NATIONAL PUBLIC
HEALTH ORGANIZATION

Epidemiological surveillance of tuberculosis in Greece, 2023

Main points:

- TB is a notifiable disease in Greece; under-reporting affects the estimated burden of disease in the population.
- In 2023, 493 active TB cases were notified, a 54% increase compared to 2022. This follows the global TB surge after the COVID-19 pandemic.
- The TB notification rate in Greece in 2023 was 4.71 per 100,000 population. Greece is a low-incidence country according to the World Health Organization (WHO) definition (less than 10 cases per 100,000 per year).
- In 2023, 47% of the total reported cases were Greeks and 53% were foreign-born. During the past decades, TB incidence had been declining in the Greek population until the COVID-19 pandemic, with the majority of cases observed among older adults. After the pandemic, an upward trend has been observed in both in the Greek and the foreign-born population. In cases originating from countries with a high TB incidence, the TB rate has steadily been increasing over the last decade. Most foreign-born TB cases pertain to adolescents and young adults (15-24 years old).
- Among foreign-born cases in 2023, an increase in central nervous system disease (tuberculous meningitis and brain TB) was noted, as well as an increase in highly transmissive cases.

Epidemiological surveillance of tuberculosis

Epidemiological surveillance of tuberculosis monitors new cases of active tuberculosis in the population. Demographic, clinical and laboratory data are collected such as age, sex, ethnicity, site of infection and drug susceptibility, as well as risk factors such as underlying diseases, exposure history etc.
Data analysis detects trends over time regarding the form and extent of the disease, risk factors for active disease and transmission and additional information, which can be used to optimize management and prevent further transmission in the setting of individual cases or clusters, as well as to guide public health strategies.
Moreover, the systematic notification of cases is essential for monitoring disease indicators set by the World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC) regarding the epidemiological surveillance of TB at European and global level.
Notification is mandatory for active TB cases in Greece. Latent tuberculosis (non-transmissible mycobacterial infection without active disease) is not currently being monitored.

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Epidemiology of tuberculosis in Greece in 2023

Number of notified cases and incidence of tuberculosis

In 2023, 493 new cases of active TB were reported, 54% more than in 2022 (Figure 1). Of those, 370 (75%) were notified by attending physicians, while 123 additional cases were recognized through active laboratory surveillance (unmatched cases) in selected tertiary hospitals.
The TB notification rate in Greece in 2023 is estimated at 4.71 per 100,000 population. A small upward trend was noted in comparison to 2019, the year preceding the COVID-19 pandemic, when the notification rate was 4.3 per 100,000 (Figure2). Due to under-reporting, the number of notified cases in 2023 is considered to be an underestimate of the true burden of disease in the country.

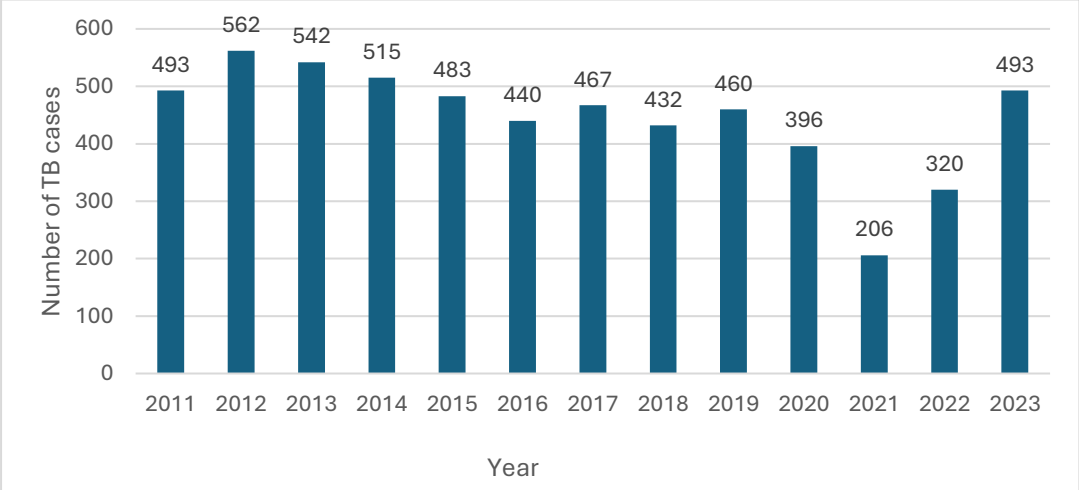


Figure 1: Number of reported active TB cases (2011-2023), including cases recognized through laboratory surveillance (unmatched cases) in selected tertiary hospitals (2022-2023) in Greece

