Peculiarities of tuberculosis in the COVID-19 pandemic

L.D. Todoriko, I.O. Semianiv

Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi **Conflict of interest:** none

OBJECTIVE. The purpose of our comprehensive analysis is to assess the prospects for the effects of the interaction between coronavirus disease 2019 (COVID-19) and tuberculosis (TB) and to strategize the risks of spreading TB infection in a coronavirus pandemic.

MATERIALS AND METHODS. Test access to full-text and abstract databases was used.

RESULTS AND DISCUSSION. An analysis of the available literature has shown that a 3-month lockdown and a long 10-month recovery worldwide could lead to an additional 6.3 million TB cases and another 1.4 million TB deaths between 2020 and 2025. On average, the detection of TB in Ukraine decreased by 27.4 %, and the incidence of TB among children decreased by 34.5 %. This is an alarming figure because we know very well that within 6 months the number of patients with TB has not decreased, they simply stopped being detected. In addition, COVID-19 may accelerate the activation of latent TB infection and thus increase the number of active cases.

CONCLUSIONS. The overall incidence of TB in 2021 will increase to the level that was last observed between 2013 and 2016. The epidemiological indicators of TB control are expected to deteriorate for at least 5-8 years due to the COVID-19 pandemic. Long-term results can be strongly affected by the rate of short-term recovery. Priority should be given to all governments, during a pandemic, to ensure the continuity of basic health care, including the implementation of national TB programs.

KEY WORDS: tuberculosis, COVID-19, epidemiology, pandemic.

Особливості перебігу туберкульозу в умовах пандемії COVID-19

Л.Д. Тодоріко, І.О. Сем'янів

Вищий державний навчальний заклад України «Буковинський державний медичний університет», м. Чернівці Конфлікт інтересів: відсутній

МЕТА. Оцінювання наслідків взаємодії між коронавірусною хворобою (COVID-19) і туберкульозом (ТБ) та подальшої тактики щодо ризиків поширення туберкульозної інфекції в сучасних умовах пандемії.

МАТЕРІАЛИ ТА МЕТОДИ. Був використаний тестовий доступ до повнотекстових і реферативних баз даних. **РЕЗУЛЬТАТИ ТА ЇХ ОБГОВОРЕННЯ.** Комплексний аналіз доступних літературних джерел показав, що в усьому світі 3-місячний локдаун і тривале 10-місячне відновлення можуть зумовити додаткові 6,3 млн випадків ТБ та ще 1,4 млн смертей від ТБ у період між 2020 і 2025 роками. У середньому виявлення ТБ в Україні зменшилося на 27,4 %, а захворюваність на ТБ серед дітей знизилася на 34,5 %. Це тривожні цифри, оскільки ми добре знаємо, що протягом півроку пацієнтів із ТБ не стало менше, їх просто перестали виявляти. Крім того, COVID-19 може прискорити активацію латентної туберкульозної інфекції та збільшити таким чином кількість активних випадків.

ВИСНОВКИ. Загальна захворюваність на ТБ у 2021 році зросте до рівня, котрий востаннє спостерігався між 2013 і 2016 роками. Передбачається погіршення щонайменше на 5-8 років епідеміологічних показників щодо контролю над ТБ через пандемію COVID-19. На довгострокові результати може сильно вплинути темп короткочасного відновлення. Пріоритетом для всіх урядів у період пандемії має бути забезпечення безперервності надання основних медичних послуг, включаючи виконання національних програм протидії ТБ.

КЛЮЧОВІ СЛОВА: туберкульоз, COVID-19, епідеміологія, пандемія.

DOI: 10.32902/2663-0338-2020-3-27-34

Особенности течения туберкулеза в условиях пандемии COVID-19

Л.Д. Тодорико, И.А. Семянив

Высшее государственное учебное заведение Украины «Буковинский государственный медицинский университет», г. Черновцы Конфликт интересов: отсутствует

ЦЕЛЬ. Оценка последствий взаимодействия между коронавирусной болезнью (COVID-19) и туберкулезом (ТБ) и дальнейшей тактики в отношении рисков распространения туберкулезной инфекции в современных условиях пандемии.

