NATIONAL PUBLIC
HEALTH ORGANIZATION

Epidemiological surveillance of tuberculosis in Greece, 2022

Main points:

- TB is a notifiable disease in Greece; under-reporting affects the estimated burden of the disease.
- In 2022, 52% more cases of active TB were notified compared to 2021. The increase is attributed to the re-initiation of TB services,which had been diverted to COVID management. It is also attributable to a pilot program ofactive TB laboratory surveillancein selected hospitals.
- As per notified cases, TB incidence in Greece in 2022 was 3.06 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 recent decadesTB incidence is declining in the Greek population, with more cases among older adults. In contrast, the TB case rate is increasing in foreign-born people from countries with a high TB incidence (55% of total cases in 2022). Most foreign-born TB cases pertain to young adults.
- In 2022 there was an increasing trend in severe cases, as well as cases with a high mycobacterial sputum load, a findingentailing high transmissibility.

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 asto 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 currentlybeingmonitored.

Tuberculosis Control Office, Dept. of Respiratory Infections
Directorate for Epidemiological Surveillance & Intervention
National Public Health Organization (NPHO)

Epidemiology of tuberculosis in Greece in 2022

Number of notified cases and incidence of tuberculosis

In 2022, 320 new cases of active TB were reported, 52% more than in 2021. Of those, 269 were notified by attending physicians, while 51 were drawn through active laboratory surveillance (unmatched cases). TB notification rate in Greece in 2022 was estimated at 3.06 per 100,000 population (Figure 1). This is higher than in 2021 (1.98 per 100,000 population); however, 2021 was not a representative year due to TB underdiagnosis and underreporting in the context of the COVID-19 pandemic. In 2019, before the outbreak of the pandemic, 449 TB cases were notified, and the estimated incidence was 4.3 per 100,000 (Figure 1). Due to under-reporting, the number of notified cases is considered to underestimate the true burden of disease in the country.

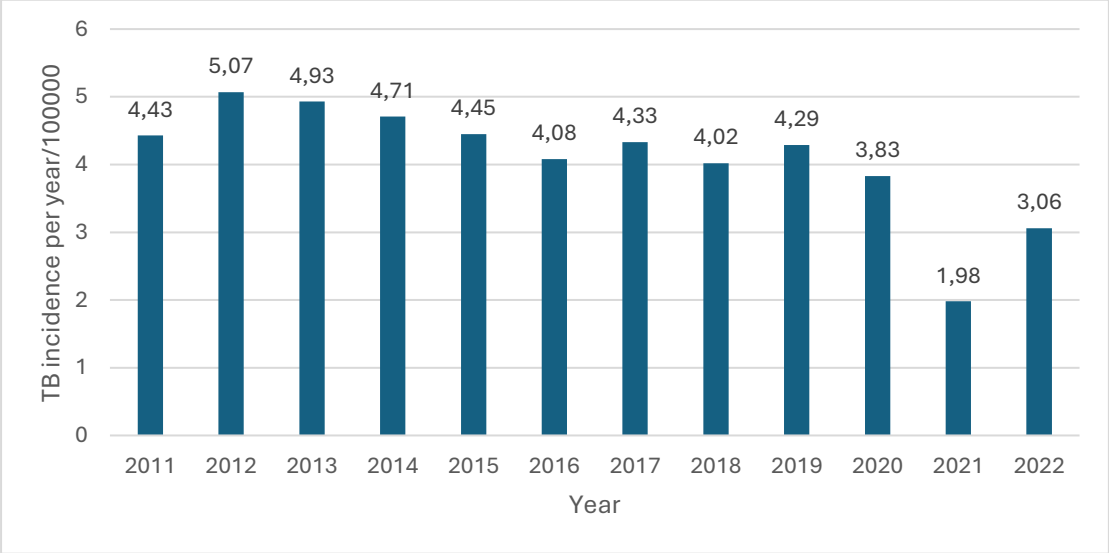


Figure 1: TB incidence per year/100000 population, 2022

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 of Thoracic Diseases “Sotiria” (Figure 2).

