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Author Affiliation:
[1]Associate professor of the department of Social Medicine and Public Health of Bukovinian State Medical University, Chernivtsi, Ukraine; ORCID ID: 0000-0003-2314-1976
[2]Associate professor of the department of Social Medicine and Public Health of Bukovinian State Medical University, Chernivtsi, Ukraine
[3]Associate professor & Head of the Department of Social Medicine and Public Health of Bukovynian State Medical University, Chernivtsi, st.Aksenina, Ukraine
[4]Vice-rector for scientific and pedagogical work and international relations of Bukovinian State Medical University, Professor of the department of Social Medicine and Public Health, Chernivtsi, Teatralnaya Square 2, Ukraine; ORCID ID: 0000-0003-1000-6417
[5]Head of the scientific and medical department with the sector of innovative development, Assistant of the department of Social Medicine and Public Health, Chernivtsi, Teatralnaya Square 2, Ukraine; ORCID ID: 0000-0003-1244-8702
[6]Associate professor of the department of Pediatric Surgery and Otolaryngology of Bukovinian State Medical University, Chernivtsi, Regional Clinical Hospital, Ukraine; ORCID ID: 0000-0003-3677-7316

✉**Corresponding author**
Associate professor of the department of Social Medicine and Public Health of Bukovinian State Medical University, Chernivtsi, Ukraine;
Email: zhanetta.chornenka.80@gmail.com

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Comparative analysis of incidence, prevalence and mortality from tuberculosis among the population of Europe and Ukraine

Chornenka Zhanetta[1]✉, Biduchak Anzhela[2], Navchuk Igor[3], Hrytsiuk Mariana[4], Domanchuk Tatyana[5], Yakovets Karolina[6]

ABSTRACT

Background: One of the most pressing socio-political and medical problems of society today is tuberculosis (TB), which today remains one of the main threats to humanity, being the leading cause of death from infectious diseases worldwide. TB is a highly contagious chronic disease that affects 10 million people each year and kills nearly 2 million people worldwide. *Methods:* Using statistical and medico-epidemiological methods, the analysis of the database of the National Registry "Tuberculosis in Ukraine" and report of Global Tuberculosis 2012-2020. *Results:* The dynamics of prevalence, morbidity and mortality from tuberculosis by sex and age in Ukraine, the WHO European Region and Chernivtsi region for the last seven years is analyzed. *Conclusion:* During the COVID-19 pandemic, all countries of the world need to join forces in the fight against tuberculosis, which is possible with the implementation of the 10 priority UN recommendations necessary to achieve the targets and reduce the colossal human and social losses from tuberculosis.

Keywords: tuberculosis, incidence, prevalence, mortality, Europe, Ukraine

1. INTRODUCTION

The transition of the millennia was marked by the tuberculosis epidemic in Ukraine, as in many countries around the world. According to the WHO, almost a third of the world's population is infected with *Mycobacterium tuberculosis* (Mtb). It is estimated that one patient can infect 10-15 healthy people. Every year there are 7-10 million people in the world with tuberculosis. The total number of TB patients in the world reaches 50-60 million. In 2019, there were 10.4 million new TB cases and 1.7 million deaths related to the disease worldwide. It is estimated that TB has killed one billion (1,000,000,000) people (Todoriko et al., 2020) in the last 200 years. In view of these figures, the World Health Organization declared tuberculosis a global

threat in 1993, (Kamenska et al., 2019) which requires active and urgent action to prevent its spread worldwide. TB affects people of all walks of life, although most TB cases occur in countries with limited resources. The problem of tuberculosis has become especially acute in Central and Eastern Europe and post-Soviet countries. The state of TB incidence and the government's approach to this problem in any country in the world is an indicator of social well-being.

