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# Breast satisfaction in adult women with Turner syndrome—An international survey employing the BREAST-Q questionnaire

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## Abstract

**Objective:** Turner syndrome (TS) is associated with short stature, delayed puberty, primary ovarian insufficiency, and other features. Most girls with TS require oestrogen replacement for pubertal induction. There is paucity of data in adult TS on pubertal outcomes, including breast satisfaction. Here, we assess breast satisfaction in TS with the BREAST-Q questionnaire, a well-validated patient-related outcome measure (PROM).

**Design:** International survey distributed online through TS support groups.

**Patients:** Adult women aged 18–45 years with TS (self-reported).

**Measurements:** The questionnaire contained demographics, health history and the four domains of the BREAST-Q. BREAST-Q scores were matched on a one-to-one basis for age, body mass index (BMI) and educational background to a normative data set derived from the 'Army of Women', an online community of healthy volunteers.

**Results:** Of 97 total responses, 74 could be matched to the control cohort. Median age was 32 years (18–45 years) and 97% were White Caucasian. Median age at menarche was 15.5 years (12–34 years), 86% had received pubertal induction therapy as teenagers. We found significantly lower BREAST-Q scores in TS in the domains 'Satisfaction with Breast' ( $p = .021$ ), 'Psychosocial Wellbeing' ( $p < .0001$ ) and

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'Sexual Wellbeing' ( $p < .0001$ ). TS who had received oestrogen replacement therapy reported lower scores compared to TS who had not received oestrogen therapy ( $p < .0001$ ). Lower BMI and previous growth hormone therapy were associated with lower breast satisfaction.

**Conclusions:** TS women who received oestrogen replacement for pubertal induction self-report lower breast satisfaction scores and late menarche, suggesting that type, mode of delivery, dose and timing of hormone supplements merit prospective study.

#### KEYWORDS

pubertal induction, patient-related outcome measures, PROM, quality of life

## 1 | INTRODUCTION

Turner syndrome (TS) affects 25–50 per 100,000 females and is associated with the partial or complete absence of a second X-chromosome on karyotype analysis.<sup>1,2</sup> Key features of TS include short stature and primary ovarian insufficiency (POI), in addition to associated features such as cardiac and renal malformations, and dysmorphism, in some. The risk of autoimmune conditions such as hypothyroidism, coeliac disease and type 1 diabetes is increased in TS. Long-term health consequences with increased morbidity and mortality are mainly due to cardiovascular disease, such as hypertension, atheroma and aortic dissection and metabolic dysfunction, which frequently manifests in adolescent age.<sup>3–5</sup> In addition, women with TS frequently have neuro- and social-cognitive problems, such as deficits in attention, executive control, working memory, facial recognition and poorer body image,<sup>6</sup> emphasizing the need for long-term surveillance in a specialized multidisciplinary service.<sup>1,2</sup>

Oestrogen replacement for the induction of puberty is required in most adolescent girls with TS since only 21%–50% have spontaneous breast development and 16%–30% have spontaneous menarche.<sup>7–9</sup> Importantly, sustained pubertal maturation highly depends on the karyotype and only a small fraction of TS women with 45,X karyotype sustains regular periods with the majority entering secondary amenorrhoea in early adulthood.<sup>7,8</sup>

The aim of oestrogen therapy for pubertal induction is to develop secondary sexual characteristics, to optimise stature and uterine growth and to maximize bone mass acquisition.<sup>10–12</sup> Pubertal induction should normally start between 11 and 12 years of age and last about 2–3 years by administering increasing doses of oestrogen followed by the addition of gestagen when break-through bleeding occurs.<sup>1,12</sup> Several studies have evaluated the effects of different modes and timings of oestrogen replacement for pubertal induction in TS, focusing on morphological changes and hormone parameters,<sup>11,13–18</sup> however, currently there is no consensus concerning dose, route of administration (i.e., oral vs. transdermal) and type of oestrogen and gestagen,<sup>1,2,19</sup> due to the lack of appropriately conducted trials.<sup>20</sup>