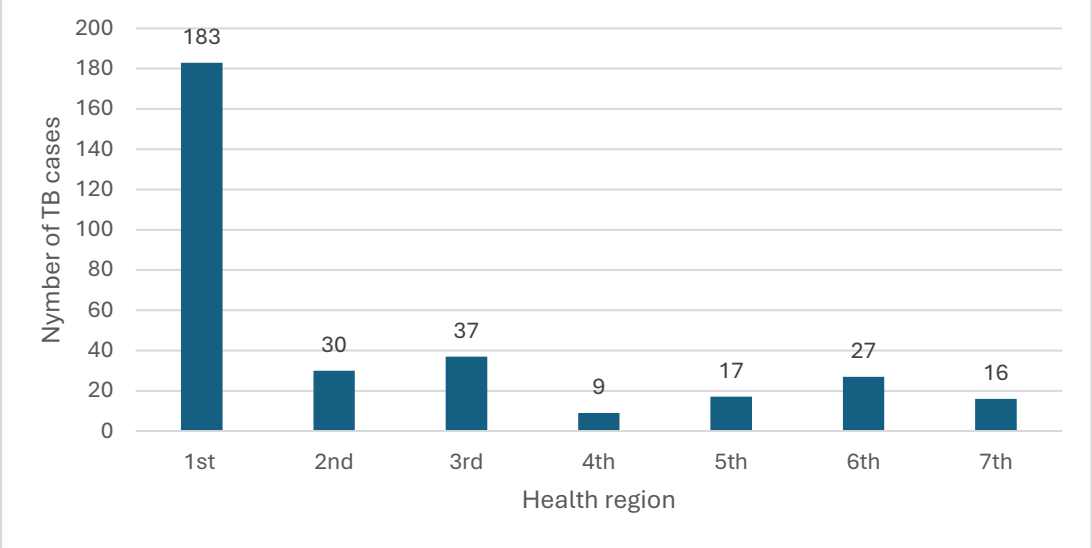
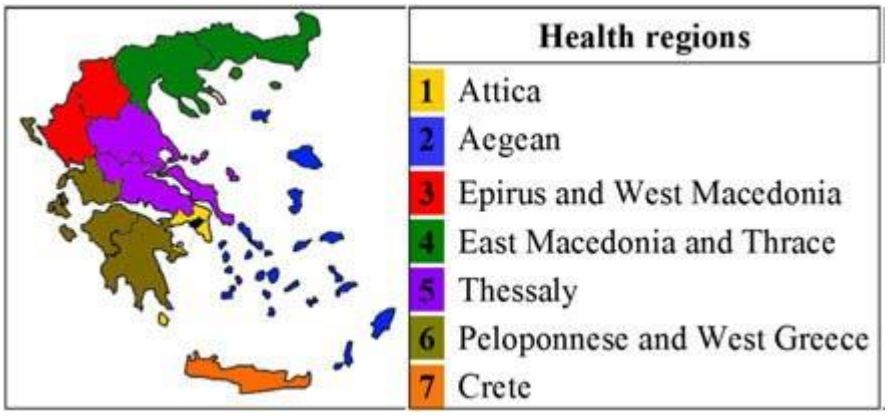


Figure 2: TB cases by Health Region, 2022



Demographic data

In 2022, 45% of the total cases were Greek, while 55% were foreign-born, namely refugees/migrants from countries with a high TB incidence (Figures 3 and 4).

