Published in final edited form as:

J Pediatr. 2018 August ; 199: 206–211. doi:10.1016/j.jpeds.2018.03.058.

Psychosocial Characteristics of Women with a Delayed Diagnosis of Turner Syndrome

Gabrielle E. Reimann, BS, Martha M. Bernad Perman, ScD, Pei-Shu Ho, PhD, Rebecca A. Parks, MS, and Leora E. Comis, MPA

National Institutes of Health, Rehabilitation Medicine Department, Bethesda, MD, 20892, USA

Abstract

Objectives—To characterize the psychosocial profiles of adult women diagnosed with Turner syndrome (TS) before (early diagnosis) and at or after (late diagnosis) age 13.

Study design—Females with TS ages 22 and older at evaluation (n=110) participated in a cross-sectional study at the National Institutes of Health. Researchers performed nonparametric and logistic regression analyses to assess early and late diagnosis cohorts on measures of depression, substance use, and perceptions of competence and identity.

Results—47% of participants received a TS diagnosis at or after age 13. Median age at diagnosis was 12.0 years (range: 0–43). Covariate-adjusted models revealed that women with late diagnoses had an increased likelihood of developing mild to severe depressive symptoms (OR = 7.36) and a decreased likelihood of being perceived as competent (OR = 0.26). Women with a late diagnosis also exhibited more frequent substance use compared with women with early diagnoses.

Conclusions—These data suggest that TS diagnoses received at or after age 13 may contribute to adverse outcomes related to depression, substance use, and perceptions of competence. Delayed TS diagnoses may place females at risk for negative psychosocial development extending into adulthood. These findings indicate it is important for pediatricians to evaluate psychosocial domains in females with TS regularly, particularly among those diagnosed at age 13 or older.

Keywords

Late diagnosis; depression; identity; alcohol; drug; growth hormone

Corresponding Author: Martha M. Bernad Perman, ScD, 10 Center Drive, Building 10, MSC-1604, CRC-1-1469 NE, Bethesda, MD 20892; Telephone: 301-469-9019; Fax: 301-480-0669; (mbernad@cc.nih.gov).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The authors declare no conflicts of interest.

Portions of this study were presented as a poster at the National Institutes of Health Summer Poster Day, 2009, Bethesda, Maryland; Women's Health 2011: The 19th Annual Congress, April 1–3, 2011, Washington, D.C.; the National Institutes of Health Summer Poster Day, 2011, Bethesda, Maryland; and the National Institutes of Health Research Festival, September 13–15, 2017, Bethesda, Maryland.

Trial registration [ClinicalTrials.gov](https://clinicaltrials.gov) NCT00006334

Turner syndrome is a common genetic disorder characterized by partial or complete absence of one X chromosome, affecting approximately 1 in 2000 female births [1]. Clinical features in women with TS may include short stature, ovarian failure, and dysmorphia, as well as medical risks such as obesity, cardiac malformations, and renal abnormalities [2]. Clinical manifestations differ by individual and as a result, age at TS diagnosis is highly variable. Schoemaker and colleagues found 55.5% of females received TS diagnoses at or after age 13 (unpublished data).

Several studies have found that growth hormone (GH) responsiveness declines as initiation age increases [4, 5]. However, there is a paucity of studies examining age at TS diagnosis as a factor of psychosocial development. Adolescence is a vulnerable time for girls with TS, and diagnoses received during this time potentially disrupt a critical period for identity formation [6]. Studies indicate that self-perception declines in early adolescence, in part due to displeasure with physical manifestations of TS (eg, amenorrhea, minimal breast development, short stature) which become increasingly evident at this time [7, 8]. Psychological profiles of females with TS frequently reveal depression and negative self-image, often beginning in adolescence and extending into adulthood [9, 10].

Previous research has shown age at TS diagnosis influences psychological well-being. However, research has yet to evaluate the long-term effect of age at diagnosis on specific psychosocial domains [11]. This study examined psychosocial development in relation to TS diagnoses received before and at or after age 13, which represents the national average age of menarche onset and a posited vital age for identity development [12, 6].