МАТЕРИАЛЫ И МЕТОДЫ. Был использован тестовый доступ к полнотекстовым и реферативным базам данных. **РЕЗУЛЬТАТЫ И ИХ ОБСУЖДЕНИЕ.** Комплексный анализ доступных литературных источников показал, что во всем мире 3-месячный локдаун и длительное 10-месячное восстановление могут обусловить дополнительные 6,3 млн случаев ТБ и еще 1,4 млн смертей от ТБ в период между 2020 и 2025 годами. В среднем выявление ТБ в Украине уменьшилось на 27,4 %, а заболеваемость среди детей снизилась на 34,5 %. Это тревожные цифры, поскольку мы хорошо знаем, что в течение полугода пациентов с ТБ не стало меньше, их просто перестали выявлять. Кроме того, COVID-19 может ускорить активацию латентной туберкулезной инфекции и увеличить таким образом количество активных случаев.

ВЫВОДЫ. Общая заболеваемость ТБ в 2021 году возрастет до уровня, который в последний раз наблюдался между 2013 и 2016 годами. Предполагается ухудшение минимум на 5-8 лет эпидемиологических показателей по контролю над ТБ из-за пандемии COVID-19. На долгосрочные результаты может сильно повлиять темп кратковременного восстановления. Приоритетом для всех правительств в период пандемии должно быть обеспечение непрерывности предоставления основных медицинских услуг, включая выполнение национальных программ противодействия ТБ.

КЛЮЧЕВЫЕ СЛОВА: туберкулез, COVID-19, эпидемиология, пандемия.

Respiratory tract infections (RTIs) remain the top cause of morbidity and mortality from infectious diseases worldwide [1, 16]. Until the end of December 2019, just three pathogens featured on the World Health Organization (WHO) Blueprint priority list for research and development: severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV), Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) and Mycobacterium tuberculosis. In January 2020, SARS-CoV-2, the cause of coronavirus disease (COVID-19), was added to the priority list [2, 12, 26]. Since then, SARS-CoV-2 has spread outside China to all continents causing death and economic disruption, and considerable concern among national, regional, and international communities. The social and psychological impact of the epidemic has been compounded by the need for strict social distancing, and the rapid spread of information and misinformation via both mainstream media and social media. Even more alarming is the disruption caused to global health services [7, 28].

Governments of high tuberculosis (TB) burden countries need to ensure the continuity of TB services in the time of COVID-19. This includes being proactive to protect the most vulnerable, including protection against economic hardship, isolation, stigma and discrimination. The global response needs to identify and mitigate potential risks to the critical mission of tackling TB (and other RTIs) [8, 29]. This includes identifying how the capabilities and infrastructure can be adapted to strengthen the response to COVID-19 and allow flexibility in programmes to enable countries to respond at pace to the evolution of COVID-19 [14, 20].

As the COVID-19 pandemic spreads into high TB burden settings, countries must put in place strategies to ease pressure on health systems and to mitigate disruption in routine health services. The current social distancing and stay-at-home measures make it particularly challenging for TB programmes to provide diagnosis, treatment and care for communities affected by TB [6, 18].

The COVID-19 pandemic has currently overtaken every other health issue throughout the world. There are numerous ways in which this will impact existing public health issues. Here we reflect on the interactions between COVID-19 and TB, which still ranks as the leading cause of death from a single infectious disease globally [4, 10]. There may be grave consequences for existing and undiagnosed TB patients globally, particularly in low and middle income countries where TB is endemic and health services poorly equipped.

TB control programmes will be strained due to diversion of resources, and an inevitable loss of health system focus, such that some activities cannot or will not be prioritised [9, 31]. This is likely to lead to a reduction in quality of TB care and worse outcomes. Further, TB patients often have underlying comorbidities and lung damage that may make them prone to more severe COVID-19. The symptoms of TB and COVID-19 can be similar, with for example cough and fever. Not only can this create diagnostic confusion, but it could worsen the stigmatization of TB patients especially in low and middle income countries, given the fear of COVID-19 [9, 17].

What is the potential impact of short-term lockdowns on TB incidence and mortality over the next 5 years? For illustration, figure shows the dynamics of TB incidence and mortality resulting from a 2-month lockdown followed by a 2-month restoration period (red curve), and the worstcase scenario of a 3-month lockdown followed by 10-month restoration. Table 1 shows estimates for the excess TB burden,

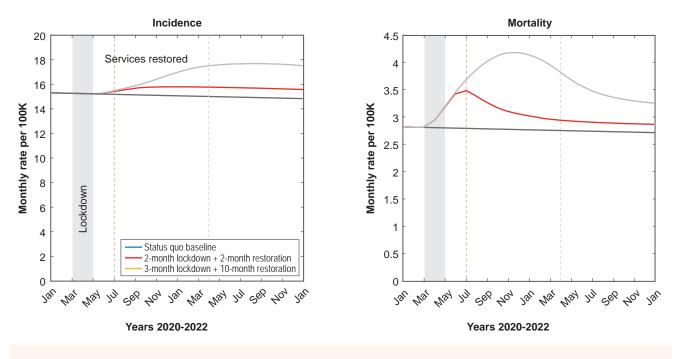


Fig. Dynamics of TB incidence and mortality following a COVID-19 lockdown

in each of the country settings. These results illustrate that it can take years for TB burden to return to pre-lockdown levels: the resulting excess TB cases and deaths can represent substantial setbacks in ending TB control in each country [27].