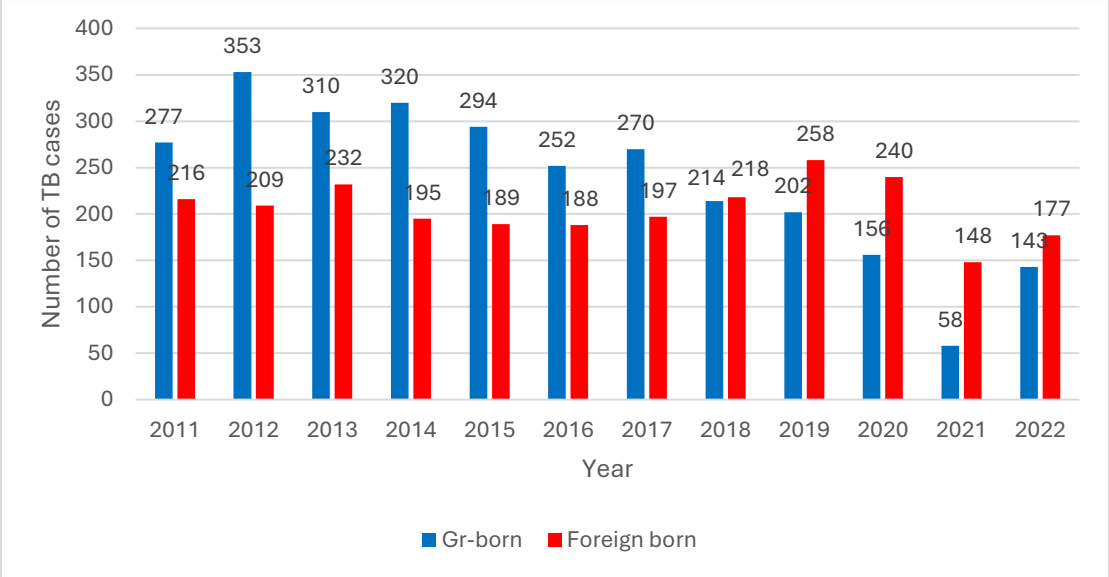


Figure 3: TB cases by year and origin, 2011-2022

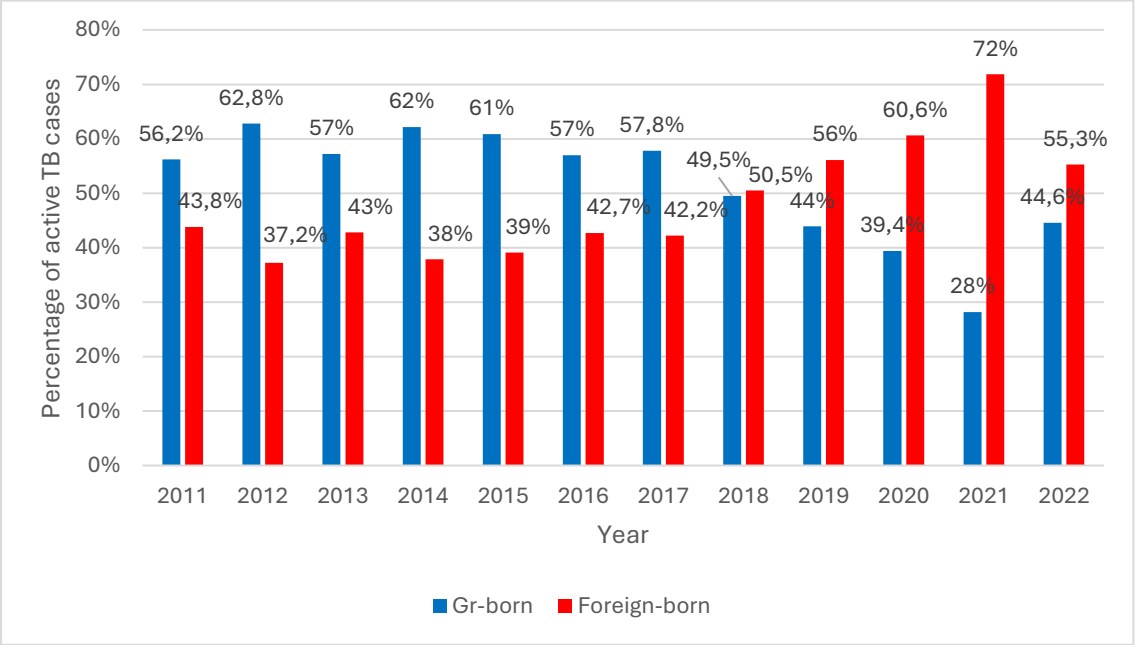


Figure 4: Percentage of TB cases by year and origin, 2011-2022

The **geographical areas of origin** of foreign-born TB cases are shown in Figure 5. Most foreign-born cases come from Central and South Asia (mostly Pakistan, Afghanistan, India, Bangladesh), accounting for 53% of foreign-born TB cases compared to 38% in 2021. Eastern Europe (mostly Georgia, Romania, Albania and Russia) is the second most prevalent geographical area of origin: 24% of foreign-born cases compared to 12% in 2021. The third most prevalent geographical region

of origin is Sub-Saharan Africa (mostly Somalia and Congo-Kinsasha) accounting for 15% of cases compared to 26% in 2021.

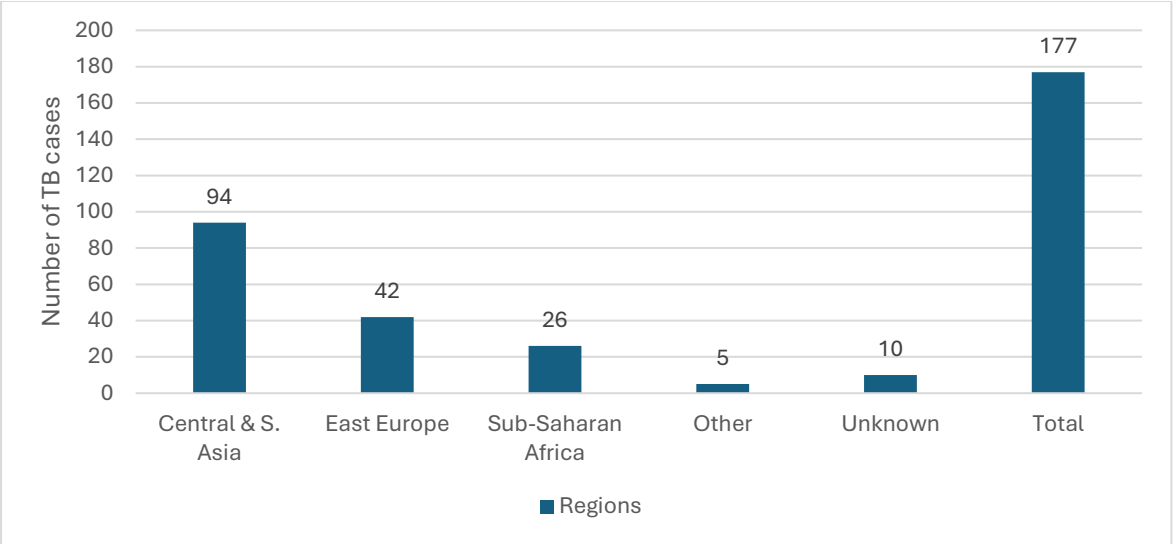


Figure 5: Foreign-born TB cases,2022

Regarding the distribution among **age groups**, people >65 years of age were the most represented age group in Greeks. In contrast, the age group most affected among foreign-born cases was15-34 years of age (Figure 6).

