Health behaviour of women with Turner Syndrome

Maristella Santi1 | Christa E. Flück1,2 | Michael Hauschild3 | Beatrice Kuhlmann4 | Claudia E. Kuehni1,5 | Grit Sommer1,2,5

1Department of Pediatric Endocrinology, Diabetology and Metabolism, Inselspital, Bern University Children's Hospital, University of Bern, Bern, Switzerland
2Department of BioMedical Research, University of Bern, Bern, Switzerland
3Department of Pediatric Endocrinology and Diabetology, CHUV, University Children's Hospital, University of Lausanne, Lausanne, Switzerland
4Children's Hospital Aarau AG, Aarau, Switzerland
5Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

Correspondence
Grit Sommer, Department of Pediatric Endocrinology, Diabetology and Metabolism, Inselspital, Bern University Children's Hospital, University of Bern, Bern, Switzerland.
Email: grit.sommer@dbmr.unibe.ch

Abstract
Aim: This study assessed lifestyle-related risk factors for cardiovascular disease in young women with Turner syndrome.

Methods: In 2012, we sent a questionnaire to women with Turner syndrome aged ≥18 years and living in Switzerland with questions on socio-demographic and medical data as well as health behaviour. We compared the reported lifestyle with that of women from the Swiss Health Survey 2012, a representative survey of the general population.

Results: Fifty-seven per cent (45/79) of women with Turner syndrome answered the questionnaire (mean age: 24 years). Eighty per cent (36/45) had never smoked compared with 58% (1156/1972) of the general population (p < 0.01). Women with Turner syndrome engaged less often in binge drinking (34% vs. 71%) (p < 0.001), but consumed alcohol equally often as the general population (p = 0.327). They performed sports as often as the general population (p = 0.34), but only one quarter (11/45) of women with Turner syndrome adhered to official physical activity recommendations.

Conclusion: Although most women with Turner syndrome had a healthy lifestyle, only a minority had sufficient physical activity. Paediatricians should promote structured physical activity in girls with Turner syndrome from early childhood onwards to reduce their cardiovascular risk in adulthood and to increase long-term health-related quality of life.

Key words
alcohol, physical activity, smoking, sports, Turner syndrome

1 | INTRODUCTION

Girls and women with Turner syndrome (TS) normally experience a healthy life, but the condition is associated with important health challenges, including obesity, dyslipidaemia, oestrogen deficiency and arterial hypertension, putting them at increased risk of cardiovascular problems. These challenges can have an impact on their health-related behaviour and physical activity. Cardiovascular disease accounted for 41% of the increased mortality in British women with TS compared with the general population, with a standardised mortality ratio of 3.0 (95% CI, 2.7–3.4). Cardiovascular diseases do not usually present clinically until adulthood, but the development of atherosclerosis actually starts in childhood and adolescence. Positive health-related behaviours, such as avoiding smoking, consuming no or only small amounts of alcohol, maintaining normal body weight and engaging in regular physical activities, are therefore important for reducing the risk of cardiovascular disease in women with TS.

Only few studies on health behaviours of girls and women with TS exist. In questionnaire studies from Norway, women with TS were reported to smoke and binge drink less than the general population. However, the impact of Turner syndrome on health behaviours has not been fully explored. The aim of this study was to assess lifestyle-related risk factors for cardiovascular disease in young women with Turner syndrome.
population. In studies from Sweden, women with TS smoked less and had lower physical activity than a female random population sample. In a recent single-centre study from the University of Colorado, USA, only one in five girls with TS adhered to physical activity recommendations, and Danish TS women reported less physical activity than healthy controls.

We aimed to assess smoking status, alcohol consumption and physical activity in women with TS aged ≥18 years living in Switzerland.