Methods

Women with a TS diagnosis participated in the cross-sectional study “Turner Syndrome: Genotype & Phenotype” at the National Institutes of Health (NIH). This study was part of a multidisciplinary, longitudinal project conducted through the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), exploring mechanisms causing TS features ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00006334): NCT00006334). The current study implemented occupational and vocational therapy measures to investigate psychosocial profiles within the TS population.

Participants were recruited through medical journal advertisements, physician referrals, TS advocacy groups, and [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00006334) online postings. Eligibility requirements included non-pregnant phenotypic females, at least 10 years of age, evidence of a X-chromosomal abnormality (or at least 80% 45, X lymphocytes for those with a 45, X/ 46XX karyotype), and no co-existing autosomal defects. Blood samplings taken at screening confirmed participant karyotype. Participants provided individual or parental informed consent. The NICHD Institutional Review Board approved this research protocol (2000-CH-0219).

Females with a TS diagnosis (n=160) enrolled between December 2008 and June 2012. This study limited participant age to 22 years and older in order to examine the psychosocial profiles of adult women. This analysis omitted 50 participants on the following bases: non-TS karyotype (n=4), incomplete testing due to intellectual disability (n=1), and pediatric age

range (n=45), as defined by the U.S. Department of Health and Human Services [13]. The final analysis included 110 participants.

Participants underwent FIVE days of comprehensive medical and psychological inpatient examination at the NIH Clinical Center in Bethesda, Maryland. Two registered occupational therapists administered the Beck Depression Inventory-II (BDI-II), Occupational Self-Assessment (OSA), and Occupational Performance History Interview-II (OPHI-II) during a 90-minute assessment [14, 15, 16]. A certified rehabilitation counselor administered the Profile of Adaptation to Life-Medical (PAL-M) during a 90-minute assessment [17]. Participant age at TS diagnosis was unknown to therapists at time of instrument administration.

Researchers conducted semi-structured interviews to collect data on height, race, education, employment, marital status, age at evaluation, and age of TS diagnosis. NIH Electronic Medical Record provided history of GH use and clinician-diagnosed depression. Age at TS diagnosis categories included early diagnosis (TS diagnosis received before age 13) and late diagnosis (TS diagnosis received at or after age 13). Karyotype categories included: 45, X (complete deletion of one X-chromosome) and) Other (mosaicism and partial deletion within the X-chromosome). Education categories included: (1) High school, GED or less (2) Some college (some college or Associate's degree), and (3) College or postgraduate degree. Race categories included: (1) Caucasian, (2) African American, (3) Hispanic, and (4) Other (Asian, Middle Eastern, Pacific Islander, or biracial). Employment status categories included: (1) Part-time, (2) Full-time, (3) Unemployed (unemployed by choice or unable to find work), (4) Other (retired, student, unable to work due to illness), and (5) Unknown (information not indicated). Marital status categories included: Married (current marriage or partnership) and Unmarried (never married or currently separated, divorced, or widowed).

BDI-II is a validated 21-item self-report measure of depression symptom severity at the time of administration. Items receive ratings on a 4-point scale ranging from 0 to 3, totaling a summary score ranging from 0 to 63. Total scores represent the following symptomology ranges: 0–13 minimal, 14–19 mild, 20–28 moderate, and 29–63 severe [13]. Scores of 14 or above indicate depressive symptoms. This instrument has well-established psychometric properties [18]. *OSA - Version 2.2* is a self-reported assessment tool used to evaluate self-perceived competence and values. “Competence” (21 items) addresses participant awareness of abilities regarding skills and behaviors. Items receive ratings on a scale from 1 (“I have a lot of problem doing this”) to 4 (“I do this extremely well”). “Value” (21 items) addresses participant-perceived importance of competence areas, on a scale of 1 (“Not so important”) to 4 (“Most important”). Analyses used standardized scores (range: 1–100) converted from Competence and Value total scores. This instrument has well-established psychometric properties [19].