Patient-reported outcome measures (PROMs) are important tools to assess the quality of care delivered from the patient's

perspective and are very popular in surgery. The BREAST-Q questionnaire was developed as a PROM to assess the impact of breast surgery from the patient's perspective focusing on psychosocial outcomes and has been rigorously validated in various areas of surgery, including breast augmentation and cancer surgery.<sup>21–23</sup> Since normative data from healthy women are published,<sup>24</sup> we have employed the BREAST-Q preaugmentation module to assess breast satisfaction in women with TS aiming to evaluate psychosocial implications and how self-reported parameters, such as BMI, karyotype or spontaneous puberty, impact on breast satisfaction in TS.

## 2 | METHODS

### 2.1 | Study design and survey distribution

We designed a questionnaire consisting of two parts: Part 1 entailed questions on basic demographics (age, country of residence, ethnicity, and highest level of education), health background (height, weight, karyotype, additional underlying chronic conditions and regular medications) and details about hormonal therapy in the past (time and mode of pubertal induction therapy, age when this was commenced, age at menarche, growth hormone treatment, previous breast augmentation). Part 2 entailed the 'preaugmentation module' of the BREAST-Q questionnaire (see below). Consent for participation was obtained online and detailed information about the study was provided via an online information leaflet. Access to the survey was only granted if all consent questions were answered with 'Yes', which also included screening for inclusion and exclusion criteria. Inclusion criteria: diagnosed by a medical professional with TS, age at the time of the survey: 18–45 years. Exclusion criteria: significant underlying conditions, such as severe rheumatoid arthritis, severe chronic inflammatory bowel disease, ongoing cancer treatment requiring chemotherapy and radiation, eating disorders and taking regular systemic glucocorticoid medications during the past year.

The online survey platform Onlinesurveys<sup>®</sup> ([www.onlinesurveys.ac.uk](http://www.onlinesurveys.ac.uk)) was employed to host and distribute the survey. The link of the survey was live between March and October 2018 and distributed

through advertisements on the websites of the Turner Syndrome International Group ([www.tsint.org](http://www.tsint.org)) and the Turner Syndrome Support Society UK ([www.tss.org.uk](http://www.tss.org.uk)). The study was also advertised via social media accounts (twitter<sup>®</sup> and Facebook<sup>®</sup>) of the above patient support groups.

## 2.2 | BREAST-Q

The BREAST-Q is a rigorously developed validated patient-related outcome instrument with an augmentation module designed for the evaluation of outcomes in patients undergoing breast augmentation.<sup>21,23,25</sup> We have employed the presurgery augmentation questionnaire (version 2.0)<sup>24,25</sup> which includes four domains: (a) Satisfaction with Breasts ( $n = 6$  items), (b) Psychosocial Well-being ( $n = 9$  items), (c) Sexual Well-being ( $n = 5$  items) and (d) Physical Well-being ( $n = 5$  items). Since the BREAST-Q scales were specifically developed and validated in women undergoing breast surgery, we performed cognitive interviews on the pre-augmentation Module in  $n = 5$  healthy women (age 23–42 years) to assess if the items and language used are appropriate for women not seeking breast augmentation. Overall, no difficulties were identified that would pose a barrier towards answering the questionnaire. Scale items are summed and transformed on a scale from 0 (worst) to 100 (best) by employing the Q-score<sup>®</sup> software (<http://qportfolio.org/score-breast-q-breast-cancer-2/>).

## 2.3 | Matching to healthy controls (Army of Women [AOW]) and data analysis

Published cumulative scores from the 'pre-augmentation module' of the BREAST-Q questionnaire in healthy women were used as normative reference data.<sup>24</sup> Those normative data were retrieved via the AOW, an online community of women engaged in breast cancer research, and who are not actively seeking breast augmentation.