2 | SUBJECTS AND METHODS

In 2012, we sent a postal questionnaire to women with TS aged ≥18 years and living in Switzerland (Supplementary Table S1). The survey was part of the nationwide Swiss Growth Study that included patients treated with recombinant growth hormone since 1985 in 11 Swiss centres of paediatric endocrinology, including university hospitals and private practice. The Swiss Growth Study has an estimated coverage of 80% of all women with TS treated with growth hormone. The two cantons of Geneva and Ticino represent the excluded 20%. Women with TS were diagnosed according to their karyotype in the paediatric endocrinology centres. Women with TS received an information letter from their paediatric endocrinology centre, followed by a questionnaire with a pre-paid return envelope. Four weeks later, we sent a reminder and another copy of the questionnaire to those who did not respond. If they still had not responded, they were contacted by phone. The questionnaire included questions on socio-demographic data, medical information and health behaviour. The Ethics Committee of the Canton of Bern approved the Swiss Growth Study (KEK number 095/15).

As comparison data, we used information from adult women aged ≥18–33 years from the Swiss Health Survey (SHS), a representative nationwide survey conducted by the Swiss Federal Statistical Office in 2012. A stratified random sample of Swiss residents received a phone call with similar questions on socio-demographic and health behaviours as the women with TS. We weighted women from the SHS according to the age distribution of the women with TS for a better comparison between the groups. We derived sampling weights from logistic regressions where study group was the outcome and age at study the explanatory variable.

We extracted the following variables from the questionnaires: age, language region of residence in Switzerland, educational level, marital status, final height, weight, smoking status, alcohol consumption, binge drinking and physical activity. We classified smoking status into (a) never smoker; (b) ex-smoker; and (c) current smoker. We categorised alcohol consumption into (a) frequently (drinking ≥1 standard drink ≥3 times per week); (b) occasionally (drinking ≥1 standard drink 1-2 times per week); (c) rarely (drinking <1 standard drink per week); and (d) never (not drinking alcohol). One standard drink was defined as 10 gram of pure ethanol. Binge drinking was classified as drinking ≥6 standard drinks during a single occasion in the last year. Women who reported binge drinking on ≥1 occasion per week were classified as binge drinking weekly, on 1–4 occasions per month as binge drinking monthly and those who did not binge drink as never binge drinking. We assessed two different types of physical activity: (a) sports: we asked women with TS whether and how frequently they engaged in gymnastic, fitness training or sporting activities. If they indicated engaging in these activities for ≥75 min/week, we classified them as doing sports (vs. no sports); (b) daily physical activity: we asked participants whether and how frequently they engaged in activities that caused some increase in breathing or made them sweat (moderate or vigorous activity). If the women indicated engaging in moderate activities for ≥150 min/week or in vigorous activities for ≥75 min/week, we categorised them as having an active vs inactive lifestyle. The classification was based on the recommendations for the healthy population from the Swiss Federal Office for Sports (BASPO) and corresponds to the guidelines from the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). Supplementary Table S1 shows the questions on smoking, alcohol consumption, daily physical activity and sport posed to women with TS and to women from the SHS, translated into English. We also asked women with TS whether they ever had experienced arterial hypertension, cardiac arrhythmia or dysfunction, heart failure, myocardial infarction, angina pectoris, stroke, deep vein thrombosis, pulmonary embolism or valvular problems and whether they had received oestrogens.

We compared self-reported health behaviour (smoking, alcohol consumption and physical activity) between women with TS and an age-adjusted sample of women from the SHS 2012 using chi-square tests for categorical variables and t tests for continuous variables. Missing values for the variables alcohol consumption (n = 2), binge drinking (n = 1), daily physical activity (n = 1) and sports (n = 2) from participating women with TS were imputed with the multivariate imputation by chained equations (MICE) method. All analyses were performed using Stata, Release 13.1 (StataCorp LP).

3 | RESULTS

In the Swiss Growth Study, 45 of 79 women with TS (57%) completed the questionnaire. Participating women with TS did not differ
from those who did not respond in terms of age, language region, final height, duration of growth hormone treatment and average growth hormone dose (data on request). In the SHS 2012, 54% of contacted persons participated. Among the 2134 women aged ≥18–33 years of the SHS, 1972 (92%) completed the questions on alcohol consumption, smoking and physical activity.