OPHI-II - Version 2.1 is a semi-structured measure used to explore a therapist's perception of an individual's ability to maintain productive lifestyle patterns. It consists of three scales: Competence (9 items), Identity (11 items), and Settings (9 items). “Competence” includes a therapist's assessment of participants' abilities, skills, and behaviors. “Identity” evaluates the degree to which a participant internalizes positive roles and values. OPHI-II Settings scale

was not relevant to the evaluation of perceptions of the participant and therefore it was not included in this analysis. Analyses used standardized scores (range: 1–100) converted from Competence and Identity total scores; higher scores represent greater abilities, productivity, and values. This instrument has well-established psychometric properties [20].

PAL-M measures psychological adjustment and physical health. Each of the 34 self-reported items receives a rating on a scale from 1 (Rarely) to 4 (Almost always). Individual items combined to create 7 composite subscale scores: Negative Emotions (5 items), Poor Well-being (5 items), Poor Income Management (3 items), Physical Symptoms (7 items), Alcohol and Drug Problems (4 items), Poor Close Relations (5 items), and Poor Child Relations (5 items). Researchers added the *PAL-M* in March 2010; 61 participants completed this instrument.

Statistical Analyses

Shapiro-Wilk tests were used to evaluate normality of variable distribution. We used chi-square tests to assess associations between age at diagnosis and GH use, depression diagnoses, and depressive symptoms. Mann-Whitney U tests were conducted to examine group differences in depression, identity, self-perception, psychological adjustment, and GH variables. We performed binary logistic regressions to examine the likelihood of mild to severe depressive symptoms and perceptions of competence and identity in relation to age at diagnosis, while controlling for chronological age, education level, GH use, karyotype, and marital status. Perceptions of self encompasses the individual's (OSA) and therapist's (OPHI-II) evaluation of the participant. All analyses were determined significant at 0.05 alpha level. We used the Statistical Package for the Social Sciences (SPSS) 23 to conduct analyses (International Business Machines Corporation SPSS, Chicago, IL, USA).

Results

Analyses included data from 110 participants (Table I). Mean age at evaluation was 42.04 ± 11.69 (SD) years (range: 22–69 years). Overall median age at TS diagnosis was 12.0 years (range: 0–43). In accordance with diagnoses categorization, 58 women received an early diagnosis, and 52 received a late diagnosis. Median age of individuals at early and late diagnoses was 1.5 and 16.25 years, respectively. Participants were predominantly Caucasian (87.3%) and unmarried (60.9%). A majority had the 45, X karyotype (70.0%) and did not use GH treatments (64.5%). At the time of evaluation, over half of the sample had a college or postgraduate degree (54.5%) and worked full time (56.4%).

In the overall sample, 25.5% of women had mild to severe depressive symptoms, whereas depressive symptoms occurred in 12.1% of early diagnosis individuals and 40.4% of late diagnosis individuals. Unadjusted comparisons displayed that those with a late TS diagnosis had significantly higher BDI-II scores than those diagnosed early ($P = .0007$). Late TS diagnosis was significantly associated with mild to severe depressive symptoms ($p = 0.001$; Table 2). There was no significant association between age at diagnosis and clinician-diagnosed depression ($p = 0.68$).

As seen in Table 3, participants who had a late diagnosis displayed significantly lower self-reported OSA Competence scores than individuals with an early diagnosis ($p = 0.012$). There was no group difference in OSA Value score ($p = 0.555$). Therapists rated those with late diagnoses significantly lower than individuals with early diagnosis on OPHI-II Competence ($p = 0.001$) and Identity ($p = 0.028$) scales.

PAL-M analyses displayed that those who received a late diagnosis reported significantly higher alcohol and drug use ($p = 0.007$), and lower scores in Income Management ($p = 0.025$). There were no significant group differences among domains of Negative Emotions, Well-being, or Physical Symptoms (Table 3). A majority of participants did not have a partner or children, resulting in low frequency of responses to PAL-M Close Relations ($n = 38$) and Child Relations ($n = 14$) scales, therefore these two subscales were not analyzed.