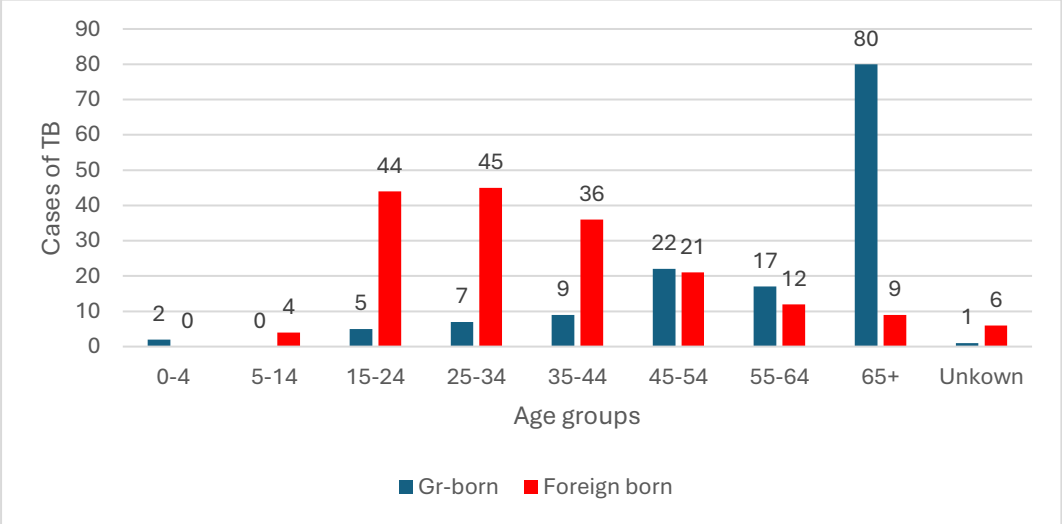


Figure 6: TB cases by age group and origin, 2022

Sex distribution was 233 males (72.8%) and 84 females (26.25%). Among Greek cases, females accounted for about 34%, while 21% were females among foreign-born cases.

There were 15 notified TB cases in **minors** (4.7%). Six cases were infants and children under 14, five of whom had a known history of TB exposure within the family. The remaining 9 were foreign-born adolescents, of which one had an history of exposure to an adult TB case within the family. Seven adolescents were residing in migrant/refugee facilities.

13% (42/320) of the notified cases lived in **group livingconditions**. Of these, 48% (20/42) resided inrefugee/migrant facilities, 14% (6/42) in detention facilities (prisons, 6 cases: 2 Greeks, 4 foreign-born), and 19% (8/42) in chronic care facilities (Table 1).

TYPE OF COMMUNAL LIVING	NUMBER OF CASES
Refugee/Migrant facility	20
Chronic care (Psychiatric Clinic, Nursing Home)	7
Detention Facility (Prison)	6
ROMA camp	4
Homeless Shelter	1
Undetermined communal living	5
TOTAL	**43**

Table 1: Number of TB cases in group living, 2022

Clinical data

Pulmonary disease (potentially transmissibletype) represented over two thirds of notified TB cases (Figure 7). Exclusively extrapulmonary TB (non-transmissible type of disease) was recorded in 12.6% of Greek and 21.5% of foreign-born cases (Figure 8). Lung cavitation, a feature associated with high transmissibility, was present in over 50% of pulmonary cases (Figure 9).

