my illness, I just want them to look at me and see me": Child perspectives on the challenges associated with disclosing an epilepsy diagnosis to others', *Epilepsy and Behavior*, 53, pp. 83–91. doi: 10.1016/j.yebeh.2015.09.026.

Bluebond-Langner, M. *et al.* (2007) 'Understanding Parents' Approaches to Care and Treatment of Children With Cancer When Standard Therapy Has Failed', *Journal of Clinical Oncology*, 25(17), pp. 2414–2419. doi: 10.1200/JCO.2006.08.7759.

Bluebond-Langner, M., Belasco, J. B. and DeMesquita Wander, M. (2010) '"I Want to Live, Until I don't Want to Live Anymore": Involving Children With Life-Threatening and Life-Shortening Illnesses in Decision Making About Care and Treatment', *Nursing Clinics of North America*, 45(3), pp. 329–343. doi: 10.1016/j.cnur.2010.03.004.

Bogdan, R. and Taylor, S. . (1975) *Introduction to qualitative research methods.* New York: John Wiley.

Brocki, J. M. and Wearden, A. J. (2006) 'A critical evaluation of the use of interpretative phenomenological analysis (IPA) in health psychology', *Psychology & Health*, 21(1), pp. 87–108. doi: 10.1080/14768320500230185.

Brown, P. and de Graaf, S. (2013) 'Considering a future which may not exist: the construction of time and expectations amidst advanced-stage cancer', *Health, Risk and Society*, 15(6–7), pp. 543–560. doi: 10.1080/13698575.2013.830081.

Burton, A.E. Shaw, R.L. and Gibson, J.M. (2015) 'Living together with age-related macular degeneration: an interpretative phenomenological analysis of sense-making within a dyadic relationship', *Journal of Health Psychology*, 20(10), pp. 1285–95. doi:10.1177/1359105313511134

Cook, R. J. and Dickens, B. M. (2014) 'Reducing stigma in reproductive health', *International Journal of*

Gynecology & Obstetrics, 125(1), pp. 89–92. doi: 10.1016/j.ijgo.2014.01.002.

Corbin, J. and Morse, J. M. (2003) 'The Unstructured Interactive Interview: Issues of Reciprocity and Risks when Dealing with Sensitive Topics', *Qualitative Inquiry*, 9(3), pp. 335–354. doi: 10.1177/1077800403009003001.

Davies, R., Davis, B. and Sibert, J. (2003) 'Parents' stories of sensitive and insensitive care by paediatricians in the time leading up to and including diagnostic disclosure of a life-limiting condition in their child', *Child: Care, Health and Development*, 29(1), pp. 77–82. doi: 10.1046/j.1365-2214.2003.00316.x.

Dodgson, J. E. (2019) 'Reflexivity in Qualitative Research', *Journal of Human Lactation*, 35(2), pp. 220–222. doi: 10.1177/0890334419830990.

Ergin, R. N. *et al.* (2018) 'Social stigma and familial attitudes related to infertility', *Turk Jinekoloji ve Obstetrik Dernegi Dergisi*, 15(1), pp. 46–49. doi: 10.4274/tjod.04307.

Gaff, C. L. and Bylund, C. L. (2010) *Family communication about genetics : theory and practice*. Oxford University Press.

Gallo, A. M., Angst, D. B. and Knafl, K. A. (2009) 'Disclosure of genetic information within families', *American Journal of Nursing*, 109(4), pp. 65–69. doi: 10.1097/01.NAJ.0000348607.31983.6e.

Gravholt, C. H. *et al.* (2003) 'Increased fracture rates in Turner's syndrome: a nationwide questionnaire survey', *Clinical Endocrinology*, 59(1), pp. 89–96. doi: 10.1046/j.1365-2265.2003.01807.x.

Grue, J. (2016) 'The social meaning of disability: a reflection on categorisation, stigma and identity', *Sociology of Health & Illness*, 38(6), pp. 957–964. doi: 10.1111/1467-9566.12417.

Hall, J. G. and Gilchrist, D. M. (1990) 'Turner syndrome and its variants', *Pediatric Clinics of North America*, 37(6), pp. 1421–1440. doi: 10.1016/S0031-3955(16)37018-3.

Humphrey, Neil and Lewis, S. (2008) '"Make me normal" The views and experiences of pupils on the autistic spectrum in mainstream secondary schools'. doi: 10.1177/1362361307085267.

Iturralde, E., Weissberg-Benchell, J. and Hood, K. K. (2017) 'Avoidant coping and diabetes-related distress: Pathways to adolescents' type 1 diabetes outcomes', *Health Psychology*, 36(3), pp. 236–244. doi: 10.1037/hea0000445.

Kaushansky, D. *et al.* (2017) 'Living a secret: Disclosure among adolescents and young adults with chronic illnesses.', *Chronic illness*, 13(1), pp. 49–61. doi: 10.1177/1742395316655855.

King, J. E. *et al.* (2016) 'Barriers in communication and available resources to facilitate conversation

about infertility with girls diagnosed with Turner syndrome', *Journal of Pediatric Endocrinology and Metabolism*, 29(2), pp. 185–191. doi: 10.1515/jpem-2015-0135.

Kitzinger, J. (1995) 'Qualitative research. Introducing focus groups.', *BMJ (Clinical research ed.)*, 311(7000), pp. 299–302. doi: 10.1136/BMJ.311.7000.299.

Kleinman, A. (1988) *The illness narratives: suffering, healing, & the human condition.* New York: Basic Books.

Larkin, M. Shaw, R. and Flowers, P. (2019) 'Multiperspectival designs and processes in interpretative phenomenological analysis research', *Qualitative Research in Psychology,* 16(2), pp. 182-198. doi: 10.1080/14780887.2018.1540655

Liedmeier, A. *et al.* (2020) 'Psychosocial well-being and quality of life in women with Turner syndrome', *Psychoneuroendocrinology*, 113. doi: 10.1016/j.psyneuen.2019.104548.

Mack, J. W. *et al.* (2006) 'Communication About Prognosis Between Parents and Physicians of Children With Cancer: Parent Preferences and the Impact of Prognostic Information', *Journal of Clinical Oncology*, 24(33), pp. 5265–5270. doi: 10.1200/JCO.2006.06.5326.

Maxted, C., Simpson, J. and Weatherhead, S. (2014) 'An Exploration of the Experience of Huntington's Disease in Family Dyads: An Interpretative Phenomenological Analysis', *Journal of Genetic Counseling*, 23(3), pp. 339–349. doi: 10.1007/s10897-013-9666-3.

Metcalfe, A. *et al.* (2008) 'Family communication between children and their parents about inherited genetic conditions: a meta-synthesis of the research', *European Journal of Human Genetics*, 16, pp. 1193–1200. doi: 10.1038/ejhg.2008.84.

Michaud, P.-A. *et al.* (2009) 'To Say or Not to Say: A Qualitative Study on the Disclosure of Their Condition by Human Immunodeficiency Virus–Positive Adolescents', *Journal of Adolescent Health*, 44(4), pp. 356–362. doi: 10.1016/J.JADOHEALTH.2008.08.004.

Mishel, M. H. (1988) 'Uncertainty in Illness', *Image: the Journal of Nursing Scholarship*, 20(4), pp. 225–232. doi: 10.1111/j.1547-5069.1988.tb00082.x.

Morgan, D. L. *et al.* (2015) 'Dyadic Interviews as a Tool for Qualitative Evaluation', *American Journal of Evaluation*, 37(1). doi: 10.1177/1098214015611244.

Morris, S. M. (2001) 'Joint and Individual Interviewing in the Context of Cancer', *Qualitative Health Research*, 11(4), pp. 553–567. doi: 10.1177/104973201129119208.

Oppenheimer, S. *et al.* (2018) 'The impact of coping patterns and chronic health conditions on health-related quality of life among children and adolescents', *European Journal of Pediatrics*, 177(6), pp. 935–

943. doi: 10.1007/s00431-018-3146-6.

Van Parys, H. *et al.* (2017) 'Multi family member interview studies: a focus on data analysis', *Journal of Family Therapy*, 39(3), pp. 386–401. doi: 10.1111/1467-6427.12169.

Quinn, D. M. and Chaudoir, S. R. (2009) 'Living With a Concealable Stigmatized Identity: The Impact of Anticipated Stigma, Centrality, Salience, and Cultural Stigma on Psychological Distress and Health', *Journal of Personality and Social Psychology*, 97(4), pp. 634–651. doi: 10.1037/a0015815.

Reimann, G. E. *et al.* (2018) 'Psychosocial Characteristics of Women with a Delayed Diagnosis of Turner Syndrome', *The Journal of Pediatrics*, 199, pp. 206–211. doi: 10.1016/j.jpeds.2018.03.058.

