

Sex distribution in tuberculosis disease in children, adolescents, and adults in a low-incidence country: a retrospective population-based cohort study

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Summary

AIM: Globally, tuberculosis incidence shows notable sex disparity, with higher rates observed in males. While this pattern is well documented in adults from high-incidence countries, the influence of sex on tuberculosis incidence in children and adolescents, particularly in low-incidence settings, remains unclear. This study investigated sex-specific tuberculosis incidence rates across all age groups, focusing on adolescents, in a low-incidence country.

METHODS: In this retrospective cohort study, data from the Swiss Federal Office of Public Health (FOPH) tuberculosis database, which centrally consolidates mandatory notifications from physicians and laboratories across Switzerland, were analysed from 2000 to 2021. Tuberculosis incidence rates and male-to-female ratios were calculated and stratified by sex and age. Adolescence was divided into early (10–14 years) and late (15–19 years) stages for detailed analysis.

RESULTS: Over 22 years, the average tuberculosis incidence in Switzerland was 6.78 per 100,000 population, with an overall male-to-female ratio of 1:0.75 ($p < 0.001$). Among the 11,872 notified cases, 832 occurred in adolescents, yielding an incidence rate of 4.39 per 100,000. In late adolescence, males had a significantly higher tuberculosis incidence rate (5.73 per 100,000) than females (2.97 per 100,000, $p < 0.001$), resulting in a male-to-female ratio of 1:0.5. Additionally, data on asylum seekers revealed nearly twice as many males as females arriving in Switzerland in late adolescence.

CONCLUSIONS: This study reveals significant sex disparity in tuberculosis incidence in a country with low tuberculosis incidence, with males showing higher rates than females beginning in late adolescence. This discrepancy is likely influenced by the higher influx of male asylum seekers in adolescence.

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Introduction

Sex distribution in tuberculosis exhibits notable disparities between males and females [1–3], with male adults accounting for the majority of cases globally. According to the 2023 global tuberculosis report by the World Health Organization (WHO), adult males represented 55% of cases, while adult females and children accounted for 33% and 12%, respectively [3]. Several studies [2, 4, 5] have shown that higher incidence rates for tuberculosis disease among males are associated with risk factors such as smoking, alcohol consumption, and exposure to mine-related silicosis, whereas females are more likely to contract tuberculosis through household contact and HIV infection [1]. Even in studies controlling for these risk factors [2, 5], males show significantly higher odds of developing tuberculosis disease, suggesting that biological factors [2, 5], particularly sex hormones, play a crucial role in modulating the immune response to tuberculosis infection [1, 6, 7]. This biological influence is further evidenced by the considerable increase in tuberculosis incidence rates during adolescence [8, 9], coinciding with hormonal changes.

Despite the well-documented sex differences in tuberculosis incidence among adults and in high-incidence countries, data are limited in adolescents, particularly in countries with low tuberculosis incidence, such as Switzerland. In such countries, tuberculosis epidemiology is heavily influenced by migration, with most tuberculosis cases occurring among foreign-born individuals, particularly asylum seekers from tuberculosis-endemic regions [10]. Although women comprise 50% of asylum seekers globally, they accounted for only 31% of asylum seekers in Europe from 2008 to 2018 [11]. This disparity underscores the importance of considering sex, age, and asylum-seeking status when analysing tuberculosis incidence in low-incidence countries. This study investigated sex-specific tuberculosis incidence rates in Switzerland – a low-incidence country – across all age groups, focusing on adolescents. Further-

more, it examined age-related trends and the impact of migration patterns on observed sex disparities.

Methods

This study was conducted in Switzerland, a country with a low incidence of tuberculosis, using national surveillance data from 2000 to 2021. The analysis focused on sex-specific tuberculosis incidence rates across all age groups, with an emphasis on adolescents. Adolescence was categorised into early adolescence (10–14 years) and late adolescence (15–19 years) [8, 9].

Data were extracted from the mandatory notification system of the Swiss Federal Office of Public Health (FOPH), which consolidates all tuberculosis notifications reported by physicians and laboratories. Notifications are required by Swiss law and include demographic, clinical, and microbiological data. Physicians report demographic information (e.g. age, sex, and nationality), clinical presentation (e.g. affected organs), and treatment details (e.g. drugs used, start dates, and outcomes). Laboratories report microbiological test results, including microscopy, culture, molecular assays, and drug susceptibility testing.

