HHS Public Access

Author manuscript

Am J Med Genet A. Author manuscript; available in PMC 2023 August 07.

Published in final edited form as:

Am J Med Genet A. 2023 May ; 191(5): 1339–1349. doi:10.1002/ajmg.a.63181.

Prevalence and descriptive epidemiology of Turner syndrome in the United States, 2000–2017: A report from the National Birth Defects Prevention Network

Bailey A. Martin-Giacalone[1,2], **Angela E. Lin**[3], **Sonja A. Rasmussen**[4,5,6], **Russell S. Kirby**[7], **Eirini Nestoridi**[8], **Rebecca F. Liberman**[8], **A. J. Agopian**[9], **John C. Carey**[10], **Janet D. Cragan**[11], **Nina Forestieri**[12], **Vinita Leedom**[6], **Aubree Boyce**[13], **Wendy N. Nembhard**[14], **Monika Piccardi**[15], **Theresa Sandidge**[16], **Xiaoyi Shan**[17], **Charles J. Shumate**[18], **Erin B. Stallings**[11], **Roger Stevenson**[19], **Philip J. Lupo**[2]

[1]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA

[2]Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA

[3]Medical Genetics Unit, Mass General for Children, Boston, Massachusetts, USA

[4]Department of Genetic Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

[5]Department of Pediatrics, University of Florida College of Medicine, Gainesville, Florida, USA

[6]Division of Population Health Surveillance, South Carolina Department of Health and Environmental Control, Columbia, South Carolina, USA

[7]Chiles Center, University of South Florida College of Public Health, Tampa, Florida, USA

Correspondence: Philip J. Lupo, Department of Pediatrics, Baylor College of Medicine, One Baylor Plaza, MS: BCM622, Houston, TX 77030, USA. philip.lupo@bcm.edu.

AUTHOR CONTRIBUTIONS

Bailey A. Martin-Giacalone: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing—Original draft, Writing—Review and editing, Visualization; **Angela E. Lin**: Conceptualization, Methodology, Writing—Original draft, Writing—Review and editing, Supervision; **Sonja A. Rasmussen:** Conceptualization, Methodology, Writing—Original draft, Writing—Review and editing; **Russell S. Kirby**: Conceptualization, Methodology, Writing—Original draft, Writing—Review and editing; **Eirini Nestoridi**: Conceptualization, Methodology, Writing—Original draft, Writing—Review and editing; **Rebecca F. Liberman**: Conceptualization, Methodology, Writing—Original draft, Writing—Review and editing; A.J. Agopian: Conceptualization, Writing—Review and editing, Funding acquisition; **John C. Carey**: Conceptualization, Writing—Review and editing; **Janet D. Cragan**: Data curation, Writing—Review and editing; **Nina Forestieri**: Data curation, Writing—Review and editing; **Vinita Leedom**: Data curation, Writing—Review and editing; **Aubree Boyce**: Data curation, Writing—Review and editing; **Wendy N. Nembhard**: Data curation, Writing—Review and editing; **Monika Piccardi**: Data curation, Writing—Review and editing; **Theresa Sandidge**: Data curation, Writing—Review and editing; **Xiaoyi Shan**: Data curation, Writing—Review and editing; **Charles J. Shumate**: Data curation, Writing—Review and editing; **Erin B. Stallings**: Data curation, Writing—Review and editing. **Roger Stevenson:** Data curation, Writing—Review and editing; **Philip J. Lupo**: Conceptualization, Methodology, Data Curation, Investigation, Resources, Supervision, Writing—Original Draft, Writing—Review & Editing, Funding Acquisition.

CONFLICT OF INTEREST STATEMENT

The authors have no relevant conflicts of interest.

The findings and conclusions in this report are solely the responsibility of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Institutes of Health.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

[8]Center for Birth Defects Research and Prevention, Massachusetts Department of Public Health, Boston, Massachusetts, USA

[9]Department of Epidemiology, Human Genetics, and Environmental Sciences, UTHealth School of Public Health, Houston, Texas, USA

[10]Department of Pediatrics, University of Utah Health, Salt Lake City, Utah, USA

[11]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[12]Division of Public Health, North Carolina Department of Health and Human Services, Raleigh, North Carolina, USA

[13]Utah Birth Defect Network, Utah Department of Health and Human Services, Salt Lake City, Utah, USA

[14]Department of Epidemiology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

[15]Office of Genetics and People with Special Health Care Needs, Maryland Department of Health, Baltimore, Maryland, USA

[16]Division of Epidemiologic Studies, Illinois Department of Public Health, Springfield, Illinois, USA

[17]Arkansas Reproductive Health Monitoring System, Arkansas Children's Research Institute, Little Rock, Arkansas, USA

[18]Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin, Texas, USA

[19]Greenwood Genetic Center, Greenwood, South Carolina, USA

Abstract

The lack of United States population-based data on Turner syndrome limits assessments of prevalence and associated characteristics for this sex chromosome abnormality. Therefore, we collated 2000–2017 data from seven birth defects surveillance programs within the National Birth Defects Prevention Network. We estimated the prevalence of karyotype-confirmed Turner syndrome diagnosed within the first year of life. We also calculated the proportion of cases with commonly ascertained birth defects, assessed associations with maternal and infant characteristics using prevalence ratios (PR) with 95% confidence intervals (CI), and estimated survival probability. The prevalence of Turner syndrome of any pregnancy outcome was 3.2 per 10,000 female live births (95% CI = 3.0–3.3, program range: 1.0–10.4), and 1.9 for live birth and stillbirth (≥20 weeks gestation) cases (95% CI = 1.8–2.1, program range: 0.2–3.9). Prevalence was lowest among cases born to non-Hispanic Black women compared to non-Hispanic White women (PR = 0.5, 95% CI = 0.4–0.6). Coarctation of the aorta was the most common defect (11.6% of cases), and across the cohort, individuals without hypoplastic left heart had a five-year survival probability of 94.6%. The findings from this population-based study may inform surveillance practices, prenatal counseling, and diagnosis. We also identified racial and ethnic disparities in prevalence, an observation that warrants further investigation.