Robinson, C. A. (2017) 'Families Living Well With Chronic Illness: The Healing Process of Moving On.', *Qualitative health research*, 27(4), pp. 447–461. doi: 10.1177/1049732316675590.

Sisk, B. A. *et al.* (2016) 'Prognostic Disclosures to Children: A Historical Perspective.', *Pediatrics*, 138(3), p. e20161278. doi: 10.1542/peds.2016-1278.

Smith, J. A., Flowers, P. and Larkin, M. (2009) *'Interpretative phenomenological analysis: Theory, method and research.'* Thousand Oaks, CA: Sage Publications Inc., (January), pp. 225.

Stein, A. *et al.* (2019) 'Communication with children and adolescents about the diagnosis of their own life-threatening condition', *The Lancet*, pp. 1150–1163. doi: 10.1016/S0140-6736(18)33201-X.

Stochholm, K. *et al.* (2006) 'Prevalence, Incidence, Diagnostic Delay, and Mortality in Turner Syndrome', *The Journal of Clinical Endocrinology & Metabolism*, 91(10), pp. 3897–3902. doi: 10.1210/jc.2006-0558.

Sutton, E. J. *et al.* (2005) 'Turner syndrome: Four challenges across the lifespan', *American Journal of Medical Genetics Part A*, 139A(2), pp. 57–66. doi: 10.1002/ajmg.a.30911.

Sutton, E. J. *et al.* (2006) 'Truth-telling and Turner Syndrome: The Importance of Diagnostic Disclosure', *The Journal of Pediatrics*, 148(1), pp. 102–107. doi: 10.1016/J.JPEDS.2005.08.022.

Tracy, S. J. (2010) *'Qualitative quality: Eight "big-tent" criteria for excellent qualitative research. Qualitative Inquiry*', 16, pp. 837–851. doi:10.1177/1077800410383121

Turner, H. E. and Hozjan, I. R. (2019) 'Diagnosis and Management of Turner Syndrome in Children and Adults', in *Advanced Practice in Endocrinology Nursing*, pp. 771–801. doi: 10.1007/978-3-319-99817-6_40.

Watts, R. *et al.* (2014) 'Family-centered care for hospitalized children aged 0-12 years: a systematic review of qualitative studies', *JBI Database of Systematic Reviews and Implementation Reports*, 12(7),

pp. 204–283. doi: 10.11124/jbisrir-2014-1683.

Whiteford, L. M. and Gonzalez, L. (1995) ‘Stigma: The hidden burden of infertility’, *Social Science and Medicine*, 40(1), pp. 27–36. doi: 10.1016/0277-9536(94)00124-C.

Appendices

Appendix 1.1 Guidelines for submission to the British Journal of Health Psychology

Title Page

You may like to use **this template** for your title page. The title page should contain**:**

- A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's best practice SEO tips);
- A short running title of less than 40 characters;
- The full names of the authors;
- The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- Abstract;
- Keywords;
- Data availability statement (see Data Sharing and Data Accessibility Policy);
- Acknowledgments.

Authorship

Please refer to the journal's Authorship policy in the Editorial Policies and Ethical Considerations section for details on author listing eligibility. When entering the author names into Editorial Manager, the corresponding author will be asked to provide a CRediT contributor role to classify the role that each author played in creating the manuscript. Please see the **Project CRediT** website for a list of roles.

Abstract

For articles containing original scientific research, a structured abstract of up to 250 words should be included with the headings: Objectives, Design, Methods, Results, Conclusions. Review articles should use these headings: Purpose, Methods, Results, Conclusions. As the abstract is often the most widely visible part of your paper, it is important that it conveys succinctly all the most important features of your study. You can save words by writing short, direct sentences. Helpful hints about writing the conclusions to abstracts can be found **here**.

Keywords

Please provide appropriate keywords.

Acknowledgments

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Statement of Contribution

All authors are required to provide a clear summary of 'what is already known on this subject?' and 'what does this study add?'. Authors should identify existing research knowledge relating to the specific research question and give a summary of the new knowledge added by your study. Under each of these headings, please provide 2-3 (maximum) clear outcome statements (not process statements of what the paper does); the statements for 'what does this study add?' should be presented as bullet points of no more than 100 characters each. The Statement of Contribution should be a separate file.

Main Text File

As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

- Title

- Main text
- References
- Tables and figures (each complete with title and footnotes)
- Appendices (if relevant)

Supporting information should be supplied as separate files. Tables and figures can be included at the end of the main document or attached as separate files but they must be mentioned in the text.

- As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors. Please do not mention the authors' names or affiliations and always refer to any previous work in the third person.
- The journal uses British spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References

References should be prepared according to the *Publication Manual of the American Psychological Association* (6th edition). This means in text citations should follow the author-date method whereby the author's last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page 1, and a DOI should be provided for all references where available.

For more information about APA referencing style, please refer to the **APA FAQ**.

Reference examples follow:

Journal article

Beers, S. R. , & De Bellis, M. D. (2002). Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. *The American Journal of Psychiatry*, *159*, 483–486. doi:**10.1176/appi.ajp.159.3.483**

Book

Bradley-Johnson, S. (1994). *Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school* (2nd ed.). Austin, TX: Pro-ed.

Internet Document

Norton, R. (2006, November 4). How to train a cat to operate a light switch [Video file]. Retrieved from **http://www.youtube.com/watch?v=Vja83KLQXZs**

Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

Click here for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the more detailed post-acceptance figure requirements.

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

Colour figures. Figures submitted in colour may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and white. If an author would prefer to have figures printed in colour in hard copies of the journal, a fee will be charged by the Publisher.

Appendix 1.2 Example of Full Search Strategy

Exact subheadings and search terms varied slightly dependent on the Database; however, the table below provides an example.

Database: Ovid Embase and Medline	
S1	Exp “Turner Syndrome” / all subheadings
S2	Exp “sex chromosome abnormalities” / all subheadings
S3	((Turner* ADJ1 Syndrome*) or Bonnevie Ullrich* or Gonadal Dysgenes* or Monosomy* or (Ullrich* ADJ1 Turner*)).ti,ab
S4	S1 or S2 or S3
S5	Exp “Growth Hormone” / all subheadings
S6	Exp “Human Growth Hormone” / all subheadings
S7	(Growth Hormone* OR Somatropin* OR Somatotrop* OR Genotropin* OR Humatrope* OR Norditropin* OR Saizen* OR Zomacton* OR Nutropin* OR Omnitrop* OR Maxomat* OR Serostim* OR Cryo Tropin* OR Umatrope* OR Norditropin* hGH or rhGH).ti,ab
S8	S5 or S6 or S7
S9	Exp “Quality of life* or “Surveys and Questionnaires” or “Health status” or “Health status indicators” or “Activities of daily living” or “Health surveys” or “Quality adjusted life years” or “Treatment outcome” or “Psychometrics” / all subheadings
S10	(Quality of life* or Life quality* or personal satisfact* or patient satisfact* or Happ* or self-concept* or Short form 36 or SF-36 or SF36 or QOL or Short form 12 or SF-12 or SF12 or HRQL or HRQOL or Euroqol or EQ-5D or Quality adjusted life year* or Quality of Wellbeing Index* or QALY or Health Utilities Index or Health stat* or Medical Outcomes Survey or (MOS)or Rosser or Health year equivalent* or HYE* or Ultilit* or Wellbeing* or Well being).ti,ab.
S11	S9 or S10
S12	Exp “Psychology” / all subheadings
S13	(Psycholog* OR Psychosocial OR Outcome*).ti,ab.
S14	S12 or 13
S15	Exp “Adaptation Psychological” OR “Emotional Adjustment” OR “Social Adjustment” / all subheadings
S16	(Adapt* OR Adjust* OR Behavio?r* OR Cope* OR Coping* OR Function* OR Emotion*).ti,ab.
S17	S15 or 16
S18	Exp “Mental Disorders” OR “Behavioral Symptoms” OR “Mental Health” / all subheadings
S19	(Mood* OR Depress* OR Anxiet* OR Distress* OR Well-being* OR Wellbeing* OR Affect* Mental Health* OR Mental Disorder* OR Anxious* OR Mental Disease*).ti,ab.

S20	S18 or 19
S21	S11 or S14 or S17 or S20
S22	S3 AND S6 AND S21

Appendix 1.3 Data Extraction Sheet

Systematic Review

Turner Syndrome, Growth Hormone Therapy and Psychological Outcomes

Data Extraction Sheet[1]

Title:				
Authors:				
Journal:				**Year**:
Keywords:				
Aims:				
Study Design:				
Randomisation:				
Blinding:				

Sample:

N:	**Mean age**:	**Country**:	**Gender:**	**Ethnicity:**
Sample:		**Control Group:**		
		Number of Controls:		
Inclusion criteria:				
Exclusion criteria:				

Measures:

Psychological outcomes:
What was measured? (Constructs):
Instrument:
(1) Self-administered or (2) Experimenter Administered?:
More than one psychological outcome measured:
What was measured? (Constructs):
Instrument:
(1) Self-administered or (2) Experimenter Administered?:
Other measures e.g. height:

Interventions:

What kind of growth hormone intervention did patients receive?:
Intervention: e.g. rhGH or hGH:
What was the dosage?:
For how long?:

Results:

Main findings:

[1] Do not leave any blank space. If it is not applicable, write "N/A". If there is no comment, write "None".