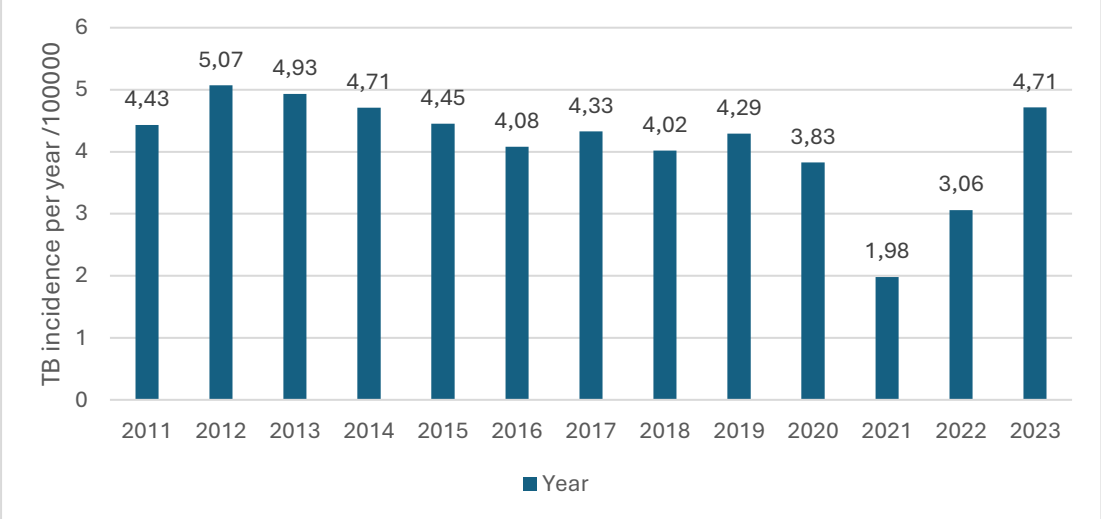


Figure 2: Active TB incidence per year/100000 in Greece, 2011-2023

Most notifications were received from the greater area of capital Athens, where most tertiary hospitals are located, including the national TB reference hospital, the General Hospital for Thoracic Diseases “Sotiria” (Figure 3).

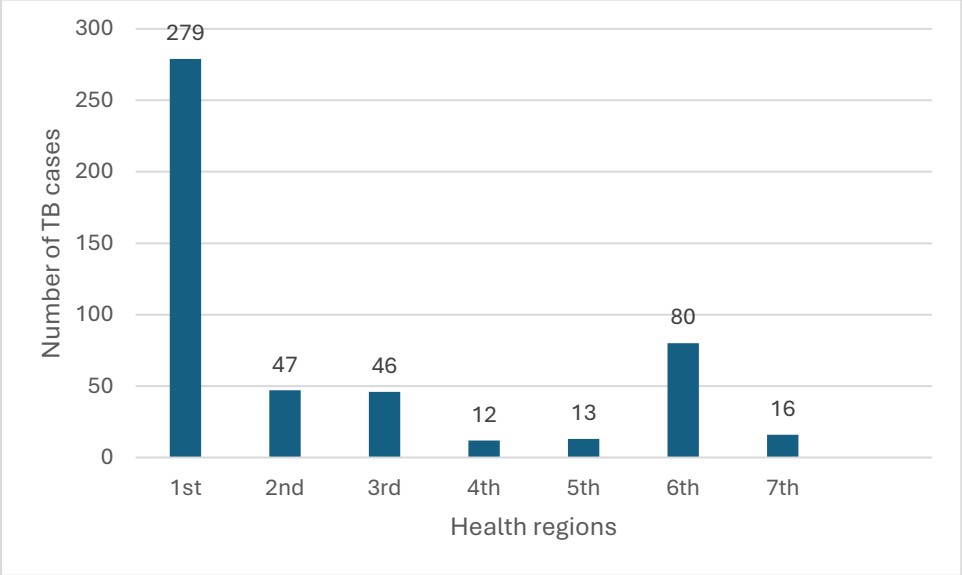
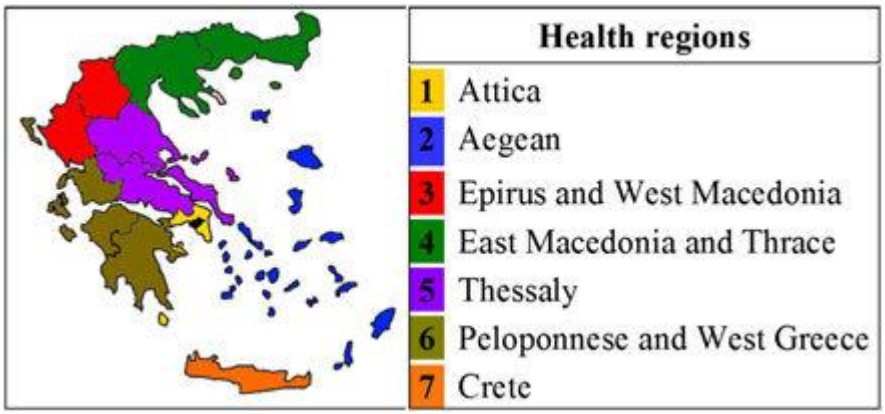


Figure 3: TB cases by Health region 2023



Demographic data

In 2023, 47% of the total cases were Greek, while 53%were foreign-born (Figures 4 and 5), a distribution similar to that of 2022.