The Swiss Federal Office of Public Health does not record information on migration status; therefore, to account for the influence of migration, additional data on asylum seekers were obtained from the Federal Statistical Office (FSO). This dataset provided sex and age at arrival for individuals who sought asylum in Switzerland during the study period.

A tuberculosis case was defined by one of the following criteria:

1. Detection of *Mycobacterium tuberculosis* by culture or molecular assays.
2. Initiation of treatment with ≥ 3 antimycobacterial drugs.

The primary outcome was the incidence rate of tuberculosis stratified by sex and age group. Incidence rates were calculated as the number of reported cases per 100,000 population per year, using annual population data from the Federal Statistical Office as the denominator.

Tuberculosis incidence rates and male-to-female ratios were calculated and compared across age groups using chi-squared (χ^2) tests. To assess the potential impact of migration, the number of male and female asylum seekers in Switzerland was analysed. Age at arrival was compared between sexes using the Mann-Whitney U-test to assess differences in distributions. All statistical analyses were performed using RStudio (version 2022.07.2) and Excel (version 2306). Descriptive statistics and graphical visualisations were used to present the results.

Ethical approval

The Swiss Epidemic Law (EpidA SR 818.101, EpidO SR 818.101.1, FPHA-ORD SR 818.101.126) provides the legal framework for collecting, analysing, and reporting notification data in an anonymised format. Ethics clearance was not required.

Results

Over the 22-year period, 11,872 cases of tuberculosis were reported in Switzerland, reflecting a mean annual incidence rate of 6.77 per 100,000 population and an overall male-to-female ratio of 1:0.75 (χ^2 , $p < 0.001$). Among these cases, 832 (7%) were adolescents, with an overall mean annual incidence rate of 4.39 per 100,000. Adolescent males had a higher mean annual tuberculosis incidence rate (5.73 per 100,000) than females (2.97 per 100,000), with a male-to-female ratio of 1:0.5 (χ^2 , $p < 0.01$).

Detailed analysis of tuberculosis incidence in adolescents in absolute numbers revealed that the increase in incidence began around the age of 10 years, with an earlier onset in females than in males (figure 1). This rise continued throughout adolescence and into young adulthood, peaking at age 25 and 30 years in males and females, respectively. Interestingly, in early adolescence, females exhibited a higher tuberculosis incidence rate (1.46 per 100,000) than males (1.15 per 100,000), with a male-to-female ratio of 1:1.2 (χ^2 , $p = 0.226$). In late adolescence, the tuberculosis incidence rate in males increased to 10.15 per 100,000, significantly higher than that in females (4.44 per 100,000), resulting in a male-to-female ratio of 1:0.41 (χ^2 , $p < 0.001$) (table 1 and figure 2). In children under 10 years of age, the tuberculosis incidence rate was low, with no significant sex difference. Notably, the incidence rates in older age groups (figure 2) may appear exaggerated due to smaller population sizes, making the rates highly sensitive to small variations in case numbers and potentially leading to overestimation.

Regarding migration, 560,575 asylum seekers arrived in Switzerland from 2010 to 2022, of whom 101,288 (18%) were adolescents. The number of male asylum seekers was nearly twice that of females, with an overall male-to-female ratio of 1:0.6 (χ^2 , $p < 0.001$) and 1:0.5 (χ^2 , $p < 0.001$) for adolescent asylum seekers. More than half of male asylum seekers arrived between the ages of 15 and 30 years, with a median age at arrival of 25 (IQR 19, 35) years. Female asylum seekers were older upon arrival, with a median age at arrival of 28 (IQR 19, 39) years (Mann-Whitney U, $p < 0.001$), and approximately one-third arrived between the ages of 15 to 30 years (table 1 and figure 3).

Discussion

Our study reveals that the overall annual tuberculosis incidence in Switzerland is influenced not only by age but also by sex, particularly during adolescence. In children and early adolescents (under 15 years of age), tuberculosis incidence rates are extremely low and show no significant sex difference. Although females may exhibit higher incidence rates in early adolescence, these differences were not significant in our dataset. This observation is consistent with existing literature suggesting a temporary dominance of tuberculosis incidence in females during adolescence [12], potentially due to the earlier onset of puberty in girls compared to boys.

However, in late adolescence, the tuberculosis incidence rate in males was significantly higher than that in females. This finding aligns with global reports showing that tuber-

culosis prevalence is significantly higher in men than in women. This disparity may be partly attributed to the biological changes associated with puberty in boys. Moreover, the disproportionate increase in male asylum seekers in this age group aligns with the higher tuberculosis incidence observed in adolescent males, suggesting that migration plays a key role in shaping the sex distribution of tuberculosis cases in Switzerland [13].