The mean age for women from both groups was 24 years after weighting the women from the SHS according to the age distribution of the women with TS (Table 1). Final height was lower in women with TS than in women from the SHS (mean height 152 cm vs. 166 cm, p < 0.001). Body mass index was higher in women with TS than in women from the SHS (25 kg/m² vs. 22 kg/m², p < 0.001). Most women from both groups came from the German-speaking region of Switzerland (67% and 65%, respectively). Educational achievement differed between the two groups (p < 0.001). More women with TS than women from the general population attended only the

| TABLE 1 Characteristics of women with Turner’s syndrome from the Swiss Growth Study and women from the Swiss Health Survey 2012 |

|                      | Women with TS (N = 45) | Women from SHS (N = 1972) |
|----------------------|------------------------|---------------------------|
| **Age at study**     | Mean (SD) Range        | Mean (SD) Range           | p-valueb |
| (years)              | 23.5 (0.9) 19–33       | 23.5 (5.7) 19–33          | n.a.      |
| **Final height (cm)**| 152.2 (8.7) 135–166    | 166.2 (1.2) 137–188       | <0.001    |
| **Weight at survey** | 57.5 (2.3) 35–90       | 61.6 (15.8) 40–180        | 0.017     |
| **Body mass index**  | 24.9 (1.0) 18–37       | 22.3 (5.4) 16–61          | <0.001    |
| (kg/m²)              |                        |                          |           |
| **Age at study**     | n (%)                  | n (%)                    | p-valuec |
| (years)              |                        |                          |           |
| 18–20                | 14 (31) (30)           |                          |           |
| 21–23                | 13 (29) (30)           |                          |           |
| 24–26                | 7 (16) (16)            |                          |           |
| 27–29                | 5 (11) (11)            |                          |           |
| >=30                 | 6 (13) (13)            |                          |           |
| **Language region**  |                        |                          | 0.776     |
| German               | 30 (67) (65)           |                          |           |
| French               | 13 (29) (28)           |                          |           |
| Italian              | 2 (4) (7)              |                          |           |
| **Education**        |                        |                          | 0.001     |
| Primary              | 16 (36) (13)           |                          |           |
| Secondary            | 26 (58) (68)           |                          |           |
| Tertiary             | 3 (7) (19)             |                          |           |
| **Marital status**   |                        |                          | 0.072     |
| Single               | 42 (93) (83)           |                          |           |
| Married, widowed,    | 3 (7) (17)             |                          |           |
| divorced             |                        |                          |           |

Abbreviations: BMI, body mass index; SD, standard deviation; SHS, Swiss Health Survey; TS, Turner syndrome.

Women from the SHS were standardised on the age at study according to women with TS.

p-value calculated from Student’s t test comparing women with TS to women from the SHS.

Women from the SHS weighted according to age distribution of women with TS.

Column percentages are given.

p-value calculated from chi-square statistics comparing women with TS to women from the SHS.

Highest educational level achieved: primary education includes persons with compulsory schooling, secondary those with vocational training and tertiary those with upper secondary or university education.
compulsory 9 years of school (36% vs. 13%, \( p = 0.001 \)). Women with TS tended to be single more often than women from the SHS (93% vs. 83%, \( p = 0.072 \)).

Of the 45 women with TS who responded to the questionnaire, ten (22%) reported having at least one cardiovascular condition; seven women had one and three women had two cardiovascular conditions. Cardiovascular conditions consisted of valvulopathy (\( n = 6 \)), cardiac arrhythmia (\( n = 1 \)), cardiomyopathy (\( n = 1 \)), arterial hypertension (\( n = 4 \)) and angina pectoris (\( n = 1 \)). None of the participants had experienced a myocardial, cerebrovascular or thromboembolic event, and no patient had diabetes mellitus (Supplementary Table S2). No data on cardiovascular disease were available from the SHS. More women with TS (39/45, 87%) reported receiving oestrogen replacement therapy or contraception than women from the SHS (937/1972, 47%) (\( p < 0.001 \)).