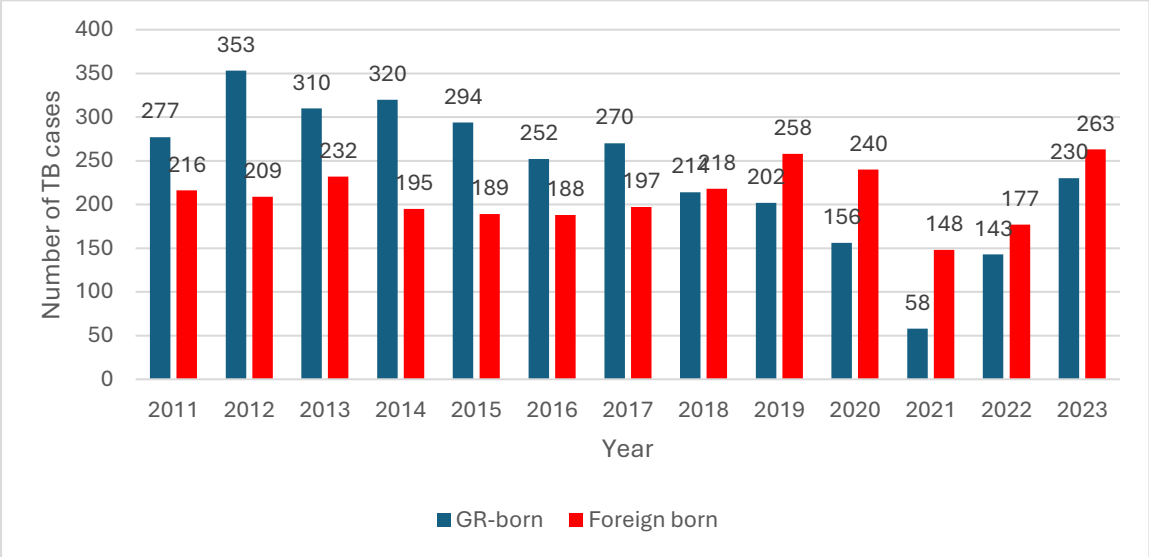


Figure 4: TB cases by year and origin, 2011-2023

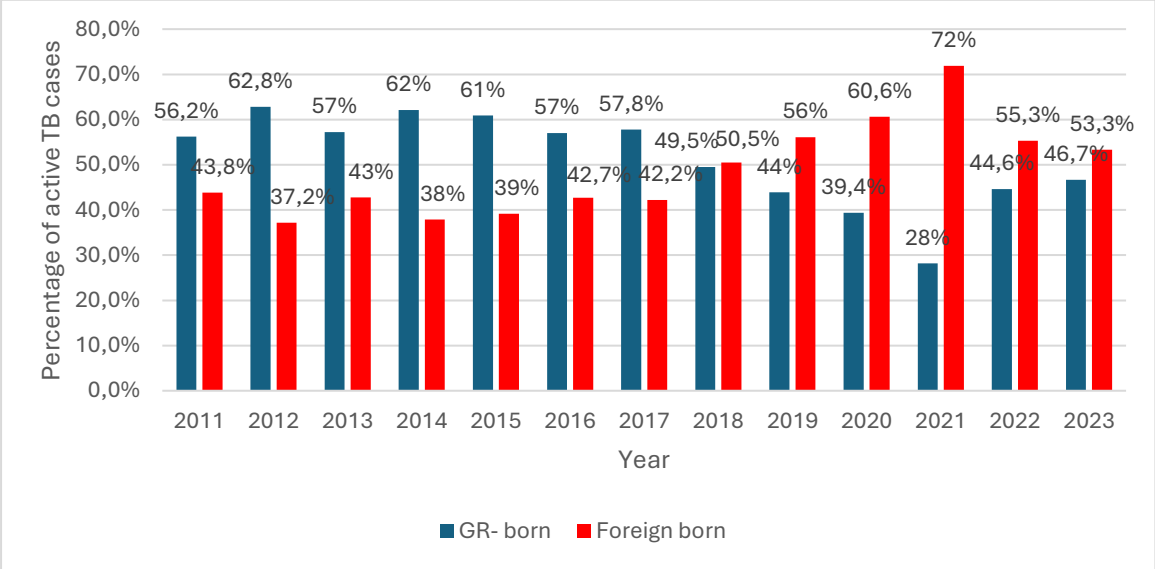


Figure 5: Percentage of TB cases by year and origin, 2011-2023

Sex distribution was 363 males (73.6%) and 130 females (26.4%). Greek women accounted for 32%, while 26% were women among foreign-born cases. In the foreign-born population, the proportion of female TB cases is significantly smaller than that of male cases, which reflects the overall gender distribution within this group. Conversely, in the Greek population, women constitute over 50% of the

general population, yet the female-to-male TB case ratio remains low. This phenomenon may be attributed either to lower TB exposure rates among women or to a lower rate of latent TB activation.

Active TB cases in the foreign-born are observed among refugees/migrants from countries with a high TB incidence.The **geographical areas of origin** of foreign-born TB cases are shown in Figure 6. Most foreign-born cases come from Central and South Asia (mostly Pakistan, Afghanistan, India, Bangladesh), accounting for 45% of foreign-born TB cases, compared to 53% in 2022. Sub-Saharan Africa (mostly Somalia, Congo and Sierra Leone) is the second most prevalent geographical area of origin: 22% of foreign-born cases, compared to 15% in 2022. The third most prevalent geographical region of origin isEastern Europe (mostly Georgia, Romania, Albania) accounting for 20% of cases, compared to 24% in 2022.