These findings should be interpreted with caution. Although our study benefits from 22 years of national sur-

veillance data, several limitations must be considered. Because data on asylum-seeking status are not included in the mandatory tuberculosis notification system, we were unable to adjust male-to-female ratios for asylum-seeking status across age groups, which represents a key limitation. Additionally, individual risk factors such as comorbidities, prior tuberculosis exposure, and health-seeking behaviour may contribute to the observed sex disparities. These potential confounders are not recorded in the national tuberculosis surveillance data; therefore, we could not assess them. Moreover, there is a mismatch in the timeframes of

Figure 1: Sex distribution in the absolute number of tuberculosis cases in children, adolescents, and adults per year of age in Switzerland based on surveillance data from the Swiss Federal Office of Public Health (FOPH) (2000–2021) and the Federal Statistical Office (FSO) (2010–2021), respectively.



Figure 2: Tuberculosis incidence rates by sex and age per 100,000 population in Switzerland.

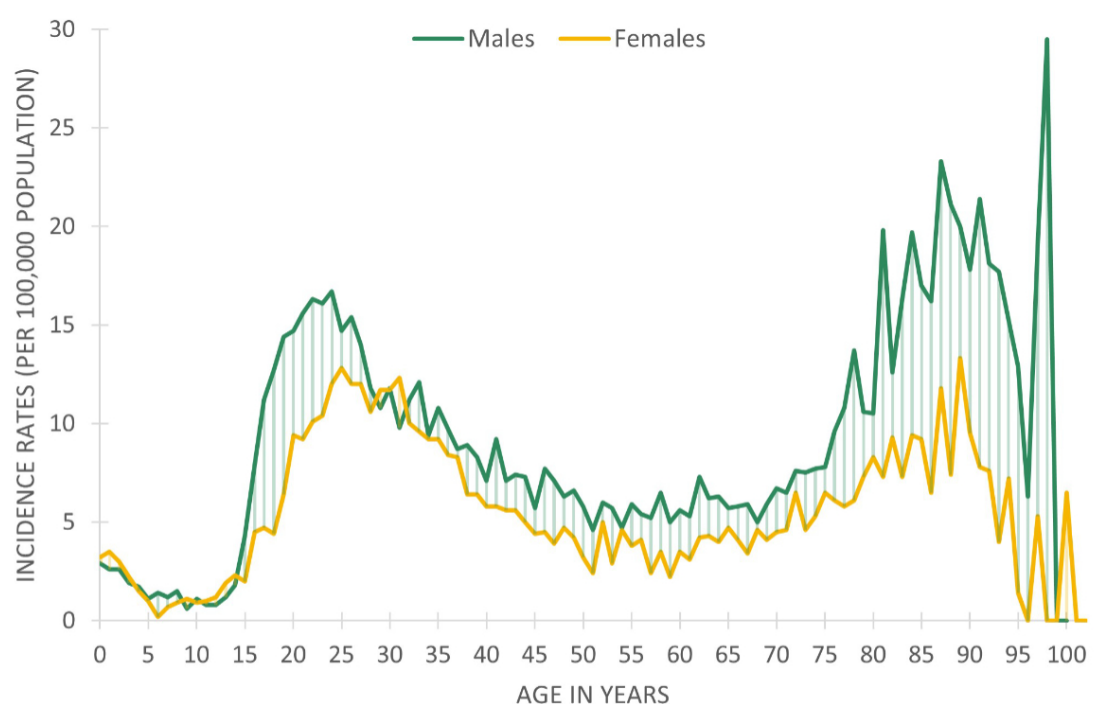
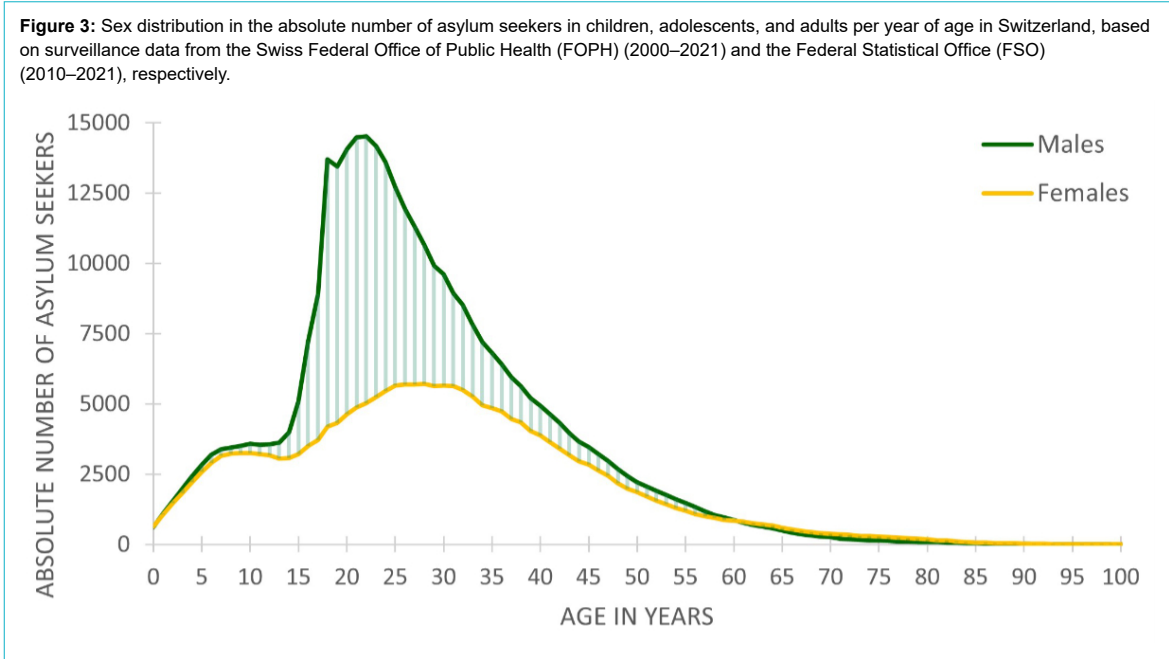


