

Vaccine Prevention of Tuberculosis in Children: Outstanding Issues Family Medicine Systems in Ukraine

Krychkovska Aelita¹, Konechna Roksolana¹, Bolibrukh Liliia¹, Lopatynska Oksana²

¹Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, Lviv Polytechnic National University, Lviv 79013, Ukraine. ²Department of Healthcare Management, Pharmacotherapy and Clinical Pharmacy, Danylo Halytsky Lviv National Medical University Lviv, 79010, Ukraine.

Abstract

The main aspects of the problems of childhood vaccination in Ukraine are studied and the ways of their solution are presented. The results of the survey on the degree of awareness of parents and future parents about the feasibility of vaccination in childhood and determining the main reason for refusal of vaccination are presented and analyzed. A SWOT analysis was conducted and the strengths and weaknesses, advantages and disadvantages of the process of children's vaccination in the opinion of their parents or future parents were defined. We have also established strategies: creation and implementation of preliminary express analyzes for vaccine tolerability; creation of an online vaccination schedule or a special application with notifications about vaccination dates individually for each child; development of a high-quality system of free vaccination and raising the level of information and sanitary and educational work of medical (pharmaceutical) institutions; increasing the responsibility of parents for refusing to vaccinate a child; a strategy for ensuring the availability of quality vaccines at the state level. The dynamics of tuberculosis incidence have been established and a study of the availability of anti-tuberculosis vaccines in the pharmaceutical market of Ukraine has been conducted. Understanding the social problems faced by the patient can help not only to solve some of them but also to consciously approach the need for vaccination and revaccination of children.

Keywords: Vaccination of children, Tuberculosis, Pharmacy, Family medicine

INTRODUCTION

Vaccination is one of the effective preventive measures to protect the world's population from several bacterial and viral diseases, especially the vaccination of children from birth to adolescence. In Ukraine, since 2020, the Calendar of Preventive Vaccination of Children (CPVC) has been amended to fully harmonize it with the CPVC of the EU and the US [1-3].

However, full harmonization is not always appropriate, as the epidemiological situation for some diseases may significantly differ from country to country and in certain territories. For example, according to WHO statistics, about nine million people worldwide suffer from tuberculosis (TB) each year. Among them, only six million are undergoing treatment. Approximately 1.7 million TB patients die each year. The main goal of the National Health Programs of many countries around the world is the prevention of TB, which is interrupting the transfer process of the activator from sick people to healthy [4]. In Ukraine, the incidence rates are higher than average, and the incidence of TB is growing from year to year [5].

However, CPVC revaccination with the BCG vaccine was removed from children aged seven years [2, 6]. According to the updated CPVC, children are vaccinated against TB for the first time on the third to fifth day after birth, and revaccination

is no longer carried out at the age of seven. Also, some newborns, who have certain developmental abnormalities, in 1-2 days of life are transferred to specialized children's inpatient departments of health care facilities (HCF), in which vaccination is not carried out, as there is no BCG vaccine in these departments. This vaccine is also not available in the children's departments of the HCF clinics, as children at the age of 7 are no longer vaccinated. To address the above issue, we have launched a study on the vaccination of children in Ukraine. Note that the study began before the Covid-19 pandemic, however, even then we encountered a generally negative attitude toward vaccinated children in Ukraine.

Address for correspondence: Krychkovska Aelita, Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, Lviv Polytechnic National University, Lviv 79013, Ukraine. aelita.m.krychkovska@lpnu.ua

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Aelita K, Roksolana K, Liliia B, Oksana L. Vaccine Prevention of Tuberculosis in Children: Outstanding Issues Family Medicine Systems in Ukraine. Arch Pharm Pract. 2022;13(4):17-23. <https://doi.org/10.51847/OMcaXT87jE>

This negative attitude, in our opinion, is because family medicine practitioners do not conduct information work with parents at the appropriate level. Also, pharmacies should be carried out educational work among the population of the country according to current legislation, however, this function, unfortunately, is also not performed by pharmacists [7].

The study aimed to investigate the dynamics of TB incidence in the country to conduct a study of the availability of anti-tuberculosis vaccines on the pharmaceutical market of Ukraine, identify existing problems with the negative attitude of citizens to the vaccination of children in Ukraine and outline ways to address them.