Covariate-adjusted comparisons showed that late diagnosis was significantly associated with an increased likelihood of developing mild to severe depressive symptoms ($OR=7.36$, $p = 0.001$) and a decreased likelihood of receiving a high therapist-rated competence score ($OR=0.26$, $p = 0.004$). Age at diagnosis was not significantly associated with OSA Competence ($p = 0.08$) or OPHI-II Identity ($p = 0.941$; Table 4) in adjusted models.

Early diagnosis was significantly associated with a history of GH treatment ($p = 0.001$). Among individuals diagnosed early, there was a significant height difference (7.5 cm) between those who reported GH use and those who did not ($p = 0.0007$). Among individuals with a late diagnosis, there was no significant height difference between those who reported GH use and who did not ($p = 0.09$). A comparative analysis showed no significant difference in height between GH users and non-GH users within the entire sample ($p = 0.67$).

Discussion

Previous studies have reported psychosocial difficulties among women with TS [7, 9, 21]. We have shown that time of diagnosis is a factor in psychosocial development among the TS population. Studies report a decline in age at time of TS diagnosis, however approximately 47% of this sample received diagnoses at or after age 13 [22]. In comparison with the early diagnosis group, results indicate that women who experienced a late TS diagnosis: 1) were more likely to develop depressive symptoms; 2) reported more frequent substance use; 3) showed decreased perception of competence; and 4) engaged in GH treatment less often.

Although 40% of women with late diagnoses reported mild to severe depressive symptoms, less than 20% had clinician-diagnosed depression. This sample's proportion of clinician-diagnosed depression was lower than the lifetime major depression seen in 36% of women with TS, as reported by Cardoso and colleagues [23]. Previous studies have reported subsyndromal depressive symptoms in women with TS; thus, those diagnosed late may experience depressive symptoms at a threshold that is prominent, but does not meet the severity necessary for a clinical diagnosis [9, 21]. Our findings indicated that those diagnosed late reported more severe feelings of self-dislike, worthlessness, personal failure, and suicidal thoughts, as identified by the BDI-II. Regardless of the absence of clinically diagnosed depression, mild to severe depression displayed in late diagnosis individuals may

indicate a concerning psychological profile that would warrant regular mental health screenings.

Greater depression in women with late diagnoses could be a consequence of potential or existing TS comorbidities (e.g., cardiac and renal anomalies, diabetes) [24]. Simultaneous disclosure of severe medical conditions associated with TS can be devastating to quality of life. Furthermore, delayed TS diagnosis may render preventive treatment options inapplicable, causing women with TS to sense a loss of control over their well-being. In cases where preventive measures are still an option, intense medical treatment for associated sequela can place mental and physical demands on women with TS. For many, childbearing is significant to a woman's identity, relationship, and culture. Therefore, disclosure of infertility can also result in vulnerability to depression. Schmidt and colleagues emphasized this, identifying similar depression profiles between women with TS and those with premature ovarian failure [25]. Potentially, women with a late TS diagnosis experience depressive symptoms after acknowledging the realities of the disorder (e.g. infertility, health complications). The current study did not collect data on past or current health conditions; however, future studies may consider gathering medical history to evaluate relationships among age at diagnosis, depression, and comorbidities.

Johannessen and colleagues reported that females without TS, but with depressive symptoms are likely to engage in frequent alcohol consumption and intoxication [26]. These researchers reference the self-medication hypothesis as a possible explanation, which is described as a person's use of substances to reduce emotional distress [27]. The present study suggests that individuals with a late diagnosis may engage in substance use to mitigate negative emotions stemming from a TS diagnosis. Few reports are available on frequency of alcohol and drug use among the TS population, however substance use is common in individuals exhibiting depressive symptoms [26]. Additional studies are necessary to analyze the prevalence of alcohol and substance use in women with TS.