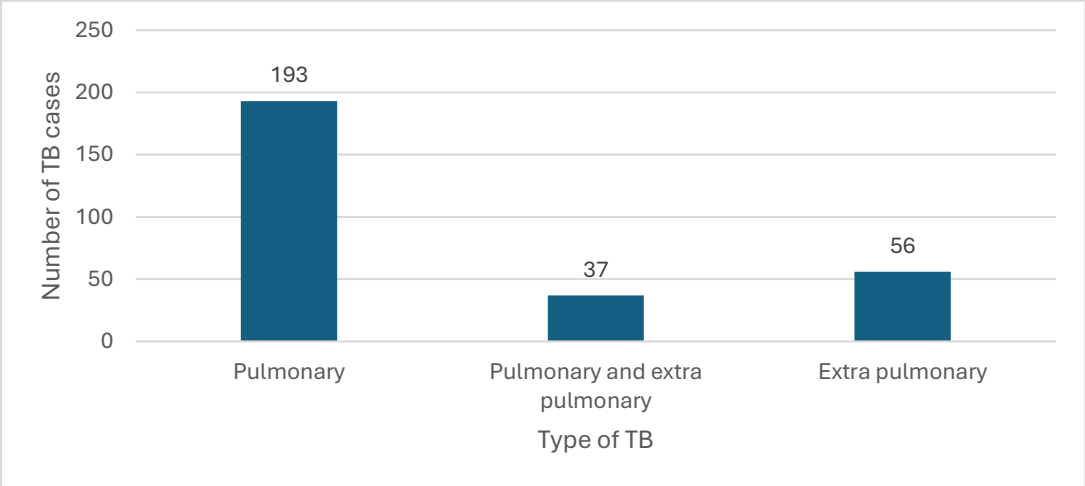


Figure 7: Type of TB,2022

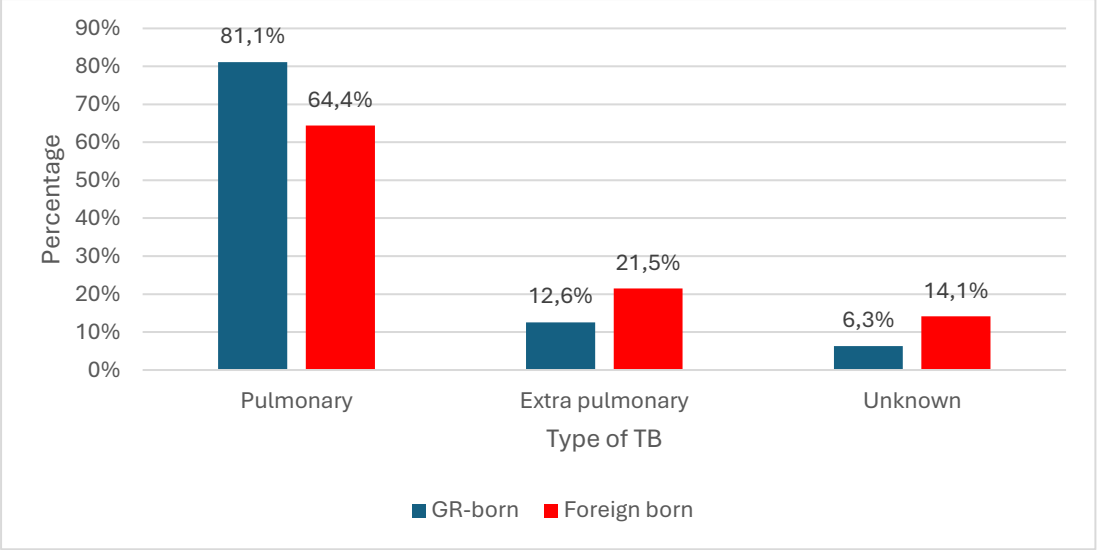


Figure 8: Percentage of pulmonary and extra pulmonary TB in GR-born and foreign-born, 2022

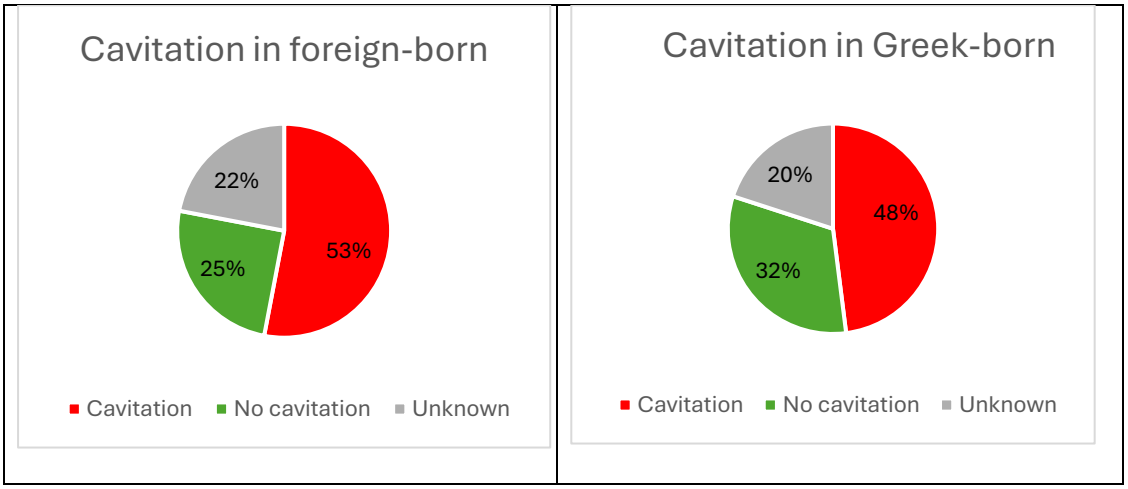


Figure 9: Cavitation in pulmonary disease, 2022

Regarding the **most severe forms of TB**, i.e. **central nervous system infection** and **miliary TB**, 2 young foreign-born TB brain abscess cases were notified, as well as 23 cases of miliary TB. Of the latter, 12 were observed in Greeks; 2 were over 65 years and 7 over 80years, while six were middle-aged, of whom 5 had significant comorbidities. In the foreign-born, 11 cases of miliary tuberculosis were recorded: 7 among young men, one of whom was living with HIV, and 4 in middle-aged men, 2 of whom had comorbidities.

