

GLOBAL TRENDS AND PROBLEMS OF INFECTIOUS DISEASES – COVID-19, HIV/AIDS, TUBERCULOSIS

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Abstract. Globalization and the interconnectedness of countries in the modern world pose new challenges to public health. Over the centuries, infectious diseases have proven to be one of the major threats to global health. Historically, several pandemics and epidemics have changed and claimed the lives of millions of people around the world. Many infectious agents continue to pose a serious problem despite advances in medicine, public health awareness campaigns and vaccination. The aim of this review is to present the global epidemiological trends and challenges related to three key infectious diseases: COVID-19, HIV/AIDS, and tuberculosis. The COVID-19 pandemic, along with the long-standing threats of HIV/AIDS and tuberculosis, is posing a serious challenge to health systems and socio-economic structures in many countries. COVID-19, caused by SARS-CoV-2, has spread rapidly around the world, resulting in significant numbers of cases, deaths, and long-term health problems. The consequences of long COVID-19 and “post-COVID-19 syndrome” have become one of the main causes of reduced work capacity and impaired quality of life in recent years. At the same time, HIV/AIDS remains a global health problem, especially in certain regions, and tuberculosis continues to constitute a serious threat, especially in conditions of limited access to health services. Each of these health problems creates specific requirements for treatment and prevention, while leading to serious health, social and economic consequences, despite global initiatives and strategies to address them.

Key words: global trends, issues, strategies, COVID-19, HIV/AIDS, tuberculosis

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has demonstrated the global health, economic, and social challenges and consequences of infectious diseases. In addition to the numerous deaths, the complications of the disease caused by the virus have led to a deterioration in the quality of life of patients. The rapid introduction of numerous anti-epidemic measures and the development of vaccines proved to be of utmost importance for controlling the disease. Adaptation by medical professionals (including in the direction of digitalization of healthcare), society and business was a necessity. At the global level, financial support for recovery was provided through various initiatives and financial packages from the European Union (EU) and the United States of America (USA). In parallel with the spread of the virus, there was a delay in the diagnosis and treatment of many other infectious (e.g. tuberculosis and HIV) and chronic diseases. Human immunodeficiency virus (HIV), the cause of acquired immunodeficiency syndrome (AIDS), continues to be a significant global health problem. Despite awareness campaigns, pre-exposure prophylaxis (PrEP) and the availability of antiretroviral treatment (ART), AIDS remains a major cause of mortality, especially in regions

such as sub-Saharan Africa, due to socio-economic barriers to effective prevention and treatment. Tuberculosis (TB) is another infectious disease that, despite efforts to control and treat it, remains a leading cause of death worldwide. In addition, HIV infection, silicosis (a specific occupational disease), and multidrug-resistant tuberculosis (MDR-TB) complicate not only the treatment but also the prevention of TB. Added to these global problems are occupational diseases caused by biological agents in the workplace, which also lead to hundreds of thousands of deaths annually. In this review, we examine global trends and some of the problems associated with these key infectious diseases, and analyze existing strategies to address future pandemics.

METHODS

Open access publications in PubMed were reviewed, as well as the official websites of the World Health Organization (WHO), the European Union (EU), the International Labour Organization (ILO), Ministry of Health of the Republic of Bulgaria (MoH), National Social Security Institute (NSI), National Center for Public Health and Analysis (NCPHA). Figure 1 presents the selection of publications according to the inclusion and exclusion criteria.