Women with TS smoked less and engaged less often in binge drinking than women from the SHS (\( p < 0.001 \)) (Figure 1 and Supplementary Table S3). Both women with TS and women from the SHS consumed alcohol with equal frequency (\( p = 0.524 \)). Women with TS were as active in their daily life and performed sports as often as women from the SHS (11/45 of TS women and 1045/1972 of SHS women, \( p = 0.455 \), and 20/45 of TS women and 394/1972 of SHS women, \( p = 0.278 \); respectively) (Figure 1). Three quarters of women with TS (75%, 34/45) did not adhere to current physical activity guidelines with vigorous-intensity activities of ≥3 days/week and/or moderate-intensity activities for ≥150 min/week,\(^{13-15}\) compared with 80% of women from the SHS (394/1972).

4 | DISCUSSION

Our nationwide study has shown that Swiss women with TS in general followed a healthier lifestyle than women from a population-based survey. However, both populations adhered poorly to national physical activity recommendations.\(^{13-15}\)

There are only two studies on smoking and alcohol consumption in women with TS. Similar to our results, these two questionnaire studies from Norway found that women with TS reported less binge drinking and less smoking than the general population.\(^{5,6}\)

Our study investigated the level of sport and physical activity in adults with TS. While women with TS were as active as women from the SHS, both groups adhered poorly to recommendations for the healthy adult population for Switzerland,\(^{13}\) from the CDC\(^{14}\) and the WHO.\(^{15}\) Our results are similar to those from a study of the University of Colorado, USA, where only 19% of girls with TS adhered to the recommendations of 1 h per day of moderate-to-vigorous physical activity.\(^{10}\) A study from Poland found that girls with TS aged 10–18 years had a lower performance in fitness tests than healthy controls.\(^{16}\) Women with TS are often smaller, heavier and have delayed puberty compared with their peers and have to cope with medical and psychosocial difficulties, which might

![FIGURE 1 Smoking status, alcohol consumption, binge drinking and physical activity in women with Turner syndrome (TS, N = 45) compared to women from the Swiss Health Survey (SHS, N = 1972)](image-url)
contribute to poor motor fitness and a low interest in sports. Persons with chronic morbidities such as cardiovascular disease are at risk of being physically inactive, which leads to a cycle of de-conditioning.\textsuperscript{17} Girls and women with TS who have a normal aortic size and no other major cardiovascular diseases benefit from regular physical activity.\textsuperscript{18} Such activity improves muscle-to-fat ratio and lowers the risk of metabolic syndrome and osteoporosis in TS.\textsuperscript{19} It also improves their body image, well-being and psychological functioning, and increases their quality of life.\textsuperscript{20,21}

Current clinical guidelines for girls and women with TS\textsuperscript{18} do not define a recommended level of activity to reduce the risk of cardiovascular disease. Physical activity should be adapted to the individual health of the patients, based on the specific comorbidity profile of girls and women with TS. Gravholt et al. did not recommend intense sports for women and girls with a moderately or severely dilated aorta.\textsuperscript{18} In the future, girls and women with TS should receive counselling on appropriate physical activity with personalised, comorbidity-adapted exercise protocols. Comprehensive information is particularly important during the sensitive phase of transition from paediatric to adult care when the young women become responsible for their own health.\textsuperscript{22} Two studies from France and Poland showed that less than 5% of adult women with TS underwent all recommended medical investigations at transition.\textsuperscript{20,21}