Follow up duration:
Author's Interpretations:
Author's Limitations:
Reviewers' Limitations:

Other comments:

Appendix 1.4 Quality Appraisal Tool

Crowe Critical Appraisal Tool (CCAT) Form (v1.4)

Reference | Reviewer

This form must be used in conjunction with the CCAT User Guide (v1.4); otherwise validity and reliability may be severely compromised.

Citation	
	Year

Research design (add if not listed)

Not research		Article | Editorial | Report | Opinion | Guideline | Pamphlet | …
Historical		…
Qualitative		Narrative | Phenomenology | Ethnography | Grounded theory | Narrative case study | …
Descriptive,		A. Cross-sectional | Longitudinal | Retrospective | Prospective | Correlational | Predictive | …
Exploratory,		
Observational		B. Cohort | Case-control | Survey | Developmental | Normative | Case study | …
Experimental	True experiment	Pre-test/post-test control group | Solomon four-group | Post-test only control group | Randomised two-factor | Placebo controlled trial | …
	Quasi-experiment	Post-test only | Non-equivalent control group | Counter balanced *(cross-over)* | Multiple time series | Separate sample pre-test post-test [no Control] [Control] | …
	Single system	One-shot experimental *(case study)* | Simple time series | One group pre-test/post-test | Interactive | Multiple baseline | Within subjects *(Equivalent time, repeated measures, multiple treatment)* | …
Mixed Methods		Action research | Sequential | Concurrent | Transformative | …
Synthesis		Systematic review | Critical review | Thematic synthesis | Meta-ethnography | Narrative synthesis | …
Other		…

Variables and analysis

Intervention(s), Treatment(s), Exposure(s)	Outcome(s), Output(s), Predictor(s), Measure(s)	Data analysis method(s)

Sampling

Total size		Group 1		Group 2		Group 3		Group 4		Control	

Population, sample, setting	

Audit/Review a) Primary | Secondary | … b) Authoritative | Partisan | Antagonist | … c) Literature | Systematic | …	Interview a) Formal | Informal | … b) Structured | Semi-structured | Unstructured | … c) One-on-one | Group | Multiple | Self-administered | …
Observation a) Participant | Non-participant | … b) Structured | Semi-structured | Unstructured | … c) Covert | Candid | …	Testing a) Standardised | Norm-ref | Criterion-ref | Ipsative | … b) Objective | Subjective | … c) One-on-one | Group | Self-administered | …

Preliminaries		Design		Data Collection	
Results		Total [/40]			
Introduction		Sampling		Ethical Matters	
Discussion		Total [%]			

General notes

Category Item	Item descriptors [Present; Absent; ■ Not applicable]	Description [Important information for each item]	Score [0–5]
1. Preliminaries			
Title	1. Includes study aims and design		
Abstract (assess last)	1. Key information 2. Balanced and informative		
Text (assess last)	1. Sufficient detail others could reproduce 2. Clear/concise writing , table(s) , diagram(s) , figure(s)		
		Preliminaries [/5]	
2. Introduction			
Background	1. Summary of current knowledge 2. Specific problem(s) addressed and reason(s) for addressing		
Objective	1. Primary objective(s), hypothesis(es), or aim(s) 2. Secondary question(s)		
	Is it worth continuing?	**Introduction [/5]**	
3. Design			
Research design	1. Research design(s) chosen and why 2. Suitability of research design(s)		
Intervention, Treatment, Exposure	1. Intervention(s)/treatment(s)/exposure(s) chosen and why 2. Precise details of the intervention(s)/treatment(s)/exposure(s) for each group 3. Intervention(s)/treatment(s)/exposure(s) valid and reliable		
Outcome, Output, Predictor, Measure	1. Outcome(s)/output(s)/predictor(s)/measure(s) chosen and why 2. Clearly define outcome(s)/output(s)/predictor(s)/measure(s) 3. Outcome(s)/output(s)/predictor(s)/measure(s) valid and reliable		
Bias, etc	1. Potential bias , confounding variables , effect modifiers , interactions 2. Sequence generation , group allocation , group balance , and by whom 3. Equivalent treatment of participants/cases/groups		
	Is it worth continuing?	**Design [/5]**	
4. Sampling			
Sampling method	1. Sampling method(s) chosen and why 2. Suitability of sampling method		
Sample size	1. Sample size , how chosen , and why 2. Suitability of sample size		

Sampling protocol	1. Target/actual/sample population(s): description and suitability 2. Participants/cases/groups: inclusion and exclusion criteria 3. Recruitment of participants/cases/groups		
	Is it worth continuing?	**Sampling [/5]**	
5. Data collection			
Collection method	1. Collection method(s) chosen and why 2. Suitability of collection method(s)		
Collection protocol	1. Include date(s) , location(s) , setting(s) , personnel , materials , processes 2. Method(s) to ensure/enhance quality of measurement/instrumentation 3. Manage non-participation , withdrawal , incomplete/lost data		
	Is it worth continuing?	**Data collection [/5]**	
6. Ethical matters			
Participant ethics	1. Informed consent , equity 2. Privacy , confidentiality/anonymity		
Researcher ethics	1. Ethical approval , funding , conflict(s) of interest 2. Subjectivities , relationship(s) with participants/cases		
	Is it worth continuing?	**Ethical matters [/5]**	
7. Results			
Analysis, Integration, Interpretation method	1. A.I.I. method(s) for primary outcome(s)/output(s)/predictor(s) chosen and why 2. Additional A.I.I. methods (e.g. subgroup analysis) chosen and why 3. Suitability of analysis/integration/interpretation method(s)		
Essential analysis	1. Flow of participants/cases/groups through each stage of research 2. Demographic and other characteristics of participants/cases/groups 3. Analyse raw data , response rate , non-participation/withdrawal/incomplete/lost data		
Outcome, Output, Predictor analysis	1. Summary of results and precision for each outcome/output/predictor/measure 2. Consideration of benefits/harms , unexpected results , problems/failures 3. Description of outlying data (e.g. diverse cases, adverse effects, minor themes)		
		Results [/5]	
8. Discussion			
Interpretation	1. Interpretation of results in the context of current evidence and objectives 2. Draw inferences consistent with the strength of the data 3. Consideration of alternative explanations for observed results 4. Account for bias , confounding/effect modifiers/interactions/imprecision		
Generalisation	1. Consideration of overall practical usefulness of the study 2. Description of generalisability (external validity) of the study		
Concluding remarks	1. Highlight study's particular strengths 2. Suggest steps that may improve future results (e.g. limitations) 3. Suggest further studies		

		Discussion [/5]	
9. Total			
Total score	1. Add all scores for categories 1–8		

Total [/40]

Appendix 2.1 Letters of Approval

NHS Board Approval

Administrator: Mrs Elaine O'Neill

Telephone Number: 0141 314 4001

E-Mail: elaine.o'neill2@ggc.scot.nhs.uk

Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/research-development/

Clinical Research & Development

Dykebar Hospital, Ward 11

Grahamston Road

Paisley, PA2 7DE

Scotland, UK

09 September 2019

Ms Mhairi Nisbet

Institute of Health and Wellbeing

Admin Building

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow G12 0XH

NHS GG&C Board Approval

Dear Ms M Nisbet,

Study Title:	A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.
Principal Investigator:	Ms Mhairi Nisbet
GG&C HB site	The Royal Hospital for Children and Queen Elizabeth University Hospital
Sponsor	NHS Greater Glasgow and Clyde

R&D reference: REC reference: Protocol no: (including version and date)	GN19MG312 19/WS/0132 V2; 18/09/19

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004 a. During the life span of the study GGHB requires the following information relating to this site
    i. Notification of any potential serious breaches.
    ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan:

    a. First study participant should be recruited within 30 days of approval date.
    b. Recruitment Numbers on a monthly basis
    c. Any change to local research team staff should be notified to R&D team
    d. Any amendments – Substantial or Non Substantial
    e. Notification of Trial/study end including final recruitment figures
    f. Final Report & Copies of Publications/Abstracts

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database. I wish you every success with this research study

Yours sincerely,

Mrs Elaine O'Neill

Senior Research Administrator

CC: Ms Emma-Jane Gault (University of Glasgow)