While stringent COVID-19 responses may only last months, they would have a lasting impact on TB in high-burden settings, through their effect mainly on TB diagnosis and treatment.

Globally, a 3-month lockdown and a protracted 10-month restoration could lead to an additional 6.3 million cases of TB between 2020 and 2025, and an additional 1.4 million TB deaths during this time.

As such, global TB incidence and deaths in 2021 would increase to levels last seen in between 2013 and 2016 respectively – implying a setback of at least 5 to 8 years in the fight against TB, due to the COVID-19 pandemic. Long-term outcomes can be strongly influenced by the pace of short-term recovery [22].

Each month taken to return to normal TB services would incur, in India, an additional 40,685 deaths between 2020 and 2025; in Kenya, an additional 1,157 deaths; and in Ukraine, an additional 137 deaths over this period.

To recover the gains made over last years through increased efforts and investments in TB, it is important to have supplementary measures and resources to reduce the accumulated pool of undetected people with TB. Such measures may include ramped-up active case-finding, alongside intensive community engagement and contact tracing to maintain awareness of the importance of recognizing and responding to symptoms suggestive of TB, using digital technology and other tools. Securing access to an uninterrupted supply of quality assured treatment and care for every single person with TB will be essential. Notifications will provide a helpful approach for monitoring the progress of such supplementary efforts [9].

Below you can see the comparing data of the incidence of TB on the first half of 2020 and first half of 2019 (table 2).

Таблиця 1. Model-estimated impact for the excess TB cases and deaths that would occur in each country, as a result of the COVID-19 response

	Excess cases between 2020-2025 (% increase)		Excess deaths between 2020-2025 (% increase)		
Country	2-month lockdown + 2-month recovery	3-month lockdown + 10-month recovery	2-month lockdown + 2-month recovery	3-month lockdown + 10-month recovery	
India	5140,370 (3.55 %)	1,788,100 (12.32 %)	151,120 (5.70 %)	511,930 (19.31 %)	
Kenya	12,154 (1.51 %)	40,992 (5.08 %)	4,873 (2.15 %)	15,800 (6.99 %)	
Ukraine	2,348 (1.19 %)	7,589 (9.86 %)	455 (2.40 %)	1,578 (8.31 %)	
Global	1,826,400 (3.1 %)	6,331,100 (10.7 %)	342,500 (4.00 %)	1,367,300 (16.0 %)	

Таблиця 2. Incidence of active TB, including relapse, among the entire population of Ukraine in the first half of 2020 compared to the same period in 2019

	In general				
Administrative area	Absolute	Absolute numbers		Per 100 thousand population	
	2019	2020	2019	2020	and first half of 2019
Avtonomna Respublika Krym	-	-	-	-	-
Vinnytska	434	280	27.7	18.2	-34.3 %
Volynska	361	295	34.9	28.7	-17.8 %
Dnipropetrovska	1189	1096	36.8	34.5	-6.2 %
Donetska	694	567	36.0	29.8	-17.2 %
Zhytomyrska	455	265	36.9	21.9	-40.7 %
Zakarpatska	475	382	37.8	30.5	-19.3 %
Zaporizka	644	412	37.4	24.4	-34.8 %
Ivano-Frankivska	379	213	27.6	15.6	-43.5 %
Kyivska	730	507	41.7	28.6	-31.4 %
Kirovohradska	375	299	39.5	32.3	-18.2 %
Luhanska	229	170	33.0	24.8	-24.8 %
Lvivska	884	611	35.2	24.5	-30.4 %
Mykolaivska	406	272	35.6	24.3	-31.7 %
Odeska	1670	1194	70.4	50.5	-28.3 %
Poltavska	382	281	27.2	20.4	-25.0 %
Rivnenska	356	207	30.7	18.0	-41.4 %
Sumska	370	248	33.9	23.3	-31.3 %
Ternopilska	252	130	24.0	12.6	-47.5 %
Kharkivska	666	493	24.9	18.7	-24.9 %
Khersonska	420	306	40.2	29.8	-25.9 %
Khmelnytska	381	266	30.0	21.3	-29.0 %
Cherkaska	363	288	29.8	24.2	-18.8 %
Chernivetska	198	101	21.9	11.2	-48.9 %
Chernihivska	334	251	33.0	25.5	-22.7 %
Kyiv	724	466	25.0	15.9	-36.4 %
Sevastopol	-	-	-	-	-
Ukraine	13 371	9600	31.7	23.0	-27.4 %

On average, the detection of TB in Ukraine decreased by 27.4 % (table 2) and the incidence of TB among children decreased by 34.5 % (table 3). This is a worrying number, because we are well aware that within 6 months there have been no fewer patients with TB, they simply stopped being detected.