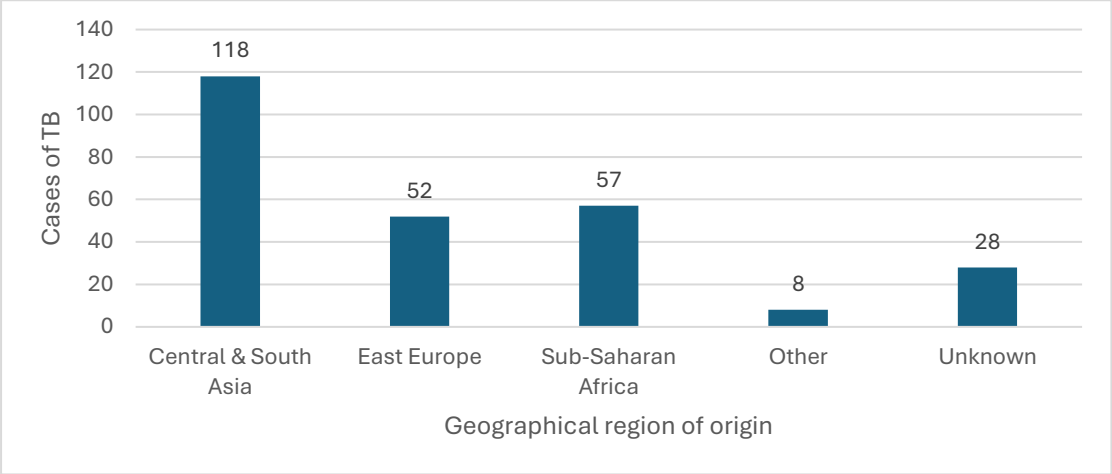


Figure 6: Origin of foreign-born TB cases in 2023

Regarding the distribution among **age groups**, people >65 years of age were the prevalent age group in Greeks. In contrast, among foreign-born cases,adolescents and young adultswere mostly affected (Figure 7).

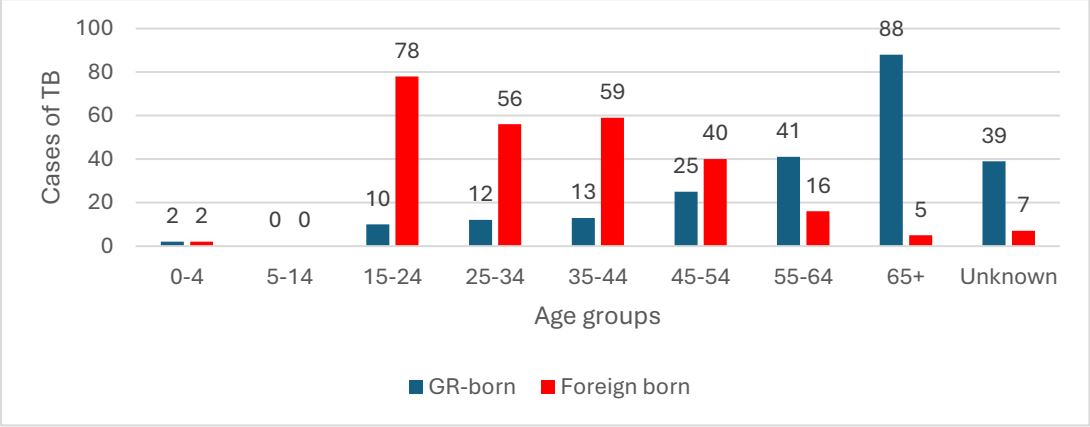


Figure 7: TB cases by age group and origin in 2023

Twenty-one TB cases in **minors** were notified (4.3%). Of those, two cases were foreign-born infants (under one year of age) and two were ROMA toddlers (under 5 years old). Of the 17 adolescent cases, one was a 15-year-old ROMA, while 16 were foreign-born adolescents residing in migrant/refugee facilities. Three minors had severe TB: two had miliary TB while a 17-year-old died of TB meningitis.

17% (83/493) of the notified cases lived in **group living conditions.** Of these, 67% (56/83) resided in refugee/migrant facilities, 7% (6/83, 2 Greeks, 4 foreign-born) in detention facilities (prisons), 9.6% (8/42) in chronic care facilities, 2.4% (2/83) in the army and 2.4% (2/83) in shelters for the homeless (Table 1).

TYPE OF COMMUNAL LIVING	NUMBER OF CASES
Refugee/Migrant facility	56
Chronic care (Psychiatric Clinic, Nursing Home)	8
ROMA camp	7
Detention Facility (Prison)	6
Homeless shelter	2
Army	2
Undetermined group living	2
TOTAL	**83**

Table 1: Number of TB cases in group living.

Clinical data

Pulmonary disease (potentially transmissible type) represented the majority of notified TB cases (87%) (Figure 8). Extrapulmonary TB (non-transmissible type of disease) was recorded in 6% of Greek and 15% of foreign-born cases (Figure 9).

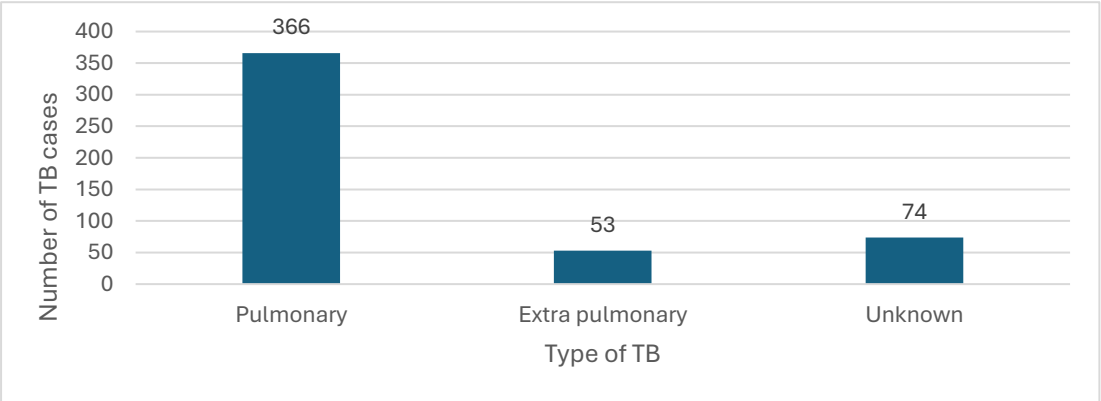


Figure 8: Cases of TB with pulmonary (with or without extrapulmonary focus) and exclusively extrapulmonary TB in 2023