REC Approval

WoSRES

West of Scotland Research Ethics Service

NHS Greater Glasgow and Clyde

Miss Mhairi Nisbet

Mental Health and Wellbeing Institute, University of Glasgow

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

G12 0XH

West of Scotland REC 4

Ward 11 Dykebar Hospital

Grahamston Road

Paisley

PA2 7DE

Date 25 September 2019

Direct line 0141 314 0214

E-mail WoSREC4@ggc.scot.nhs.uk

Dear Miss Nisbet

Study title:	**A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.**
REC reference:	**19/WS/0132**
Protocol number:	**1**
IRAS project ID:	**263560**

Thank you for your email of 25 September 2019. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 25 September 2019.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Participant information sheet (PIS) [PIS 16-25 yrs - tracked changes]	3	25 September 2019

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Advertisement]	1	10 June 2019
Interview schedules or topic guides for participants [Interview Schedule]	1	10 June 2019
IRAS Application Form [IRAS_Form_07082019]		07 August 2019

Document	*Version*	*Date*
Letter from funder [Proceed to Ethics letter (Univ of Glas)]	N/A	28 May 2019
Letters of invitation to participant [Letter of invitation 1 (To child)]	1	10 June 2019
Letters of invitation to participant [Letter of invitation 2 (To parent/guardian)]	1	10 June 2019
Other [University Insurance Document]	N/A	24 July 2019
Other [Assent Form 12-15 yrs]	1	18 September 2019
Other [Responses to REC Provisional opinion]	1	18 September 2019
Participant consent form [Consent form 12-15]	1	28 June 2019
Participant consent form [16-25 and parent Consent Form]	1	28 June 2019
Participant information sheet (PIS) [PIS 12-15 yrs_tracked changes]	2	18 September 2019
Participant information sheet (PIS) [PIS parents/guardians_tracked changes]	2	18 September 2019
Participant information sheet (PIS) [PIS 16-25 yrs - tracked changes]	3	25 September 2019
Research protocol or project proposal [Protocol_tracked changes]	2	18 September 2019
Summary CV for Chief Investigator (CI) [CI CV - Rory O'Connor]		01 March 2017
Summary CV for student [Student CV - Mhairi Nisbet]		10 June 2019
Summary CV for supervisor (student research) [Supervisor CV - Rory O'Connor]		01 March 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Recruitment Flowchart]	1	28 June 2019

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

Yours sincerely

Rozanne Suarez

REC Manager

Copy to: Professor Rory O'Connor, University of Glasgow

Emma-Jane Gault, University of Glasgow

nhsg.NRSPCC@nhs.net

[redacted]

Appendix 2.2 Participant Information Sheets

12-15-year-old Participant Information Sheet

Participant information sheet (Aged 12-15 years old)

Study title

A study looking into how girls with Turner Syndrome were told about their condition, and how they feel talking about their condition to other people.

Invitation to take part

You are invited to take part in a research project. We are looking for young people aged between 12-15 years old who have been diagnosed with Turner Syndrome (TS) and their parents/guardians. Before deciding whether you want to take part or not it is important to understand why this research is being carried out. You also need to know what taking part will involve. This information is written below. Please take the time to read this carefully and, if you'd like, talk about it with others. If there is anything that is not clear or you would like more information on, please feel free to ask. Take time to decide whether you would like to take part.

If you decide to take part in this study, please contact one of the researchers, using the contact details below. If you attend the Turner Syndrome clinic in Glasgow, Dr Mason will also ask you and your parent/guardian if you would like to take part the next time you attend. You will be given a copy of this Participant Information Sheet and the signed consent form to keep. Thank you for taking the time to read this information sheet.

Who is conducting the research?

The research is being carried out by Mhairi Nisbet (Trainee Clinical Psychologist), Professor Rory O'Connor (Professor of Health Psychology), Dr Avril Mason (Consultant Endocrinologist), Dr Marie Freel (Consultant Endocrinologist) and Dr Elizabeth Hunter (Clinical Psychologist). The study is being carried as part of Mhairi Nisbet's training course at the University of Glasgow.

What is the purpose of the study?

This study is looking at how girls with Turner Syndrome (TS) were told about their condition. We know that TS is quite a common genetic condition. Some girls are diagnosed when they are a baby, while others are diagnosed when they are a child or teenager.

The study will look at how girls found out they had TS, what they feel comfortable telling others about their condition and their parent/guardians experience of talking about TS with their daughters. The aim of this study is to gain a better understanding about the best way to tell families and young people about TS for the first time.

Why have I been invited to take part?

You have been invited to take part because you have TS and are aged between 12-15 years old.

What would taking part involve?

If you decide to take part, you will be contacted by Mhairi Nisbet to arrange a good time to attend either the Royal Hospital for Children, Glasgow or the Area G clinics within the Queen Elizabeth University Hospital, Glasgow. You should come with at least one of your parents/guardians. If you already attend one of the TS clinics in Glasgow, then we'll try to invite you on the same day as you are attending the TS clinic anyway. If this doesn't work for you then we will arrange another date that suits you and your parent/guardian. If we arrange a date that's different from when you would usually attend the clinic, you will be reimbursed for any travel expenses.

If you don't attend one of the Glasgow TS clinics, then we will arrange a day and time that suits you to come along to one of the hospitals above. We will reimburse you for any travel expenses.

The research visit will last around about one hour in total. The first thing we will do is ask you and at least one of your parents/guardians to sign a form to say you are both happy for you to take part in the study. You and your parent/guardian will also have the chance to ask any more questions.

Then we will ask you and your parent/guardian some questions about how you found out you had TS, and how you feel talking about your condition with other people. We'll also ask about what having a diagnosis of TS means to you.

Sometimes young people don't want to talk about certain subjects in front of their parents. We will ask your parent/guardian to wait outside the room while we ask you if there is anything else you would like to talk about or add. We will then ask you to wait outside and ask your parent/guardian if there is anything else they'd like to talk about. If not, the interview will be finished. With your permission, your interview will be recorded using an audio recorder, so we remember everything that you tell us. All information will be confidential.

What are the possible benefits of taking part?

The advantages of taking part are mainly around helping us to get a better understanding of what it's like talking about TS for the first time, and what it's like to live with TS. This is so we can help others with TS in the future. There are no direct benefits to taking part in the study.

What are the possible disadvantages and risks of taking part?

It's possible you might feel upset when talking about your experience of having TS and the impact it's had on you and your family. If this happens then the interview will be paused, and you will be offered support from the Trainee Clinical Psychologist doing the interview, or another Clinical Psychologist. You can also spend some time talking to your parent/guardian alone about how you feel.

If you feel okay to continue, the interview will carry on. If you decide you don't want to then the interview will stop. There are no other risks to taking part.

Do I have to take part?

No, you don't. It is your choice if you want to take part and you can always change your mind. You don't have to answer any questions that you don't want to. Just tell your parent/guardian and the people carrying out the research that you don't want to take part any more. You don't have to give a reason. It is your choice.

Will my information be confidential?

All personal information collected about you during the study will be kept completely confidential. If any information about you was required to leave the hospital, your name and address will be removed so that you can't be recognised from it.

What happens to my information?

We may be collecting and keeping personal information from you to do this study. Information will be anonymised and stored within a locked filing cabinet in the locked Psychology Department or in 'OneDrive for Business', one of the University of Glasgow's secure storage providers, on a password protected computer. This means data will be held on University computer systems and premises but that data held on University computers will be anonymised with the code linking to identifiable information held separately.

Researchers from the University of Glasgow collect, store and process all personal information in line with the General Data Protection Regulation (2018) and the Data Protection Act (2018). This means that it will be stored securely and not shared with other people unless you say so. If any findings from this study are published, your name and any other information which means someone could recognise you will not be included. This means no one will be able to tell it's you. However, we might use direct quotes in the final report, as examples of the kinds of topics we talk about during the interview.

NHS Greater Glasgow and Clyde is the sponsor for this study based in Scotland. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. NHS Greater Glasgow and Clyde will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting Professor O'Connor and/or at: https://www.nhsggc.org.uk/patients-and-visitors/faqs/data-protection-privacy/.

What will happen to the results of the study?

At the end of the study, the finished report will be handed in to the University of Glasgow. We hope that the findings will be published in a medical journal or may be presented at a conference. This is to make sure other researchers and clinicians working with girls with TS know what we have found. If you like, you will be sent a written summary of the report of the findings in plain English. This will be easier to read. Your identity and personal information will not be reported or published following this study.

Who is funding the research?

The research is funded by the Clinical Psychology course at the University of Glasgow.

Who has reviewed the study?

The study has been reviewed by Glasgow University to make sure that it meets the necessary standards. The West of Scotland Research Ethics Committee 4 board has also reviewed this study to make sure it meets ethical standards.

Thank you very much for taking the time to read this Information Sheet.