The state of the environment, geographical and environmental factors also play an important role in the prevalence of tuberculosis. Overcrowding and time of contact with patients are key factors in tuberculosis infection. Today, tuberculosis reaches the highest number of cases in absolute numbers in history (DeRiemer et al., 2007) due to the mass urbanization of populations. The situation with tuberculosis in Ukraine is quite complicated. Tuberculosis is not just a medical problem. This is a social problem that reflects the socio-economic condition of the country, the cultural and educational level and well-being of the population, the degree of development of health care, including tuberculosis (Pyatnochka et al., 2016). And this disease has recently caused great concern in Ukraine and in the Ministry of Health of Ukraine in particular. Along with well-established risk factors (such as human immunodeficiency virus (HIV), malnutrition, and young age), variables such as diabetes, indoor air pollution, alcohol, immunosuppressive drugs, and tobacco smoke play an important role at both the individual and the general population (Zhurilo et al., 2018; Recalova et al., 2017). Socio-economic and behavioural factors have also been shown to increase susceptibility to infections. Certain groups, such as health workers and indigenous peoples, also have an increased risk of contracting and contracting tuberculosis.

In addition to providing effective treatment and reducing mortality, the main goal of TB control programs in countries with high TB incidence is to reduce the transmission of TB infections. Active tuberculosis develops in only 10% of people who have Mycobacterium tuberculosis. In other cases, the immune system controls the reproduction of mycobacteria and the pathogen persists in the lymph nodes and alveolar macrophages (Stalenhoef et al., 2008) - latent tuberculosis infection. At primary infection, the disease develops in people with defective immune systems (especially in HIV-infected) and in children. In HIV-infected patients develop generalized forms of tuberculosis in children - primary tuberculosis complex - a lesion in the lungs and loss of regional hilar lymph nodes on the side of the lung lesion. In other cases, the disease develops with the reactivation of latent tuberculosis infection (Protsyuk, 2020) due to weakening of the immune system or exogenous super infection. In these cases, there are secondary forms of tuberculosis with local damage to the lungs or other organs, because the immune system is already activated by Mtb (Matsyuk & Nedospasova, 2017). In the absence of treatment, this disease can kill about half of patients within five years, and inadequate therapy can lead to drug-resistant strains of *Mycobacterium tuberculosis*, which, of course, will be even harder to fight. It is also worth noting that the untimely diagnosis of tuberculosis among the population has a negative impact on those around the patients, and may even lead to an outbreak of infection in even more people.

An important role in reducing the incidence of tuberculosis in the population is the prevention of the disease, i.e. its timely detection, for which fluorography examinations of the population. Such reviews contribute to a significant reduction in the number of patients with tuberculosis, and this fact affects the positive dynamics of reducing mortality from tuberculosis.

2. MATERIALS AND METHODS

Using analytical-synthetic and statistical methods, the study of dynamic models of TB incidence for men and women of different ages was conducted. The study was conducted on the basis of personalized information from the database of the report on Global Tuberculosis 2012-2020 analytical and statistical guide "Tuberculosis in Ukraine" 2013-2019 and on the basis of anti-tuberculosis dispensaries of Chernivtsi region. The main accounting and statistical medical documentation of the relevant dispensaries "Notification of a patient who was diagnosed with active tuberculosis for the first time in his life" (f.089/r) was analyzed.

3. RESULTS AND DISCUSSION

In 1993, for the first time in its history, the WHO sounded the alarm and recognized tuberculosis as a global threat, and said that if governments did not consider the fight against tuberculosis as their first priority and did not fund the fight against the disease, tuberculosis would cause enormous damage to our economies and populations. Highly developed countries have allocated significant funds to overcome the tuberculosis epidemic and in 1 - 3 years have taken control of the TB situation in their countries. Poor countries have been unable to fund TB measures, and the TB epidemic progressed approximately until 2005, and since 2006, in most of these countries, as in Ukraine, the TB epidemic has slowly receded.

According to EuroTB (this is the WHO monitoring structure), in 2019 there were 10.0 million cases of tuberculosis in the world, 1.2 million cases of death from tuberculosis among people without HIV, and about 208,000 cases death from HIV-associated tuberculosis. If we take the mortality of HIV-infected people as 100%, then one quarter of they die from tuberculosis. Men (aged ≥15

years) accounted for 56% of people diagnosed with tuberculosis in 2019; women accounted for 32% and children (under 15) for 12%. Among all victims, 8.2% were people living with HIV.