Women with TS from our data set were matched for educational background, body mass index (BMI) and age on a one-to-one basis with women from the AOW control cohort. The R-package MatchIt<sup>®</sup> was used for the computations.<sup>26</sup> The method 'Optimal' was applied using the Mahalanobis distance measure to obtain a matched sample for the TS cohort using women from the AOW collective. Matching was performed on the variables 'age', 'educational background' and 'BMI'. The rounded BMI on full number compared with the original values was used for matching due to better performance. For the sake of compatibility, four educational categories as assessed in the TS cohort were defined for matching between the cohorts: no formal education (AOW category 1), high school education (AOW category 2), college or university education (AOW categories 3 and 4), and postgraduate education (AOW categories 5 and 6).<sup>24</sup>

Descriptive statistics were computed, including the mean, standard deviation and 95% confidence intervals. Individual delta

scores (TS women *minus* matched control) were generated to compare overall scores (TS vs. controls), and to facilitate subgroup analysis for dichotomous values as follows: Pubertal induction therapy in the past: Yes versus No; Karyotype: 45,X versus mosaic; Growth Hormone therapy in the past: Yes versus No. In addition, continuous values were converted into dichotomous values as follows: BMI < 25 kg/m<sup>2</sup> versus > 25 kg/m<sup>2</sup>; Age at diagnosis: <9 years versus > 9 years; Age at menarche: <15 years versus > 15 years.

The nonparametric Wilcoxon signed-rank test was employed to analyse overall matched pairs and delta values for subsequent subgroup analysis. A  $p < .05$  was considered as being statistically significant.

## 2.4 | Regulatory approval

Ethical approval for the study was obtained by the Ethics Review Board at the University of Birmingham, UK (reference: ERN\_17-1392).

## 3 | RESULTS

### 3.1 | Matching and characterization of the TS cohort of survey participants

Overall, we received  $n = 97$  responses. Fifteen participants were excluded:  $n = 7$  met exclusion criteria,  $n = 3$  had breast augmentation in the past,  $n = 4$  participants were older than 45 years and  $n = 1$  participant did not complete the questionnaire, leaving  $n = 82$  valid responses in total. Of these 82 women, it was possible to match 74 women with women from the AOW control cohort ( $n = 1211$ ),<sup>24</sup> while suitable matches could not be found for 8 women. Table 1 contains balance summary measures for the variables 'age' (row 1), 'education' (row 2), and 'BMI' (row 3), which were used for matching between the case (TS) and the control group (AOW).

#### 3.1.1 | Basic demographics (Table 2)

The median age of participation was 33 years. Most participants categorized themselves of White Caucasian ethnicity ( $n = 69/72$  responses), and one woman each was of New Zealand, Japanese and African origin. Sixty-one percent ( $n = 45$ ) of study participants were UK residents, 11% from the US ( $n = 18$ ), 7% from Australia ( $n = 5$ ) and 5% from Ireland ( $n = 4$ ). Other countries of residence with one or two participants include Austria, Bulgaria, Cameroon, Canada, France, Portugal, Slovakia, South Africa and Spain (combined total 16%). Seventy percent ( $n = 52$ ) of participating women declared College or University Education as educational background, 22% ( $n = 16$ ) had postgraduate education, 8.2% ( $n = 5$ ) high school education and one participant had no formal education.

**TABLE 1** Balance summary measures for the case and the matched control cohort ( $n = 74$ ) calculated for the matching variables age, education, and BMI (rounded)

	Means TS	Means control	Std. mean diff.	Variance Ratio	eCDF Mean	eCDF Max	Std. pair distance
Age	31.49	33.73	-0.3	1.32	0.04	0.16	0.32
Educational background	3.12	3.15	-0.05	1.23	0.01	0.01	0.05
BMI	27.72	27.43	0.04	1.08	0.01	0.05	0.1

Note: Means of case (TS) and control cohort, their standardized mean difference (std. mean diff.), variance ratio, eCDF mean and max and the standardized average of the absolute differences of a variable between pairs are presented.

Abbreviations: BMI, body mass index; eCDF, empirative cumulative distribution function; TS, Turner syndrome.