Contact details

If you have any questions you can contact the research team who will be carrying out the research:

Mhairi Nisbet (Trainee Clinical Psychologist)

Email:

Tel: 07743304734

Professor Rory O'Connor (Professor of Health Psychology)

Email: rory.oconnor@glasgow.ac.uk

Tel: (0)141 211-0690/3927

Dr Avril Mason (Consultant in Paediatric Endocrinology)

Email: avrilmason@nhs.net

Tel: 0141 201 0000

Dr Marie Freel (Clinical Senior Lecturer in Diabetes and Endocrinology)

Email: marie.freel@glasgow.ac.uk

Tel: 0141 451 6189

Dr Elizabeth Hunter (Clinical Psychologist)

Email: Elizabeth.Hunter2@ggc.scot.nhs.uk

Tel: 0141 451 661

16-25-year-old/Parent and Guardian Participant Information Sheet

Participant information sheet (Aged 16-25 years old)/(Parent/Guardian)

Study title

A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.

Invitation to take part

You are invited to take part in a research project. We are looking for young people aged between 16-25 years old/12-25 years old who have been diagnosed with Turner Syndrome (TS) and their parents/guardians. Before deciding whether you want to take part or not it is important to understand why this research is being carried out. You also need to know what taking part will involve. This information is written below. Please take the time to read this carefully and, if you'd like/if you wish, talk about it with others. If there is anything that is not clear or you would like more information on, please feel free/do not hesitate to ask. Take time to decide whether you would like to take part.

If you decide to take part in this study, please contact one of the researchers using the contact details below. If you/your daughter attend's one of the Turner Syndrome clinics in Glasgow then Dr Mason or Dr Freel will also ask you and your parent/guardian if you would like to take part the next time you attend. If you usually attend this appointment with your daughter, you will also be asked if you would like to take part. You will be given a copy of this Participant Information Sheet and the signed consent form to keep. Thank you for taking the time to read this information sheet.

Who is conducting the research?

The research is being carried out by Mhairi Nisbet (Trainee Clinical Psychologist), Professor Rory O'Connor (Professor of Health Psychology), Dr Avril Mason (Consultant Endocrinologist), Dr Marie Freel (Consultant Endocrinologist) and Dr Elizabeth Hunter (Clinical Psychologist). The study is being carried as part of Mhairi

Nisbet's training course at the University of Glasgow/the University of Glasgow's Doctorate in Clinical Psychology degree course.

What is the purpose of the study?

This study is looking at/investigating how girls with Turner Syndrome (TS) were told about their condition. We know that TS is a fairly common genetic condition. Some girls are diagnosed when they are a baby, while others are diagnosed when they are a child or teenager.

The study will look at how girls found out they had TS, what they feel comfortable telling others about their condition and their parent/guardians experience of talking about/discussing TS with their daughters. The aim of this study is to gain a better understanding about the best way to tell families and young people about TS for the first time.

Why have I been invited to take part?

You have been invited to take part because you have TS and are aged between 16-25 years old. You have been invited to take part because your child has the condition Turner Syndrome and she is aged between 12-25 years old. This study aims to explore how girls learned they had TS and your experience of this as a parent/guardian.

What would taking part involve?

If you decide to take part, you/and your daughter will be contacted by Mhairi Nisbet to arrange a good time to attend the Royal Hospital for Children, Glasgow or the Area G clinics within the Queen Elizabeth University Hospital, Glasgow. You should come with at least one of your parents/guardians. If you/your daughter already attend one of the TS clinics in Glasgow, then we'll try to invite you both on the same day as you are attending the TS clinic anyway. If this doesn't work for you/isn't suitable then we will arrange another date that suits you both. If we arrange a date that's different from when you/your daughter would usually attend the clinic, you will be reimbursed for any travel expenses.

If you/your daughter don't attend one of the Glasgow TS clinics, then we will arrange a day and time that suits you to come along to one of the hospitals/locations above. We will reimburse you for any travel expenses. We hope to interview girls with at least one parent/guardian.

The research visit will last around about one hour in total. The first thing we will do is ask you to sign a form to say that you are happy to take part in the study. We will also ask your parent/guardian to sign a form to say they are happy to take part in the study. We will also ask your daughter to sign a form to say she is happy to take part, and if she is under the age of 16 you will be required to sign her consent form. You and your parent/guardian/daughter will also have the chance to ask any more questions.

Then we will ask you and your parent/guardian/daughter some questions about how you/she found out you/she had TS, and how you/she feel talking about your/her condition with others. We'll also ask about what having a diagnosis of TS means to you/your daughter and your family.

Sometimes young people don't want to talk about certain subjects in front of their parents. We will ask your parent/guardian/you to wait outside the room while we ask you/your daughter if there is anything else you/she would like to talk about or add. We will then ask you/her to wait outside and ask your parent/guardian/you if there is anything else they'd/you like to talk about. If not, the interview will be finished. With your permission, your interview will be recorded using an audio recorder, so we remember everything that you tell us. All information will be confidential.

What are the possible benefits of taking part?

The advantages of taking part are mainly around helping us to get a better understanding of what it's like talking about TS for the first time, and what it's like to live with TS. This is so we can help others with TS in the future. There are no direct benefits to taking part in the study.

What are the possible disadvantages and risks of taking part?

It's possible you/or your daughter might feel upset when talking about your/the experience of having TS and the impact it's had on you and your family. If this happens then the interview will be paused, and you will be

offered support from the Trainee Clinical Psychologist doing the interview or another Clinical Psychologist. You can also spend some time talking to your parent/guardian/daughter alone about how you feel.

If you both feel okay to continue, the interview will carry on. If you decide you don't want to then the interview will stop. There are no other risks to taking part.

Do I have to take part?

No, you don't. It is your choice if you want to take part and you can always change your mind. You don't have to answer any questions that you don't want to. Just tell the people carrying out the research that you don't want to take part any more. You don't have to give a reason. It is your choice.

Will my information be confidential?

All information collected about you during the study will be kept completely confidential. If any information about you was required to leave the hospital, your name and address will be removed so that you can't be recognised from it. Please note that assurances on confidentiality will be strictly adhered to unless we think you or someone else is at risk. In such cases, the University may be obliged to contact relevant statutory bodies/agencies.

What happens to my information?

We may be collecting and keeping personal information from you to do this study. Information will be anonymised and stored within a locked filing cabinet in the locked Psychology Department or in 'OneDrive for Business', one of the University of Glasgow's secure storage providers, on a password protected computer. This means data will be held on University computer systems and premises, but that data held on University computers will be anonymised with the code linking to identifiable information held separately.

Researchers from the University of Glasgow collect, store and process all personal information in line with the General Data Protection Regulation (2018) and the Data Protection Act (2018). This means that it will be stored securely and not shared with other people unless you say so. If any findings from this study are published, your name and any other information which means someone could recognise you will not be included. This means no one will be able to tell it's you. However, we might use direct quotes in the final report, as examples of the kinds of topics we talk about during the interview.

NHS Greater Glasgow and Clyde is the sponsor for this study based in Scotland. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. NHS Greater Glasgow and Clyde will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting Professor O'Connor and/or at: https://www.nhsggc.org.uk/patients-and-visitors/faqs/data-protection-privacy/.

What will happen to the results of the study?

At the end of the study, the finished report will be handed in to the University of Glasgow. We hope that the findings will be published in a medical journal or may be presented at a conference. This is to make sure the general public other researchers and clinicians working with girls with TS know what we have found. If you like/wish, you will be sent a written summary of the report of the findings in plain English. This will be easier to read. Your identity and personal information will not be reported or published following this study.

Who is funding the research?

The research is funded by the Clinical Psychology course at the University of Glasgow.

Who has reviewed the study?

The study has been reviewed by Glasgow University to make sure that it meets the necessary standards. The West of Scotland Research Ethics Committee 4 board has also reviewed this study to make sure it meets ethical standards.

Thank you very much for taking the time to read this Information Sheet.

Contact details

If you have any questions you can contact the research team who will be carrying out the research:

Mhairi Nisbet (Trainee Clinical Psychologist)

Email:

Tel: 07743304734

Professor Rory O'Connor (Professor of Health Psychology)

Email: rory.oconnor@glasgow.ac.uk

Tel: (0)141 211-0690/3927

Dr Avril Mason (Consultant in Paediatric Endocrinology)

Email: avrilmason@nhs.net

Tel: 0141 201 0000

Dr Marie Freel (Clinical Senior Lecturer in Diabetes and Endocrinology)

Email: marie.freel@glasgow.ac.uk

Tel: 0141 451 6189

Dr Elizabeth Hunter (Clinical Psychologist)

Email: Elizabeth.Hunter2@ggc.scot.nhs.uk

Tel: 0141 451 661

Appendix 2.3 Consent forms

12-15-year-old consent form

Centre Number:

Project Number:

Participant Identification Number for this trial:

Title of Project: A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.