About one third of the world's population is infected with Mycobacterium tuberculosis. This means that 10% of people infected with Mycobacterium tuberculosis can develop tuberculosis (Todoriko et al., 2020) during their lifetime, especially people with HIV, diabetes, smokers, malnutrition, stress, and so on. And in a year one tuberculosis patient can infect up to 10-15 other people with whom he will come into contact. This is how tuberculosis spreads. It is estimated that one third of TB cases worldwide are not registered, i.e. the real situation is undoubtedly worse than statistically registered. Geographically, most people who contracted tuberculosis in 2019 lived in WHO regions: Southeast Asia (44%), Africa (25%) and the Western Pacific (18%); a lower incidence rate was observed in the Eastern Mediterranean (8.2%), America (2.9%) and Europe (2.5%).

The prevalence of TB, which covers two-thirds of the world's population, is among eight countries: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), and Pakistan (5.7%), Nigeria (4, 4%), Bangladesh (3.6%) and South Africa (3.6%). The other 22 countries included in the WHO list of the 30 countries with a high burden of TB account for 21% of the global figure.

Incidence of tuberculosis

The national incidence of TB ranges from less than 5 to more than 500 new case and recurrences per 100,000 populations per year. In 2019, 54 countries had a low incidence of TB (<10 cases per 100,000 population per year), mainly in the United States and the WHO European Region, as well as in a few countries in the Eastern Mediterranean and the Western Pacific. These countries have every opportunity to eliminate active TB. Drug-resistant tuberculosis continues to pose a threat to public health. Worldwide, in 2019, about half a million people contracted rifampicin-resistant tuberculosis (RR-TB), of which 78% had multidrug-resistant tuberculosis (MDR-TB), (Todoriko et al., 2019; Moskalyuk & Kolotilo, 2018). The largest share of the global burden of TV falls on three countries: India (27%), China (14%) and the Russian Federation (8%). Globally, in 2019, 3.3% of new TB cases and 17.7% of previously treated cases had MDR / RR-TB. The highest percentage (> 50% of previously treated cases) was in the countries of the former Soviet Union. As of the end of 2019, most WHO regions in the world and many countries with high levels of TB incidence have not reached the benchmarks of the TB Elimination Strategy to 2020.

Worldwide, the incidence of tuberculosis is declining, but not fast enough to reach the limit of 2020 - a decrease of 20% between 2015 and 2020. The overall incidence reduction from 2015 to 2019 was 9% (from 142 to 130 new cases per 100,000 population), including a decrease of 2.3% between 2018 and 2019. The WHO European Region achieved the most positive results, reducing the incidence of TB by 19% between 2015 and 2019, and the African region made significant progress by reducing the incidence by 16%. Globally, the incidence of tuberculosis is declining by about 2% per year. In order to achieve the targets set by the TB Elimination Strategy, these rates of decline need to be accelerated to 4-5% per year.