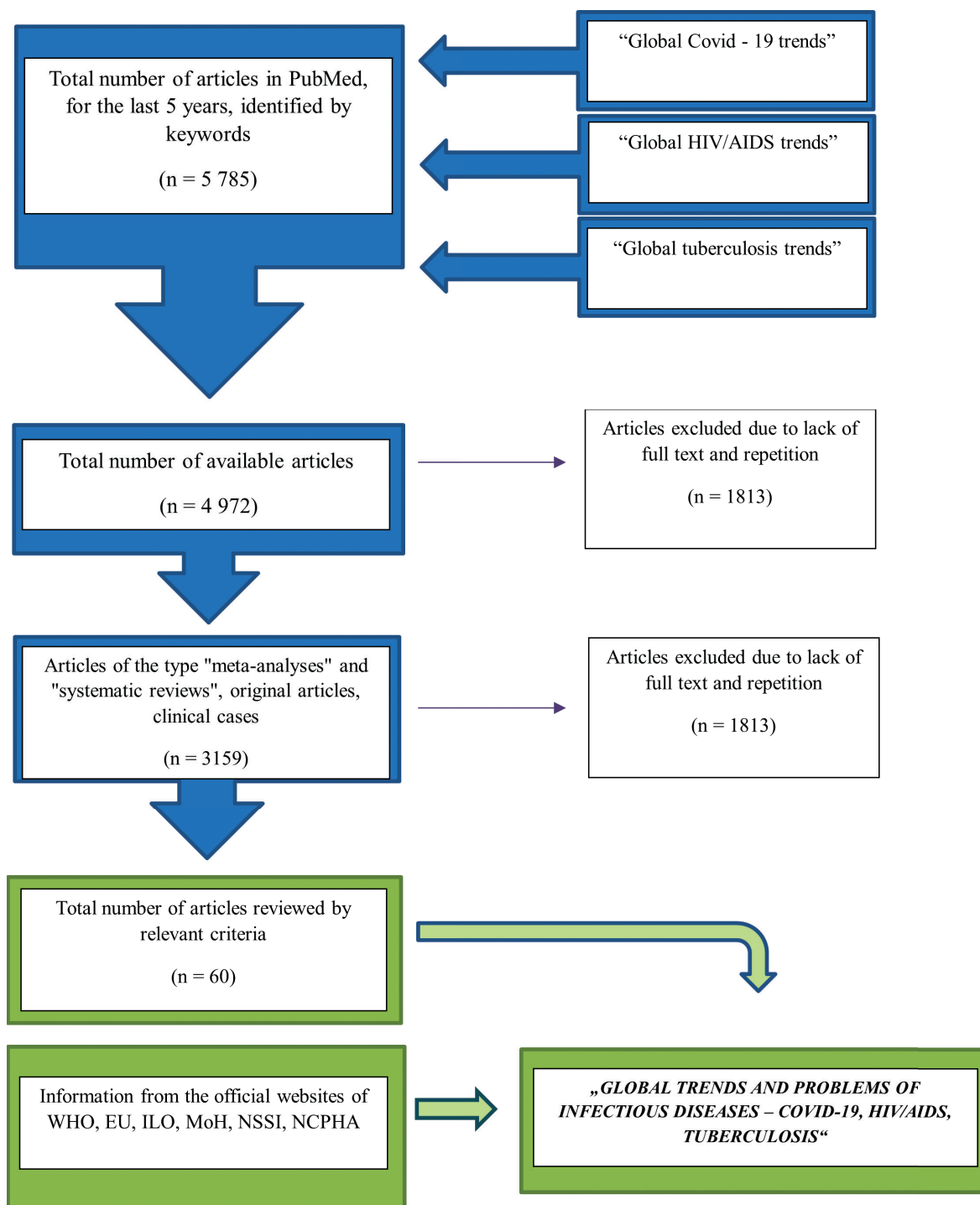


Fig. 1. Selection of publications based on inclusion and exclusion criteria

COVID-19: Epidemiology, challenges and global control efforts

In December 2019, numerous patients with symptoms of a previously unknown infection with a wide spectrum of clinical manifestations were registered in the city of Wuhan (Hubei province, eastern China). The extremely worrying trend of multi-organ and multi-system involvement, the high mortality rate

and serious complications necessitated the declaration of an epidemic, which subsequently expanded globally and became a pandemic. Complications of the disease have led to a reduced quality of life and disability, and in some cases to severely limited work capacity for months after infection [1-12]. According to WHO data, the COVID-19 pandemic has rapidly reached global proportions, affecting over 776 mil-

lion people by the end of 2024 and causing over 7 million deaths[13]. Symptoms can persist for weeks or months after the onset of infection (so-called “long COVID”, post-COVID syndrome (PCS)), which has led to a significant increase in absenteeism from work due to temporary disability, as well as to the search for alternative options for remote work and learning. Illness and isolation have caused not only health but also socio-economic problems [14-22]. The main challenges, especially at the beginning of the pandemic, were the lack and/or uneven distribution of resources (medical, financial, logistical, organizational, etc.) [23]. Affected countries have tried to flatten the epidemiological curve and avoid overburdening health systems by imposing specific hygiene measures, restricting social contact, wearing a mask, keeping physical distance, raising public awareness, impose travel restrictions, border closures, and mandatory quarantine for infected people and their contacts [1, 22]. Multiple vaccines (Pfizer-BioNTech, Moderna, AstraZeneca) have been developed in a short period of time with high efficacy, most with mild side effects after administration [1, 11, 22, 24-27]. Poor and developing countries have received support through international funds and initiatives such as COVAX [28]. COVAX was a joint initiative of the Global Alliance for Vaccines (Gavi), the Coalition for Epidemic Preparedness Innovation (CEPI), WHO and UNICEF from 2020 to 2023, which aimed to accelerate the development of COVID-19 vaccines and ensure equal and equitable access to them for all [28].