### 3.1.2 | Health history (Table 2)

The median height of participants was 152.2 cm (range 125–168 cm), mean weight 68.6 kg (range 38–150 kg;  $SD \pm 5.3$  cm); calculated mean BMI was 28.07 kg/m<sup>2</sup> (range 16.8–60.0 kg/m<sup>2</sup>;  $SD \pm 7.6$  kg/m<sup>2</sup>). The karyotype was reported in  $n = 49$  (66%) of participants;  $n = 23$  reported a 45,X karyotype (31%) and  $n = 26$  (35%) a mosaic karyotype, further specified as 45,X/46,XX in  $n = 7$ , 45,X/46,XY in  $n = 2$ , isochromosome X in  $n = 2$  and ring chromosome in  $n = 2$  participants. Age of diagnosis with TS ( $n = 72$  responses) was in  $n = 13$  (18%) participants during infancy,  $n = 17$  (23%) before the age of 10 years,  $n = 35$  (49%) during adolescence (10–18 years) and  $n = 7$  (10%) participants in adulthood (18–35 years). Seventy percent of participating women reportedly received growth hormone therapy in the past and 86.5% received pubertal induction therapy during adolescence. The median age at menarche ( $n = 63$  responses) was 15.5 years (range 12–34 years); two participants stated that they never achieved menarche. The reported mode of pubertal induction was oral oestrogen preparations in most respondents (38/40) and transdermal oestrogens in 2/40 responses;  $n = 24$  participants did not disclose the mode of pubertal induction therapy.

Significant comorbidities were disclosed by  $n = 36$  participants and are also listed in Table 2.

### 3.2 | BREAST-Q scores

Direct comparison of the overall scores for each individual domain of the BREAST-Q pre-augmentation module in the entire TS cohort with the matched control cohort shows significantly lower scores in TS women for the domains 'Satisfaction with Breasts' ( $p = .04$ ), 'Psychosocial Wellbeing' ( $p < .0001$ ) and 'Sexual Wellbeing' ( $p < .0001$ ) (Figure 1A); there were no differences in the domain 'Physical Wellbeing'.

To determine individual ranks of satisfaction for each domain, delta scores were calculated by subtracting each score from a control from that of the matched TS woman (Figure 1B). A delta score less than '0', therefore, indicates lower satisfaction in a TS woman compared to their match.

We performed subgroup analysis by direct comparison of delta scores (Figure 2). TS women who received pubertal induction therapy

had overall lower delta scores compared to TS women who did not receive pubertal induction therapy in all domains but 'physical wellbeing', which reached statistical significance for the domain 'satisfaction with breasts' ( $p = .017$ ) (Figure 2A). Delta scores did not differ between TS women who achieved menarche after or before the age of 15 years (Figure 2B). Women with TS and a BMI of less than 25 kg/m<sup>2</sup> reported lower delta BREAST-Q scores than women who were overweight or obese, which reached statistical significance in the domains 'satisfaction with breasts' ( $p = .01$ ) and 'sexual wellbeing' ( $p = .01$ ) (Figure 2C). There were no statistically significant differences in delta BREAST-Q scores in TS women who were diagnosed before the age of 9 years (Figure 2D) or who had a 45,X or mosaic karyotype (Figure 2E). In TS women who reported to have received growth hormone therapy during childhood, delta scores were lower compared to TS women who had not received growth hormone in the 'psychosocial wellbeing' domain ( $p = .047$ ), but no statistically significant differences were observed in the other domains (Figure 2F).

## 4 | DISCUSSION

In this carefully designed study, we employed the BREAST-Q questionnaire in a cohort of women with TS as a PROM on breast satisfaction as an indirect means of assessing the effectiveness of pubertal induction using oestrogen replacement therapy. Our data suggest that TS women are less satisfied with their breasts overall, in their psychosocial and their sexual life compared to matched non-TS women.