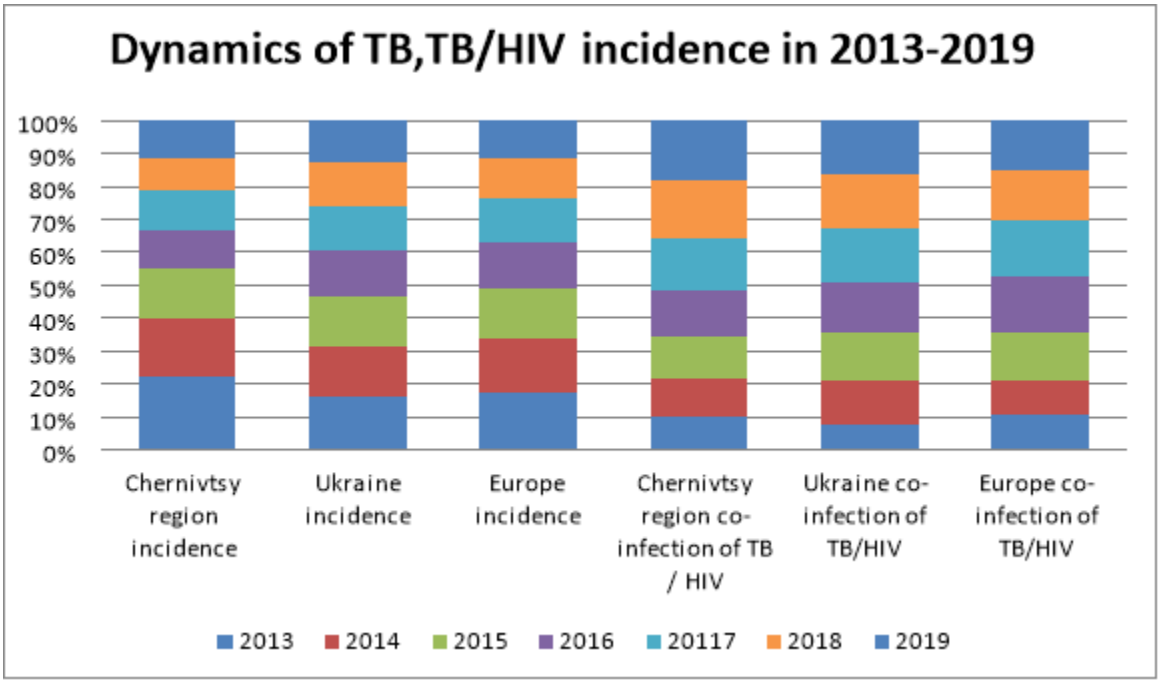

Figure 1 Dynamics of TB and TB with HIVper 100,000 population in Ukraine, WHO European Region and Chernivtsi region for 7 years

In Ukraine, the incidence of tuberculosis is significantly declining. According to WHO estimates, the incidence of TB in 2018 was 80 new cases and relapses per 100,000 population. The average annual reduction in the estimated incidence of TB over the last five years was about 4.0%, which is lower than the observed average annual reduction in the incidence of TB in 5.6 priority countries in the WHO European Region over the same period (Fig. 1).

According to routine surveillance, the incidence of tuberculosis in 2018 is 62.3 per 100.000 populations. Thus, in Ukraine in 2018, about 22% of TB cases were undetected. In 2019, the incidence of TB (new cases + relapses) was 60.1 per 100.000 population, which is 3.6% lower than in 2018. (62.3 per 100.000 population). Over the past five years, the incidence has decreased by 17.3% (from 70.5 in 2015 to 60.1 per 100 thousand population in 2019), and there has been a decrease in incidence of approximately 4% annually in the period from 2013 to 2019 (in the WHO European Region for the corresponding period of decrease by 5% per year). During the above period, only in Zakarpattia, Dnipropetrovsk, Vinnytsia, Kirovohrad, and Chernivtsi regions there was a tendency to increase the incidence of TB (new cases and relapses), respectively, from 2.2% to 14.7%. In the regions of Ukraine there is a significant fluctuation in the incidence of TB (from 40.6 to 138.5 per 100 thousand populations).

The highest rates of TB incidence were registered in Odesa (138.5), Dnipropetrovsk (79.1), Kherson (77.9), Kirovohrad (75.4) oblasts; lower indicators - in Chernivtsi (40.6), Ternopil (42.3), Kharkiv (48.7) regions and in Kyiv (45.0). To implement the strategy to eliminate TB, Ukraine must achieve by 2035 a reduction in the incidence of TB by 90% compared to 2015 (from 70.5 to 7.1 per 100.000 populations).

According to routine surveillance between 2015 and 2019, the absolute number of TB / HIV co-infections decreased from 6,292 to 5,807, but relative to the reported new cases and relapses, the proportion of patients with HIV / TB co-infection remained broadly stable, at 20.7 % to 23.0% (Fig. 2). The highest incidence of TB / HIV was observed in Odesa region - 64.3 per 100 thousand populations, the lowest in Ivano-Frankivsk region - 2.0 per 100 thousand populations. The highest share of patients with TB / HIV co-infection in the structure of active TB incidence in 2019 was in Odesaregion - 46.4%, the lowest - in region Zakarpattia - 3.1%. In 2019, there was a very strong geographical heterogeneity in the percentage of HIV-infected among new cases and recurrences of tuberculosis: from 3.1% in the Transcarpathian region to 46.4% in Odessa. Despite this heterogeneity, the trend of TB / HIV spread in the period from 2014 to 2019 by region is quite stable: out of 25 regions, in 20 there was an increase in HIV prevalence by more than 1%, in particular in Chernivtsi region this figure increased by 2%.