Name of Researcher(s): Mhairi Nisbet

CONSENT FORM

	Please initial box
I've had the chance to read and think about the information in the Participant Information Sheet for girls aged 12-15 years old (Version 2 dated 18/07/19).	☐
I've had the chance to think about the information and ask any questions I might have had and understand the answers I have been given.	☐
I understand it's up to me if I want to take part and that I can decide not to take part at any time, without giving any reason, without my legal rights being affected.	☐
I confirm that I agree to the way my data will be collected (through doing the interview) and processed and that data will be stored for up to 10 years in the University in line with relevant Data Protection policies and regulations.	☐
I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐
I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project.	☐
I understand that if I decide to stop taking part, my data collected up to then will be kept and used for the remainder of the study.	☐
I agree to my interview being audio-recorded.	☐
I understand that the recorded interview will be transcribed (typed out) word by word and the transcription stored for up to 10 years in the University in line with Data Protection policies and regulations.	☐

I understand that my information and things that I say in an interview might be quoted in reports and articles that are published about the study, but my name or anything else that could tell people who I am will not be revealed. ☐

I agree to take part in the study. ☐

_____	_____	_____
Name of participant	*Date*	*Signature*
_____	_____	_____
Name of participant's parent/guardian	*Date*	*Signature*
_____	_____	_____
Researcher	*Date*	*Signature*

(1 copy for participant; 1 copy for researcher)

Centre Number:

Project Number:

Participant Identification Number for this trial:

Title of Project: A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.

Name of Researcher(s): Mhairi Nisbet

CONSENT FORM

	Please initial box
I confirm that I have read and understood the Participant Information Sheet for either girls aged 16-25 (Version 3 dated 25/09/19) or for parents/guardians (Version 2 dated 18/09/19).	☐
I have had the opportunity to think about the information and ask questions, and understand the answers I have been given.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	☐
I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	☐
I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐
I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project.	☐
I understand that if I withdraw from the study, my data collected up to that point will be retained and used for the remainder of the study.	☐
I agree to my interview being audio-recorded.	☐
	☐

I understand that the recorded interview will be transcribed word by word and the transcription stored for up to 10 years in University archiving facilities in accordance with Data Protection policies and regulations.

I understand that my information and things that I say in an interview may be quoted in reports and articles that are published about the study, but my name or anything else that could tell people who I am will not be revealed. ☐

I agree to take part in the study. ☐

_____	_____	_____
Name of participant	*Date*	*Signature*

Parent/guardian of:

(if applicable)

_____	_____	_____
Researcher	*Date*	*Signature*

(1 copy for participant; 1 copy for researcher)

Appendix 2.4 Interview Schedule

A. (Topic) diagnostic narrative

Opening Questions:

Girls with TS:

1. Can you tell me a bit about how long you've been coming to the clinic?
2. Can you tell me a bit about how you found out you had Turner Syndrome?

Parent/guardian:

3. Where you involved in telling (participant) they had Turner Syndrome?
4. Can you tell me how you found telling (participant) about the aspects of their condition?
5. Do you have anything to add around (participants) diagnosis?

Prompts:

- How old were you when you received your diagnosis?
- What do you remember being told about your diagnosis?
- What was good about it?
- What could have been better?
- Did you suspect that you were not given information about TS?

B. (Topic) aspects of the condition

Opening questions:

Girls with TS:

6. Can you tell me what having TS means for you?
7. Do you have any health problems relating to TS?

Prompts:

- Do you know of any other health problems that others with TS might have?

C. (Topic) what is disclosed to others e.g. peers

Opening question:

Girls with TS:

8. How do you feel talking about your condition to others?

Prompts:

- Who do you feel comfortable talking about it with?
- What aspects are easier to talk about?
- What aspects are harder to talk about?
- What would be your worries around talking about your condition to others?

D. (Topic) advice around disclosure

Opening questions:

Girls with TS:

9. What advice would you give to girls that have been diagnosed when talking about their condition to others?

Parent/guardian:

10. What advice would you give to parents talking to their daughter about TS?

Both girls with TS and parent/guardian:

11. What advice would you give to HCP's talking to a girl with TS at diagnosis and beyond?

E. (Topic) Impact

Opening question:

Girls with TS:

12. Has having TS had any impact on you and your life?

Both girls with TS and parent/guardian:

13. Do you think your TS diagnosis has had an impact on your family?

Prompts:

- How does this impact you day to day?
- Has it affected your relationships e.g. with friends?
- How does this impact your family day to day?

F. Opportunity to speak without parent/guardian/daughter present

Opening question:

14. Are there any topics you'd like to talk about again?
15. Is there anything else you'd like to add?

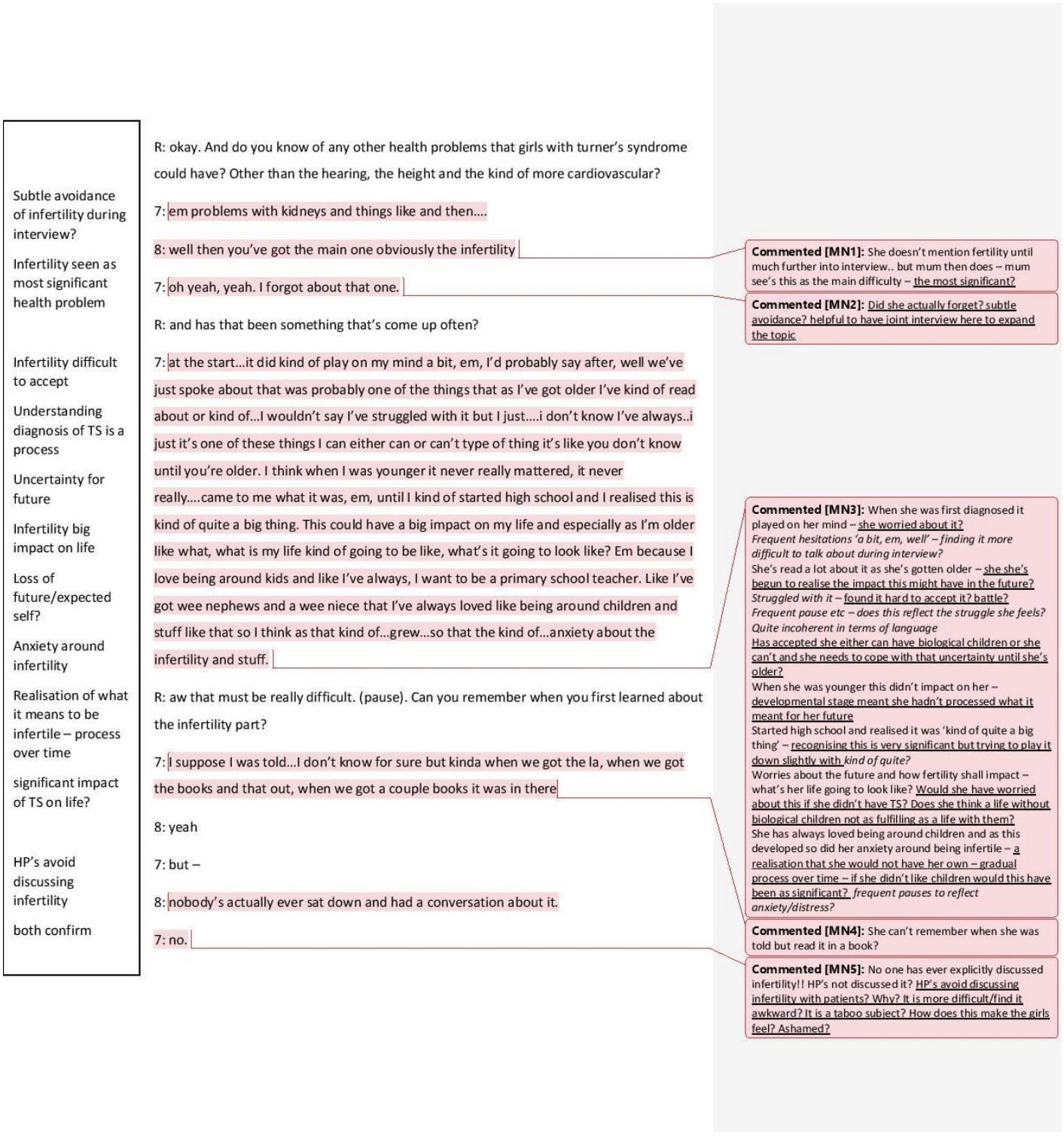
If no:

Closing

Do you have any further questions?

Thank you very much for taking part.

Appendix 2.5 Example of coding and analysis



Appendix 2.6 Project Proposal

A qualitative study exploring various aspects of disclosure in girls with Turner Syndrome: disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others.