Both surveys, the Swiss Growth Study and the Swiss Health Survey 2012, may suffer from social desirability bias, as women may have answered the questionnaire in a way that may be more accepted by social norms. Thus, our results may have overestimated health-related behaviour in both groups, such that women may have under-reported smoking and alcohol consumption and over-reported levels of physical activity and sports. However, we compared the answers of women with TS to responses from the general population during telephone interviews, which are even more prone to social desirability bias than postal questionnaires.\textsuperscript{23} The data on cardiovascular outcomes of women with TS were self-reported, which may have led to underreporting of cardiovascular problems, because participating women may not recall their diagnostic results in detail. The small sample size runs the risk of not detecting differences in physical activities and sports between women with TS to women from the SHS. The women with TS who participated in our study may not be representative for the entire population of women with TS. Due to the design of the Swiss Growth Study, we included TS women treated with recombinant human growth hormone since 1991, when TS became an approved indication for growth hormone treatment in Switzerland. We could not include TS patients who did not receive growth hormone because they or their parents declined treatment or because they were diagnosed late during adolescence when the growth plates were almost closed. Thus, women with mild TS phenotypes may have been underrepresented in our sample, potentially resulting in an underestimation of physical activity. On the other hand, the 57% of participating women with TS in our survey may be more motivated to engage in physical activity than non-participants, which may have led to an overestimation of physical activity in our study. We included women with TS from both public hospitals and from private practice, increasing the representativeness of our study population for women with TS treated with GH in Switzerland. Our study assessed a broad range of modifiable risk factors for cardiovascular diseases, including health behaviour measures and the amount of daily physical activity and sports.

In conclusion, a sedentary lifestyle was common in young women with TS. New strategies to encourage physical activity are needed, beginning in childhood. Children may adapt to sporting and movement patterns more easily and may be more flexible in increasing their physical activity levels than adults. They can build on their childhood repertoire as they reach adolescence and continue this into adulthood. Paediatricians should therefore promote a structured physical activity programme for girls with TS from early childhood onwards to promote well-being and reduce cardiovascular risk in adulthood. Clinical practice guidelines for girls and women with TS should include personalised physical activity recommendations, with the aim to increase long-term health-related quality of life.

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**CONFLICT OF INTEREST**

We report no conflict of interest.

**ORCID**

Maristella Santi \url{https://orcid.org/0000-0003-0675-8130}

Grit Sommer \url{https://orcid.org/0000-0002-4205-7932}

**REFERENCES**

1. Mavinkurve M, O’Gorman CS. Cardiometabolic and vascular risks in young and adolescent girls with Turner syndrome. BBA Clin. 2015;3:304-309.

2. Brun S, Berglund A, Mortensen KH, et al. Blood pressure, sympathetic tone, exercise capacity and metabolic status are linked in Turner syndrome. Clin Endocrinol (Oxf). 2019;91(1):148-155.