A range of studies have assessed the morphological development of breasts in TS girls on oestrogen therapy, mainly to assess optimal timing and dosages of oestrogen therapy for pubertal induction.<sup>8,11,13–15,17,18</sup> Some reports suggest that about half of TS girls receiving pubertal induction therapy do not progress to Tanner breast stage B5.<sup>14,16,27</sup> Another prospective study in  $n = 21$  TS women did not find any major morphological differences in breast size and shape compared to a reference population, but slightly reduced breast volumes and more bulky thorax volumes were observed.<sup>15</sup> In general, subjective breast-satisfaction is widely under-reported and only one recent report from the dsd-LIFE initiative assessed breast satisfaction in a large multicentre cohort

**TABLE 2** Demographics and health history, and treatment details of 74 women with Turner syndrome women

Age (years)	32 (18–45)
Height (cm)	152 (125–168)
Weight (kg)	65 (48–92)
BMI (kg/m <sup>2</sup> )	28 (16.9–60.8)
Country of origin <sup>a</sup>	
United Kingdom	45 (60.8%)
United States	8 (10.8%)
Australia	5 (6.8%)
Ireland	4 (5.4%)
Canada, France	2 each (2.7%)
Austria, Bulgaria, Cameroon, New Zealand, Portugal, Slovakia, South Africa, Spain	1 each (1.4%)
Highest level of education	
Postgraduate	16 (21.6%)
College or University	52 (70.3%)
High School	5 (6.8%)
No formal education	1 (1.3%)
Age at diagnosis (years) <sup>a</sup>	11.0, 0.02–35.0
Age at menarche (years) <sup>b</sup>	15.5, 12–34.0
Karyotype	
45,X	23 (31.1%)
Mosaic	26 (35.1%)
Not known/reported	25 (33.8%)
Hormone replacement therapy	
Yes	62 (83.8%)
None	8 (10.8%)
Not disclosed	4 (5.4%)
Growth hormone therapy (in the past)	
Yes	52 (70.2%)
No	21 (28.4%)
Not known	1 (1.4%)
Pubertal induction therapy	
Yes	63 (85.1%)
Ethinylestradiol	19 (25.7%)
Other oral oestrogen	18 (24.3%)
Oestrogen patches	2 (2.7%)
Not disclosed	24 (32.4%)
No	11 (14.9%)

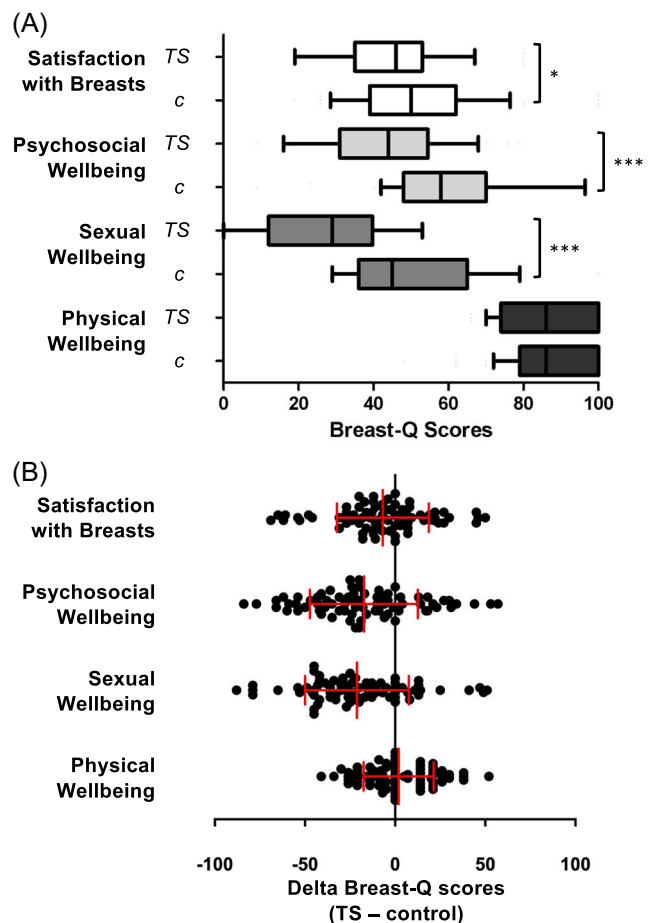
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Comorbidities	
Diabetes mellitus	5 (6.8%)
Hypothyroidism	10 (13.5%)
High blood pressure	7 (9.5%)
Coeliac disease	1 (1.4%)
Eczema/asthma	10 (13.5%)
Psoriasis	5 (6.8%)
Osteoarthritis	3 (4.1%)
None	16 (21.7%)
None disclosed	22 (29.8%)