Abstract

Background

Turner syndrome (TS) is a genetic condition occurring in around 1/2500 female births. Although most girls are diagnosed by adolescence, a previous study found 45/322 participants were unaware of their TS diagnosis. Preliminary research suggests parents may withhold information from their daughters, particularly around the infertility component. Current literature around TS and disclosure is limited and has not yet investigated the impact of having TS on the girls and their families.

Aims

The primary aim of this study is to explore the nature of disclosure in girls with TS; disclosure of the diagnosis to girls by their parents/professionals and girls experience of disclosing their condition to others. The secondary aim is to explore whether TS has had an impact on girls and their family's lives.

Methods

This study shall be qualitative in nature, to gain a fuller insight into the nature of disclosure in girls with TS. Semi structured qualitative interviews will be conducted with both girls and their parents.

Applications

We hope this project could provide further recommendations for parents and professionals about factors that facilitate disclosure in girls with TS. It may also highlight the potential barriers to parents disclosing aspects of the condition to their children.

Introduction

Turner Syndrome

Turner syndrome (TS) is a genetic condition resulting from a sex chromosome anomaly that occurs in approximately 1/2000 to 1/2500 live female births (Apperley *et al.*, 2018). The condition is most often caused by the absence of all or part of the second sex chromosome. Typically, women with TS exhibit short stature, reproductive, cardiovascular, endocrine, renal, vision and/or hearing abnormalities (Morgan, 2007; Bondy, 2014). Research also suggests women with TS experience psychosocial difficulties in areas such as social skills, self-esteem and perceptions of competence, compared to their peers (Reimann *et al.*, 2018). Most girls are diagnosed with the condition by the time they reach adolescence, however the time of diagnosis can vary from the second trimester of pregnancy through to adulthood (Apperley *et al.*, 2018).

Disclosure to children with disabilities/illnesses

Historically, research suggests clinicians took a 'protective approach' when communicating diagnosis and prognosis to children, the rationale being that patients should be shielded from distress (Sisk *et al.*, 2016). However as objective evidence has accumulated, a more open approach has been recommended, taking hope and prognosis (Mack *et al.*, 2006), individual differences e.g. developmental stage (Bluebond-Langner, Belasco and DeMesquita Wander, 2010) and family culture (Bluebond-Langner *et al.*, 2007) into consideration.

While most studies focus on children with intellectual disabilities, HIV or cancer, there appears to be less research exploring disclosure in children with genetic conditions. Hill, Sahhar, Aitken, Savarirayan, & Metcalfe, (2003) conducted qualitative research to explore parents experience of being told their child had bone dysplasia which results in significantly short stature. They found the way in which the diagnosis is explained to be the most important thing to parents, including factors such as having written information around the condition, potential medication complications and how to access support. Dennis, Howell, Cordeiro, & Tartaglia, (2015) surveyed the parents of and individuals with a sex chromosome aneuploidy affecting fertility, and found that both groups valued full, early disclosure.

Poor disclosure or withholding a diagnosis appears to result in a number of negative consequences for both children and their families. Research exploring children with a diagnosis of cancer found that poor communication between clinicians parents and children can increase the suffering of patients and their families (Sisk et al., 2016). Gaff & Bylund (2010) noted that if a diagnosis is withheld it could expand into a family secret, resulting in an environment of distrust and strain amongst family interpersonal relationships. An atmosphere of secrecy might also dissuade children from asking questions; Metcalfe, Plumridge, Coad, Shanks, & Gill (2011) found that if parents did not acknowledge that their child had a genetic condition then siblings of the affected child felt inhibited from asking questions because they did not want to upset their parents.

Turner Syndrome and Disclosure

Gravholt et al., (2003) conducted a study that assessed the characteristics and risk factors of bone fractures in women with TS (average age 30 years old). Unexpectedly, they discovered 45/322 participants they surveyed were unaware of their TS diagnosis. Further qualitative research by Sutton et al., (2005) explored the challenges experienced by 97 girls and women with TS across the lifespan, ranging from 7-59 years of age. The average age of diagnosis was 12 years old; however, they found many participants had some aspect of the TS diagnosis kept secret from them. Secondary analysis examining the impact of secret-keeping on girls and women with TS suggests that parents are the most likely individuals to withhold diagnostic information from their daughters, particularly the infertility component (Sutton *et al.*, 2006). Sutton et al., (2006) found patients with TS from whom information was withheld about their condition were at higher risk of depression and generally mistrusted health care professionals.

A recent cross sectional study from King, Plamondon, Counts, Laney, & Dixon, (2016b) explored the timing for parents to discuss infertility with their daughters with a diagnosis of TS and the potential barriers that hinder their ability to facilitate this conversation. They found that age and emotional maturity were key factors in determining when parents would choose to discuss infertility. Being afraid of negative emotion and

struggling with the balance of educating plus protecting their daughters were two of the main barriers which affected parent's ability to have the conversation.

It can be seen that previous research exploring the nature of disclosure in girls with TS is fairly limited. The issue of diagnostic disclosure was highlighted by chance through a quantitative study, and King et al., (2016b)'s research is similarly quantitative in nature. Although there are benefits to quantitative research, such as generalisability and being able to test a hypothesis (Black, 1999), qualitative methods can be valuable to initially develop theories around complex or under researched conditions, arguably providing a more holistic view (Bogdan and Taylor, 1975). Sutton et al., (2005, 2006) studies were qualitative; however, the primary objective was to determine the general concerns and challenges faced by girls with TS, rather than explore their experience of disclosure. Therefore, it could be useful to conduct further qualitative research to develop a richer understanding of disclosure in girls with TS. Moreover, King et al., (2016b) only collected data from parents/carers of girls with TS. Therefore, it could be useful to examine disclosure and infertility from the perspectives of girls themselves.

Research exploring adolescents views and experiences of disclosing conditions such as autism and HIV found teenagers are often reluctant to tell others about their diagnosis, for fear of being treated differently or experiencing stigma (Humphrey, Neil and Lewis, 2008; Michaud *et al.*, 2009). Metcalfe, Coad, Plumridge, Gill, & Farndon (2008) found children with genetic conditions rarely discussed the condition or its risks with their siblings. Most communication took place between the child and parent(s). As far as we are aware, there has been no prior research conducted to explore how girls with TS feel about disclosing their condition to others.

Lastly, current literature has not yet explored the impact that receiving a diagnosis of TS has had on the girls and how the condition affects their day to day lives. It is also unclear how having a child with TS impacts upon parents and families.

Aims:

The primary aim of this study is to explore the nature of disclosure in girls with Turner Syndrome. It's anticipated this will involve exploring at least three topics:

1. How adolescent girls learned they had TS
2. Parents experience of discussing and potentially disclosing aspects of TS to their children
3. How girls with TS feel about disclosing their condition to others

The secondary aim of this study is to explore whether TS has an impact on girls and their family's lives. It is anticipated this will explore:

1. The impact of having TS on the girls, for example, has it affected their relationships or self-concept
2. The impact that having a child with TS has on families

Plan of investigation

Participants:

Participants will be girls diagnosed with Turner Syndrome, recruited from two designated Turner Syndrome clinics. The first clinic is for children and adolescents based within the Royal Hospital for Children, Glasgow. The number of girls that typically attend the clinic is around 40, and 8 girls in total attend each monthly clinic. The second clinic is based in the Area G clinics within the Queen Elizabeth University Hospital, Glasgow, and similarly around 40 adults typically attend. Girls' parents/guardians will also be invited to participate. Girls aged over 18 years old who may not attend the clinic with a parent, will be asked to distribute Patient Information Sheets (PIS) to their parents/guardians inviting them to take part. It is recognised that this is a relatively small sample to recruit from, however the clinical team has reassured there will be people willing to take part, and fully support the recruitment procedure. We are therefore confident we will reach the participant target.

If we are not able recruit enough participants through the clinic, participants may be reached through publication of an advert in a newsletter produced by the Turner Syndrome Support Society, UK.

No. of participants: This study aims to recruit 6-8 adolescent girls and at least one of their parents/guardians.

Participants with TS Inclusion criteria:

- Girls aged between 12-25 years old.
- Received diagnosis of Turner Syndrome.
- Have at least one parent/guardian who also wishes to take part.

Exclusion criteria:

- Participants with a significant learning disability. Participants who do not or did not attend main stream school shall not be included.
- Participants that do not speak English.

Parents/guardians inclusion criteria:

- Be the parent/guardian to a girl aged between 12-25 years old diagnosed with TS.

Exclusion criteria:

- Participants that do not speak English.

Recruitment procedures:

Girls and their parents/guardians will be posted a PIS and Cover letter inviting them to take part. Patients with TS aged over 18 years old, who may not live with their parents, will also be sent the parent/guardian PIS sheet and shall be asked to distribute this. The lead clinician's (Dr Mason and Dr Freel) will post the information. Three separate Information Sheets will be written, one for girls aged 12-15 years old, another

for girls aged 16-25 years old and a third for parents/guardians. As some participants are under the age of 16, an Information Sheet that includes parental/guardian consent is necessary for informed consent.