MATERIALS AND METHODS

The materials were data from official statistical databases on the incidence of TB population in Ukraine, the State Register of Medicines, and data from the survey of employees and students of higher education institutions (HEIs) on vaccination. The research methods were: a meta-analysis, statistical analysis, marketing office, field methods, and SWOT analysis.

RESULTS AND DISCUSSION

Every year, specialists of the Public Health Center of the Ministry of Health of Ukraine and the Center for Medical Statistics of the Ministry of Health of Ukraine are preparing an analytical and statistical reference book "Tuberculosis in Ukraine" and a package of documents on the incidence of TB in the regions of Ukraine [4]. We have worked out statistical data on the incidence of the TB population in the last four years (**Table 1**).

Table 1. Statistics on the incidence of tuberculosis in Ukraine

No	Nosology/years	2018*	2019	2020	2021
	<i>Total number of TB patients (ICD-10-CM code)</i>	8306	8103	6738	9825
1.	1.1. Pulmonary tuberculosis (ICD-10-CM code: A15.0 - 3, A16.0 - 2, A19)	7668	7461	6238	9014
	1.2. Extrapulmonary tuberculosis (ICD-10-CM code: A15.0 - 3, A16.0 - 2, A19)	638	642	500	811
2.	Relapses	1447	1315	1121	1863
3.	New cases	5775	5852	4944	7096
4.	Others	1084	936	673	866
5.	Men / women	6011/2295	5989/2114	4849/1889	7167/2658

*1st quarter of 2018

According to statistics of disease dynamics among the adult population, TB tends to decrease in relapses, however, for new cases this trend is unstable. The reduction of morbidity and recovery of patients should be associated, first of all, with the appearance on the pharmaceutical market of new drugs that act on resistant forms of mycobacteria. It should be noted that the vast majority of the country's adult population is vaccinated in the first days of life and revaccinated at the age of seven. Sometimes, if necessary, revaccination was performed at the age of 14.

In terms of the reliability of data on diagnostic studies of TB incidence, there are data until 2019, as further attention was focused on the problems that arose with the Covid-19 pandemic [8-10]. The coverage of the adult population with preventive and fluorographic examinations decreased to 45.9% in 2017, and the percentage of children aged 4–14 covered by tuberculin diagnosis decreased from 64.4% in 2012 to 49.7% in 2017 [3]. The percentage of detection of patients during preventive examinations to the total number of newly diagnosed patients decreased to 51.1% in 2017, a detection of patients with tuberculin diagnosis, although it increased to only 51.1%, but with insufficient preventive coverage of children aged 0-14 years (49.7% in 2017). The number of children under 1 year of age who received BCG prophylactic vaccination decreased to 83.6% in 2017, as did the number of children aged 7 and over to 46.0% in 2017.

Significantly increased the number of deaths from TB, in particular, according to observations in 2017 to 25.0%, the number of deaths from TB patients out of inpatient treatment gradually increased to 32.8%, indicating a late diagnosis of TB and underdiagnosis of patients [4].

The incidence rate of children (from 0 to 17 years) with TB in 2014 compared to 2013 decreased by 15% (respectively 11.9 and 10.1 per 100 thousand population, or 948 and 770 in absolute numbers). However, the incidence of TB among children in 2018 increased by compared to 2014 by 2.9%. In 2014, the incidence was 10.1 per 100 thousand population, and in 2018 - 10.4 per 100 thousand, or 770 and 788 in absolute terms, respectively [11].

In 2021 (**Table 1**) the incidence of TB in all indicators had a positive trend, which we explain as an increase in the number of diagnostic studies conducted on the population associated with the Covid-19 pandemic, and the detection of new cases and recurrences of the disease.

Thus, the question arises as to the expediency of abolishing BCG revaccination in Ukraine of children at the age of 7 and, if necessary, at the age of 14. Particular attention should be paid to solving the problem of supplying children's wards of polyclinics of HCF with the BCG vaccine.