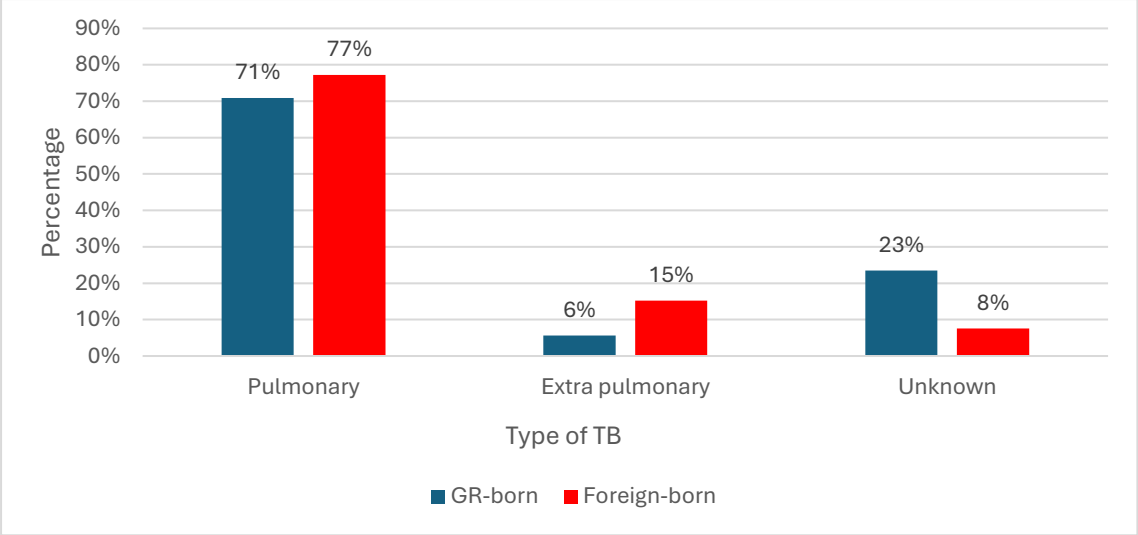


Figure 9: Percentage of pulmonary and exclusively extra pulmonary TB in Greek and foreign-born cases in 2023

A significant proportion of pulmonary cases presented with lung **cavitation,** a feature associated with high transmissibility (Figure 10). In 2023, compared to 2022, lung cavitation decreased in Greeks, but increased in the foreign-born.

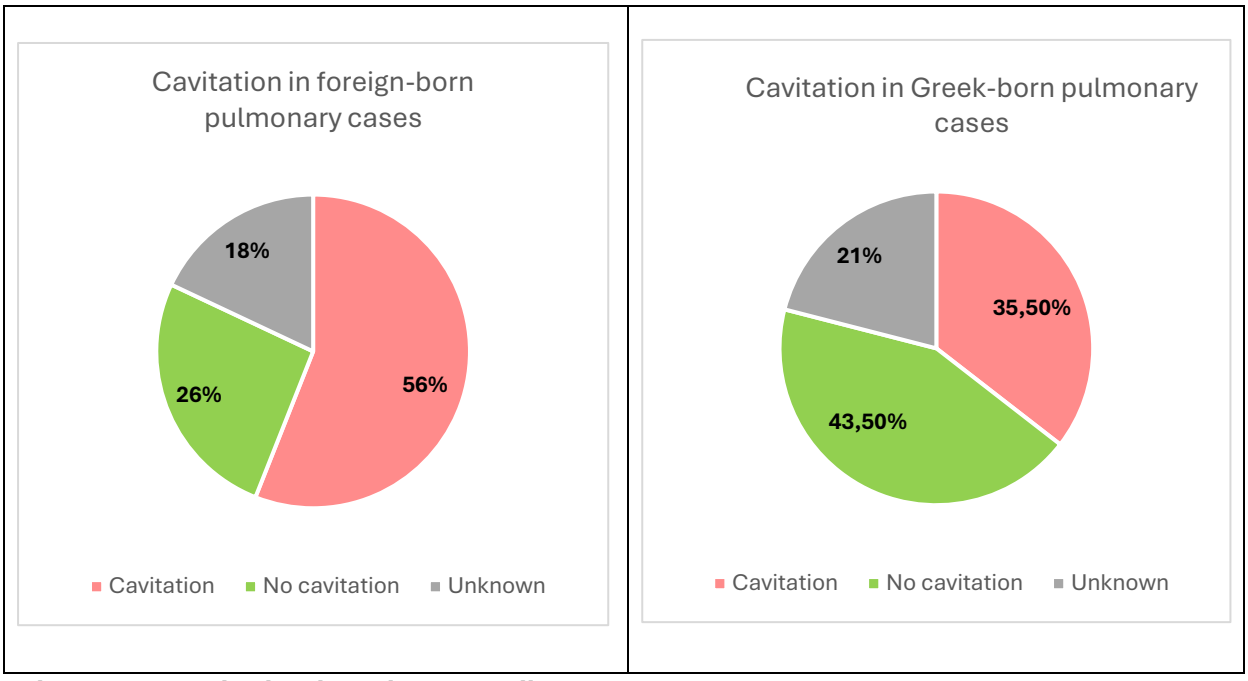


Figure 10: Cavitation in pulmonary disease, 2023

The **most severe forms** of TB are disease of the central nervous system (CNS) and miliary TB. In 2023 there was a substantial increase in **CNS disease** (tuberculous meningitis and cerebral TB): 8 foreign-born cases were notified (17-39 years old), while only 2 in 2022. Out of the 8 CNS TB cases, only one was immunosuppressed (HIV). 23 **miliary TB** cases were reported. Of the latter, 8 were observed in Greeks