Poor self-perception is a widely recognized issue among the TS population; studies indicate concerns with body image, infertility prognosis, and acceptance of TS limitations [21, 28, 10]. Though the current study's comparative analyses showed differences in identity in relation to age at TS diagnosis, these differences did not sustain after controlling for various factors. Instead, these findings indicate that marital status and chronological age affected identity to a greater extent than age at TS diagnosis (Table 4). Self-perceived competence was also not significantly associated with age at diagnosis. However, both adjusted and unadjusted models showed that therapists perceived the competence of women with late diagnoses as lower than women diagnosed early. Therapists perceived individuals with a late diagnosis as less capable of meeting expectations, fulfilling goals, and addressing responsibilities. Based on these objective evaluations, there may be salient differences in abilities between those diagnosed early and late. Studies show women with TS benefit from therapeutic interventions promoting self-management skills, however these interventions ameliorate difficulties only after they have already been embedded [29]. Early detection may allow time for girls with TS to develop compensatory strategies from a young age.

Pursuit of available treatment offers a sense of control over a chronic disorder. Early diagnosis may permit the timely induction of puberty, allowing girls with TS to develop secondary sex characteristics alongside their peers. Additionally, previous reports identified a positive relationship between growth-promoting treatments and self-perception of intelligence and attractiveness in girls with TS [30]. Unfortunately, growth-promoting options become less effective and pursued as age at treatment initiation increases [5]. The present study's results support this observation; significantly more women with an early diagnosis received GH therapy (50%) compared with late diagnosis GH users (10%). Although some studies report that older girls with TS may still benefit from GH treatment, early initiation positively affects height [4, 5]. For this reason, clinical practice guidelines strongly recommend that GH initiation occurs no later than age 13 for girls to see benefit [31]. Those diagnosed early have the potential to benefit from improved body image through growth-promoting treatments, as opposed to those with a late diagnosis who likely missed the age at which GH treatment is most effective. Future studies may consider collecting growth rate and severity of TS clinical features in childhood to explore the relationships between childhood TS presentation, depression and perceptions of self.

There are limitations within the present study. The sample's small size (n=110) may contribute to wide logistic analyses confidence intervals (Table 4). Late inclusion of the PAL-M measures resulted in smaller sample sizes in analyses of psychosocial adjustment and physical health (n=61). Furthermore, the PAL-M intended to provide preliminary data on alcohol and substance use in women with TS. Future studies should use an instrument with high validity to examine these variables further. Additionally, the demographic interview did not inquire about several potentially impactful variables. For example, this study was unable to control for health care access, which could potentially influence timing of TS diagnosis (i.e. availability of diagnostic technology, socioeconomic status). This study also did not collect data on the influence or proximity of other psychosocial events (i.e. losses, financial stressors, job difficulties, divorce). These factors warrant acknowledgement in future studies, as they may also contribute to depressive symptoms. Additionally, several of this study's measures included self-report questionnaires, introducing potential report and recall biases. This study also recruited on a voluntary basis, and results potentially represent a demographically skewed sample. For example, this sample was predominately Caucasian (87%) with college or post-graduate degrees (54.5%); therefore, results potentially best depict the psychosocial characteristics of well-educated Caucasian women with TS.

Nevertheless, these data indicate that a late diagnosis is associated with adverse psychosocial outcomes of women with TS. Therefore, this study concludes that early childhood is a vital time for TS diagnosis in order for individuals to adjust to their prognoses and consider growth-promoting treatments. Based on these study results, we recommend that pediatricians karyotype females with unexplained short stature, amenorrhea, pubertal delays, or other TS-related features [22]. Results also highlight the need for pediatricians to regularly screen for depressive symptoms and substance use in all females with TS, especially those who experienced a diagnosis at or after age 13. Finally, physicians should refer females with TS to appropriate specialists to meet their psychological needs and provide a better quality of life.

Acknowledgments

We thank the girls and women with TS who participated in our study. We also thank the NIH Fellows Editorial Board for their contributions in the editing process. We dedicate this article to the memory of Carolyn A. Bondy, M.D.

Supported by Intramural Research Programs of the National Institutes of Child Health and Human Development. Sponsors were not involved in the design, collection, analysis, writing, or submission process of this article.