Table 1: Distribution of sex in tuberculosis in the Swiss population, focusing on early and late adolescence, based on surveillance data (2000–2021) from the Swiss Federal Office of Public Health (FOPH) and sex distribution in asylum seekers based on surveillance data (2012–2021) from Federal Statistical Office (FSO).

	Early adolescence		Late adolescence		Adolescence		All ages	
	10–14 years		15–19 years		10–19 years		0–100 years	
	M	F	M	F	M	F	M	F
Number of tuberculosis cases (2000–2021)	121		711		832		11,872	
	55	66	503	208	558	274	6789	5083
Male-to-female ratio of tuberculosis cases	1:1.2		1:0.41		1:0.49		1:0.75	
	Chi ² , p = 0.226		Chi ² , p <0.001		Chi ² , p <0.001		Chi ² , p <0.001	
Incidence per 100,000	1.30		7.37		4.39		6.77	
	1.15	1.46	10.15	4.44	5.73	2.97	7.85	5.71
Number of asylum seekers (2010–2021)	33,998		67,290		101,288		560,575	
	18,274	15,724	48,377	18,913	66,651	34,637	348,909	211,666
Male-to-female ratio of asylum seekers	1:0.86		1:0.39		1:0.52		1:0.61	
	Chi ² , p <0.001		Chi ² , p <0.001		Chi ² , p <0.001		Chi ² , p <0.001	

Chi²: chi-squared test.



the available datasets: national tuberculosis notification data are available from 2000 to 2021, while asylum seeker data are available from 2010 to 2021. This discrepancy may introduce bias, leading to over- or underestimation of the influence of migration on male-to-female tuberculosis incidence ratios.

The generalisability of our findings is limited to Switzerland and other low-incidence countries with similar health-care systems and migration patterns. The observed male predominance in tuberculosis incidence, particularly in late adolescence, is consistent with findings from a pooled analysis including data from Europe, the Americas, and Australia, suggesting that biological and behavioural risk factors contribute beyond high-incidence settings [14].

Our findings provide important epidemiological insights into the sex distribution of tuberculosis in Switzerland, particularly among adolescents. This knowledge is valuable for informing public health strategies and may help clinicians improve tuberculosis diagnosis, especially in adolescents. Future research incorporating individual-level risk factors, social influences, and longitudinal follow-up would provide a more comprehensive understanding of

sex-specific tuberculosis disparities, particularly in children and adolescents.

Data sharing statement

Due to the stringent data protection and privacy terms outlined by the Swiss Federal Office of Public Health, the study data are not available for open sharing. The data provided by the Swiss Federal Office of Public Health was anonymised and aggregated, with strict regulations on its use to prevent any identification of individuals. Therefore, while the analysis is based on the Swiss Federal Office of Public Health data, sharing the raw data is not permissible under the data use agreement.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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