Note: Data are given in as median (range), unless stated otherwise.

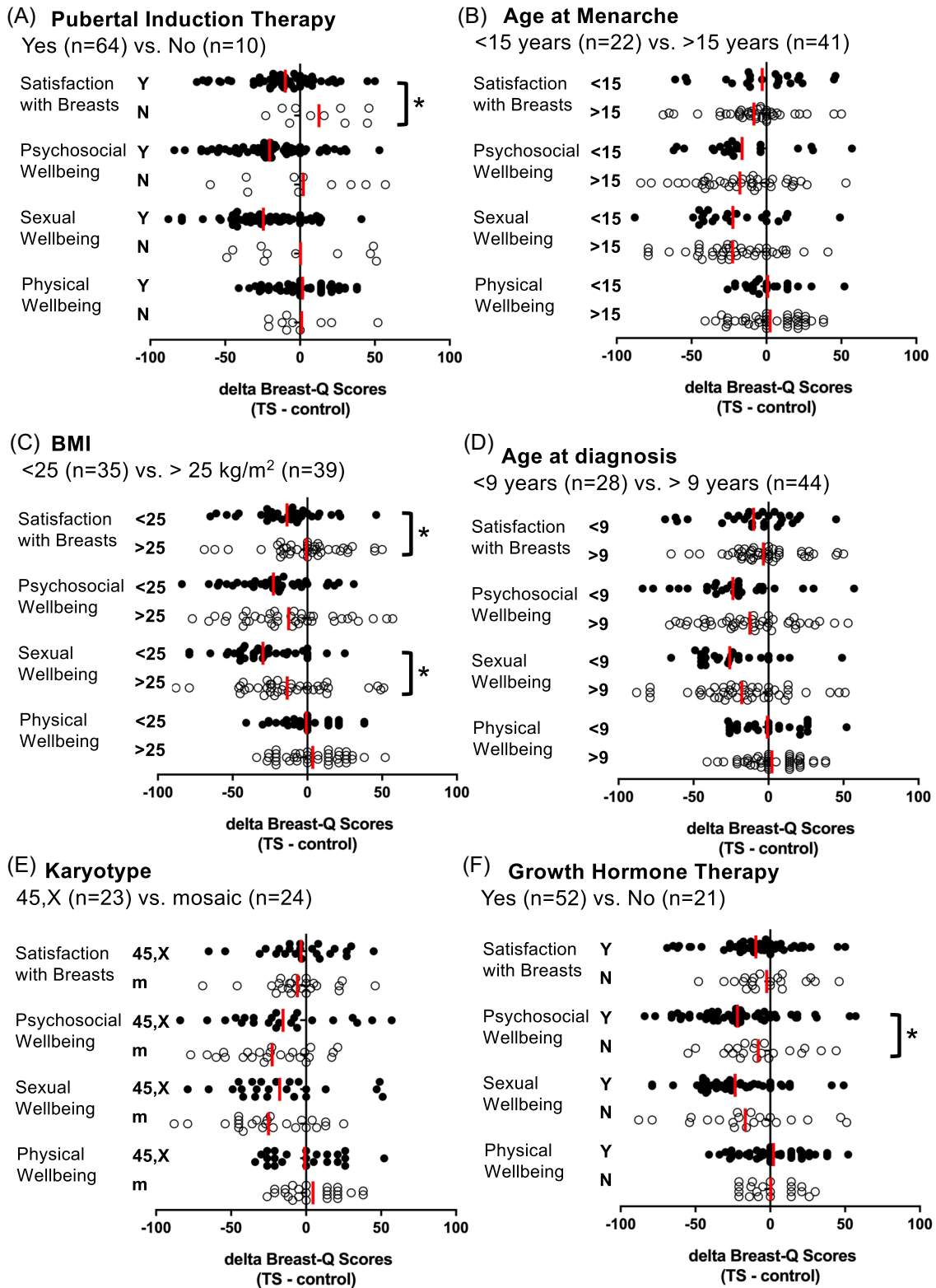
<sup>a</sup>n = 72 responses.