3. Gravholt CH, Naeraa RW, Nyholm B, et al. Glucose metabolism, lipid metabolism, and cardiovascular risk factors in adult Turner’s
syndrome. The impact of sex hormone replacement. Diabetes Care. 1998;21(7):1062-1070.
4. Schoemaker MJ, Swerdlow AJ, Higgins CD, Wright AF, Jacobs PA. United Kingdom Clinical Cytogenetics G. Mortality in women with turner syndrome in Great Britain: a national cohort study. J Clin Endocrinol Metab. 2008;93(12):4735-4742.
5. Fjermestad KW, Naess EE, Bahr D, Gravholt CH. A 6-year Follow-up survey of health status in middle-aged women with Turner syndrome. Clin Endocrinol (Oxf). 2016;85(3):423-429.
6. Naess EE, Bahr D, Gravholt CH. Health status in women with Turner syndrome: a questionnaire study on health status, education, work participation and aspects of sexual functioning. Clin Endocrinol (Oxf). 2010;72(5):678-684.
7. Krantz E, Landin-Wilhelmsen K, Trimpou P, Bryman I, Wide U. Health-related quality of life in Turner syndrome and the influence of growth hormone therapy; a 20-year follow-up. J Clin Endocrinol Metab. 2019;104(11):5073-5083.
8. Landin-Wilhelmsen K, Bryman I, Wilhelmsen L. Cardiac malformations and hypertension, but not metabolic risk factors, are common in Turner syndrome. J Clin Endocrinol Metab. 2001;86(7):4162-4170.
9. Landin-Wilhelmsen K, Bryman I, Wilhelmsen L. Osteoporosis and fractures in Turner syndrome-importance of growth promoting and oestrogen therapy. Clin Endocrinol (Oxf). 1999;51(4):497-502.
10. Thompson T, Zieba B, Howell S, Karakash W, Davis S. A mixed methods study of physical activity and quality of life in adolescents with Turner syndrome. Am J Med Genet A. 2020;182(9):386-396.
11. Sommer G, Gianinazzi ME, Kuonen R, et al. Health-related quality of life of young adults treated with recombinant human growth hormone during childhood. PLoS One. 2015;10(10):e0140944.
12. Swiss Federal Statistical Office. Swiss Health Survey 2012 2013 [Accessed: June 24 2020]. Available from: https://www.bfs.admin.ch/bfs/en/home/statistics/catalogues-databases/publications.asset/detail.349060.html
13. Swiss Federal Office for Sports (BASPO). Gesundheitswirksame Bewegung bei Erwachsenen. Empfehlungen für die Schweiz. 2013 [Accessed: December 07 2020]. Available from: https://www.baspo.admin.ch/de/sportfoerderung/breitensport/gesundheit/bewegungsempfehlungen.html#ui-collapse-857
14. U.S. Department of Health and Human Services. Physical activity guidelines advisory committee report. 2018 [Accessed: June 24 2020]. Available from: https://health.gov/our-work/physical-activity/current-guidelines/scientific-report
15. World Health Organisation. Global recommendations on physical activity for health 18 - 64 years old. 2011 [Accessed: June 24 2020]. Available from: https://www.who.int/dietphysicalactivity/publications/recommendations18_64yearsold/en/
16. Milde K, Tomaszewski P, Stupnicki R. Physical fitness of schoolgirls with Turner syndrome. Pediatr Exerc Sci. 2013;25(1):27-42.
17. Durstine JL, Gordon B, Wang ZZ, Luo XJ. Chronic disease and the link to physical activity. J Sport Health Sci. 2013;2(1):3-11.
18. Gravholt CH, Andersen NH, Conway GS, 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(3):G1-G70.
19. Sienkiewicz-Dianzenza E, Milde K, Tomaszewski P, Frac M. Physical activity of girls with Turner’s syndrome. Pediatric Endocrinol Diabetes Metab. 2011;17(3):134-137.
20. Devernay M, Ecosse E, Coste J, Carel JC. Determinants of medical care for young women with Turner syndrome. J Clin Endocrinol Metab. 2009;94(9):3408-3413.
21. Gawlik A, Kaczor B, Kaminska H, Zachurzok-Buczynska A, Gawlik T, Malecka-Tendera E. Quality of medical follow-up of young women with Turner syndrome treated in one clinical center. Horm Res Paediatr. 2012;77(4):222-228.
22. Rubin KR. Turner syndrome: transition from pediatrics to adulthood. Endocr Pract. 2008;14(6):775-781.
23. Bowling A. Mode of questionnaire administration can have serious effects on data quality. J Public Health (Oxf). 2005;27(3):281-291.
24. Swerdlow AJ, Cooke R, Albertsson-Wikland K, et al. Description of the SAGhE cohort: a large European study of mortality and cancer incidence risks after childhood treatment with recombinant growth hormone. Horm Res Paediatr. 2015;84(3):172-183.
25. Swerdlow AJ, Cooke R, Beckers D, et al. Cancer risks in patients treated with growth hormone in childhood: the SAGhE cohort study. J Clin Endocrinol Metab. 2017;102(5):1661-1672.
26. Swerdlow AJ, Cooke R, Beckers D, et al. Risk of meningioma in European patients treated with growth hormone in childhood: results from the SAGhE cohort. J Clin Endocrinol Metab. 2019;104(3):658-664.
27. Savendahl L, Cooke R, Tidblad A, et al. Long-term mortality after childhood growth hormone treatment: the SAGhE cohort study. Lancet Diabetes Endocrinol. 2020;8(8):683-692.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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