Most **extrapulmonary** TB pertained to tuberculous lymphadenitis (47 cases) and tuberculous pleurisy (22 cases). Skeletal TB (mainly vertebral) was found in 6 cases,

gastrointestinal TB in 2, urinary tract TB in 2, hepatic TB in one and peritoneal TB in one.

In 2022, 7.5% (24/320) were **relapsed** cases, usually due to incomplete treatment.

HIV status data was available for 69% of reported cases. Of the 221 cases with a known HIV status, 9**T B/HIV co-infection** cases were recognized (4%, median age: 39 years, range: 19 - 54): 2 were Greek and 7 foreign-born. One Greek and one foreign-born case were imprisoned at the time of diagnosis.

Laboratory data

Regarding bacteriological testing, 66% (210/320) of the total number of notified cases were laboratory-confirmed at the time of reporting (Table 2).

In 15 of the 320 cases (4.6%), the TB diagnostic results became available **post - mortem**.

Of all pulmonary TB cases with a known microscopy result, 64% (121/189) were positive, a finding associated with **high transmissibility** (Figure 10). Of the cases with a known laboratory result, 96% had a positive culture and 87.5% had a positive molecular test (Figure 11).

Classification*	Number
Confirmed	210 (66%)
Probable	78 (24%)
Possible	32 (10%)