Meanwhile, more complex cases and ongoing processes will begin to be registered, and patients with bacterial excretion will endanger all contact persons without knowing their pathology. Here is a clear example of the future problem we will deal with in the coming years.

Now we would like to answering the important questions of the combination of TB and COVID-19.

COVID-19 could accelerate activation of dormant TB [28]. According to the WHO, dormant TB already affects a quarter of the world's population. If the novel coronavirus activates a sizable proportion of these dormant infections, it could severely upset the global health and economic situation.

Many viruses, including SARS-CoV-2, cause a temporary immunosuppressive effect, which causes dormant bacterial infections to come back to life. This was the case with the Spanish flu pandemic of 1918-1920, which caused an increase in the number of lung TB cases. The highest death rate was in the patient subgroup, which had influenza with TB.

The 2009 H1N1 flu pandemic also showed the same trend, with poorer outcomes in patients coinfected with TB or multidrug-resistant strains. Patients with SARS or MERS infections were also found to develop lung TB.

Are people with TB likely to be at increased risk of COVID-19 infection, illness and death [28]? While experience

Таблиця 3. Incidence of children aged 0-17 years, including active TB, including its relapse, in the first half of 2020 compared to the same period in 2019

		Children aged 0-17 years			
Administrative area	Absolute	Absolute numbers		Per 100 thousand population	
	2019	2020	2019	2020	of 2020 and first half of 2019
Avtonomna Respublika Krym	-	-	-	-	-
Vinnytska	19	15	6.7	5.3	-20.9 %
Volynska	7	11	2.9	4.6	+1,6 times
Dnipropetrovska	48	27	8.3	4.7	-43.4 %
Donetska	18	4	5.9	1.3	-4,5 times
Zhytomyrska	17	8	7.1	3.4	-2,1 times
Zakarpatska	13	10	4.5	3.4	-24.4 %
Zaporizka	29	23	9.9	7.9	-20.2 %
Ivano-Frankivska	12	6	4.3	2.2	-48.8 %
Kyivska	38	21	11.0	5.9	-46.4 %
Kirovohradska	10	12	6.0	7.3	+21.7 %
Luhanska	5	1	4.7	1.0	-4,7 times
Lvivska	21	12	4.3	2.5	-41.9 %
Mykolaivska	4	9	1.9	4.4	+2,3 times
Odeska	58	32	12.4	6.8	-45.2 %
Poltavska	5	4	2.1	1.7	-19.0 %
Rivnenska	8	3	2.9	1.1	-2,6 times
Sumska	12	3	7.1	1.8	-3,9 times
Ternopilska	4	2	2.0	1.0	-2,0 times
Kharkivska	22	21	5.1	4.9	-3.9 %
Khersonska	22	8	11.2	4.1	-2,7 times
Khmelnytska	3	1	1.3	0.4	-3,2 times
Cherkaska	11	15	5.5	7.7	+40.0 %
Chernivetska	2	2	1.1	1.1	=
Chernihivska	14	7	8.7	4.4	-49.4 %
Kyiv	16	12	2.9	2.1	-27.6 %
Sevastopol	-	-	-	-	-
Ukraine	418	269	5.5	3.6	-34.5 %

on COVID-19 infection in TB patients remains limited, it is anticipated that people ill with both TB and COVID-19 may have poorer treatment outcomes, especially if TB treatment is interrupted.

Older age, diabetes and chronic obstructive pulmonary disease are linked with more severe COVID-19 and are also risk factors for poor outcomes in TB.

TB patients should take precautions as advised by health authorities to be protected from COVID-19 and continue their TB treatment as prescribed.

People ill with COVID-19 and TB show similar symptoms such as cough, fever and difficulty breathing. Both diseases attack primarily the lungs and although both biological agents transmit mainly via close contact, the incubation period from exposure to disease in TB is longer, often with a slow onset.