Keywords

birth defects; epidemiology; prevalence; sex chromosome abnormality; Turner syndrome

1 | INTRODUCTION

Turner syndrome is a sex chromosome abnormality that is caused by the partial or complete loss of one X chromosome. Individuals with Turner syndrome experience a wide array of comorbidities, including short stature, delayed puberty, and left-sided heart defects (Fuchs et al., 2019; Gravholt et al., 2017; Lin et al., 2019). Congenital heart defects, such as bicuspid aortic valve and coarctation of the aorta, are common in Turner syndrome, and some are associated with early mortality (Silberbach et al., 2018).

There have been no United States (US) population-based estimates of the prevalence of Turner syndrome, which limits the ability to monitor prevalence trends and compare studies. While there are some existing state-specific reports of Turner syndrome prevalence (National Birth Defects Prevention Network, 2022), these reports often lack karyotype information. Additionally, few studies have used population-based data to evaluate descriptive characteristics or survival (Buckway et al., 2000), knowledge that could be helpful for patient monitoring and management. Another limitation of the current Turner syndrome literature is the exclusion of non-live birth outcomes (Berglund et al., 2020; Gravholt et al., 2022; Stochholm et al., 2006), which can result in underestimates of some severe birth defects (Heinke et al., 2020). Non-live birth outcomes are reported in approximately 70%–80% of prenatal Turner syndrome cases (Buckway et al., 2000; Gruchy et al., 2014; Iyer et al., 2012), and thus, their inclusion may be necessary for accurate prevalence estimates.

The primary objective of our study was to provide more evidencebased data on Turner syndrome for research and clinical knowledge. To address this aim, we formed a multistate, collaborative study using data from seven surveillance programs within the National Birth Defects Prevention Network (NBDPN), a large group of state- and population-based birth defects surveillance programs (Mai et al., 2016). In this study, we estimated the prevalence of karyotype-confirmed cases with Turner syndrome diagnosed up to the first year of life. We also calculated the proportion of cases with specific birth defects, evaluated associations of maternal and infant characteristics, and conducted survival analyses.

2 | MATERIALS AND METHODS

2.1 | Editorial policies and ethical compliance

This study was approved by the Institutional Review Board for Human Subjects Research at Baylor College of Medicine. If required by the state or institution, each surveillance program received specific approval through its respective institutional review board.

2.2 | Data sources

We obtained data on cases with Turner syndrome from seven, population-based birth defects surveillance programs (hereafter, programs) and on female live births from state birth records or state vital statistics offices. The programs were Arkansas, South Carolina, Texas, and Utah (statewide for birth years 2000–2017), California (10 counties for 2010–2012 and 2017, eight counties for 2013–2016), Massachusetts (statewide for 2011–2017), and the Metropolitan Atlanta Congenital Defects Program (MACDP; five counties for 2000–2011, three counties for 2012–2017).

2.3 | Study population

Programs ascertained cases with Turner syndrome diagnosed within the first year of life. All cases were clinically reviewed and coded using the following codes: World Health Organization's (WHO) International Classification of Disease (ICD) 9th revision: 758.6; ICD 10th revision: Q96.0-Q96.9; or the British Pediatric Association Classification of Diseases: 758.600–758.690 (Table S1). Case inclusion required confirmation by karyotype or chromosomal microarray analysis. Cases with a Turner syndrome phenotype that were diagnosed only by fluorescence in situ hybridization or noninvasive prenatal screening were excluded, as were those with <10 cell mosaic karyotype. Per recent diagnostic guidelines (Gravholt et al., 2017; Lin et al., 2019), we excluded the following karyotypes, which do not strictly result in Turner syndrome: 45,X/46,XY with male sex assigned at birth; X-autosome translocations and 45,X with trisomy 21; 46,XX,del(q24) and 46,X,del(X)(q25); and 46,X,idic(X) (q24). Case eligibility was confirmed by a medical geneticist (A.E.L.).

2.4 | Data collection

Programs abstracted the following demographic and clinical information on cases and female live births from medical or vital records: clinical and calculated estimates of infant gestational age at delivery (continuous), infant birth weight (continuous), maternal age at delivery (continuous), maternal race and ethnicity (Hispanic, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian or Pacific Islander, non-Hispanic Black, non-Hispanic White, or other/unknown), and year of delivery (continuous). Programs submitted data on pregnancy outcomes as live birth, stillbirth (fetal death ≥20 weeks gestation), elective termination, miscarriage/unspecified non-live birth (fetal death <20 weeks gestation), or unknown. Massachusetts ascertained "other pregnancy losses," defined as elective terminations and miscarriages <20 weeks. MACDP did not collect data on miscarriages occurring <20 weeks gestation.

Diagnoses of any of the "core" birth defects included in the NBDPN Guidelines for Conducting Birth Defects Surveillance Appendix 3.1 (National Birth Defects Prevention Network, 2021) were collected for each case. These defects were chosen because they are commonly ascertained by surveillance programs, although not all programs collected all birth defects across all years of the study. Importantly, these "core" birth defects do not represent all major defects that could occur or be characteristic of a Turner syndrome phenotype.

We collected survival data for live birth cases from states that follow cases up to at least 1 year of age: California and Massachusetts (follow-up data through 1 year of age) and Arkansas, Utah, Texas, and MACDP (follow-up data through 5 years of age). Survival data included infant death (yes/no) and length of follow-up time (if death occurred, the number of days from birth to death; if death did not occur, length of time in days for which the program ascertained deaths). All programs obtained death information through linkage to vital records or medical record abstraction.

2.5 | Study variables

We used data for gestational age based on the clinical (ultrasound) estimate. If the clinical estimate was missing, we used the calculated estimate (based on date of last menstrual period) or an estimate based on standard neonatal exam. Using the WHO definition, we classified birth weight for gestational age as small (birth weight < 10th centile), appropriate, and large (birth weight > 90th centile) using a published US birth weight reference (Talge et al., 2014). In analyses that assessed birth weight for gestational age, we excluded cases (N = 630) and live births (denominator data, N = 4261) with gestational age < 22 weeks to be consistent with the birth weight range used in the reference.

Due to small case counts, we grouped cases with maternal race and ethnicity designated as “non-Hispanic American Indian or Alaska Native” or “non-Hispanic Asian or Pacific Islander” into a single category, labeled as “non-Hispanic Alaska Native, American Indian, Asian, or Pacific Islander.” Across all programs, we also categorized pregnancy outcomes as live birth, other pregnancy loss (elective termination at any gestational age and miscarriage <20 weeks gestation), stillbirth (fetal death ≥20 weeks gestation), or unknown. Prevalence estimates and karyotype proportions were stratified by type of pregnancy outcome: (1) all pregnancy outcomes, and (2) live birth and stillbirth cases only.