Table 2: Classification of cases according to the case definition, 2022

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

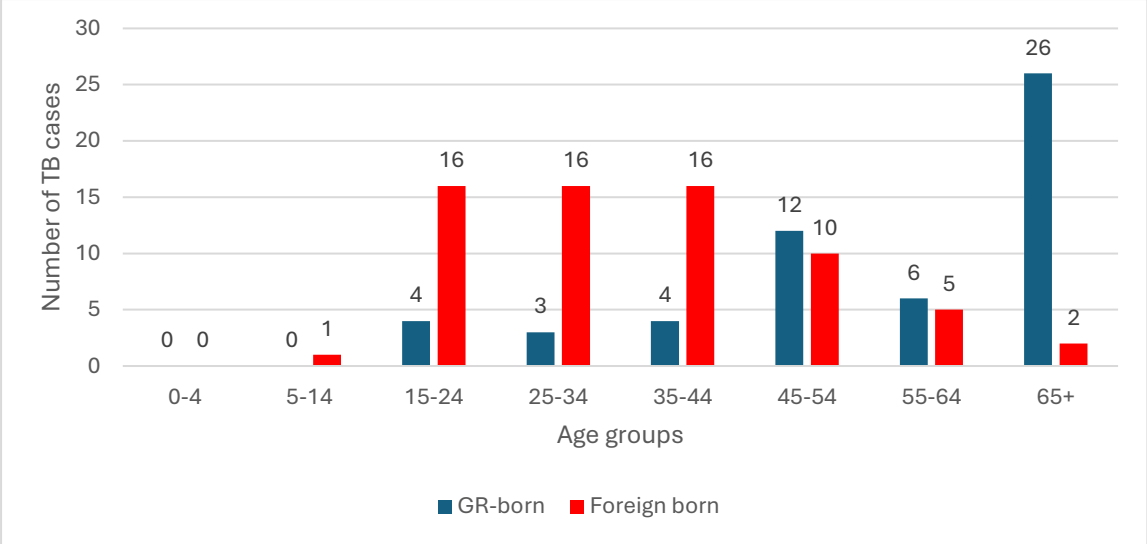


Figure 10: Pulmonary cases with known positive microscopy, 2022

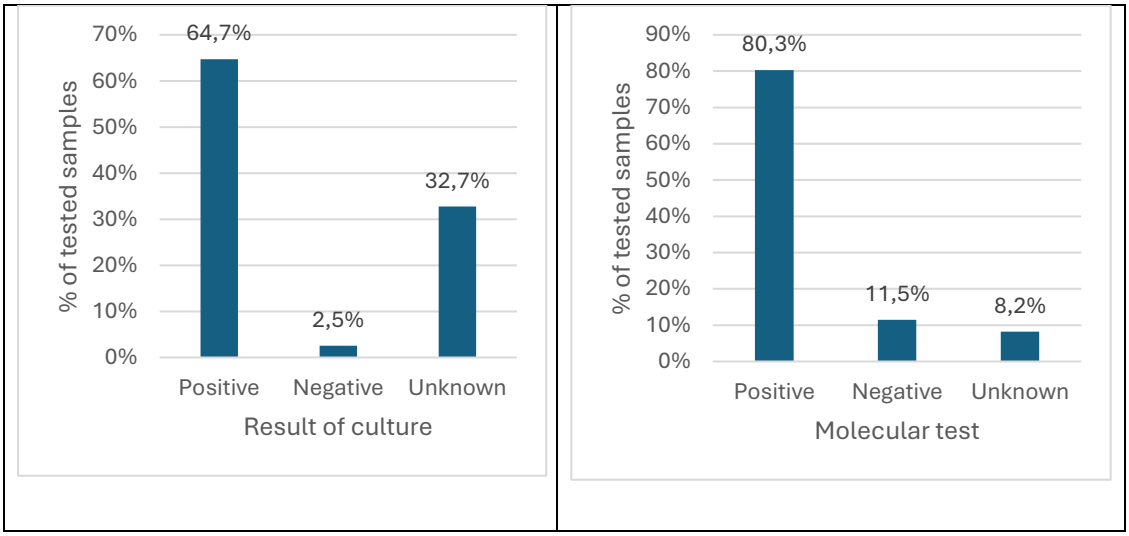


Figure 11: Laboratory confirmation of active TB cases in 2022: result of mycobacterial cultures and molecular testing

Sensitivity to antituberculosis drugs

Susceptibility results to primary antituberculosis drugs were available for 60% (192/320) of total TB cases.83.8% (161/192) were **sensitive** to all primary antituberculosis drugs: 87.5% of Greek and 82.7% of foreign-born cases (Table 3). **Isolated isoniazid resistance** was reported in 2.6% (5/192) of cases, whereas no isolated rifampicin resistance was observed. Of note, isoniazid and rifampicin are the most critical drugs in TB treatment (Figure 12). Combined resistance to isoniazid and

rifampicin (**multidrug-resistant tuberculosis, MDR**) was present in 4.7% (9/192). Resistance to quinolones (**extended resistance, pre-XDR**) was reported in one case (Figure 13).

Type of resistance	**Number of strains with known susceptibility result**	**Number (%) of resistant strains**	**Greeks (n=82)**	**Foreign-born (n=110)**
Isolated isoniazid(**R-INH**)	192	5(2,6%)	0	5(4,5%)
Isolated rifampicin (**R-RIF**)	192	0		
Isolated streptomycin (**R-STR**)	182	8(4,4%)	4(4,8%)	4(3,6%)
Isolated pyrazinamide (**R-PZA**)*	160	2(1,25)	1(1,2%)	1(0,9%)
Isolated ethambutol (**R-ETH**)	182	0		
Isoniazidand rifampicin (multi-drug resistance, **MDR**)	192	9	4,48%	5(4,5%)
Extended **pre-XDR****	7MDR	1	0	1(0,9%)

Table 3: Sensitivity and resistance in reported cases with known sensitivity score.

* probably*M bovis* strain

** Pre-XDR: Isoniazid, rifampicin AND fluoroquinolone

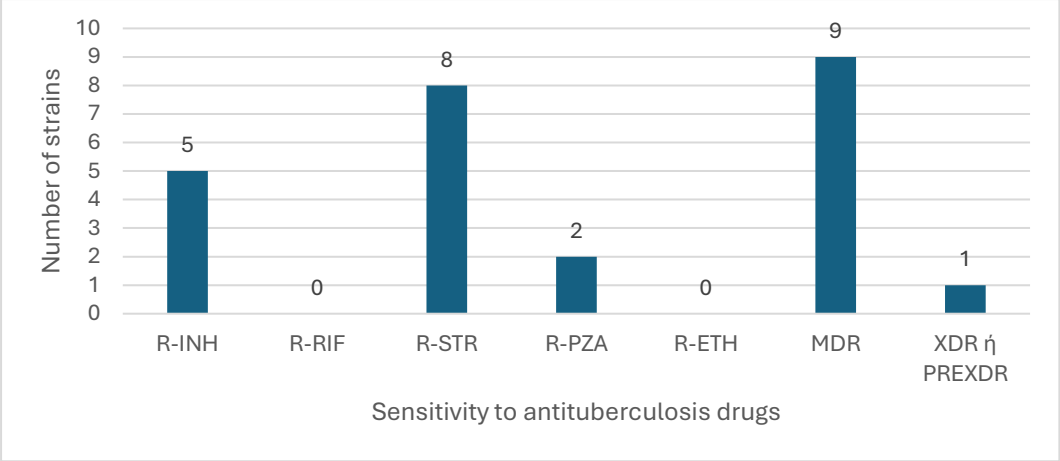


Figure 12: Number of resistant *M. tuberculosis*strains, 2022.

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).