DOI: 10.32902/2663-0338-2020-3-27-34

Do COVID-19 and TB spread in the same way [28]? While both TB and COVID-19 spread by close contact between people the exact mode of transmission differs, explaining some differences in infection control measures to mitigate the two conditions.

TB bacilli remain suspended in the air in droplet nuclei for several hours after a TB patient coughs, sneezes, shouts, or sings, and people who inhale them can get infected. The size of these droplet nuclei is a key factor determining their infectiousness. Their concentration decreases with ventilation and exposure to direct sunlight.

COVID-19 transmission has primarily been attributed to the direct breathing of droplets expelled by someone with COVID-19 (people may be infectious before clinical features become apparent). Droplets produced by coughing, sneezing, exhaling and speaking may land on objects and surfaces, and contacts can get infected with COVID-19 by touching them and then touching their eyes, nose or mouth. Handwashing, in addition to respiratory precautions, are thus important in the control of COVID-19.

What should health authorities do to provide sustainability of essential tuberculosis services during the COVID-19 pandemic [28]? People-centred delivery of TB prevention, diagnosis, treatment and care services should be ensured in tandem with the COVID-19 response.

Prevention. Measures must be implemented to limit transmission of TB and COVID-19 in congregate settings and health care facilities. Administrative, environmental and personal protection measures apply to both. Provision of TB preventive treatment should be maintained as much as possible.

Diagnosis. Tests for TB and COVID-19 are different and both should be made available for individuals with respiratory symptoms, which may be similar for the two diseases.

Treatment and care. People-centred outpatient and community-based care should be strongly preferred over hospital treatment for TB patients (unless serious conditions require hospitalization) to reduce opportunities for transmission.

Anti-TB treatment, in line with the latest WHO guidelines, must be provided for all TB patients, including those in quarantine and those with confirmed COVID-19 disease. Adequate stocks of TB medicines should be provided to all patients to reduce trips to collect medicines.

Use of digital health technologies for patients and programmes should be intensified. In line with WHO recommendations, technologies like electronic medication monitors and video-supported therapy can help patients complete their TB treatment.

What services can be leveraged across both disease [28]? The response to COVID-19 can benefit from the capacity building efforts developed for TB over many years of investment by national authorities and donors. These include infection prevention and control, contact tracing, household and community-based care, and surveillance and monitoring systems.

Although modes of transmission of the two diseases are slightly different, administrative, environmental and personal protection measures apply to both.

TB laboratory networks have been established in countries with the support of WHO and international partners. These networks as well as specimen transportation mechanisms could also be used for COVID-19 diagnosis and surveillance.

Respiratory physicians, pulmonology staff of all grades, TB specialists and health workers at the primary health care level may be points of reference for patients with pulmonary complications of COVID-19. They should familiarize themselves with the most current WHO recommendations for the supportive treatment and containment of COVID-19.

TB programme staff with their experience and capacity, including in active case finding and contact tracing, are well placed to support the COVID-19 response.

How can we protect people seeking TB care during the COVID-19 pandemic [28]? In a context of widespread restriction of movement of the population in response to the pandemic and isolation of COVID-19 patients, communication with the healthcare services should be maintained so that people with TB, especially those most vulnerable, get essential services. This includes management of adverse drug reactions and comorbidities, nutritional and mental health support, and restocking of the supplies of medicines.

Enough TB medicines will need to be dispensed to the patient or caregiver to last until the next visit. This will limit interruption or unnecessary visits to the clinic. Mechanisms to deliver medicines at home and even to collect specimens for follow-up testing may become expedient. Home-based TB treatment is bound to become more common. Alternative arrangements to reduce clinic visits may involve limiting appointments to specific times to avoid exposure to other clinic attendees; using digital technologies to maintain treatment support [21]. Community health workers become more critical as treatment is more decentralized.

More TB patients will probably start their treatment at home and therefore limiting the risk of household transmission of TB during the first few weeks is important.

Vulnerable populations who have poor access to healthcare should not get further marginalized during the pandemic.

Is tuberculosis treatment different in people who have both TB and COVID-19 [28]? In most cases TB treatment is not different in people with or without COVID-19 infection.

Experience on joint management of both COVID-19 infection and TB remains limited. However, suspension of TB treatment in COVID-19 patients should be exceptional. TB preventive treatment, treatment for drug-susceptible or drug-resistant TB disease should continue uninterrupted to safeguard the patient's health, reduce transmission and prevent the development of drug-resistance.

While treatment trials are ongoing, no medication is currently recommended for COVID-19 and therefore no cautions on drug-drug interactions are indicated at present. TB patients on treatment should nonetheless be asked if they are taking any medicines, including traditional cures, that may interact with their medication.