(one ROMA infant and seven elderly patients with comorbidities). In the foreign-born, 15 miliary TB cases were recorded (8 in previously healthy young men and 7 in middle-aged men, two of whom had comorbidities).

In the cases with exclusively **extrapulmonary TB**, the majority pertained to tuberculous lymphadenitis (20/53 or 38%) and bone TB (12/53 or 23%), mainly vertebral. 8 cases presented with tuberculous pleurisy (15%), 5 (9%) with gastrointestinal TB, 2 (4%) with urinary tract TB, one with peritoneal TB (2%) and one with ocular TB.

In 2023, 6.5% (32/493) of cases reported a previous TB diagnosis, mostly **relapse** due to incomplete treatment, compared to 7.5% in 2022.

Of the 493 total cases, 336 were reported to have negative HIV status, 11 were positive and 146 had an unknown HIV status. **TB/HIV co-infection** cases correspond to 3% (11/347) of the cases with known HIV status compared to 4% in 2022. Of the 11 TB/HIV co-infection cases (median age: 39 years, range: 17 - 51), 5 were Greek and 6 were foreign-born. One Greek and one foreign-born case were prisoners.

Laboratory data

Regarding bacteriological testing, 90% (442/493) of the total notified cases in 2023 were laboratory-confirmed at the time of reporting, either by culture or by molecular testing plus positive microscopy (Table 2). However, it is noted that laboratory confirmed cases are more likely to be reported compared to cases that received therapeutic treatment based on clinical criteria only.

Classification*	Number
Confirmed	442 (90%)
Probable	22 (4%)
Possible	29 (6%)

Table 2: Classification of cases according to the case definition, 2023

*For case definitions, see: https://eody.gov.gr/wp-content/uploads/2022/04/orismoi-loimodon-nosimaton-20220413.pdf

Among pulmonary TB cases with a known sputum microscopy result in 2023, 49% (155/315) had positive microscopy, a finding associated with **high transmissibility** (Figure 11).

Culture results were known for 75% (367/493) of cases (Figure 12), of which 96% (353/367) were positive.

Molecular testing results were available for 76% (375/493) of cases (Figure 12), of which 90% (339/375) were positive.

In 3% of cases (17/493), TB was confirmed **post-mortem**, compared to 4.6% in 2022.