References

1. Stochholm K, Juul S, Juel K, Naeraa RW, Gravholt CH. Prevalence, incidence, diagnostic delay, and mortality in Turner syndrome. *J Clin Endocrinol Metab.* 2006; 91:3897–3902. [PubMed: 16849410]
2. Al Alwan I, Khadora M, Amir I, Nasrat G, Omair A, Brown L, et al. Turner syndrome genotype and phenotype and their effect on presenting features and timing of diagnosis. *Int J Health Sci.* 2014; 8:195–202.
3. Schoemaker MJ, Swerdlow AJ, Higgins CD, Wright AF, Jacobs PA. Mortality in Women with Turner Syndrome in Great Britain: A National Cohort Study. *J Clin Endocrinol Metab.* 2008; 93:4735–4742. [PubMed: 18812477]
4. Bucerzan S, Miclea D, Popp R, Alkhzouz C, Lazea C, Pop IV, et al. Clinical and genetic characteristics in a group of 45 patients with Turner syndrome (monocentric study). *Ther Clin Risk Manag.* 2017; 13:613–622. [PubMed: 28496331]
5. Ross J, Lee PA, Gut R, Germak J. Impact of age and duration of growth hormone therapy in children with Turner syndrome. *Horm Res Paediatr.* 2011; 76:392–399. [PubMed: 22156541]
6. Steensma TD, Kreukels BP, de Vries AL, Cohen-Kettenis PT. Gender identity development in adolescence. *Horm Behav.* 2013; 64:288–297. [PubMed: 23998673]
7. McCauley E, Feuillan P, Kushner H, Ross J. Psychosocial development in adolescents with Turner syndrome. *J Dev Behav Pediatr.* 2001; 22:360–365. [PubMed: 11773800]
8. McCauley E, Ross J, Kushner H, Cutler G Jr. Self-esteem in and behavior in girls with Turner syndrome. *J Dev Behav Pediatr.* 1995; 16:82–88. [PubMed: 7790519]
9. Kilic BG, Ergur AT, Ocal G. Depression, levels of anxiety and self-concept in girls with Turner's syndrome. *J Pediatr Endocrinol Metab.* 2005; 18:1111–1117. [PubMed: 16459458]
10. Freriks K, Timmermans J, Beerendonk CCM, Verhaak CM, Netea-Maier RT, Otten BJ, et al. Standardized multidisciplinary evaluation yields significant previously undiagnosed morbidity in adult women with Turner syndrome. *J Clin Endocrinol Metab.* 2011; 96:E1517. [PubMed: 21752892]
11. Wide Bowman U, Bryman I, Möller A. Psychological well-being in women with Turner syndrome: Somatic and social correlates. *Psychosom Obstet Gynecol.* 2004; 25:211–219.
12. Chumlea WC, Schubert CM, Roche AF, Kulin HE, Lee PA, Himes JH, et al. Age at menarche and racial comparisons in US girls. *Pediatr.* 2003; 111:110–113.
13. U.S. Department of Health and Human Services. Pediatric Expertise for Advisory Panels; Guidance for Industry and FDA Staff 2015 Jun 29. Retrieved from: <https://www.fda.gov/RegulatoryInformation/Guidances/ucm082185.htm>
14. Beck AT, Steer RA, Brown GK. BDI-II, Beck depression inventory: Manual San Antonio, Tex: Psychological Corp; 1996
15. Baron K, Kielhofner G, Lyenger A, Goldhammer V, Wolenski J. A user's manual for the occupational self assessment (OSA). Version 2.2 University of Illinois; 2006
16. Kielhofner G, Mallinson T, Crawford C, Nowak M, Rigby M, Henry A, et al. A user's manual for the occupational performance history interview (OPHI-II). Version 2.1 University Illinois; 2004
17. Brintzenhofesoc K, Aron M, Jacobsen MP, Koziol DE, Callahan C. The development of the profile of adaptation to life within a medically ill population. *Soc Work in Health Care.* 2007; 45:43–58.
18. Doziois DJA, Dobson KS, Ahnberg JL. A psychometric evaluation of the beck depression inventory-II. *Psychol Assess.* 1998; 2:83–89.