2.6 | Statistical analysis

We estimated the prevalence of Turner syndrome per 10,000 female live births (number of Turner syndrome cases divided by the number of female live births within the individual state or for the total surveillance catchment area, multiplied by 10,000) for (1) each program and (2) all programs combined. Non-live births were not included in the denominator since including non-live births has not been shown to significantly impact prevalence estimates of other birth defects (Marshall et al., 2015). We also estimated the prevalence by maternal race and ethnicity. Sensitivity analyses of the crude prevalence included (1) case and denominator data excluding early losses (≤20 weeks gestational age) and (2) leave-one-out analysis to identify variability in program ascertainment. To calculate the proportion of cases with core birth defects and 95% confidence intervals (CI), we used the exact binomial method.

We estimated prevalence ratios (PR) for maternal age at delivery (categorical: <25, 25–29 [reference], 30–34, 35–39, or ≥ 40 years), maternal race and ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White [reference], or non-Hispanic Alaska Native, American Indian, Asian, or Pacific Islander), infant birth weight for gestational age (small, appropriate [reference], or large), and year of delivery (categorical: 2000–2002 [reference], 2003–2005,

2006–2008, 2009–2011, 2012–2014, or 2015–2017) using Poisson regression. Cases with missing values for a specific variable were excluded from the respective analysis.

We estimated survival probability of infants with Turner syndrome at 1 day, 7 days, 28 days, 1 year, 2 years, and 5 years. Survival probability was defined as the time between birth and death due to any cause or length of follow-up. We estimated the survival probability among (1) all cases and (2) cases without hypoplastic left heart (HLH), a congenital anomaly that is associated with poor survival (Lara et al., 2017).

We constructed Kaplan–Meier curves and used the log-rank test to determine differences in survival by maternal race and ethnicity, year of delivery category, presence of at least one core birth defect, or karyotype category (45,X; mosaicism; structural abnormalities of the X; or other, defined as any karyotype not included in the previous groupings). Associations with p-values <0.05 were considered significant, and all log-rank tests met the proportional hazards assumption. All statistical analyses were conducted in R version 4.0.4.

3 | RESULTS

3.1 | Crude prevalence of Turner syndrome

For the study period 2000–2017, we identified 1872 cases with Turner syndrome diagnosed up to the first year of life among 5,911,109 female live births across the seven surveillance programs. The prevalence of Turner syndrome among all pregnancy outcomes was 3.2 per 10,000 female live births (95% CI = 3.0–3.3, Table 1). When we restricted the numerator to live birth and stillbirth cases, the prevalence of Turner syndrome was 1.9 per 10,000 live births (95% CI = 1.8–2.1). Turner syndrome prevalence among all outcomes was highest in Massachusetts (10.4, 95% CI = 9.2–11.8) and lowest in South Carolina (1.0, 95% CI = 0.8–1.3).

The crude prevalence also differed by maternal race and ethnicity. The prevalence was highest among cases born to women who identified as non-Hispanic White (3.6 per 10,000 female live births, 95% CI = 3.4–3.9) followed by cases born to women who identified as Hispanic (2.6 per 10,000 female live births, 95% CI = 2.4–2.8), non-Hispanic Alaska Native, American Indian, Asian, or Pacific Islander (2.3 per 10,000 female live births, 95% CI = 1.8–2.9), and non-Hispanic Black (1.7 per 10,000 female live births, 95% CI = 1.4–2.0).

3.2 | Crude prevalence sensitivity analysis

Recognizing that Massachusetts ascertains very early losses and that MACDP does not collect data on miscarriages <20 weeks gestation, we conducted a sensitivity analysis to address skewness in the data. We estimated the prevalence among cases of any pregnancy outcome and female live births (denominator data) that were born >20 weeks gestation (Table S2). In this analysis, the prevalence across all programs was 2.1 per 10,000 female live births (95% CI = 2.0–2.2). For Massachusetts, the prevalence was 1.7 per 10,000 female live births.

To determine the effect of each individual program's data on the combined overall prevalence estimate, we also conducted a leave-one-out sensitivity analysis, which estimated

the overall prevalence by leaving out exactly one program in subsequent iterations. We found significant differences between the combined prevalence estimate and the resulting prevalence estimate after removing data from Utah, Massachusetts, Texas, and South Carolina (Figure S1).

3.3 | Descriptive proportions

Among all cases, 40.5% (N = 759) were live births, 20.6% (N = 386) were stillbirths, 35.0% (N = 655) were other pregnancy losses, and 3.9% (N = 72) were of unknown outcome. The most frequent karyotype among all cases was 45,X (75.4%, Table 2). Mosaicism and structural X abnormalities comprised 9.2% and 6.5% of the study cohort, respectively. The proportion of all cases with at least one core birth defect was 25.2% (N = 472). The most common defects were coarctation of the aorta (11.6%), atrial septal defect (6.8%), and ventricular septal defect (3.8%, Table 3).

3.4 | Prevalence by maternal and infant characteristics

We excluded cases and female live births (denominator data) with missing data for maternal age (48 cases; 123,210 live births), maternal race and ethnicity (223 cases; 169,598 live births), and birth weight for gestational age (876 cases; 455,368 live births). Resulting counts are shown in Table 4.

The prevalence of Turner syndrome did not significantly differ for any maternal age group compared to the 25–29 year group nor by any year of birth category compared to 2000–2002 (Table 4). We did find that the prevalence of Turner syndrome was 50% lower for cases born to women who identified as non-Hispanic Black (PR = 0.5, 95% CI = 0.4–0.6) compared to women who identified as non-Hispanic White. We also observed a significantly lower prevalence of Turner syndrome among cases born to women who identified as Hispanic (PR = 0.7, 95% CI = 0.6–0.8) or non-Hispanic Alaska Native, American Indian, Asian, or Pacific Islander (PR = 0.6, 95% CI = 0.5–0.8) compared to women who identified as non-Hispanic White.

3.5 | Survival

Among all cases, overall survival for individuals with Turner syndrome was >90% at all-time points from 1 to 5 years (Table 5). Among cases without HLH, survival was also >90% at all-time points. One-year survival did not significantly differ by karyotype, maternal race and ethnicity, year of delivery, or the presence of at least one core birth defect among all cases nor the subset of cases without HLH (Figures S2–S4).