In Ukraine, the CPVC in 2019 provides for vaccination against 10 diseases. All vaccinations before the age of 18 are free. People at risk, including doctors, students, the military, and educators, can get free vaccinations against measles, rubella, and mumps. However, in the absence of BCG vaccine supply to outpatient pediatric departments of HCF,

there is a need to purchase them at their own expense. Marketing analysis of the BCG and tuberculin market in Ukraine, allowed them to establish their presence in the State Register of Medicines, as well as their availability and cost in pharmacies (**Table 2**) [12].

Table 2. Availability of BCG vaccine and tuberculin according to the state drug registry

Name/dosage form	The composition of active substances	Producer	The applicant
RC № UA/14884/01/01 , validity RC unlimited from 16.12.2020:			
TUBERCULOSIS PREVENTION VACCINE LIVE, DRY BCG 10 powder and solvent for suspension for intradermal injection, 0.5 mg (10 doses), 5 ampoules of powder, and 5 ampoules of solvent in 1 ml (isotonic sodium chloride solution) in a cardboard box	one ampoule of BCG vaccine 10 (10 doses) contains 0.5 mg of live BCG mycobacteria; one dose (0.1 ml) of vaccine contains 50 µg of semi-dry mass of BCG mycobacteria, from 150,000 to 600,000 live BCG mycobacteria	BIOMED-LUBLIN, Poland POLPHARMA SA Pharmaceutical Works (solvent manufacturer), Poland	BIOMED-LUBLIN, Poland
RC № UA/16739/01/01 , the validity of RC from 06/05/2018 to 06/05/2023:			
TUBERCULIN PPD RT 23 SSI solution for injection 2 TO / 0.1 ml of 1.5 ml of solution (15 doses) in a vial; 1 or 10 vials in a cardboard box	One dose (0.1 ml) contains: 0.04 µg of tuberculin PPD RT 23 (2 TO) One vial (1.5 ml) contains: 15 doses of Tuberculin PPD RT 23 SSI (2 TO / 0.1 ml)	AJ Vaccines A / EU, Denmark	AJ Vaccines A / EU, Denmark
RC № UA/16761/01/01 , the validity of the RC from 06/15/2018 to 06/15/2023:			
TUBERCULIN PPD RT 23 SSI solution for injection 2 TO / 0.1 ml of 1.5 ml in bulk: in vials № 1300-1400 in a plastic bag	one dose (0.1 ml) contains: 0.04 µg of tuberculin PPD RT 23 (2TO); one bottle (1.5 ml) contains: 15 doses of Tuberculin PPD RT 23 SSI (2 TO / 0.1 ml)	AJ Vaccines A / EU, Denmark	AJ Vaccines A / EU, Denmark
RC № UA/16762/01/01 , the validity of the RC from 06/15/2018 to 06/15/2023:			
TUBERCULIN PPD RT 23 SSI solution for injection 2 TO / 0.1 ml; 1.5 ml of solution (15 doses) in a vial; 1 vial complete with 15 self-locking syringes in contour honeycomb packaging or without contour honeycomb packaging in a cardboard box	one dose (0.1 ml) contains: 0.04 µg of tuberculin PPD RT 23 (2 TO); one bottle (1.5 ml) contains: 15 doses of Tuberculin PPD RT 23 SSI (2 TO / 0.1 ml)	LUMIER PHARMA LLC (production in bulk packaging of the manufacturer AJ Vaccines A / ES, Denmark), Ukraine	LUMIER PHARMA LLC, Ukraine
RC № UA/15772/01/01 , RC validity is unlimited from 15.02.2017:			
BIOLIC TUBERCULIN PPD-L solution for injection with an activity of 2 TO / dose in bulk: 30 ampoules of 0.6 ml (6 doses), or 1 ml (10 doses), or 20 ampoules of 3 ml (30 doses) in a cardboard cell packaging; 10 or 20 cardboard honeycomb packages in a cardboard package	one dose of 0.1 ml contains allergen-tuberculoprotein - 2 TO (tuberculin units)	JSC "BIOLIK", Ukraine	JSC "BIOLIK", Ukraine
RC № UA/15771/01/01 , RC validity is unlimited from 15.02.2017:			
BIOLIC TUBERCULIN PPD-L solution for injection with an activity of 2 TO / dose of 0.6 ml (6 doses), 1 ml (10 doses), 3 ml (30 doses) in ampoules № 10; or set: 1 ampoule of 0.6 ml (6 doses), 3 syringes with needles for extraction, 3 needles for injection; or set: 1 ampoule of 1 ml (10 doses), 5 syringes with needles for extraction, 5 needles for injection	one dose of 0.1 ml contains allergen-tuberculoprotein - 2 TO (tuberculin units)	JSC "BIOLIK", Ukraine	JSC "BIOLIK", Ukraine