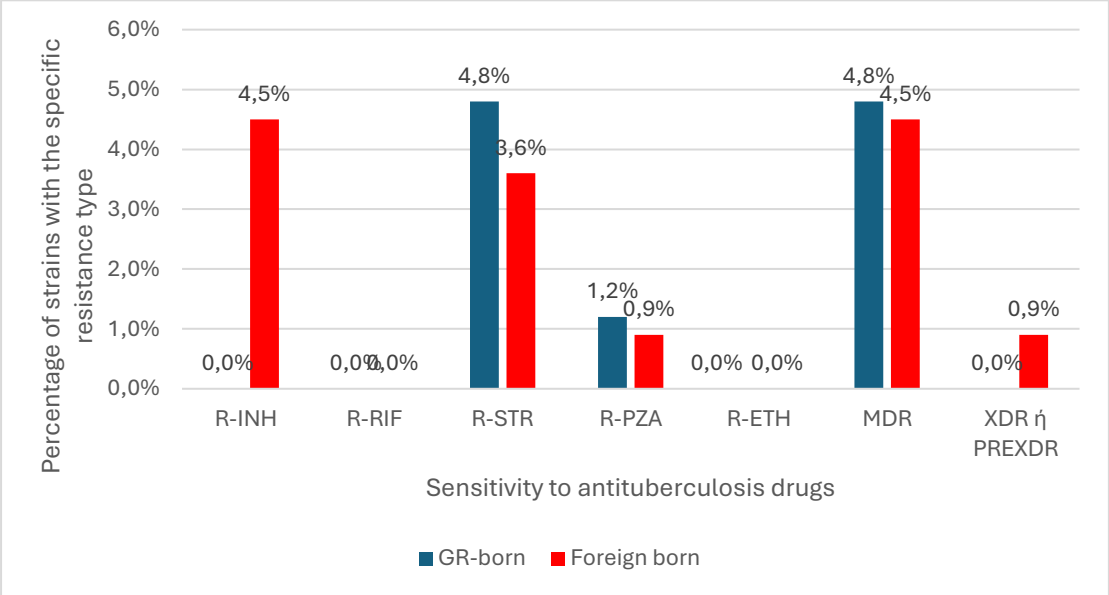


Figure 13: Percentage of resistant strains *M. tuberculosis*, 2022.

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

A pilot active laboratory surveillance was conducted in 2022 in four tertiary hospitals of the greater area of capital Athens, in order to address under-reporting, which was exacerbated during the COVID-19 pandemic. Active surveillance yielded an additional 19% (51 cases) and increased data completion rates of drug susceptibility results by 50%.

During the last decade, the annual reported number of active TB cases has been decreasing in the Greek population, while increasing among the foreign-born. Due to the pandemic, 2021 was a non-representative year for TB surveillance. In 2022, despite reduced migration/refugee inflows compared to previous years, the number of cases among the foreign-born was higher than the number of cases among Greeks, a phenomenon observed yearly since 2018.

Foreign-born TB cases are mostly young adults (under 45 years of age), while Greek TB cases were generally older. 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.

Pediatric tuberculosis in Greece follows a downward trend. While 20 years ago about 10% of TB cases were children <14 years of age, in 2022 the rate was 1.9%, compared to 2% in 2021 and 3.5% in 2019. In children <14 years with active TB, exposure to a known adult TB case in the immediate family environment was recorded, i.e. the source of infection of young children was within the family.

An upward trend was noted in **miliary tuberculosis**, a **severe form of TB**: 23 cases (7%) in 2022, compared to 2 (0.9%) in 2021. Almost all Greek military TB cases were older people (latent disease reactivation), while foreign-born miliary TB cases were mainly young adults with no underlying morbidity (presumably new TB infection).

Pulmonary TB was the 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. Extrapulmonary disease, a non-transmissible type of TB, accounted for 1/5 of cases, compared to 1/6 in 2021.

Advanced lung disease with positive sputum microscopy complicated by **cavitation** follows an increasing trend. In comparison with the pre-pandemic rate (41% in 2019), pulmonary TB cases with positive sputum microscopy in 2022 accounted for 64%. This was higher than the already high 2021 rate (55.56%). In cases with a known imaging result, lung cavitation was observed in 53.5% of foreign-born cases (vs. 51% in 2021) and in 48% of Greeks (vs. 40% in 2021). This phenomenon is an indirect indicator of delayed diagnosis, which may be due to low awareness of the disease among health professionals, delayed patient presentation or access barriers in health services.

In 2022, 66% of notified cases were **laboratory confirmed**. Antituberculosis drug susceptibility data were available for 60% of cases (40% in 2021). Among the culture-

positive cases, 2.6% showed isolated isoniazid **resistance** (vs. 4.7% in 2021), while 4.7% had combined isoniazid and rifampicin resistance (multi-drug-resistant strains, MDR), vs. 5.9% in 2021. While in 2021 MDR cases were all foreign-born, in 2022 MDR cases were also reported in Greeks. One foreign-born case with extensive resistance (preXDR) was reported.