4 | DISCUSSION

4.1 | Crude prevalence of turner syndrome

Using data from seven NBDPN birth defects surveillance programs, we report the population-based estimate of the prevalence of Turner syndrome in the United States, which, in previous reports, has largely been unaccompanied by karyotype examination, assessments of the association of demographic characteristics, or survival analyses. The lack of such data in the United States compared to European countries (Berglund et al., 2019, 2020;

Gravholt et al., 2022; Ji et al., 2016; Schoemaker et al., 2008; Zelinska et al., 2018) can be largely attributed to differences in health care structure. Unlike European countries, which often have access to nationalized health care registry data (Laugesen et al., 2021; Schmidt et al., 2019), the United States does not have a nationwide birth defects or Turner syndrome registry and relies on medical care centers and state birth defects surveillance programs for case ascertainment.

Within the present study, there were substantial differences by program. For example, the prevalence of Turner syndrome was lowest in South Carolina. Turner syndrome cases in South Carolina were primarily ascertained through the Greenwood Genetic Center, which contributed data for approximately one-third of the state (National Birth Defects Prevention Network, 2022); data from cytogenetic centers in other regions of the state were not available. Although the South Carolina Department of Health and Environmental Control began an active case-finding birth defects program in 2006, these ascertainment issues likely resulted in a significant underestimate of the true prevalence of Turner syndrome in this state. These data can serve as a reference to inform strategies that aim to improve case ascertainment.

Turner syndrome prevalence across all pregnancy outcomes was highest in Massachusetts and was significantly different compared to other programs. In 2011, Massachusetts began collecting data on other pregnancy losses, including early miscarriages and terminations, in addition to live births and stillbirths (Massachusetts Department of Public Health, 2013). For this reason, our analyses did not include data from Massachusetts prior to 2011. Although five other programs conducted surveillance for these outcomes, Massachusetts ascertains karyotype information from very early losses (<18 weeks gestational age) at several large, tertiary care hospitals in the state. Our sensitivity analysis showed that the prevalence of Turner syndrome in Massachusetts was similar to other states when excluding early losses.

We also observed a significantly higher prevalence of Turner syndrome in Utah compared to other programs. After a study from the Utah Birth Defect Network found that 12.6% of infant girls with coarctation of the aorta had a confirmed Turner syndrome karyotype, Utah's Primary Children's Hospital began offering cytogenetic testing to all girls who presented with this congenital heart defect (Eckhauser et al., 2015), which might be responsible for the higher prevalence. Additional factors that could have contributed include the unique position of the Primary Children's Hospital as the sole referral and speciality care center in the state, which may simplify the ascertainment of individuals with Turner syndrome.

4.2 | Karyotypes and NBDPN "core" birth defects

We found that 75.4% of Turner syndrome cases had karyotype 45,X, a proportion that is consistent with a retrospective French study of prenatally diagnosed Turner syndrome (79.6% with 45,X; Gruchy et al., 2014). However, this proportion is higher than clinical estimates (Gravholt et al., 2017). This discrepancy is likely due to a delay in diagnosis, which is more common among individuals with mosaic karyotypes, who often present with milder phenotypes compared to individuals with 45,X (Stochholm et al., 2006).

Like previous assessments (Gravholt et al., 2017), coarctation of the aorta, atrial septal defect, and ventricular septal defect were among the most common anomalies. The proportion of cases with bicuspid aortic valve (3.5%) or horseshoe kidney (3.4%), two other common anomalies associated with Turner syndrome, were lower than previous estimates of 14%–34% and 10%, respectively. The challenges of diagnosing these defects prenatally and at birth (Silberbach et al., 2018; Strauss et al., 2000) may explain this discrepancy. Notably, we restricted this study's collection of major birth defects to the NBDPN "core" birth defects (National Birth Defects Prevention Network, 2021) for consistent data collection across the seven surveillance programs. However, further research should address this limitation by including population-based assessments of the proportion of cases with other birth defects that are observed within the Turner syndrome phenotype.

4.3 | Prevalence by maternal characteristics

We found that the prevalence of Turner syndrome did not significantly differ by maternal age. Findings that conclude that advanced maternal age (≥40 years) is associated with Turner syndrome (Hagman et al., 2010) are likely a reflection of incidental diagnosis due to increased screening for other birth defects in older women (Papp et al., 2006; Saenger et al., 2001). Others have found that the majority of Turner syndrome cases retain the maternal X chromosome and that loss or abnormality of the second X chromosome is due to paternal meiotic errors (Uematsu et al., 2002), which could be part of the explanation for why Turner syndrome is not thought to be associated with advanced maternal age (Gunther et al., 2004). Although this study did not collect paternal age data, future studies should consider evaluating the effect of paternal age on Turner syndrome prevalence. Such investigation could support hypotheses related to the paternal mechanisms underlying Turner syndrome development (Huang et al., 2021).

Few studies have described Turner syndrome among racial and ethnic groups in the United States. In a study of 81 individuals with Turner syndrome in North Carolina, 86.4% identified as White and 13.6% identified as African American, American Indian, or Asian. Of the individuals who were diagnosed prenatally, all were White (Savendahl & Davenport, 2000). We found that the prevalence of Turner syndrome was significantly lower for individuals born to women who were Hispanic, non-Hispanic American Indian, Alaska Native, Asian, Pacific Islander, or non-Hispanic Black compared to non-Hispanic White. Importantly, our findings could be explained by differences in case ascertainment by race and ethnicity. Therefore, surveillance programs should consider evaluating and improving current ascertainment strategies by maternal race and ethnicity to enhance ascertainment of birth defects in these populations.

We also hypothesize that these findings could be a result of structural racism in healthcare, including lack of access to and utilization of prenatal testing and care, lower likelihood of affordable care, and distrust in the healthcare system, all of which are known to disproportionately affect Black women (Gadson et al., 2017) and some of which have also been shown to impact attitudes toward prenatal testing for Down syndrome in Black women (Kuppermann et al., 2006; Learman et al., 2003). An assessment of the association of Turner syndrome prevalence with structural racism and the effects of structural racism

might identify factors related to inequitable access to maternal and infant care, which could also be influencing case ascertainment. Findings from such studies could inform diagnostic protocols, medical management, and engagement strategies, especially for the populations that we identified to be at highest risk in this study: Hispanic, non-Hispanic American Indian, Alaska Native, Asian, or Pacific Islander, and non-Hispanic Black populations.

