Public health

THE PRIORITIZATION OF ZOONOSES IN THE REPUBLIC OF NORTH MACEDONIA – DO WE NEED ONE HEALTH APPROACH

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Abstract

Zoonoses have a different impact on public health, determined by geographical and socio-economic factors, which requires their prioritization for prevention and control purposes to be performed at the national level. Prioritization of zoonoses is a mechanism used in policy-making, primarily in allocating available resources.The aim of the paper was to compare two different methods used for prioritization of zoonoses by the Institute of Public Health (IPH) and Food and Veterinary Agency (FVA). Material and methods: IPH used a method prepared by the U.S. Centers for Disease Control and Prevention (CDC), - One Health Zoonotic Disease Prioritization (OHZDP) tool, adapted to national conditions (2019). FVA used a standardized semi-quantitative method based on the OIE Methodological Manual (List and Categorization of priority diseases in animals including those transmitted to humans). A total of 21 zoonoses were selected, based on their importance for the human and veterinary sector. These diseases were ranked according to the stated criteria of the two previously conducted prioritizations and their comparison was performed. Results: With the prioritization conducted by IPH and FVA the first 5 ranked zoonoses were: hemorrhagic fevers with renal syndrome, leishmaniasis, tularemia, brucellosis and listeriosis. With the prioritization carried out by the FVA the first 5 ranked zoonoses were: bovine brucellosis, bovine tuberculosis, salmonellosis, avian influenza and West Nile fever. A Cumulative Annual Incidence was taken as a control parameter. Regarding this, the 5 first ranked zoonoses were: echinococcosis, brucellosis, Lyme fever, leishmaniasis and tularemia. Conclusions: A comparative analysis of the separate lists of priorities for human and veterinary medicine shows that only a certain percentage overlap. Also, the presence of a number of zoonoses with endemic character, but also a more pronounced risk of new emergent diseases, determines the need to provide consensus on the methodology of prioritization of zoonoses, and its formalization and institutionalization, as a crucial step towards identification and prioritization of zoonoses that would be the subject of joint programs and interventions.

Јавно здравје

ПРИОРИТИЗАЦИЈА НА ЗООНОЗИТЕ ВО РЕПУБЛИКА СЕВЕРНА МАКЕДОНИЈА – ДАЛИ Е ПОТРЕБЕН ПРИСТАП НА ЕДНО ЗДРАВЈЕ

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Извадок

Зоонозите имаат различен импакт врз јавното здравство, детерминирано од географските и социоекономските фактори, што условува нивната приоритизација за цели на превентива и контрола да биде изведена на национално ниво. Целта на трудот беше да се споредат два различни метода што се користат за приоритизирање на зоонозите од Институтот за јавно здравје (ИЈЗ) и Агенцијата за храна и ветеринарство (АХВ). Материјал и методи: ИЈЗ користеше метод подготвен од U.S. Centers for Disease Control and Prevention (CDC), - One Health Zoonotic Disease Prioritization (OHZDP) алатка, прилагодена на националните услови (2019). АХВ користеше стандардизиран полуквантитативен метод заснован на методолошкиот прирачник на OIE (List and Categorization of priority diseases in animals including those transmitted to humans). Беа селектирани вкупно 21 зоонози, врз основа на нивната важност за хуманиот и ветеринарниот сектор. Овие зоонози беа рангирани според наведените критериуми на двете претходно спроведени приоритизации и беше извршена нивна споредба. Резултати: Со приоритизација спроведена од ИЈЗ и АХВ (семиквантитативен метод Rist CDC), први 5 рангирани зоонози беа: хеморагични трески со бубрежен синдром, лајшманијаза, туларемија, бруцелоза и листериоза. Со приоритизација спроведена од АХВ (модификација на квантитативниот метод на OIE), први 5 рангирани зоонози беа: бруцелоза кај говеда, туберкулоза кај говеда, салмонелоза, авијарна инфлуенца и западнонилска треска. Како контролен параметар беше земена кумулативната годишна инциденца (КГИ). Првите 5 рангирани зоонози согласно КГИ беа: ехинококоза, бруцелоза, лајмска треска, лајшманијаза и туларемија. Заклучоци: Споредбената анализа на одделните листи на приоритетни зоонози за хумана и ветеринарна медицина покажува дека само одредени зоонози се преклопуваат. Исто така, присуството на голем број зоонози со ендемичен карактер, но и поизразен ризик од појава на нови заболувања, ја одредува потребата да се обезбеди консензус за методологијата на приоритизација на зоонози, како и нејзино формализирање и институционализација, како клучен чекор кон идентификување и приоритизирање на зоонози кои би биле предмет на заеднички програми и интервенции.

Introduction

Zoonoses are infectious diseases that can be transmitted between animals and humans, directly or indirectly, and especially through direct contact and / or through food. Zoonoses pose a persistent public challenge due to the dynamic and complex nature of the problem[1]. Apart from the basic characteristics of infectious diseases that make them a subject of special interest for human and veterinary medicine, zoonoses have a special feature that makes them a common problem for both disciplines. The importance of zoonoses for human medicine and public health stems from their pathogenicity to humans, but also the economic losses they can directly and indirectly inflict on farmers and business operators, as well as their overall socio-economic impact[2-4].