The cost of tuberculin in pharmacies in Ukraine ranged from 176 to 189 UAH or about € 6. The cost of the BCG vaccine has not been established, as it comes directly to maternity hospitals. Only the Uro-BCG vaccine, which costs UAH 3,000, can be purchased at pharmacies. or ~€ 95. Vaccination is offered in private HCF as a service with a pediatrician's

examination and the cost is from one hundred to 1 thousand UAH. However, BCG vaccination is not offered.

Several publications on the negative attitude of some citizens to preventive vaccinations and vaccination, in general,

prompted us to develop a specialized electronic questionnaire [13-15] (Table 3).

Table 3. Questionnaire on parents' awareness of the expediency of vaccination in childhood

Questionnaire on vaccination of children (16 questions)	
The purpose of the survey according to this questionnaire is to analyze the degree of awareness of parents and future parents about the feasibility of vaccination in childhood and determine the main reason for refusal of vaccination.	
1.	Specify your age
	a) 18-21 years b) 22-35 years c) 35-50 years d) over 50 years
2.	Education level, academic title
	a) student b) Ph.D. student c) academic d) associate professor e) professor
3.	In what locality do you live?
	a) a big city b) a small town c) a village (settlement, urban-type settlement)
4.	Are you already a parent or just planning to?
	a) yes, I have a child (ren). b) no, but I plan to shortly. c) no, and not planning.
5.	Have you been vaccinated against 10 diseases, which are carried out in the clinic free of charge in childhood?
	a) yes b) no
6.	If not, why?
	a) refusal of parents. b) lack of free vaccines. c) intolerance to vaccination.
7.	If so, were there any adverse reactions?
	a) yes b) no
8.	If so, did they lead to serious consequences?
	a) yes b) no adverse reactions were minor.
9.	Do you consider it appropriate to vaccinate your children?
	a) yes b) no
10.	The main reason for refusing to immunize a child:
	a) religious beliefs; b) the harm from vaccinations outweighs the risks of infection; c) I am afraid of side effects; d) I do not see the need; e) I believe that a child should not be vaccinated until a certain age; f) other (specify): _____
11.	Do you prefer paid or free vaccinations?
	a) payment. b) free of charge.
12.	Are you sufficiently informed about the benefits of vaccination?
	a) yes, enough. b) no.
13.	Where you get information about vaccinations:
	a) from the media (television, radio, newspapers, internet) (emphasis added); b) from a medical professional; c) not informed (a) about the need for vaccinations; d) other: _____
14.	Are you ready to permit vaccination if you receive detailed and reliable information about the vaccine?
	a) yes b) difficult to answer. c) no
15.	Do you understand and evaluate the consequences of an outbreak of an infection in the absence of vaccination?
	a) yes b) no c) difficult to answer.
16.	Are you ready to talk to a healthcare professional for a sufficient level of information about vaccination?
	a) yes b) no

The survey consisted of 16 questions, part of which was aimed at establishing the contingent of respondents, the second part of the questions concerned the respondent's own experience of vaccination, and a third part of the questions was asked to establish his attitude and desire for today and in the future regarding the vaccination of children.

The questionnaire was electronic, anonymous, and offered voluntarily to students, academics, employees of the administration, researchers, and other staff of two universities: Lviv Polytechnic National University (NU LP) and Danylo Halytsky Lviv National Medical University (LNMU).

As a result of the survey, the total contingent of respondents was: 173 people from OU LP and 73 people from LNMU, a total of 246 respondents. Our analysis of the passport part of the questionnaire in terms of age, level of education, and gender allow us to say that the sample of respondents is representative. The distribution of respondents in the two universities by age and level of education is presented in **Figures 1 and 2**.