19. Kielhofner G, Forsyth K, Kramer J, Iyenger A. Developing the occupational self assessment: the use of Rasch analysis to assure internal validity, sensitivity and reliability. *British J Occup Ther.* 2009; 72:94–104.
20. Kielhofner G, Mallinson T, Forsyth K, Lai JS. Psychometric properties of the second version of the occupational performance history interview (OPHI-II). *Am J Occup Ther.* 2001; 55:260–267. [PubMed: 11723966]
21. Rickert VI, Hassed SJ, Hendon AE, Cunniff C. The effects of peer ridicule on depression and self-image among adolescent females with Turner syndrome. *J Adolesc Health.* 1996; 19:34–38. [PubMed: 8842858]
22. Massa G, Verlinde F, De Schepper J, Thomas M, Bourguignon JP, Craen M, et al. Trends in age at diagnosis of Turner syndrome. *Arch Dis Child.* 2005; 90:267–268. [PubMed: 15723912]
23. Cardoso G, Daly RJ, Haq NA, Hanton L, Rubinow DR, Bondy CA, et al. Current and lifetime psychiatric illness in women with Turner syndrome. *Gynecol Endocrinol.* 2004; 19:313–319. [PubMed: 15726728]
24. Carvalho AB, Guerra G, Baptista MT, de Faria AP, Marini SH, Guerra AT. Cardiovascular and renal anomalies in Turner syndrome. *Rev Assoc Med Bras.* 2010; 56:655–659.
25. Schmidt PJ, Cardoso GM, Ross JL, Haq N, Rubinow DR, Bondy CA. Shyness, social anxiety and impaired self-esteem in Turner syndrome and premature ovarian failure. *J Am Med Assoc.* 2006; 295:1373–1378.
26. Johannessen EL, Andersson HW, Bjørngaard JH, Pape K. Anxiety and depression symptoms and alcohol use among adolescents- a cross sectional study of Norwegian secondary school students. *BMC Public Health.* 2017; 17:494. [PubMed: 28535753]
27. Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harv Rev Psychiatry.* 1997; 4:231–244. [PubMed: 9385000]
28. Bannink EMN, Raat H, Mulder PGH, de Muinck Keizer-Schirama MPF. Quality of life after growth hormone therapy and induced puberty in women with Turner syndrome. *J Pediatrics.* 2006:95–101.
29. Chadwick PM, Smyth A, Liao L. Improving self-esteem in women diagnosed with Turner syndrome: Results of a pilot intervention. *Pediatr Adolesc Gynecol.* 2014; 27:129–132.
30. Rovet J, Holland J. Psychological aspects of the Canadian randomized controlled trial of human growth hormone and low-dose ethinyl oestradiol in children with Turner syndrome. *Horm Res.* 1993; 2:60–64.
31. Gravholt CH, Andersen NH, Conway GS, Dekkers OM, Geffner ME, Klein KO, et al. Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. *Eur J Endocrinol.* 2017; 177:1–70. [PubMed: 28404594]

Abbreviations

TS	Turner syndrome
GH	Growth Hormone
NIH	National Institutes of Health
BDI-II	Beck Depression Inventory-II
OSA	Occupational Self-Assessment
OPHI-II	Occupational Performance History Interview-II
PAL-M	Profile of Adaptation to Life-Medical

Table 1

Participant demographics (N=110) of women who received early (age<13) and late (age ≥ 13) diagnoses

Characteristics	Early Diagnosis n (%)	Late Diagnosis n (%)	Total n (%)
Race			
White	51 (87.9)	45 (86.5)	96 (87.3)
African American	2 (3.4)	5 (9.6)	7 (6.4)
Hispanic	3 (5.2)	1 (1.9)	4 (3.6)
Other ^a	2 (3.4)	1 (1.9)	3 (2.7)
Marital Status			
Married	22 (37.9)	21 (40.4)	43 (39.1)
Unmarried	36 (62.1)	31 (59.6)	67 (60.9)
Education			
High School, GED or less	10 (17.2)	14 (26.9)	24 (21.8)
Some College	11 (19.0)	15 (28.8)	26 (23.7)
College or Postgraduate	37 (62.7)	23 (44.2)	60 (54.5)
Employment Status			
Part time	11 (19.0)	12 (23.1)	23 (20.9)
Full time	34 (58.6)	28 (53.8)	62 (56.4)
Unemployed	8 (13.8)	2 (3.8)	10 (9.1)
Other ^b	5 (8.6)	9 (17.3)	14 (12.7)
Unknown	0 (0)	1 (1.9)	1 (0.9)
Karyotype			
45,X	46 (79.3)	31 (59.6)	77 (70.0)
Other	12 (20.7)	21 (40.4)	33 (30.0)
Growth Hormone			
Yes	29 (50)	10 (19.2)	39 (35.5)
No	29 (50)	42 (80.8)	71 (64.5)