Effective treatments to prevent TB and to treat active TB have been scaled up and are in use worldwide. The risk of death in TB patients approaches 50 % if left untreated and may be higher in the elderly or in the presence of comorbidity. It is critical that TB services are not disrupted during the COVID-19 response.

Now let's look at the relationship **between Bacillus Calmette-Guerin (BCG) vaccination and COVID-19** [13, 25]. There is no evidence that the BCG protects people against infection with COVID-19 virus. Two clinical trials addressing this question are underway, and WHO will evaluate the evidence when it is available. In the absence of evidence, WHO does not recommend BCG vaccination for the prevention of COVID-19. There is experimental evidence from both animal and human studies that the BCG vaccine has non-specific effects on the immune system. These effects have not been well characterized and their clinical relevance is unknown.

On 11 April 2020, WHO updated its ongoing evidence review of the major scientific databases and clinical trial repositories, using English, French and Chinese search terms for COVID-19, coronavirus, SARS-CoV-2 and BCG.

The review yielded three preprints, in which the authors compared the incidence of COVID-19 cases in countries where the BCG vaccine is used with countries where it is not used and observed that countries that routinely used the vaccine in neonates had less reported cases of COVID-19 to date. Such ecological studies are prone to significant bias from many confounders, including differences in national demographics and disease burden, testing rates for COVID-19 virus infections, and the stage of the pandemic in each country [19].

The review also yielded two registered protocols for clinical trials, both of which aim to study the effects of BCG vaccination given to health care workers directly involved in the care of patients with COVID-19.

BCG vaccination prevents severe forms of TB in children and diversion of local supplies may result in neonates not being vaccinated, resulting in an increase of disease and deaths from TB. In the absence of evidence, WHO does not recommend BCG vaccination for the prevention of COVID-19. WHO continues to recommend neonatal BCG vaccination in countries or settings with a high incidence of TB [5].

Problem of stigma and discrimination only escalates during a pandemic [24]. The COVID-19 pandemic has provoked social stigma and discriminatory behaviours against people of certain ethnic backgrounds as well as anyone perceived to have been in contact with the virus. Stigma can undermine social cohesion and prompt social isolation of groups, which might contribute to a situation where the virus and TB are more likely to spread. This can:

- drive people to hide the illness to avoid discrimination;
- prevent people from seeking health care immediately;
- discourage them from adopting healthy behaviours.

Stigma and fear around communicable diseases like TB hamper the public health response. What works is building trust in reliable health services and advice, showing empathy with those affected, understanding the disease itself, and adopting effective, practical measures so people can help keep themselves and their loved ones safe. Governments, citizens, media and communities have an important role to play in preventing and stopping stigma. We all need to be intentional and thoughtful when communicating on social media and other communication platforms, showing supportive behaviours around COVID-19, as well as older diseases like TB.

Consider the likely impact of COVID-19 on children with TB [7, 30]. Amongst the 1.5 million annual deaths from TB, an estimated 205,000 occur in children with the majority occurring in resource-poor settings. Child survival from TB depends on timely diagnosis, prompt initiation of treatment, community and health systems support for continuous availability of child friendly medication as well as prevention of transmission from sputum-smear positive index casesusually adults-to vulnerable young children in households.

These important elements of the cascade of care are at stake at a time when resources will be focused on providing care for individuals affected by COVID-19. The diagnosis of childhood TB is not only made at dedicated clinics of National TB control programs but equally in generic child health clinics and hospital wards. Many of these facilities will be closed or overwhelmed with other tasks, and as a result diagnostic opportunity in children will be missed. The majority of children in low and middle income countries are not seen by dedicated paediatric specialists, and many general physicians and nurses usually available for their care will be seconded to dealing with adult patients affected by severe respiratory symptoms of COVID-19 instead [15]. Available specialist expertise in respiratory medicine switched to diagnosing and treating this new viral disease, which does not appear generally to have similarly severe manifestations in children compared to adults. Hence it will be assumed that children will cope better and do not need similar attention from the health services during the COVID-19 pandemic. We are already witnessing this trend in HIC where routine clinics are cancelled and paediatric intensive care beds are handed over to adult services. Laboratories are likely to be overwhelmed with analyses of respiratory specimens sent for COVID-19 rather than M. tuberculosis or other pathogens, and once the eagerly anticipated Xpert cartridges for COVID-19 are rolled out it is easy to imagine that GeneXpert platforms will be seconded for COVID-19 diagnostics.