4.4 | Survival

We found that survival for Turner syndrome was greater than 90% from birth to 5 years. Additionally, previous studies have shown that individuals with HLH-associated Turner syndrome have a significantly greater risk of death compared to those without HLH (Lara et al., 2017; Reis et al., 1999). Our analysis showed that Turner syndrome without HLH had survival probabilities greater than 90% at all-time points that we analyzed. This information is important for counseling parents about survival when HLH is not a part of the Turner syndrome phenotype.

5 | STRENGTHS AND LIMITATIONS

Strengths of this study include the use of data from seven active case-finding, population-based birth defects surveillance programs. Our study is not limited to live births but also includes stillbirths, elective terminations, and miscarriages <20 weeks gestation. Furthermore, the extensive dataset generated by this multistate collaboration enabled us to analyze associations of prevalence with maternal and infant characteristics and estimate survival probability.

There are also important study limitations. First, our study required a karyotype-confirmed diagnosis to reduce false screening findings, which resulted in the exclusion of cases diagnosed through other screening methods or based on clinical signs without a karyotype. Additionally, there is a well-known delay in Turner syndrome diagnosis (Swauger et al., 2021), which means that our study likely represents the prevalence of early diagnosis of Turner syndrome. Since half of Turner syndrome cases are diagnosed after the first year of life, our findings might reflect potential selection bias toward more severe phenotypes and might not be generalizable to individuals diagnosed later in life.

We also recognize that not all women receive access to care and cytogenetic testing, potentially resulting in cases that were not captured in this study. Therefore, the prevalence estimates reported in this study likely underestimate the true prevalence of Turner syndrome. The surveillance variability among state programs (National Birth Defects Prevention Network, 2019) also likely contributed to an underestimate of the prevalence. This limitation highlights the importance of improving ascertainment consistency across surveillance programs.

6 | CONCLUSIONS

We provide a US population-based estimate of the prevalence of Turner syndrome. Our findings confirm several previous observations and highlight the importance of including non-live birth outcomes in prevalence estimates of Turner syndrome. Overall, this study

provides a reference for individual US states and care centers to evaluate differences in prevalence by geographic locations, consider epidemiologic factors that are associated with prevalence, and develop educational programming for providers and the public (Canfield et al., 2006). Our results support future evaluations of the impact of structural racism on Turner syndrome prevalence among individuals born to mothers who identify as Hispanic, non-Hispanic American Indian, Alaska Native, Asian, Pacific Islander, and non-Hispanic Black populations. These efforts might identify potential barriers and facilitators related to prenatal screening, diagnosis, and care for these populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This research would not have been possible without the many individuals at each state birth defects program who assisted in the data collection for this study. This study was funded in part through R01HD093660 (MPI: Agopian/Lupo) and DOD W81XWH-20-1-0567 (PI: Lupo). Bailey A. Martin-Giacalone was also supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number T32GM088129 (PI: Van den Veyver) and by the National Cancer Institute of the National Institutes of Health under Award Number T32CA190194 (MPI: Colditz/James), the Foundation for Barnes-Jewish Hospital, the Siteman Cancer Center, and the Department of Defense (W81XWH-20-1-0567).

DATA AVAILABILITY STATEMENT

Research data are not shared.

REFERENCES

Berglund A, Stochholm K, & Gravholt CH (2020). The epidemiology of sex chromosome abnormalities. American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 184(2), 202–215. 10.1002/ajmg.c.31805 [PubMed: 32506765]

Berglund A, Viuff MH, Skakkebæk A, Chang S, Stochholm K, & Gravholt CH (2019). Changes in the cohort composition of turner syndrome and severe non-diagnosis of Klinefelter, 47,XXX and 47,XYY syndrome: A nationwide cohort study. Orphanet Journal of Rare Diseases, 14(1), 16. 10.1186/s13023-018-0976-2 [PubMed: 30642344]

Buckway CK, Magenis RE, Bissonnette JM, Olson S, & Rosenfeld RG (2000). Prenatal diagnosis of turner syndrome: The Portland experience. In Saenger P & Pasquino AM (Eds.), Optimizing health care for Turner patients in the 21st century: Proceedings of the 5th international turner symposium held in Naples on 23–25 March 2000, (p. 336). Elsevier Science.

Canfield MA, Honein MA, Yuskiv N, Xing J, Mai CT, Collins JS, Devine O, Petrini J, Ramadhani TA, Hobbs CA, & Kirby RS (2006). National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999–2001. Birth Defects Research. Part A, Clinical and Molecular Teratology, 76(11), 747–756. 10.1002/bdra.20294 [PubMed: 17051527]

Eckhauser A, South ST, Meyers L, Bleyl SB, & Botto LD (2015). Turner syndrome in girls presenting with coarctation of the aorta. The Journal of Pediatrics, 167(5), 1062–1066. 10.1016/j.jpeds.2015.08.002 [PubMed: 26323199]

Fuchs MM, Attenhofer Jost C, Babovic-Vuksanovic D, Connolly HM, & Egbe A (2019). Long-term outcomes in patients with Turner syndrome: A 68-year follow-up. Journal of the American Heart Association, 8(11), e011501. 10.1161/JAHA.118.011501 [PubMed: 31131660]

Gadson A, Akpovi E, & Mehta PK (2017). Exploring the social determinants of racial/ethnic disparities in prenatal care utilization and maternal outcome. Seminars in Perinatology, 41(5), 308–317. 10.1053/j.semperi.2017.04.008 [PubMed: 28625554]

Gravholt CH, Andersen NH, Conway GS, Dekkers OM, Geffner ME, Klein KO, Lin AE, Mauras N, Quigley CA, Rubin K, Sandberg DE, Sas TCJ, Silberbach M, SoderstromAnttila V, Stochholm K, van Alfen-van derVelden JA, Woelfle J, Backeljauw PF, & International Turner Syndrome Consensus, G. (2017). Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2016 Cincinnati international Turner syndrome meeting. European Journal of Endocrinology, 177(3), G1–G70. 10.1530/EJE-17-0430 [PubMed: 28705803]

Gravholt CH, Viuff M, Just J, Sandahl K, Brun S, van der Velden J, Andersen NH, & Skakkebaek A (2022). The changing face of Turner syndrome. Endocrine Reviews, 44, 33–69. 10.1210/endrev/bnac016