On 21 July 2020, EU leaders agreed on a total budget of €1.824 billion for the period 2021-2027. Combining the Multiannual Financial Framework (MFF) and an emergency recovery effort of over €750 billion, the package helps the EU recover from the COVID-19 pandemic and supports investment in the environmental and digital transition. These elements complement the three €540 billion backstops the EU has already put in place to support workers, businesses and countries (from 9 April 2020). In 2024, the EU has allocated an incentive package worth €2,018 billion to promote recovery in various sectors [29, 30]. In 2021 The United States has provided \$3,500,000,000 under the American Rescue Plan Act (ARPA) [31]. Federal funding supports the nation's public transportation systems as they continue to respond to the COVID-19 pandemic and support the President's call to vaccinate the U.S. population [32]. ARPA supports workers by: improving the unemployment insurance system (modernizing the insurance system to help workers get the benefits they deserve), ensuring worker safety

(by providing additional funding to help vulnerable workers be healthy and protected by COVID-19), and assisting with health insurance premiums (helping workers who lost their jobs or had their hours reduced during the pandemic to pay for health insurance by fully subsidising premiums) [33].

A major problem in the implementation of these global control measures has been the resistance of a segment of the population to social distance and vaccination. However, the collaborative efforts of multiple institutions have achieved their goal of reducing morbidity and mortality worldwide [34].

The COVID-19 pandemic has had a significant impact on health tourism, leading to a sharp reduction in international travel and disruption of many medical services. Many healthcare institutions and tourism operators have been forced to adapt their services, introducing new requirements to ensure the safety and health of travelers [29]. Despite these difficulties, the pandemic has also sparked new interest in medical tourism in the post-pandemic period, with a focus on safe destinations and innovations in telehealth and virtual consultations. These trends highlight the need for the industry to adapt to new consumer and regulatory demands [35]. In addition, the COVID-19 pandemic delayed and prevented examinations with various specialists for months. Patients with rheumatic diseases were particularly affected, as they could not access a rheumatologist for months. According to the literature, in most Central and Western European countries, consultation with a rheumatologist takes about 30 weeks [36]. Fuchs et al. and other sources reported that in Germany, it takes more than 6 months from the onset of the first symptom of inflammatory joint disease until a consultation with a specialist is scheduled [37]. This trend is also relevant for other non-EU countries. Widdiefield et al. published data showing that in Canada it takes an average of 74 days to appoint such a consultation, which significantly worsens the quality of health care to patients with rheumatic diseases [37, 38].

HIV/AIDS: Global pandemic and the fight against the virus

By 2024, AIDS (AIDS) caused by HIV continues to be a challenge and a global health problem. Despite significant advances in diagnosis and treatment in recent decades, the disease remains one of the major contributors to mortality in some regions, particularly in Africa (sub-Saharan Africa) [39-41]. According to the Joint United Nations Programme on HIV and AIDS (UNAIDS) and WHO, by the end

of 2023 about 1.3 million people are newly infected, about 40 million are living with HIV, and there are about 630,000 deaths [39]. About 28 million people worldwide are receiving antiretroviral treatment, which significantly improves quality of life and reduces viral load [39, 40].