There shall be two ways participants can indicate consent. Firstly, the PIS will invite them to contact a member of the research team prior to their appointment if they would like to take part. Alternatively, the lead clinicians will ask all potential participants if they would like to take part when they attend the clinic. If they indicate they would like to take part, the researcher shall contact them to provide any further information required and arrange the interview. The Trainee Clinical Psychologist shall also attend both clinics to provide further information about the study and answer any questions from potential participants. Potential participants shall firstly be approached by either lead clinician and asked whether or not they wish to speak to the trainee.

Two separate consent forms shall be distributed once participants have agreed with the researcher to take part: one for girls aged 12-15 years old and another for girls aged 16-25 years old and the parents/guardians. Uptake rates shall be monitored, and as we get close to 8 participants, we will be careful about offering additional invitations.

Measures:

Semi structured qualitative interviews will be conducted with both girls with Turner Syndrome and at least one of their parents/guardians.

Design:

This study shall be qualitative in nature, to gain a fuller insight into the nature of disclosure in girls with TS.

Research procedures:

Girls and their parents/guardians shall be initially interviewed together using a dyadic interview approach. Advantages of dyadic interviews include the opportunity to bring interaction into the interview (Kitzinger, 1995) and expand the coverage of the research topic by participants sharing their point of view (D. L. Morgan, Eliot, Lowe, & Gorman, 2016). However, previous research indicates family members may not talk openly in front of one another to an interviewer if they worry about criticising or raising sensitive topics which could hurt another's feelings or damage the relationship (Morris, 2001)(Corbin and Morse, 2003). It could be the case that girls may not respond as openly if their parents/guardians are within the same interview. A parent may also feel more comfortable discussing the challenges of disclosure without their child present. Therefore, both parties shall then be interviewed individually, unless they choose to decline.

One interviewer shall conduct the semi structured, in-person interviews, lasting between 45-60 minutes. Interviews shall be conducted either directly after their appointment as part of the monthly clinic or scheduled for another time that suits them. Please see Appendix 1 for a draft interview schedule.

All interviews will be audio taped and transcribed verbatim.

Please see Appendix 2 for a draft timetable.

Data Analysis:

Transcripts will be coded using standard qualitative research methods. Data shall be analysed using NVivo software. Qualitative methods considered for this study included inductive approach such as Interpretative phenomenological analysis (IPA) and Grounded Theory and deductive approaches such as Framework Analysis. The aim of IPA is to explore in detail the processes through which participants make sense of their own experiences, focusing on their own perceptions, understanding and views (Brocki and Wearden, 2006). Categories to describe and explain phenomena are derived inductively, which means they are gradually obtained from the data.

Grounded theory was first described by (Glaser and Strauss, 1967), and aimed to generate a “grounded theory” to describe and explain the phenomenon under study. Grounded theory includes all data sources that might contribute to theory development such as diaries and observations, unlike IPA which uses mainly interviews. A literature review is carried out after collecting and analysing data, rather than before.

Framework Analysis is deductive in its approach meaning the categories are derived at the beginning or part way through analysis. It is better tailored to qualitative research that is time limited, has explicit questions, and a pre-designed sample, for example working professionals. Framework analysis can generate theories, however the primary interest is to describe and interpret what is happening in a particular setting (Ritchie, J. & Spencer, 1994)

IPA is the method which will be employed in this study. A systematic review from (Smith, 2011) found that illness experience accounted for the largest proportion of IPA research, which is unsurprising given that IPA was first established in Health Psychology. As this study explores patients lived experience of having a condition, which naturally plays a significant part in their lives and concerns of those with the condition and their families, IPA was decided to be the most appropriate method of analysis. Furthermore, it was necessary to carry out a literature review before analysis to provide the researcher with a better understanding of TS, and so grounded theory would have been inappropriate. Lastly, because this is a subject lacking in research, open-ended, explorative questions will enable richer responses from participants, rather than explicit questioning. Qualitative interviews will therefore be conducted as best practice within IPA methodology (Smith, 2009).

All audio data shall be anonymised during transcription, and any identifiable information removed. Audio recordings will be stored within a locked filing cabinet in the locked Psychology Department and anonymised transcriptions will be stored on ‘OneDrive for Business’, one of the University of Glasgow’s secure storage providers, on a password protected computer. Researchers from the University of Glasgow collect, store and process all personal information in accordance with the General Data Protection Regulation (2018) and the Data Protection Act (2018). This means that it will be stored securely and not shared with other people without permission. If any findings from this study are published, participants identity will be anonymised.

The data will be stored in facilities in line with the University of Glasgow retention policy of up to 10 years and will not pass this information to a third party without express permission from participants. After this, further retention may be agreed, or the data will be securely destroyed in accordance with the relevant standard procedures.

Justification of sample size:

We expect that we will reach saturation of themes by interviewing 6-8 girls and at least one of their parents/guardians. Similar qualitative studies interviewing dyads recruited around the same number of participants; Akeson, Worth, & Sheikh (2007) explored the psychosocial impact of anaphylaxis on young people and their parent's, interviewing seven adolescents and their parent's. Another study explored the experience of having Huntingdon's disease, interviewing seven parent/adult – child dyads jointly (Maxted, Simpson and Weatherhead, 2014). They similarly used IPA to analyse the resultant data. Due to the depth and detail of analysis and understanding of how girls and their parents/carers experience TS, a small, purposively selected sample will be appropriate.

We recognise this study includes a fairly wide age range of participants. The reason for this is because the sample population we are recruiting from is relatively small. The study population is small because Turner syndrome is a rare disease; diagnosis can occur throughout childhood, adolescence or even into adulthood and, therefore, reducing the age range to be included would limit the size of the population from which we could recruit. This would impact on the study being adequately powered to answer the research question. Moreover, although a 12 year old's experience of having TS may be different from that of a 25 year old; this is not the primary focus of the research. The primary aim of this study is to explore how girls learned they had TS and their parents/guardians experience of discussing and potentially disclosing aspects of the condition. We are including girls who received their diagnosis across all time points from birth to adolescence. Including girls aged 12-25 may better inform the perspective of girls from early to late adolescence, as outlined in the study aims. We hope including a wider age range may generate a wider range of themes, which may be grouped together during analysis.

Setting and equipment:

Interviews will be conducted within the Royal Hospital for Children, Glasgow and the Area G clinics within the Queen Elizabeth University Hospital, Glasgow in a private clinic room. The equipment needed includes an audio recorder and interview questions.

Health and safety issues

As the topic of the interview may be sensitive for some participants, it could be the case that girls or their parents/guardians become distressed during the interview. If this does happen, the interviewer will ask the participant if they would like a break or would like to stop the interview altogether. If they would like a break, the audio recording shall be paused, and the researcher will ask whether they would like a moment alone, or

whether they would like to talk about what has caused them distress. If they are then comfortable to continue, the interview shall be resumed, if not the participant shall be debriefed.

Dissemination

The findings of this study shall be disseminated through the Trainee Clinical Psychologist's doctorate thesis and may be submitted to a peer reviewed journal for publication. Participants will be able to read the final paper if it is published in a peer reviewed journal and will also be asked if they would like to read a plain English summary of the final report.

Ethical issues

The main ethical issues arising from this study are around consent and potential distress to participants caused by procedural risks. The study includes participants under the age of 16 and so it is essential all participants have been able to provide informed consent. It is possible a participant becomes distressed during their interview due to the sensitive nature of the topic discussed. The above protocol will be employed, and a member of the Psychology team will be made aware the interviews are taking place, in case anyone does become distressed and wishes to speak to another member of staff. This study shall be submitted for ethical approval to the NHS Greater Glasgow and Clyde Ethics Committee. Management approval from the Health Board R&D will also be required.

Financial issues

Costs that shall be covered will include printing (participant information sheets and consent forms) and for audio recording equipment. It might also be necessary to provide travel costs if participants are interviewed out with their usual clinic appointment at the hospital. Travel costs have been estimated at no more than £30 per participant family group, totalling £240. This will be funded by the University of Glasgow.

Practical applications

We would hope this research project could provide further recommendations for parents and health care professionals about factors that facilitate disclosure of a TS diagnosis to girls. It may also highlight the potential barriers to parents disclosing aspects of the condition to their children and provide tools and/or advice to help reduce these barriers. Previous research indicates infertility can be a challenging topic for parents to discuss with their children and so this study could provide a greater understanding around why and provide practical suggestions for the way to frame this conversation. If the way in which their condition was disclosed to them has had any lasting impact on girls with TS, it's essential that parents feel confident in talking to their children about their condition, to minimise any further distress.

References

*See Major Research Project reference list for all references including within the proposal.