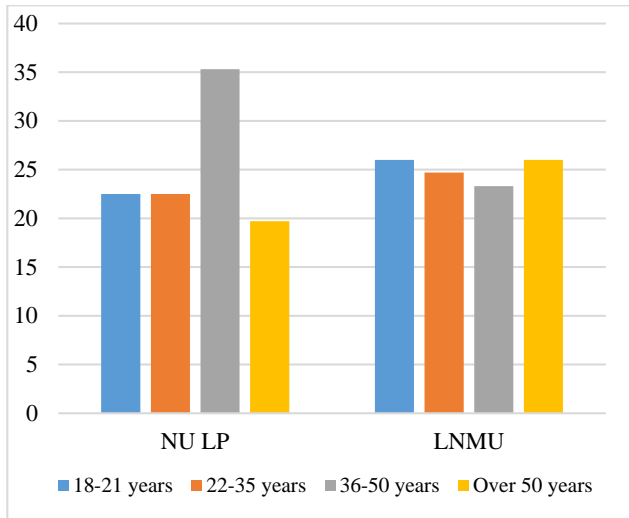


Figure 1. Distribution (%) of respondents by age of NU LP (173 answers) and LNMU (73 answers).

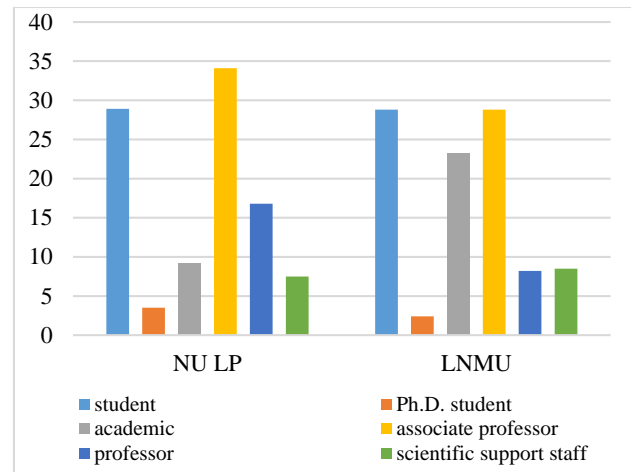


Figure 2. Distribution (%) of respondents of NU LP (173 answers) and LNMU (73 answers) by the level of education.

The presented distribution in the percentage of respondents of NU LP and LNMU by the level of education (**Figure 2**) indicates a high activity of respondents from among students and associate professors in the two HEIs. It is these two categories of respondents are parents or future parents.

The analysis of the data obtained as a result of the questionnaire on all questions allowed us to conduct a SWOT analysis and identify strengths and weaknesses, advantages and disadvantages of the process of vaccination of children in the opinion of their parents or future parents. The matrix of the SWOT analysis is presented in **Table 4**.

Table 4. Matrix of SWOT-analysis of vaccination of children in Ukraine

Component SWOT analysis	Possibility	Threats
	A. The state provides quality-free vaccines.	a) increase in child mortality in case of refusal of parents to vaccinate (in case of outbreaks).
B. Informing parents and future parents about the benefits and advantages of vaccination.	b) insufficient provision of vaccines to clinics;	
B. Checking children for vaccination idiosyncrasies.	c) poor quality vaccines, which may carry the risk of serious reactions, and parents will refuse to vaccinate their children.	
Strengths	SO - strategies	ST - strategies
I. Vaccination protects children from infections and prevents the severe course of the disease and complications - in case of infection.	- Develop a program or online application to inform parents about vaccination (B, a).	- Control at the state level over the provision of quality free vaccines (II, III, b, c.)
II. Vaccinations necessary for a child against 10 diseases are carried out in the clinic free of charge.	-Distribute information among the population about the benefits and advantages of vaccination (I, IV).	- Conduct conversations of future parents with doctors
III. Ukraine purchases only WHO-qualified vaccines.	- Conduct medical examinations with mandatory tests for the safety of vaccination (B, V.)	on the need for childhood vaccination (I, V, a)
IV. There are no alternatives to vaccination.		

V. If for some reason the child has not been vaccinated according to the calendar, vaccination is carried out according to an individual schedule drawn up by a doctor by the recommendations of the Ministry of Health of Ukraine.