Numerous international campaigns have been created to raise awareness and reduce the stigma surrounding the disease. PrEP (pre-exposure prophylaxis) - taking medication to prevent infection - is one of the main prevention programmes. This is particularly effective in certain at-risk groups (people with multiple sexual partners, people with addictions or homosexuals) [39, 41]. The main components of the tablet are Tenofovir (TDF) and Emtricitabine (FTC). The best known patented name for this combination is Truvada®, but generic versions of PrEP are now available. In Bulgaria, the drug is available under the name Tenofovir Disoproxil Emtricitabine [42]. There are active efforts in researching vaccines and new therapies that can cure AIDS, but they are currently of limited clinical use [40, 43]. The United Nations Programme to Fight HIV/AIDS, known as UNAIDS, is working towards the goal of eliminating HIV as a global health problem by 2030 [39]. There are several types of drugs against HIV, the infection that targets different phases of the virus' replication process. Because the virus mutates rapidly and becomes resistant to any single drug taken, patients must take combination anti-HIV therapy (antiretroviral therapy, ART). Unfortunately, ART cannot completely eliminate the infection [44]. The treatment is covered by the Ministry of Health, regardless of the patient's health insurance status [45].

The main challenges on the agenda are socio-economic barriers to prevention and treatment (lack of awareness and access to health services, low social status and education). Another major problem is long-term non-adherence to treatment and lack of health infrastructure in countries with low gross domestic product (GDP) [40, 41].

Tuberculosis: An Ancient Disease in the Modern World

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB), is a chronic, systemic infectious disease that usually affects the lungs but can develop in all organs and systems of the body. It is usually spread by the airborne route by patients with pulmonary TB (PTB). Despite the availability of an aetiological treatment and global efforts to effectively control it, TB still poses a public health threat due to the persistence of its prevalence and the number

of deaths [46, 47]. Silicosis (a specific occupational disease) and HIV infection are the most significant risk factors for TB and complement each other, especially in low GDP countries [47-50]. HIV infection increases the incidence of TB by increasing the risk of reactivation of latent TB infection (LTBI) with MTB and rapid progression to active TB [47]. The problem with BCG (*Bacillus Calmette-Guerin*) vaccination, despite its compulsory nature according to the immunization calendar of R. Bulgaria, is becoming increasingly popular. According to the WHO, in 2021, TB is the second deadliest infectious disease in the world after COVID-19, causing an estimated 1.5 million deaths each year [46]. In 2023, WHO estimates that about 10.8 million people were newly infected with TB, and approximately 1.25 million deceased from the disease. Of these, 6.1% are persons living with HIV. The majority of cases are in Southeast Asian countries (45%), Africa (24%) and the Western Pacific (17%). More than two-thirds of cases are concentrated in 8 countries: India (26%), Indonesia (10%), China (6.8%), Philippines (6.8%), Pakistan (6.3%), Nigeria (4.6%), Bangladesh (3.5%), and Democratic Republic of Congo (3.1%). Women affected by the disease account for 3.6 million (33% of all estimated cases) and children aged 0-14 years account for 1.3 million (12%) [46]. The spread of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) complicates the fight against the disease. Other challenges include inadequate access to diagnosis and treatment in poor and remote countries/regions, the impact of HIV on TB susceptibility, and the duration of treatment with a combination of anti-TB drugs – a minimum of 6 months for susceptible TB, including 2 months with 4 drugs and 4 months with 2 drugs [46]. The COVID-19 pandemic has had a major impact on TB control by delaying access to diagnosis and treatment. According to the WHO, there is an increase in mortality and the number of undiagnosed TB cases (hidden morbidity) in 2020 and 2021 as a result of the pandemic [46].

In an effort to control and prevent the disease, initiatives have been organized to raise awareness, improve immunization coverage (the BCG vaccine remains the main vaccine for TB prevention), early diagnosis, treatment with new therapies, and programs to improve access to treatment in developing countries. The Stop TB Partnership was founded in 2001 and is part of the United Nations (UN), administered by the United Nations Office for Project Services (UNOPS) based in Geneva, Switzerland [51]. Stop TB Partnership brings together the efforts of

various international organizations with the goal of eliminating TB. The goals of the current WHO End TB Strategy are to reduce TB incidence by 90% and deaths by 95% by 2035 compared to 2015 levels, and even to eliminate TB by 2050 (less than 1 new case per 1 million population per year) [46, 47, 51].

About 1/4 of the world's population has latent tuberculosis infection (LTBI), i.e. these individuals are infected with MTB but are not (yet) sick and cannot spread this infection. LTBI is probably the most important factor in the lack of desired progress in TB control. It is defined as a state of persistent immune response to stimulation by MTB antigens without clinical evidence of active disease. It represents a huge reservoir for the development of a TB epidemic, as about 1/10 of infected persons develop active TB during their lifetime. Immunocompromised individuals are particularly at risk of LTBI activation, which is closely linked to the ability of host immunity to provide an adequate response. Persons infected with HIV, persons with immune-mediated inflammatory diseases, those receiving treatment with systemic corticosteroids and tumor necrosis factor- α (TNF- α) antagonists, hemodialysis patients, transplant candidates, and recipients are at increased risk of TB reactivation.