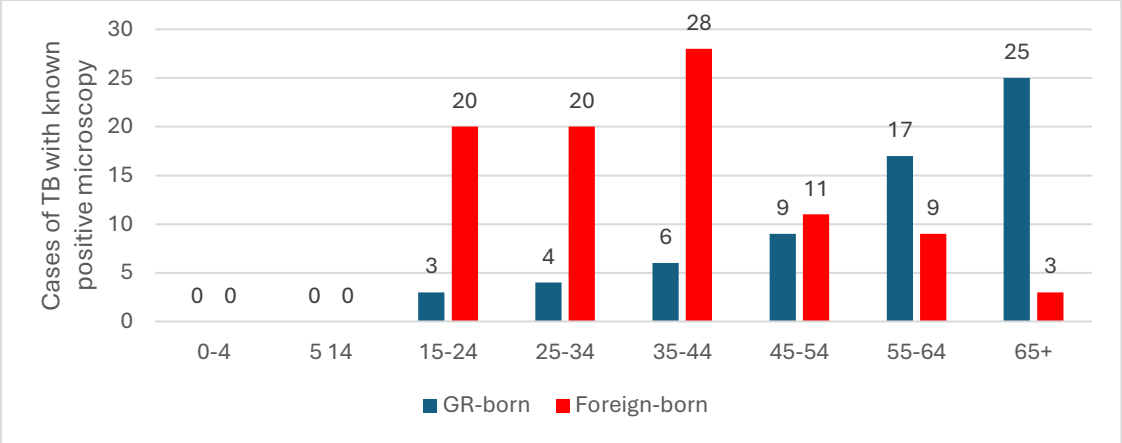


Figure 11: Pulmonary cases with known positive microscopy, 2023

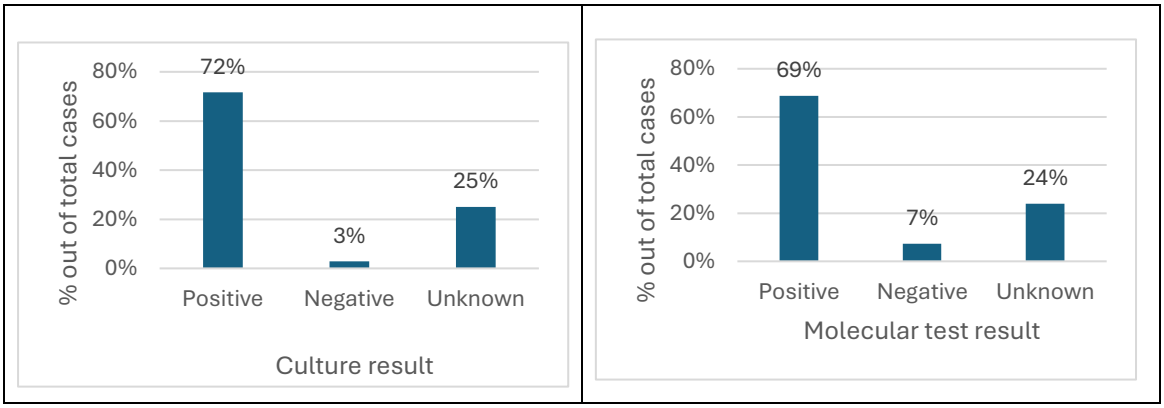


Figure 12: Culture and molecular testing results, 2023

Sensitivity to antituberculosis drugs

Susceptibility results to primary antituberculosis drugs were available for 59% (293/493) of cases, a proportion comparable to 2022. 42% of susceptibility results were retrieved through active laboratory surveillance in selected tertiary hospitals.

Among the cases with known susceptibility results, 84% (234 out of 293) were **sensitive** to all primary antituberculosis drugs. Sensitivity was higher among Greeks: 88% (97/110) compared to 82.5% (151/183) of foreign-born cases, similar to the rates observed in 2022 (see Table 4).

Isolated isoniazid resistance was reported in 2.3% (7/293) of cases. **Isolated rifampicin resistance** was present in 0.6% (2/295) of cases, while none had been recorded in 2022. Of note, isoniazid and rifampicin are the most critical drugs in TB treatment (Figure 14).

Multidrug-resistance (MDR) and extended resistance (XDR) was reported in 6 cases (6/293 or 2%): 5 foreign-born cases from Eastern Europe and one Greek XDR case. The latter had no past TB history and no known TB exposure.

Type of resistance	Number of strains with known susceptibility result	Number (percentage) of strains with the specific resistance type	Greek-born with known susceptibility result (N= 110)	Foreign-born with known susceptibility result (n=183)
Isolatedisoniazid (**R-INH**)	293	7 (2.3%)	3 (2.7%)	4 (2.2%)
Isolated rifampicin (**R-RIF**)	295	2 (0.6%)	0	2 (1%)
Isolated streptomycin (**R-STR**)	293	22 (8%)	4 (4%)	18 (10%)
Isolated pyrazinamide (**R-PZA**)- probably *M bovis* strain	271	0	-	-
Isolated ethambutol (**R-ETH**)	293	0	-	-
Isoniazid and rifampicin (multi-drug resistance, **MDR**)	293	3 (1%)	0	3 (1,6%)
Extended (**pre-XDR&XDR**)*	**	3	1	2

Table 4: Sensitivity and resistance in reported cases with known sensitivity results, 2023

* Pre-XDR: Isoniazid, rifampicin AND fluoroquinolone, XDR: Isoniazid, rifampicin,fluoroquinolone AND bedaquiline or linezolid.

** There are no susceptibility data for bedaquiline and linezolid for the strains with combined resistance to isoniazid and rifampicin.

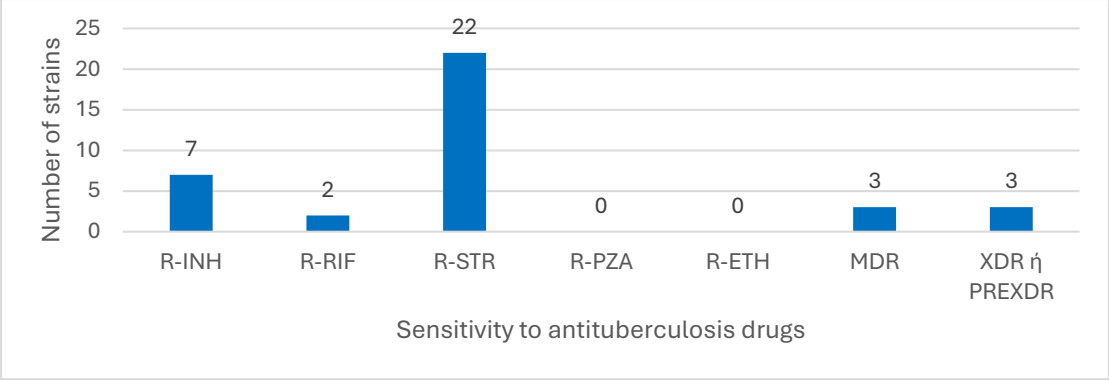


Figure 13: Number of resistant *M. tuberculosis* strains, 2023

R-INH: Isolated isoniazid resistance,**R-RIF**: Isolated rifampicin resistance, **R-STR**: Isolated streptomycin resistance, **R-PZA**: Isolated pyrazinamide resistance, **R-ETH**: Isolated ethambutol resistance, **MDR**: Multi-drug resistance (Resistance to isoniazid AND rifampicin), **preXDR**: Extended (Resistance to isoniazid, rifampicin AND fluoroquinolone), **XDR**: Extended (Resistance to isoniazid, rifampicin, fluoroquinolone AND bedaquiline or linezolid).