<sup>b</sup>n = 63 responses.



**FIGURE 1** BREAST-Q scores for the entire matched cohort of 74 women with TS. (A) Direct comparison of the overall scores (0–100) in women with Turner syndrome (TS) and controls (c). Boxplots represent the mean with interquartile ranges, whiskers represent two standard deviations of the mean. (B) Individual delta scores obtained by subtracting the BREAST-Q scores from each control from their matched TS woman. Red lines represent the mean with one standard variation. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]





**FIGURE 2** Delta BREAST-Q scores in different TS subgroups. (A) Comparison for TS women who reported to have received pubertal induction therapy (closed circles) compared to TS who did not receive pubertal induction (open circles). (B) Comparison for TS women who reported to have achieved menarche younger before (closed circle) or after the age of 15 years (open circles). (C) Comparison for TS women who are lean (BMI < 25 kg/m<sup>2</sup>; closed circles) or overweight/obese (BMI > 25 kg/m<sup>2</sup>; open circles). (D) Comparison for TS women who were diagnosed before (closed circles) or after their 9th birthday (open circles). (E) Comparison for TS women who reported to have a 45,X karyotype (closed circles) compared to those who reported mosaicism (open circles). (F) Comparison for TS women who reported to have received growth hormone therapy (closed circles) compared to those who did not receive growth hormone therapy (open circles). Number or received responses for each subgroup are provided for each panel. The red line represents the mean of delta BREAST-Q values for each subgroup. Asterisks indicate where direct comparison reached statistical significance level. BMI, body mass index; TS, Turner syndrome. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

of women with differences in sexual development (DSD), which included 332 TS women.<sup>28</sup> The authors report lower satisfaction with breasts in TS based on a categorical scale in comparison to published data from the literature as no control data was collected as part of the study. Breast satisfaction was associated with a lower degree of sexual satisfaction and 'feelings of femininity' in the overall dsd-LIFE cohort, a finding we could confirm in our TS cohort based on the domains of the BREAST-Q questionnaire. We did not assess breast size in our cohort, which is a limitation of our analysis. Three TS women in our cohort received breast augmentation in their twenties, which suggests a higher rate of breast augmentation compared to the normal population<sup>29</sup> (4.1% vs. 0.9%), likely reflecting dissatisfaction with breast shape/morphology. To our knowledge, breast augmentation in TS is not systematically captured elsewhere and should be addressed in ongoing studies assessing health care outcomes in TS such as registries (i.e., the iTS Registry; [www.i-turnersyndrome.org](http://www.i-turnersyndrome.org)).