The increase in the incidence of tuberculosis is due both to the increase in the incidence of new cases and to the improvement of the organization of tuberculosis detection and the introduction of unified statistical reporting on tuberculosis. Chernivtsi region is one of the regions with an increased level of registered tuberculosis (18.4 cases per 100 thousand population), although there is a clear downward trend compared to the statistics of 2014-2015.

Prevalence of tuberculosis

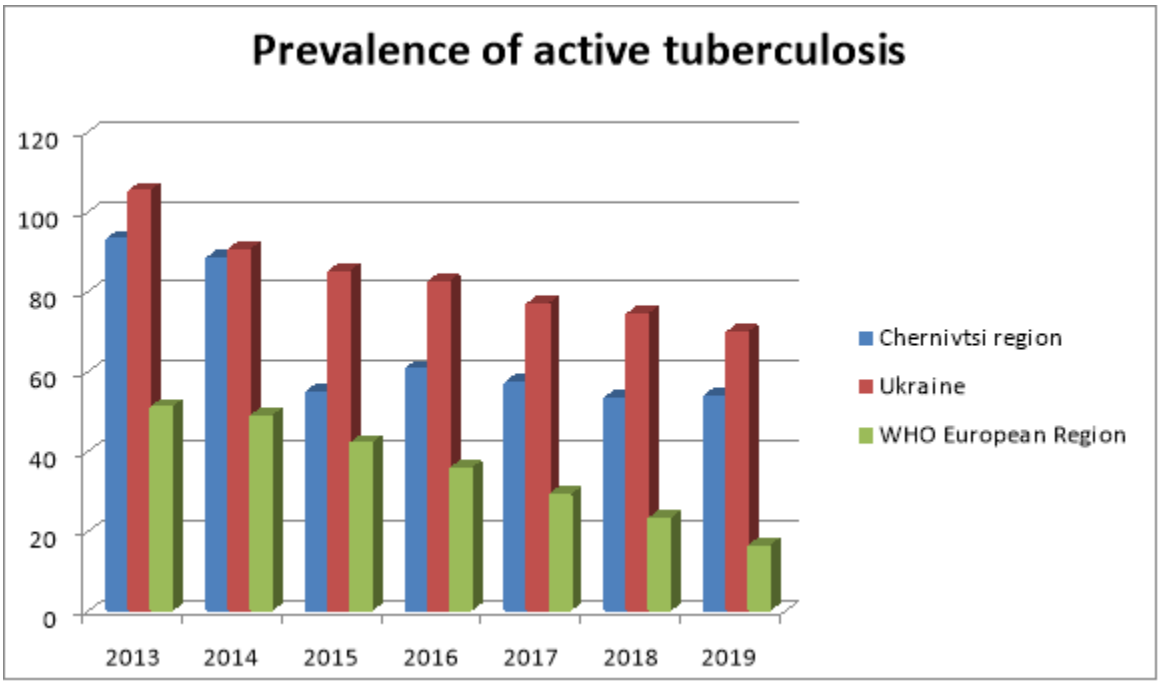

Figure 2 The prevalence of active TB among the population of Ukraine, Chernivtsi region and Europe for 7 years.

The prevalence of TB over the past seven years has tended to decrease, in 2019 the prevalence decreased by 6.6% compared to 2018. However, the current prevalence of TB in Ukraine is almost more than twice the target of the Partnership "Stop TB" - 36 cases per 100,000 population registered in the WHO European Region. The highest levels of TB prevalence in Ukraine were registered in Odesa (150.3), Mykolaiv (113.9), Dnipropetrovsk (109.6) and Kirovohrad (95.3) oblasts. Compared to 2018, the prevalence of TB prevalence in Vinnytsia (10.6%), Zakarpattia (4.3%) and Chernivtsi (1.1%) regions (Fig. 2).