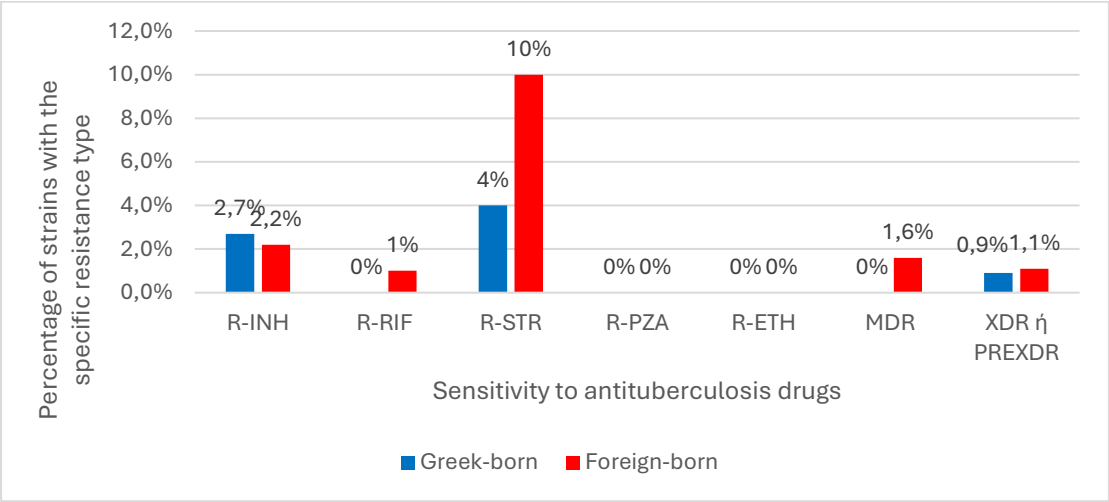


Figure 14: Percentage of resistant *M. tuberculosis* strains, 2023

R-INH: Isolated isoniazid resistance, **R-RIF**: Isolated rifampicin resistance, **R-STR**: Isolated streptomycin resistance, **R-PZA**: Isolated pyrazinamide resistance, **R-ETH**: Isolated ethambutol resistance, **MDR**: Multi-drug resistance (Resistance to isoniazid AND rifampicin), **preXDR**: Extended (Resistance to isoniazid, rifampicin AND fluoroquinolone), **XDR**: Extended (Resistance to isoniazid, rifampicin, fluoroquinolone AND bedaquiline or linezolid).

Discussion

In 2023, the number of notified active TB cases was higher among the foreign-born than among the natives, a constant phenomenon since 2018. Foreign-born TB cases were predominantly adolescents and young adults from high TB incidence countries. In contrast, TB cases among Greeks primarily involve older individuals, with a significant percentage of cases in those over 80 (reactivation of latent TB acquired at a young age). TB in the foreign-born is generally more advanced and/or severe upon diagnosis and more cases of resistant TB are noted in this group. Regardless of

ethnic background, cases are observed in groups with social risk factors and/or precarious living conditions, such as intravenous drug users and prisoners.

Pulmonary TB was the most prevalent type of active disease, with or without additional extrapulmonary sites (most often lymph nodes). Pulmonary disease confers a risk for transmission and is therefore particularly relevant from a public health perspective. Exclusively extrapulmonary TB, a non-transmissible type of disease, accounted for 1/7 of cases, compared to 1/5 in 2022.

Lung cavitation, a finding that indicates **high transmissibility**, presented an upward trend in foreign-born cases (56% in 2023 compared to 53.5% in 2022). This phenomenon is an indirect indicator of delayed diagnosis, which may be due to delayed seeking of care or access barriers in reaching health services. In Greek-born cases, cavitation showed a decreasing trend (35.5% in 2023 compared to 48% in 2022). A positive sputum smear test, another indicator of high transmissibility, was reported in 49% of cases, compared to 64% in 2022.

Pediatric tuberculosis in Greece is steadily declining. While 20 years ago about 10% of TB cases were children <14 years of age, in 2023 the rate was 0.6%, compared to 1.9% in 2022 and 2% in 2021. In 2022 children <14 years old with active TB had a history of TB exposure within the immediate family environment, i.e. the source of infection of young children was within the family. In 2023, the cases in children <14 years old pertained to infants and toddlers, in whom exposure presumably happened within the family.

With respect to **severe forms** of TB, there was a proportional decline in **miliary** TB, namely 4.7% (23/493 cases) in 2023, compared to 7% (23/320 cases) in 2022. Greek miliary TB cases were mostly elderly, while foreign-born cases were mainly previously healthy young adults. Tere was an increase in **central nervous system** TB: 8 young foreign-born cases were reported (compared to 2 cases in 2022), of whom one previously healthy teenager died of tuberculous meningitis.

In 2023, 90% of notified cases were **laboratory confirmed** with a positive culture or molecular testing plus microscopy. Antituberculosis drug susceptibility data were available for 59% of cases, a rate similar to 2022. Among the culture-positive cases, 2.3% showed isolated isoniazid **resistance** (vs. 2.6% in 2022), while 1% had combined isoniazid and rifampicin resistance (multi-drug-resistant strains, MDR), vs. 4.7% in 2021. In 2021, MDR cases were all foreign-born, while in 2022 and 2023 MDR cases were also reported in Greeks, but multi-resistance in steadily more prevalent in foreign-born cases. In 2023, three cases of extensive resistance (preXDR/XDR) were reported (one Greek, two foreign-born), while in 2022 only one of preXDR case had been reported.