The BREAST-Q augmentation module is a rigorously developed and well-validated PROM used successfully in a number of studies in patients seeking breast augmentation.<sup>23,30</sup> Normative data from a large North American sample was published recently, allowing for comparison and expansion of the tool for clinical care and research.<sup>24</sup> The BREAST-Q questionnaire was developed through literature reviews, focus groups, patient interviews and expert panels to enable the assessment of treatment outcomes that are relevant to patients undergoing breast surgery. Although the questionnaire was developed for patients receiving surgery to meet their specific needs, it appears reasonable to use this tool for other patient groups, such as TS, who have received treatment that affects the development of secondary sexual characteristics for adequate assessment of treatment outcomes. Since the BREAST-Q, to date, had not been used outside breast surgery, we took care to conduct qualitative interviews with healthy women under guidance with the developers of the BREAST-Q to ensure the items of the questionnaire were relevant for our study population. In addition to satisfaction with breast (domain 1), the BREAST-Q questionnaire also captures specific quality of life (QoL), such as the domains 'psychosocial wellbeing' (domain 2), 'sexual wellbeing' (domain 3) and 'physical wellbeing' (domain 4) *in relation* to breast, which provide more detailed insights into QoL of the study population. TS women in our cohort report lower scores for 'satisfaction with breasts' and 'psychosocial/sexual wellbeing', suggesting a negative impact of lower breast satisfaction on these QoL domains. In the subgroup analysis, the age at menarche, the age at diagnosis and the karyotype did not seem to impact on BREAST-Q scores. However, lower scores were observed in TS women who received pubertal induction therapy and who had a lower BMI. In the dsd-LIFE study, higher BMI in TS was not found to be associated with greater breast satisfaction but lower self-esteem and reduced body image.<sup>27,28</sup> In contrast, the normative data set from the AOW shows higher satisfaction scores in healthy women with lower BMI,<sup>24</sup> which possibly reflects the higher proportion of women with larger breasts in the control cohort compared to DSD with smaller breast size.

TS women who have received GH therapy in the past have lower psychological wellbeing scores compared to TS women who have not received GH therapy, which is a surprising finding, however, this is likely confounded by the fact that TS women who had GH therapy also received pubertal induction therapy; in our sample, 93% of TS women who had GH therapy also received pubertal induction therapy compared to 71% of TS women who did not receive GH therapy. Due to the small sample size, a further subanalysis was not feasible and these observations need to be scrutinized in future studies with larger cohorts.

Various methods of pubertal induction are used around the world, using different timing, oestrogen preparations, modes of delivery and dosing. To date, no large prospective study has compared the outcomes of different regimens on uterine size, breast size, shape and satisfaction, height, and body composition.<sup>20</sup> There is general expert consensus that 17 $\beta$ -estradiol delivered through the transdermal route is the most physiological and probably safest oestrogen preparation,<sup>12</sup> although there is no data from clinical trials to underpin this guidance.<sup>20</sup> The timing of menarche is indicative of sufficient oestrogen delivery. Interestingly, however, no difference in breast satisfaction was found between women with menarche before/after age 15 years. In our cohort, subgroup comparison of TS women who received ethinylestradiol for pubertal induction compared to other oral oestrogen preparations did not show any differences in BREAST-Q delta scores, but we have not included those results due to bias caused by the heterogeneity of oestrogen preparations (nine different formulations).

The strength of our study includes the use of a validated tool and the matched design using health control women from the AOW. Limitations include potential selection bias assuming more breast-dissatisfied TS women respond to an online survey than satisfied ones. In addition, the sample size is limited although various efforts were made to increase recruitment via patient support groups, possibly because addressing sexual characteristics remain a social taboo. Respondents were mostly white with a higher educational background, which likely represent the traditional membership of patient support groups. Self-reporting itself may introduce inaccuracy of information but assessing PROMs through engagement with support groups is nonetheless generally regarded as reliable, real-life evidence.<sup>31</sup> Finally, the BREAST-Q questionnaire has not been strictly validated in TS women but in women who are about to receive breast surgery, however, through our qualitative interviews with healthy women and its recent use in a large cohort,<sup>24</sup> we believe that the survey can and should be used for a wider purpose, such as to evaluate breast satisfaction in women with TS. To our knowledge, the BREAST-Q is the only fully validated and most comprehensive tool available to assess these patient-related outcomes.

In conclusion, our results demonstrate that breast satisfaction is reduced in young adult women with TS, which prompts speculation on the type, dose, and timing of pubertal induction treatment as well as the optimal hormone replacement therapy in young adult life. Paediatric endocrinologists strive for physiological hormone replacement therapy. Our results call for larger prospective studies to



compare the outcomes of different pubertal induction regimens including breast satisfaction, breast size- and shape, uterine size, height, body composition, bone mass and cardiovascular health.

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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