The prevalence of tuberculosis by sex and age

From 2014 to 2019 in Ukraine, the decline in registration of TB cases among men and women was largely proportional, and as a result, the share of all new and recurrences of TB among men remained stable at about 70% (in 2019 - 70.4%). The most populous age group - men aged 35-44 years, but the largest absolute number of undetectable patients with TB, are men aged 25-34 years (Fig. 3). People aged 35-44 have the greatest burden of tuberculosis in Ukraine. In the period from 2014 to 2018, the incidence of tuberculosis decreased for all age groups over 14 years, but at different rates: thus, the fastest decrease was observed in the age group "25-34 years" (-8.0% annually) and the group " 15 -24 years "(-6.3% annually), while the decline in TB registration among the elderly was relatively slow.

In contrast to Ukraine, in the countries of the WHO European Region, the greatest burden of TB falls on the age of 35-44 for men and 25-34 for women, and for the latter it varies slightly in all age groups (Fig. 4). TB in Ukraine has significantly rejuvenated. Thus, the incidence of tuberculosis in children increased 2.1 times (from 4.7 to 8.8 per 100 thousand population), which is an unfavourable prognostic sign. In addition, 67.4% of first-time patients with tuberculosis are people of the most able-bodied and reproductive age - from 20 to 50 years, but an increase in the incidence of tuberculosis is observed in all age groups.

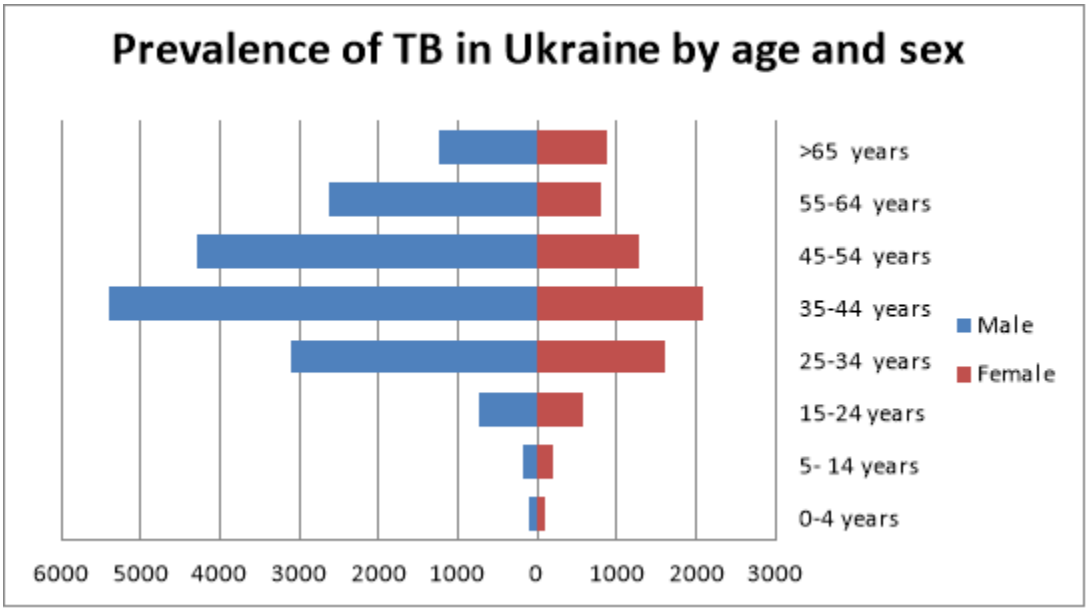

Figure 3 Prevalence of tuberculosis in Ukraine by age and sex by 2020

This model of temporary change is consistent with a common understanding of the epidemiology of TB - the "aging epidemic", which is a sign of reducing the burden of TB in the real population. Because tuberculosis in the elderly most often occurs as a result of reactivation of latent infection; therefore, a reduction in the rate of transmission has little effect on the incidence of tuberculosis in this age group. In contrast, early-stage tuberculosis is the result of recent infection, and a reduction in the number of reported TB cases in these age groups implies a reduction in the annual risk of infection and, consequently, a reduction in tuberculosis transmission among the general population. The lack of reduced registration of TB cases in children can be explained by improved TB diagnosis or a change in the practice of TB diagnosis in children, improved TB diagnostic procedures in the country. This picture persists mainly in regions with a rapid decline in the disease, except for areas with a slow decline or without it.