Gruchy N, Vialard F, Blondeel E, Le Meur N, Joly-Helas G, Chambon P, Till M, Herbaut-Graux M, Vigouroux-Castera A, Coussement A, Lespinasse J, Amblard F, Jimenez M, Lebel Roy Camille L, Carre-Pigeon F, Flori E, Mugneret F, Jaillard S, Yardin C, … Leporrier N (2014). Pregnancy outcomes of prenatally diagnosed Turner syndrome: A French multicenter retrospective study including a series of 975 cases. Prenatal Diagnosis, 34(12), 1133–1138. 10.1002/pd.4439 [PubMed: 24961405]

Gunther DF, Eugster E, Zagar AJ, Bryant CG, Davenport ML, & Quigley CA (2004). Ascertainment bias in Turner syndrome: New insights from girls who were diagnosed incidentally in prenatal life. Pediatrics, 114(3), 640–644. 10.1542/peds.2003-1122-L [PubMed: 15342833]

Hagman A, Wennerholm UB, Kallen K, Barrenas ML, Landin-Wilhelmsen K, Hanson C, & Bryman I (2010). Women who gave birth to girls with Turner syndrome: Maternal and neonatal characteristics. Human Reproduction, 25(6), 1553–1560. 10.1093/humrep/deq060 [PubMed: 20237051]

Heinke D, Nestoridi E, Hernandez-Diaz S, Williams PL, Rich-Edwards JW, Lin AE, Van Bennekom CM, Mitchell AA, Nembhard WN, Fretts RC, Roberts DJ, Duke CW, Carmichael SL, Yazdy MM, & National Birth Defects Prevention Study. (2020). Risk of stillbirth for fetuses with specific birth defects. Obstetrics and Gynecology, 135(1), 133–140. 10.1097/AOG.0000000000003614 [PubMed: 31809437]

Huang AC, Olson SB, & Maslen CL (2021). A review of recent developments in Turner syndrome research. Journal of Cardiovascular Development and Disease, 8(11), 138. 10.3390/jcdd8110138 [PubMed: 34821691]

Iyer NP, Tucker DF, Roberts SH, Moselhi M, Morgan M, & Matthes JW (2012). Outcome of fetuses with Turner syndrome: A 10-year congenital anomaly register based study. The Journal of Maternal-Fetal & Neonatal Medicine, 25(1), 68–73. 10.3109/14767058.2011.564688

Ji J, Zöller B, Sundquist J, & Sundquist K (2016). Risk of solid tumors and hematological malignancy in persons with Turner and Klinefelter syndromes: A national cohort study. International Journal of Cancer, 139(4), 754–758. 10.1002/ijc.30126 [PubMed: 27061708]

Kuppermann M, Learman LA, Gates E, Gregorich SE, Nease RF Jr., Lewis J, & Washington AE (2006). Beyond race or ethnicity and socioeconomic status: Predictors of prenatal testing for Down syndrome. Obstetrics and Gynecology, 107(5), 1087–1097. 10.1097/01.AOG.0000214953.90248.db [PubMed: 16648415]

Lara DA, Ethen MK, Canfield MA, Nembhard WN, & Morris SA (2017). A population-based analysis of mortality in patients with Turner syndrome and hypoplastic left heart syndrome using the Texas birth defects registry. Congenital Heart Disease, 12(1), 105–112. 10.1111/chd.12413 [PubMed: 27685952]

Laugesen K, Ludvigsson JF, Schmidt M, Gissler M, Valdimarsdottir UA, Lunde A, & Sorensen HT (2021). Nordic health registry-based research: A review of health care systems and key registries. Clinical Epidemiology, 13, 533–554. 10.2147/CLEP.S314959 [PubMed: 34321928]

Learman LA, Kuppermann M, Gates E, Nease RF Jr., Gildengorin V, & Washington AE (2003). Social and familial context of prenatal genetic testing decisions: Are there racial/ethnic differences? American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 119C(1), 19–26. 10.1002/ajmg.c.10004 [PubMed: 12704634]

Lin AE, Prakash SK, Andersen NH, Viuff MH, Levitsky LL, Rivera-Davila M, Crenshaw ML, Hansen L, Colvin MK, Hayes FJ, Lilly E, Snyder EA, Nader-Eftekhari S, Aldrich MB, Bhatt AB, Prager LM, Arenivas A, Skakkebaek A, Steeves MA, … Gravholt CH (2019). Recognition and management of adults with Turner syndrome: From the transition of adolescence through

the senior years. American Journal of Medical Genetics. Part A, 179(10), 1987–2033. 10.1002/ajmg.a.61310 [PubMed: 31418527]

Mai CT, Kirby RS, Correa A, Rosenberg D, Petros M, & Fagen MC (2016). Public health practice of population-based birth defects surveillance programs in the United States. Journal of Public Health Management and Practice, 22(3), E1–E8. 10.1097/PHH.0000000000000221

Marshall J, Salemi JL, Tanner JP, Ramakrishnan R, Feldkamp ML, Marengo LK, Meyer RE, Druschel CM, Rickard R, Kirby RS, & National Birth Defects Prevention, N. (2015). Prevalence, correlates, and outcomes of omphalocele in the United States, 1995–2005. Obstetrics and Gynecology, 126(2), 284–293. 10.1097/AOG.0000000000000920 [PubMed: 26241416]

Massachusetts Department of Public Health. (2013). Massachusetts Birth Defects Among Live and Stillbirths 2008–2010. https://www.mass.gov/doc/2008-2010-report-0/download

National Birth Defects Prevention Network. (2019). Special issue: 2019 congenital malformations surveillance report: A report from the National Birth Defects Prevention Network. Birth Defects Research, 111(18), 1321–1447.