Weak sides

1. There are cases when children are contraindicated on vaccination.
2. A child who has not received all vaccinations (due to parental refusal), may prohibit from attending a crèche or school during outbreaks of certain vaccine-preventable diseases.
3. Adherence to the vaccination schedule (some vaccines, such as rotavirus and Haemophilus type b infection, should not be given unless they have been started or completed by a certain age)
4. Some inconveniences of free vaccination (queues at the clinic, insufficient number of vaccines) and high cost of paid vaccines.

WO – strategies

- 1) Creation of rapid tests for vaccine tolerability (1, B,)
- 2) Creating an online vaccination schedule or a special application with notifications of vaccination dates (3,4, B)
- 3) Development of a quality system of free vaccination and raising the level of work of medical institutions (4, A)

WT – strategies

- 1) Strengthen the responsibility of parents for refusing vaccination (2, a)
- 2) Ensure at the state level the availability of quality vaccines (4, b, c)

The development of a matrix of SWOT-analysis of vaccination allowed to analyze of five strategies that will positively influence the attitude of parents toward the process of vaccination of children in Ukraine, namely: a strategy for the creation and implementation of preliminary rapid tests for vaccine tolerability; creating an online vaccination schedule or a special application with notifications about the dates of vaccination individually for each child; development of a high-quality free vaccination system and raising the level of information and sanitary-educational work of medical (pharmaceutical) institutions; strengthening the responsibility of parents for refusing to vaccinate their children; strategy to ensure quality vaccines at the state level. It should be noted that cases of misdiagnosis of tuberculosis in adults occur. These cases have serious consequences for mental and social health of the patient [16].

In the study, we did not consider drugs that are used for the pharmacotherapy of tuberculosis in adults [17], as well as the problem of tuberculosis resistance to known drugs [18].

A number of scientists are studying the problems of developing new types of anti-tuberculosis vaccines, as well as the possibility of improving existing vaccines [19, 20]. These questions are relevant and provide a perspective for further research.

CONCLUSION

It is necessary to introduce a new approach to the BCG vaccination process for newborns who are transferred in the first days of life to specialized inpatient departments of other CHCs and who have not been vaccinated in maternity hospitals. Understanding the social problems faced by the patient can help not only to solve some of them but also to consciously approach the need for vaccination and revaccination of children.

Early and timely detection of TB patients is a necessary condition for their rapid and complete treatment, and is also crucial to prevent the spread of infection, as patients with pulmonary TB are epidemiologically dangerous.

The informational and educational work of medical and pharmaceutical workers is an integral part of their professional responsibilities and should cover the issue of vaccination of children, as opinion, unfortunately, is mainly influenced by inaccurate information from Internet resources. It is important to implement developed strategies to promote the vaccination of children among the population, especially strategies such as creating an online vaccination schedule or a special application with notifications about vaccination dates and developing a quality system of free vaccination, and improving the level of medical (pharmaceutical) HCF.

ACKNOWLEDGMENTS: None

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

ETHICS STATEMENT: All measures accomplished in this scientific trial containing human supporters remained in similarity through the ethical principles of the institutional advisory group.

REFERENCES

1. Order of the Ministry of Health of Ukraine dated 11.11.2021 No. 2506 "On approval of the Amendments to the Regulation on the organization and implementation of vaccination prevention, the Procedure for ensuring proper conditions of storage, transportation, use, and vaccination, accounting for toxoids and allergen for tuberculosis: <https://alergova.ua/zakon.rada.gov.ua/laws/show/z1527-21#Text>
2. Order of the Ministry of Health of Ukraine dated May 18, 2018 No. 947 "On Amendments to the Calendar of Preventive Vaccinations in Ukraine" - Access mode: <https://zakon.rada.gov.ua/laws/show/z0659-18#Text>
3. Order of the Ministry of Health of Ukraine dated July 3, 2020 No. 1510 "Changes to the calendar of preventive vaccinations in Ukraine" - Access mode: <https://zakon.rada.gov.ua/laws/show/z1013-20#Text>
4. The situation with tuberculosis in Ukraine during the period of health care reform [Electronic resource] / Yu.V. I. Feshchenko, V. M. Melnyk, V. G. Matusevich. – Access mode: <http://amnu.gov.ua/sytuacziya-z-tuberkulozu-v-ukrayini-v-period-reformuvannya-ohorony-zdorov-ya/>
5. Analytical and statistical materials on TV. [Electronic resource] Access mode: <https://phc.org.ua/kontrol-zakhvoryuvan/tuberkuloz/statistika-z-tb/analitichno-statistichni-materiali-z-tb>In Ukraine, the National Calendar of preventive vaccinations has been updated. [Electronic resource] Access mode: <https://moz.gov.ua/article/news/v-ukraini-onovleno-nacionalnij-kalendar-profilaktichnih-sheplen2018>