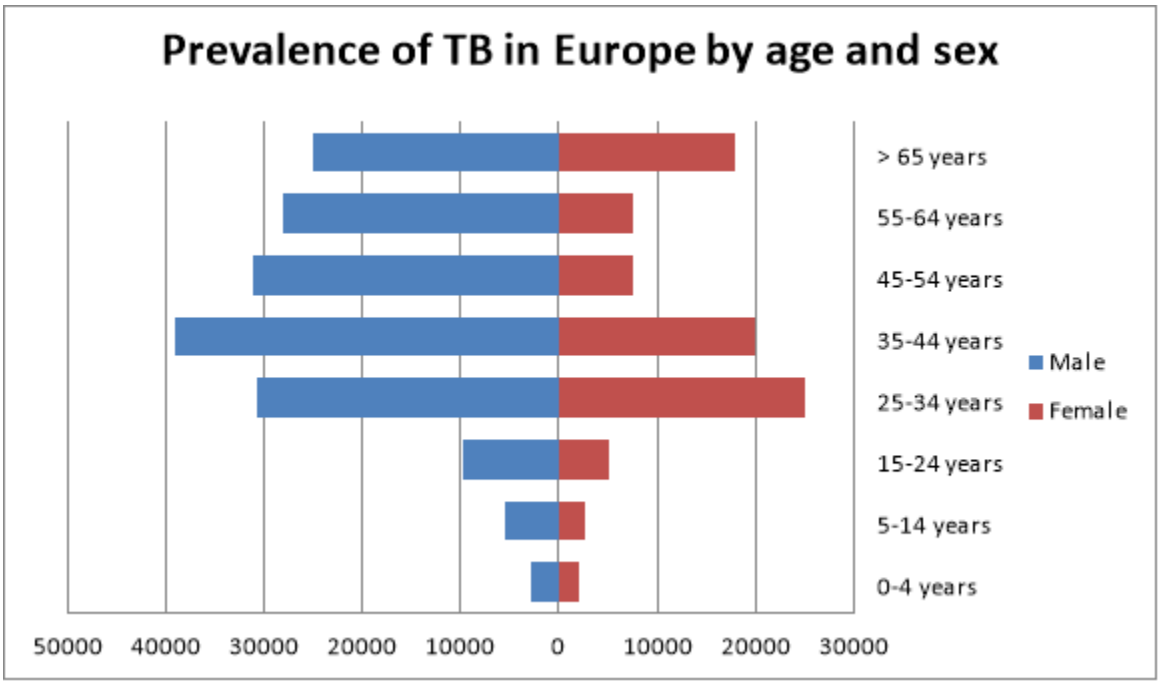

Figure 4 Prevalence of tuberculosis in WHO European Region by age and sex by 2020

Mortality from tuberculosis

Worldwide, the leading cause of death among infectious diseases is TB, which is also one of the 10 most common causes of death in general. In 2019, TB caused 1.4 million deaths, including 208,000 among HIV-positive people. The annual number of TB deaths is declining worldwide, but not fast enough to reach the first phase of the End TV Strategy; i.e. a reduction of 35% between 2015 and 2020. The cumulative reduction between 2015 and 2019 was only 14%, which is less than half the way to reach this limit. From 2015 to 2019, the WHO European Region achieved significant results towards reaching this limit, reducing TB mortality by 31%, and the African region made significant progress, reducing mortality by 19%. Reductions in other WHO regions were 6.1% in the United States, 11% in the Eastern Mediterranean, 10% in Southeast Asia, and 17% in the Western Pacific. A total of 46 countries are on track to reach the 2020 limit. These include the seven countries with a high TB burden that have already achieved this (Bangladesh, Kenya, Mozambique, Myanmar, the Russian Federation, Sierra Leone and the United Republic of Tanzania) and one other that is on the way-Vietnam).