The WHO-recommended tests to detect LTBI are the Mantoux tuberculin skin test (TST) and interferon-gamma release assays (IGRAs), immunological methods based on the release of interferon-gamma (IFN- γ) from sensitized T cells of TB-infected individuals upon repeated exposure to MTB antigens. Two types of IGRAs are currently available that use different immunological methods: the QuantiFERON-TB Gold Plus (QFT-Plus) and the T-SPOT.TB.

It is extremely important to emphasize that the diagnosis of LTBI is not based on TFTs or IGRAs alone, but is always made after exclusion of active TB with appropriate medical evaluation (history and physical examination, microbiological examination of sputum and other biological samples for the presence of MTB, chest radiography, pathomorphological and other examinations). In the exclusion of active disease, especially in immunosuppressed persons, young children and close family contacts, the preventive treatment of LTBI caused by MTB strains presumed to be drug-susceptible would be: monotherapy with isoniazid (H) for at least 6 months and treatment with regimens containing the rifamycin antibiotic: rifampicin (R) or rifapentine (P).

Adding to the problem are occupational diseases caused by biological agents [52]. In 2005, biological hazards at work were responsible for around 320 000 deaths per year worldwide and around 5 000

deaths in the EU. According to Corrao CR et al. occupational diseases due to infections accounted for about 0.8% of all deaths, mainly in health and social services (65.21%) [52, 53]. According to the European Working Conditions Survey 2015, the proportion of workers in the European Union exposed to infectious agents at work was 13%, which is 1.5 times higher than the situation 10 years ago [54]. Experts estimate that there were 550 000 deaths worldwide in 2021 due to exposure to biological agents in the work environment. COVID-19 accounts for the largest share in 2021 as a cause of work-related death in 230,000 people [55]. According to a UNI Global Union study, only 98 countries in the world have recognized COVID-19 as an occupational disease, covering only 2% of the population. [56] o date, COVID-19 and long COVID-19 are not included in the lists of occupational diseases provided by international organizations (ILO, WHO, EU) and are not recognized as an occupational disease in Bulgaria and in most countries [22, 57]. The precarious financial situation of many workers reduces their ability to afford health care costs. This in turn leads to personal economic losses, but also affects their families, employers and the state [14-22].

The situation in Bulgaria:

The National Health Strategy 2020 of the Republic of Bulgaria pays particular attention to the surveillance of communicable diseases, the protection of the country from the import and spread of these infections, the containment of outbreaks and epidemics, the provision of high immunisation coverage of the population against vaccine-preventable infections and the organisation of a rapid response to situations threatening public health (including the use of biological agents for terrorist purposes) [58]. A priority task is the reduction of hospital-acquired infections (HAIs) and antimicrobial resistance (AMR), which are criteria for assessing the quality of medical services and patient safety. It has been pointed out that HAIs are among the top ten leading causes of increased patient mortality, although they are largely preventable. The emergence of polyresistance leads to a permanent limitation of treatment and prevention options for bacterial infections [58].

According to the NCDC, there were 563,079 cases of COVID-19 and 38,106 deaths in the country in 2022, yet a decrease in lethality from the previous year was reported. As of 1 July 2024, the National COVID-19 System has been discontinued, as well as the Single Information Portal – coronavirus. bg. Information on cases registered in the country is

published once a week on the websites of the Ministry of Health and the National Centre for Infectious and Parasitic Diseases [59-61].