National Birth Defects Prevention Network. (2021). NBDPN Guidelines for Conducting Birth Defects Surveillance Appendix 3.1. https://www.nbdpn.org/docs/Appx3__1_BDDescriptions2015.pdf

National Birth Defects Prevention Network. (2022). Major Birth Defects Data from Population-based Birth Defects Surveillance Programs in the United States, 2014–2018. https://www.nbdpn.org/docs/Birth_Defects_Data_and_Directory_2022.pdf

Papp C, Beke A, Mezei G, Szigeti Z, Ban Z, & Papp Z (2006). Prenatal diagnosis of Turner syndrome: Report on 69 cases. Journal of Ultrasound in Medicine, 25(6), 711–717. 10.7863/jum.2006.25.6.711 [PubMed: 16731887]

Reis PM, Punch MR, Bove EL, & van de Ven CJ (1999). Outcome of infants with hypoplastic left heart and Turner syndromes. Obstetrics and Gynecology, 93(4), 532–535. 10.1016/s0029-7844(98)00462-1 [PubMed: 10214828]

Saenger P, Wikland KA, Conway GS, Davenport M, Gravholt CH, Hintz R, Hovatta O, Hultcrantz M, Landin-Wilhelmsen K, Lin A, Lippe B, Pasquino AM, Ranke MB, Rosenfeld R, Silberbach M, & Fifth International Symposium on Turner, S. (2001). Recommendations for the diagnosis and management of Turner syndrome. The Journal of Clinical Endocrinology and Metabolism, 86(7), 3061–3069. 10.1210/jcem.86.7.7683 [PubMed: 11443168]

Savendahl L, & Davenport ML (2000). Delayed diagnoses of Turner's syndrome: Proposed guidelines for change. The Journal of Pediatrics, 137(4), 455–459. 10.1067/mpd.2000.107390 [PubMed: 11035820]

Schmidt M, Schmidt SAJ, Adelborg K, Sundboll J, Laugesen K, Ehrenstein V, & Sorensen HT (2019). The Danish health care system and epidemiological research: From health care contacts to database records. Clinical Epidemiology, 11, 563–591. 10.2147/CLEP.S179083 [PubMed: 31372058]

Schoemaker MJ, Swerdlow AJ, Higgins CD, Wright AF, Jacobs PA, & Group UKCC (2008). Cancer incidence in women with Turner syndrome in Great Britain: A national cohort study. The Lancet Oncology, 9(3), 239–246. 10.1016/S1470-2045(08)70033-0 [PubMed: 18282803]

Silberbach M, Roos-Hesselink JW, Andersen NH, Braverman AC, Brown N, Collins RT, De Backer J, Eagle KA, Hiratzka LF, Johnson WH Jr., Kadian-Dodov D, Lopez L, Mortensen KH, Prakash SK, Ratchford EV, Saidi A, van Hagen I, Young LT, American Heart Association Council on Cardiovascular Disease in the Young, … Council on Peripheral Vascular. (2018). Cardiovascular health in turner syndrome: A scientific statement from the American Heart Association. Circulation: Genomic and Precision Medicine, 11(10), e000048. 10.1161/HCG.0000000000000048 [PubMed: 30354301]

Stochholm K, Juul S, Juel K, Naeraa RW, & Gravholt CH (2006). Prevalence, incidence, diagnostic delay, and mortality in Turner syndrome. The Journal of Clinical Endocrinology and Metabolism, 91(10), 3897–3902. 10.1210/jc.2006-0558 [PubMed: 16849410]

Strauss S, Dushnitsky T, Peer A, Manor H, Libson E, & Lebensart PD (2000). Sonographic features of horseshoe kidney: Review of 34 patients. Journal of Ultrasound in Medicine, 19(1), 27–31. 10.7863/jum.2000.19.1.27 [PubMed: 10625187]

Swauger S, Backeljauw P, Hornung L, Shafer J, Casnellie L, & Gutmark-Little I (2021). Age at and indication for diagnosis of turner syndrome in the pediatric population. American Journal of Medical Genetics. Part A, 185(11), 3411–3417. 10.1002/ajmg.a.62459 [PubMed: 34390317]

Talge NM, Mudd LM, Sikorskii A, & Basso O (2014). United States birth weight reference corrected for implausible gestational age estimates. Pediatrics, 133(5), 844–853. 10.1542/peds.2013-3285 [PubMed: 24777216]

Uematsu A, Yorifuji T, Muroi J, Kawai M, Mamada M, Kaji M, Yamanaka C, Momoi T, & Nakahata T (2002). Parental origin of normal X chromosomes in Turner syndrome patients with various karyotypes: Implications for the mechanism leading to generation of a 45,X karyotype. American Journal of Medical Genetics, 111(2), 134–139. 10.1002/ajmg.10506 [PubMed: 12210339]

Zelinska N, Shevchenko I, & Globa E (2018). Nationwide study of turner syndrome in Ukrainian children: Prevalence, genetic variants and phenotypic features. Journal of Clinical Research in Pediatric Endocrinology, 10(3), 256–263. 10.4274/jcrpe.5119 [PubMed: 29537378]

TABLE 1

Crude prevalence of Turner syndrome by surveillance program and pregnancy outcome.

	Cases			Prevalence per 10,000 live births	
Program	**All cases**	**Live births and stillbirths only**	**Female live births**	**Total[a]**	**Live births and stillbirths only**
Massachusetts	256	37	245,466	10.4 (9.2–11.8)	1.5 (1.1–2.1)
Utah	316	178	459,106	6.9 (6.2–7.7)	3.9 (3.3–4.5)
California	181	78	400,099	4.5 (3.9–5.2)	1.9 (1.6–2.4)
MACDP[b]	138	90	410,259	3.4 (2.8–4.0)	2.2 (1.8–2.7)
Arkansas	65	53	320,780	2.0 (1.6–2.6)	1.7 (1.3–2.2)
Texas	856	697	3,477,737	2.5 (2.3–2.6)	2.0 (1.8–2.1)
South Carolina	60	12	597,662	1.0 (0.8–1.3)	0.2 (0.1–0.4)
Total	1872	1145	5,911,109	3.2 (3.0–3.3)	1.9 (1.8–2.1)

[a] Live births, stillbirths (fetal death ≥20 weeks gestation), and other pregnancy losses (elective termination at any gestational age and miscarriage <20 weeks gestation).

[b] Metropolitan Atlanta Congenital Defects Program.

Am J Med Genet A. Author manuscript; available in PMC 2023 August 07.

TABLE 2

Distribution of Turner syndrome karyotype by pregnancy outcome (N = 1872).