The source of registration of data on tuberculosis mortality in Ukraine is the Civil Status Registration System, which is considered to be the best source of data on TB mortality. As the Registry Office in Ukraine is of high quality and coverage, WHO TB mortality estimates are accurate within a fairly narrow range of uncertainty. According to WHO estimates, in 2000 the TB mortality rate (excluding TB / HIV deaths) was estimated at 23 cases per 100,000 populations. Mortality from TB peaked in 2005 at 27 cases per 100,000 populations, and has since declined by an average of 9.1%. By the end of 2018, the estimated TB mortality rate in Ukraine was 8.3 per 100,000 populations (Table 1). Over the past five years, Ukraine has maintained a steady trend towards a gradual reduction in TB mortality by an average of 8% per year, from 10.8 per 100,000 populations in 2015 to 8.8 per 100,000 populations in 2019. . To implement the TB strategy by 2035, the mortality rate must be reduced by 95% compared to 2015 (from 10.8 to 0.5 per 100,000 populations).

Table 1 Dynamics of mortality from TB, TB / HIV for 2013-2020 (per 100,000 population)

Years	Deaths from TB (per 100,000 population)			Deaths from TB / HIV (per 100,000 population)		
	Ukraine	WHO European Region	Chernivtsy region	Ukraine	WHO European Region	Chernivtsy region
2013	14,1	4,1	10,3	5,6	0,42	0,2
2014	12,2	3,6	8,4	4,6	0,36	0,7
2015	10,8	3,5	7,6	4,5	0,54	0,9
2016	9,5	2,8	7,7	4,2	0,56	0,4
2017	9,3	2,6	6,8	3,9	0,54	0,9

2018	9,4	2,5	7,9	3,9	0,47	0,6
2019	8,8	2,1	5,8	3,4	0,45	0,8

In contrast to TB mortality, TB / HIV mortality in Ukraine has been broadly stable over the past 20 years. Between 2000 and 2019, TB / HIV mortality ranged from 2.1 to 7.0 per 100,000 population without any clear trend over time. Since 2015, mortality from TB / HIV co-infection has decreased by an average of 4.0% per year (from 4.6 per 100,000 population to 3.9 per 100,000 population, respectively). In 2019, as in the past, in 8 regions of Ukraine mortality from TB / HIV co-infection exceeded the average Ukrainian value of 3.4 per 100 thousand population (Odessa - 14.1, Dnepropetrovsk - 9.4, Mykolaiv - 6.3, Donetsk - 5.7, Kyiv - 6.0, Chernihiv - 3.6, Luhansk - 3.5 regions and Kyiv - 3.8).

Thus, over the last 10 years in Ukraine there has been a 2.5-fold decrease in the death rate from tuberculosis. According to the State Statistics Service, at the beginning of 2019 the mortality rate from tuberculosis was 8.8 per 100 thousand people in Chernivtsi region (5.8 per 100 thousand population).

4. CONCLUSION

The WHO European Region and a number of high tuberculosis burden countries are on track to meet the 2020 targets for reducing morbidity and mortality. At the same time, the whole world is still far from reaching the agreed indicators, and currently the COVID-19 pandemic could slow down or even nullify all the gains made. The high level of morbidity and mortality on TB at the present stage is associated with the socio-economic crisis both in Ukraine and in the world as a whole, short coming in the health care system, increasing proportion of multidrug-resistant strains of the Office, the HIV epidemic, and low effectiveness of TB control measures among vulnerable groups. Thus, only the conscientious implementation of the proposed measures, with the support of the highest state levels, will allow further containing and subsequently improving the epidemic situation with TB both in Ukraine and in the world.

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Author Contributions

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Ethical approval

The study acquired the ethical approval from the Commission on Biomedical Ethics for compliance with moral and legal rules of medical research of Bukovynian State Medical University of the Ministry of Health of Ukraine, (letter number Nr. 2 from 18.02.2021-project number 0120U102625).

Data and materials availability

All data associated with this study are present in the paper.

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