In terms of the other two infections, a total of 4048 persons with HIV infection have been registered by the end of 2022, with 327 new cases registered in the corresponding year. In 9% of those diagnosed with AIDS, the diagnosis was made in the presence of tuberculosis as an opportunistic infection [59]. In the period 2004-2017, the implementation of the "HIV/AIDS Prevention and Control Programme", funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria, introduced prevention services among the most vulnerable groups in the country through the establishment of low-threshold centres and networks of trained non government organization teams [59]. The national programmes respond to the requirements and commitments made by the country in implementation of international recommendations and a number of policy documents such as: the UN Sustainable Development Goals, the Declaration of Commitment on HIV (Dublin Declaration); the Third Union Programme of Action on Health (2014-2020), the draft Global HIV Strategy of the Joint United Nations Programme on HIV/AIDS (2021-2026) [39, 62, 63]. Within the framework of the National Programme for the Prevention and Control of HIV and Sexually Transmitted Infections in the Republic of Bulgaria 2021-2025, four annual Anti-AIDS campaigns continue to be held: on the 14th of February, the International Day of Compassion for those Affected by HIV/AIDS (the third Sunday in May), the summer Anti-AIDS campaign (August) and on the 1st of December – World AIDS Day. AIDS prevention programs focus on educating young people, at-risk groups, and increasing awareness about ways to prevent HIV infection, including condom use and PrEP [64].

Bulgaria occupies an intermediate level compared to the high prevalence of TB in the countries of Eastern Europe and Central Asia, and its low prevalence in the countries of Western Europe. In line with measures taken worldwide, our country has developed its own programmes for the control of this socially important disease since 1951, applying established models and practices to reduce the societal burden of TB. Thanks to the efforts undertaken in the implementation of the „National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria“, the country is witnessing a downward trend in the incidence of TB from 48.8 per 100 000 in 2001 to 13.5 per 100 000 in 2023. Over the last 4 years, the same trends have been reported

in our country due to the COVID-19 pandemic as globally – a decrease in registered TB cases due to restructuring and disrupted functions of specialized TB control facilities by districts, non-appearance of TB cases and patients in health facilities since the introduction of lockdown and stigma due to similar symptoms of the two diseases; persistent household contact and increased risk of transmission among family members. The total number of people registered with TB in the country according to the National Center for Public Health and Analysis in 2023 is 869, which corresponds to 13.5 per 100,000 population. The number of men with the disease is usually twice the number of women. The most affected age groups are 45-54, 65+ and 55-64. The administrative districts with incidence rates above the national average in 2023 are: Sofia District – 32.2; Vratsa – 22.9; Montana – 24.3; Pernik – 18.9; Yambol – 18.7 per 100 000 [65].

According to the National Social Insurance Institute (NSI), for the period 2009-2022, a total of 13 cases of occupational diseases caused by biological agents have been recognized, with 7 cases of TB – 1 case each reported for 2009, 2013 and 2014, and 4 cases for 2015. From the data provided by the NSI, no correlation can be made between the reported cases and their distribution by sex, age groups, occupation/activity of the patient, category of work, work characteristics, duration of exposure and severity of the illness [66, 67]. The main difficulties in occupational risk assessment are related to the lack of systematic information on biological agents in many work activities, insufficient awareness and inadequate training of workers on occupational health and safety, lack of standardized criteria for occupational exposure to airborne biological agents. Awareness of biological agents is critical for the prevention of related diseases and mortality.

Modern strategies for addressing the challenges of socially significant infectious diseases

1. The basis of strategies to combat infectious diseases is global cooperation, the development of international initiatives related to information exchange, health education, as well as financial and material support (donations/purchase of vaccines) for countries with low GDP.

2. Accessibility to medical services, medical facilities, modern medical equipment, medicinal products and vaccines is fundamental to reducing morbidity, prophylaxis and prevention.

3. Funding and development of new molecules to treat the three infections is a key mechanism for reducing and preventing their consequences.

4. International campaigns to fight stigma and prejudice, together with social support programs for those affected, can reduce social isolation and improve the psychosocial health of affected individuals.

5. The development of strict standards for safety in the work environment (with priority in healthcare), as well as effective protocols for the protection and training of personnel are a top priority for limiting the spread of infections.

6. Development of special programs and health insurance to alleviate the economic consequences of infectious diseases.

CONCLUSION

The COVID-19 pandemic highlighted the vulnerability of the global public system to emerging health crises. Infectious diseases (COVID-19, HIV/AIDS and tuberculosis) remain serious global problems that require coordinated efforts at global, national and local levels. Despite advances in diagnosis and treatment, and international prevention and control efforts, many challenges remain, including socioeconomic barriers and shortages of health services in many regions. Many of the problems lie in unequal access to health services, stigma and resource scarcity in poor and developing countries. Success in the fight against these diseases depends on global solidarity, scientific innovation and effective health policies.

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Постъпил за печат: 05.03.2025 г.

Submitted: 05.03.2025

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