Karyotype	Total[a] (%)	Live births and stillbirths only (%)
45,X	1412 (75.4)	792 (69.2)
Mosaicism		
45,X/46,XX	123 (6.6)	76 (6.6)
45,X/47,XXX or 45,X/46,XX/47,XXX	27 (1.4)	25 (2.2)
45,X/47,XXX or 45,X/46,XX/47,XXX	27 (1.4)	25 (2.2)
45,X/46,XY	23 (1.2)	16 (1.4)
Structural abnormalities of the X		
46,XX,del(Xp22.3)	20 (1.1)	18 (1.6)
46,X,r(X)/46,XX	47 (2.5)	36 (3.1)
46,X,i(Xq) or 46,X,idic(Xp)	55 (2.9)	48 (4.2)
Other[b]	30 (1.6)	27 (2.4)
Not otherwise specified	135 (7.2)	107 (9.3)

[a] Live births, stillbirths (fetal death ≥20 weeks gestation), and other pregnancy losses (elective termination at any gestational age and miscarriage <20 weeks gestation).

[b] "Other" includes cases with rare karyotypes that did not fit within the other karyotype classifications.

TABLE 3

Counts and proportions of core birth defects in Turner syndrome cases ($N = 1872$) by karyotype.

Birth defect	45,X	Other	Total[a]	Percent of all cases (95% CI)
Coarctation of the aorta	163	55	218	11.6 (10.2–13.2)
Atrial septal defect	82	46	128	6.8 (5.7–8.1)
Ventricular septal defect	48	25	73	3.8 (3.1–4.9)
Hypoplastic left heart syndrome	49	18	67	3.6 (2.8–4.5)
Bicuspid aortic valve	50	15	65	3.5 (2.7–4.4)
Horseshoe kidney	46	17	63	3.4 (2.6–4.3)
Aortic valve stenosis	27	16	43	2.3 (1.7–3.1)
Renal agenesis/hypoplasia	16	5	21	1.1 (0.7–1.7)
Omphalocele	18	0	18	1 (0.6–1.5)
Mitral valve stenosis	5	4	9	0.5 (0.2–0.9)
Clubfoot	6	4	10	0.5 (0.3–1.0)
Atrioventricular septal defect	6	1	7	0.4 (0.2–0.8)
Cleft palate alone	5	3	8	0.4 (0.2–0.8)
Limb deficiencies (reduction defects)	6	1	7	0.4 (0.2–0.8)
Rectal and large intestinal atresia/stenosis	5	0	5	0.3 (0.1–0.6)
Spina bifida without anencephaly	2	2	4	0.2 (0.1–0.5)
Anophthalmia/microphthalmia	3	1	4	0.2 (0.1–0.5)
Interrupted aortic arch	3	1	4	0.2 (0.1–0.5)
Pulmonary valve atresia and stenosis	3	1	4	0.2 (0.1–0.5)
Transposition of the great arteries	2	1	3	0.2 (0.0–0.5)
Tricuspid valve atresia and stenosis	2	1	3	0.2 (0.0–0.5)
Cleft lip with cleft palate	3	1	4	0.2 (0.1–0.5)
Cleft lip alone	3	0	3	0.2 (0.0–0.5)
Esophageal atresia/ Tracheoesophageal fistula	0	2	3	0.2 (0.0–0.5)
Diaphragmatic hernia	2	2	4	0.2 (0.1–0.5)
Encephalocele	1	0	1	0.1 (0.0–0.3)
Ebstein anomaly	0	2	2	0.1 (0.0–0.4)
Tetralogy of Fallot	0	2	2	0.1 (0.0–0.3)

Birth defect	45,X	Other	Total[a]	Percent of all cases (95% CI)
Choanal atresia	0	1	1	0.1 (0.0–0.3)
Biliary atresia	1	0	1	0.1 (0.0–0.3)
Small intestinal atresia/stenosis	1	0	1	0.1 (0.0–0.3)
Gastroschisis	2	0	2	0.1 (0.0–0.3)

[a]Counts indicate the number of defects and do not reflect the number of cases, as a case can be counted in more than one category.

TABLE 4

Prevalence ratios and 95% confidence intervals for associations of maternal and infant birth characteristics with Turner syndrome.

Characteristic	Cases	Live births	Prevalence ratio (95% CI)
Maternal age			
<25 years	644	2,103,546	1.0 (0.9–1.1)
25–29 years	493	1,613,425	1.0 (Reference)
30–34 years	427	1,315,475	1.1 (0.9–1.2)
35–39 years	204	614,645	1.1 (0.9–1.3)
≥40 years	56	140,808	1.3 (1.0–1.7)
Maternal race and ethnicity			
Hispanic	568	2,199,288	0.7 (0.6–0.8)
Non-Hispanic Alaska Native, American Indian, Asian, or Pacific Islander	68	295,254	0.6 (0.5–0.8)
Non-Hispanic Black	137	821,185	0.5 (0.4–0.6)
Non-Hispanic White	876	2,425,784	1.0 (Reference)
Birth weight for gestational age			
Small	313	622,408	3.9 (3.4–4.5)
Appropriate	554	4,342,689	1.0 (Reference)
Large	129	490,644	2.1 (1.7–2.5)
Year of birth			
2000–2002	254	838,896	1.0 (Reference)
2003–2005	243	880,320	0.9 (0.8–1.1)
2006–2008	274	940,718	1.0 (0.8–1.1)
2009–2011	359	1,069,032	1.1 (0.9–1.3)
2012–2014	357	1,101,556	1.1 (0.9–1.3)
2015–2017	385	1,080,587	1.2 (1.0–1.4)

TABLE 5

Survival probabilities and 95% confidence intervals for individuals with Turner syndrome.

	Number at risk		Number of deaths		Overall survival probability	
Survival time	**All cases**	**Cases without HLH[a]**	**All cases**	**Cases without HLH**	**All cases**	**Cases without HLH**
1 day	745	702	13	13	98.4 (97.2–99.1)	98.2 (96.9–98.9)
7 days	731	693	23	17	97.0 (95.6–98.0)	97.6 (96.2–98.5)
28 days	719	687	33	22	95.6 (94.0–96.9)	96.9 (95.3–97.9)
1 year[b]	593	581	64	37	91.8 (89.6–93.5)	94.8 (92.8–96.2)
2 years	568	558	66	37	91.4 (89.3–93.2)	94.8 (92.8–96.2)
5 years[c]	485	478	68	38	91.1 (88.9–92.9)	94.6 (92.6–96.0)

[a] HLH = hypoplastic left heart.

[b] All programs except South Carolina provided data to assess survival up to and including one year.

[c] Arkansas, Utah, Texas, and Metropolitan Atlanta Congenital Defects Program (MACDP) provided data to assess 2- and 5-year overall survival.