These issues are not specific for childhood TB as adult TB services are likely to be similarly affected. However, the timely diagnosis of TB in children is even more essential to prevent deaths. Families are reluctant to bring unwell children to the hospitals for investigation as everyone is discouraged from using health services at this stage, unless severely unwell. Apart from TB meningitis, TB rarely presents as an acute, severe illness in children but progresses silently until tipping points are reached. Such subtle presentations are likely to be missed if children cannot be reviewed regularly. Given the overlapping presentations of TB and pneumonia in children in the first place, many children are initially placed on a trial of antibiotics but ought to be reviewed in a timely fashion [7, 23].

Another important part of services for children is the provision of preventive therapy for TB infection in the community, which requires resources to contact trace, screen and eventually implement drug therapy. These services are rudimentary in low and middle income countries at the best of times. Provision of preventive therapy works, and given that the under 5 year olds are particularly at risk of progressing to TB disease in its absence, the number of cases of childhood TB will most likely rise as a consequence [3].

As most TB in young children is acquired in their own household, social distancing measures that keep a family together for long periods of time are likely to result in more exposure of children to infectious TB index cases. Contact screening for COVID-19 should therefore include questions about TB in the household in order to protect young children from additional risks [11].

Conclusions

A priority for all governments during this difficult time should be to ensure continuity of essential health services, including national programmes to end TB. During the 2014-2015 Ebola outbreak in West Africa, additional deaths from TB (as an indirect consequence of the outbreak) exceeded deaths directly caused by Ebola.

Access to treatment for people with TB was interrupted because community health workers, doctors and laboratories devoted their energies and resources to the Ebola outbreak. The same is now likely to happen with the COVID-19 pandemic, but on a global scale.

As the relatively weak health systems in high-burden settings struggle to respond to COVID-19, there is a significant risk that prevention and treatment programmes for the existing conditions will be disrupted.

References

- Bhimraj A., Morgan R., Shumaker A. et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Available at: https://www.idsociety.org/practiceguideline/ covid-19-guideline-treatment-and-management.
- Brodin P. Why is COVID-19 so mild in children? Acta Paediatr. 2020; 109: 1082-1083. https://doi.org/10.1111/apa.15271.
- Castagnoli R., Votto M., Licari A. et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. JAMA Pediatr. 2020. Available at: https://jamanetwork.com/ journals/jamapediatrics/fullarticle/2765169.
- Gandhi R., Lynch J., Del Rio C. Mild or moderate COVID-19. N. Engl. J. Med. 2020. doi: 10.1056/NEJMcp2009249.
- Guan W.J., Ni Z.Y., Hu Y. et al. China Medical Treatment Expert Group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. *N. Engl. J. Med.* 2020; 382 (18): 1708-1720. doi: 10.1056/NEJMoa2002032.
 He X., Lau E.H.Y., Wu P. et al. Temporal dynamics in viral shedding and
- He X., Lau E.H.Y., Wu P. et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat. Med.* 2020; 26 (5): 672-675. doi: 10.1038/ s41591-020-0869-5.
- Kincaid E. COVID-19 Daily: HCQ Hospital Protocols, ED Physician Death. Medscape. 2020. Available at: https://www.medscape.com/viewarticle/929383.
- Lavezzo E., Franchin E., Ciavarella C. et al. Suppression of COVID-19 outbreak in the municipality of Vo, Italy. *medRxiv*. 2020. doi: 10.1101/2020.04.17.200 53157.
- Li X., Geng M., Peng Y. et al. Molecular immune pathogenesis and diagnosis of COVID-19. J. Pharm. Anal. 2020; 10 (2): 102-108. doi: 10.1016/j. jpha.2020.03.001.
- McIntosh K. Coronavirus disease 2019 (COVID-19): epidemiology, virology, clinical features, diagnosis, and prevention. Available at: https://www. uptodate.com/contents/coronavirusdisease-2019-covid-19-epidemiologyvirology-clinical-featuresdiagnosis-and-prevention.
- Pathak L., Gayan S., Pal B. et al. (2020). Coronavirus activates a stem cell mediated defense mechanism that accelerates activation of dormant tuberculosis: implications for the COVID-19 pandemic. *bioRxiv* preprint. doi: https://doi.org/10.1101/2020.05.06.077883.
- Tadolini M., Codecasa L., García-García Jé-Mía et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur. Respir. J.* 2020. DOI: 10.1183/13993003.01398-2020.
- Togun T., Kampmann B., Stoker N. et al. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. *Annals of Clinical Microbiology and Antimicrobials*. 2020; 19: 21. DOI: 10.1186/s12941-020-00363-1.
- Wong H.Y.F., Lam H.Y.S., Fong A.H. et al. Frequency and distribution of chest radiographic findings in COVID-19 positive patients. *Radiology*. 2020: 201160. doi: 10.1148/radiol.2020201160.