6. Law of Ukraine "On Ensuring Sanitary and Epidemic Welfare of the Population" dated 24.02.1994 No. 4004-XII, as amended from 14.01.2021. Access mode: <https://zakon.rada.gov.ua/laws/show/4004-12#Text>
7. Global research on coronavirus disease (COVID-19). Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov>
8. Casey MF, Price L, Markwalter D, Bohrmann T, Tsujimoto TM, Lavin K, et al. Advance Care Planning for Emergency Department Patients with COVID-19 Infection: An Assessment of a Physician Training Program. *Am J Hosp Palliat Care*. 2022;10499091211072850. doi:10.1177/10499091211072850
9. European Commission, Directorate-General for Communication, The EU and the Coronavirus pandemic, 2022. Available from: <https://data.europa.eu/doi/10.2775/401085>
10. Ustinov AV. Tuberculosis in Ukraine: equal morbidity is decreasing. Morion Publishing House [Electronic resource] Access mode: <https://www.umj.com.ua/article/139407/tuberkuloz-v-ukrayini-riven-zahvoryuvanosti-znizhuetsya>
11. State Register of Medicinal Products of Ukraine. Available from: <http://www.drz.com.ua/>
12. Wu Q, Dudley MZ, Chen X, Bai X, Dong K, Zhuang T, et al. Evaluation of the safety profile of COVID-19 vaccines: a rapid review. *BMC Med*. 2021;19(1):1-6. doi:10.1186/s12916-021-02059-5
13. Walach H, Klement RJ, Aukema W. The safety of covid-19 vaccinations—we should rethink the policy. *Vaccines*. 2021;9(7):693. doi:10.3390/vaccines9070693
14. Machingaidze S, Wiysonge CS. Understanding COVID-19 vaccine hesitancy. *Nat Med*. 2021;27(8):1338-9. doi:10.1038/s41591-021-01459-7
15. Freitas BC, Meneguello JE, Eugenio LG, Lemos R, Scodro RB, Siqueira VL, et al. Cord factor producer *Mycobacterium abscessus* subsp. *bolletii* in asymptomatic immunocompetent host sputa samples. *Braz J Pharm Sci*. 2022;58. doi:10.1590/s2175-97902022e19504
16. Ibnouf EO, Elegami AA, Waggiallah HA. The Effect of Some Sudanese Medicinal Plant Extracts on Some Clinically Isolated Pulmonary Tuberculosis Bacteria. *Int J Pharm Phytopharmacol Res*. 2021;11(2):31-7. doi:10.51847/wvOdR4Dg15
17. Pulingam T, Parumasivam T, Gazzali AM, Sulaiman AM, Chee JY, Lakshmanan M, et al. Antimicrobial resistance: prevalence, economic burden, mechanisms of resistance and strategies to overcome. *Eur J Pharm Sci*. 2021;106103. doi:10.1016/j.ejps.2021.106103
18. Firouzi Z, Jaafari MR, Sankian M, Zare S, Tafaghodi M. A novel nanomicelle composed from PEGylated TB di-peptide could be successfully used as a BCG booster. *Iran J Basic Med Sci*. 2022;25(2):223-31.
19. Garg NK, Dwivedi P, Jain A, Tyagi S, Sahu T, Tyagi RK. Development of novel carrier (s) mediated tuberculosis vaccine: More than a tour de force. *Eur J Pharm Sci*. 2014;62:227-42. doi:10.1016/j.ejps.2014.05.028