^a. Race (Asian, Middle Eastern Pacific Islander, biracial)^b. Employment Status (Retired, student, unable to work due to illness)

Note: Percentages may be subject to rounding errors

Table 2

Associations between age at diagnosis and depressive variables

Characteristics	Early Diagnosis (%)	Late Diagnosis (%)	χ^2	p
Depressive Symptoms				
Minimal	87.9	59.6	11.59	0.001 **
Mild to Severe	12.1	40.4		
Depression Diagnosis				
Yes	22.4	19.2	0.17	0.68
No	77.6	80.8		

*
p = 0.05;**
p = 0.01

Early diagnosis (age < 13); Late diagnosis (age ≥ 13)

Table 3

Unadjusted comparisons of scores (median) between early and late diagnosis groups

Characteristics	Early Diagnosis	Late Diagnosis	p
BDI-II (<i>n</i> =110)			
Total Score	5.0	10.0	0.0007**
OSA (<i>n</i> =110)			
Competence	58.0	53.5	0.012*
Value	57.5	59.0	0.555
OPHI-II (<i>n</i> =110)			
Competence	63.0	47.0	0.001**
Identity	58.0	53.5	0.028*
PAL-M (<i>n</i> =61)			
Negative Emotions	46.5	45.0	0.630
Well Being	51.0	49.0	0.159
Income Management	49.0	36.0	0.025*
Physical Symptoms	45.0	45.0	0.415
Alcohol and Drug Use	52.0	58.0	0.007**

*
p 0.05;**
p 0.01

Early diagnosis (age < 13); Late diagnosis (age ≥ 13)

Table 4

Adjusted logistic regression of covariates with depression, self-perceived competence, and therapist-perceived competence and identity

	BDI- II		OSA Competence		OPHI-II Competence		OPHI-II Identity	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age at Diagnosis	7.36 **	2.52 – 25.12	0.472	0.19 – 1.12	0.26 **	0.11 – 0.66	1.04	0.41 – 2.62
Growth Hormone	0.56	0.17 – 1.79	1.41	0.54 – 3.69	0.49	0.17 – 1.43	0.54	0.19 – 1.58
Marital Status	0.92	0.34 – 2.50	1.422	0.62 – 3.25	0.77	0.31 – 1.91	2.74 *	1.05 – 7.15
Karyotype	0.88	0.30 – 2.52	1.173	0.49 – 2.83	0.67	0.26 – 1.76	0.79	0.29 – 2.07
Education								
Some College	0.53	0.14 – 2.09	1.108	0.35 – 3.56	3.56	0.94 – 13.55	1.92	0.45 – 8.17
College or higher	0.71	0.22 – 2.23	1.427	0.53 – 3.85	4.69 **	1.46 – 15.03	3.42	0.96 – 12.19
Age by Decade								
31–40	1.29	0.29 – 5.90	0.673	0.19 – 2.33	1.69	0.42 – 6.75	1.44	0.34 – 5.99
40–71	0.56	0.12 – 2.72	0.816	0.23 – 2.91	2.50	0.63 – 9.98	4.73 *	1.07 – 20.84

* p 0.05;

** p 0.01

Reference categories: Age at Diagnosis (Early Diagnosis); GH (GH Users); Marital Status (Married); Karyotype (45,X); Education (High School, GED or less); Age by Decade (22–30)