- 15. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19-11 May 2020. Available at: https://www. who.int/dg/speeches/detail/who-directorgeneral-s-opening-remarks-at-the-media-briefing-on-covid-19-11-may-2020.
- World Health Organization. Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases. 2020. Available at: https://www. who.int/publications-detail/laboratory-testingfor-2019-novel-coronavirusin-suspected-human-cases20200117.
- Wu C., Chen X., Cai Y. et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern. Med. 2020. doi: 10.1001/jamainternmed.2020.0994.
- Zhang T., Wu Q., Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr. Biol.* 2020; 30 (7): 1346-1351. doi: 10.1016/j.cub.2020.03.022.
- 19. Zheng J. SARS-CoV-2: an emerging coronavirus that causes a global threat. Int. J. Biol. Sci. 2020; 16 (10): 1678-1685. doi: 10.7150/ijbs.45053.
- Zhu N., Zhang D., Wang W. et al. A novel coronavirus from patients with pneumonia in China. *N. Engl. J. Med.* 2020; 382: 727-733. doi: 10.1056/NEJ-Moa2001017.
- Zumla A., Niederman M. The explosive epidemic outbreak of novel coronavirus disease 2019 (COVID-19) and the persistent threat of respiratory tract infectious diseases to global health security. *Curr. Opin. Pulm. Med.* 2020. doi: 10.1097/MCP.0000000000676.
- Available at: https://www.news-medical.net/news/20200510/COVID-19could-accelerate-activation-of-dormant-tuberculosis-(TB).aspx.
- 23. Available at: http://www.stoptb.org/covid19maps.asp.
- Available at: https://ann-clinmicrob.biomedcentral.com/articles/10.1186/ s12941-020-00363-1.
- 25. Available at: https://erj.ersjournals.com/content/ early/2020/05/13/13993003.01398-2020.article-info.
- Available at: https://www.who.int/news-room/commentaries/detail/bacillecalmette-gu%C3%A9rin-(bcg)-vaccination-and-covid-19.
- Available at: https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid-19.%20onset.
- Available at: https://www.who.int/teams/global-tuberculosis-programme/ covid-19.
- Available at: https://www.who.int/news-room/q-a-detail/tuberculosis-and-the-covid-19-pandemic#.
- Available at: https://www.theunion.org/news-centre/news/covid-19-and-tuberculosisthreats-and-opportunities.
- Available at: https://www.sciencedirect.com/science/article/pii/ S2531043720301033.

ВІДОМОСТІ ПРО АВТОРІВ / INFORMATION ABOUT AUTHORS Тодоріко Лілія Дмитрівна

Завідувачка кафедри фтизіатрії та пульмонології Вищого державного навчального закладу України «Буковинський державний медичний

університет».

Д-р мед. наук, професор.

2, пл. Театральна, м. Чернівці, 58002, Україна. ORCID iD: orcid.org/0000-0001-9042-0073

Сем'янів Ігор Олександрович

Доцент кафедри фтизіатрії та пульмонології Вищого державного навчального закладу України «Буковинський державний медичний

університет». Канд. мед. наук.

2, пл. Театральна, м. Чернівці, 58002, Україна. ORCID iD: orcid.org/0000-0003-0340-0766

КОНТАКТНА ІНФОРМАЦІЯ / CORRESPONDENCE ТО

Тодоріко Лілія Дмитрівна

2, пл. Театральна, м. Чернівці, 58002, Україна. Тел./факс: +38 (0372) 55-37-54. E-mail: pulmonology@bsmu.edu.ua

Todoriko Liliia Dmytrivna

Head of Department of Phthisiology & Pulmonology, Higher State Educational Establishment of Ukraine "Bukovinian State Medical University". DM, professor. 2, Theatralna sq., Chernivtsi, 58002, Ukraine. ORCID iD: orcid.org/0000-0001-9042-0073

Semianiv Igor Oleksandrovych

Associate Professor of Department of Phthisiology & Pulmonology, Higher State Educational Establishment of Ukraine "Bukovinian State Medical University". PhD. 2, Theatralna sq., Chernivtsi, 58002, Ukraine.

2, Theatralna sq., Chernivtsi, 58002, Ukraine ORCID iD: orcid.org/0000-0003-0340-0766