Prioritization is defined as a process of evaluation of a group of entities and their ranking in order of their importance or urgency, i.e. systematization in relation to certain predefined criteria - a process of defining priorities in most areas of public health[3]. Defining the priorities in the field of infectious diseases and classification of the most important pathogens in terms of their importance for a certain country - prioritization is applied by several institutions and countries. Prioritization as an instrument is especially important when creating certain policy and allocating public health resources in a given country.

In the past, recognized prioritization methods were used by a range of health professionals to identify infectious diseases in the domain of public health and animal health, for national surveillance and risk assessment programs, including zoonoses.

Prioritization methodologies have been developed and discussed for different goals and priorities. Methods, depending on the selection criteria and the ranking of pathogens, are defined as qualitative, semi-quantitative and quantitative[5]. Different methods have been used by researchers. The published materials on the process of prioritization of diseases differ in the number of pathogens that are ranked, the number of criteria by which they are ranked and the methods used. Quantitative methods are applied when there is empirical data, such as disease burden, and socio-economic impact as well as when there are effective surveillance systems. Semiquantitative and qualitative methods are used when data are insufficient or not available at all[2].

The aim of the paper was to compare two different methods used for prioritization of zoonoses by the Institute of Public Health (IPH) and Food and Veterinary Agency (FVA).

Materials and methods

IPH used the method developed by the U.S. Centers for Disease Control and Prevention (CDC), - One Health Zoonotic Disease Prioritization (OHZDP) tool, adapted to national conditions (2019)[5].

FVA used the standardized semi-quantitative method based on the OIE Methodological Manual (List and Categorization of priority diseases in animals including those transmitted to humans). The methodology is based on the document of the World Organization for Animal Health - Office International des Epizooties (OIE)[6]. The methodology is officially adopted by the Food and Veterinary Agency[7].

The categorization itself is conducted in three phases:

- Preparation of a List of infectious diseases in animals that are categorized and prioritized (with special reference to zoonoses) and a list of infectious diseases - zoonoses in humans, according to the national legislation for zoonoses that are legally regulated in human and veterinary medicine [8, 9].

- Provision and processing of data on zoonoses in the human population and animal population.

- Implementation of categorization and prioritization of zoonoses from the previously defined list in accordance with certain criteria and values and comparison with the list of IPH and the cumulative annual incidence (CAI) [10].

Phase 1 List of zoonoses that are categorized and prioritized

The lists of zoonoses that are categorized and prioritized are prepared on the so-called legal basis, i.e. only the diseases that are legally regulated are included. The list of infectious diseases in animals that are categorized and prioritized is prepared as a joint combined list of diseases that are legally regulated in accordance with the national legislation of North Macedonia and a list of diseases that are legally regulated in accordance with EU legislation. This list also includes zoonoses that are important from the aspect of veterinary public health (foodborne infections and intoxications and vector borne diseases).

Phase 2

The first prioritization was made by the Institute of Public Health (IPH),

in cooperation with representatives of the FVA, with the methodology of the U.S. Centers for Disease Control and Prevention (CDC), - One Health Zoonotic Disease Prioritization (OHZDP) tool, adapted to national conditions (2019). Prioritization is based on the One Health Approach methodology developed by CDC Atlanta in several steps[5]:

First step - preparation of a working group with representatives from the human and veterinary sector and preparation of a list of zoonoses that should be ranked. The list of diseases that are subject to ranking (prioritization) is composed of selected zoonoses and vector communicable diseases that are subject to mandatory reporting in the public health sector and in the veterinary sector. Second step - defining criteria for selection of public health significance of zoonoses, selected in the first step. Third step - developing questions by defining a categorical question for each of the criteria selected in the second step. Fourth step - ranking of the criteria with individual ranking of the criteria specified in step 2 by each representative, and then the individual grades are combined and a common list of ranked criteria is obtained. Fifth step - ranking the zoonoses where each zoonosis is scored based on the answers for each criterion, the scores for each disease are summed and normalized according to the maximum score, thus obtaining the final list of priority diseases.

Results

List of ranked zoonoses according to the methodology of IPH is presented in Table 1.

Table 1. List of ranked zoonoses according to the methodology of IPH

Zoonosis	Total points	Normalized result	Rank
Hemorrhagic fevers with renal syndrome	24.00	1.00	1
Leishmaniasis	23.17	0.97	2
Tularemia	23.17	0.97	3
Brucellosis	22.58	0.94	4
Listeriosis	21.92	0.91	5
West Nile Virus Infections	21.67	0.90	6
Salmonellosis	20.67	0.86	7
Leptospirosis	19.75	0.82	8
Tetanus	19.75	0.82	8
Echinococcosis	19.08	0.80	10
Verotoxigenic E. coli infection	18.42	0.77	11
Trichinellosis	17.83	0.74	12
Avian Influenza (HPAI, LPAI)	17.67	0.74	13
Anthrax	16.50	0.69	14
Lyme fever	16.33	0.68	15
Rabies	13.75	0.57	16
Q Fever	13.00	0.54	17
Prion diseases	11.25	0.47	18
Pestis	10.25	0.43	19
Encephalitis (arthoborne)	9.75	0.41	20
Campylobacteriosis	9.00	0.38	21
Rift Valey Fever	0.00	0.00	22
Japanese encephalitis	0.00	0.00	22
Glanders	0.00	0.00	22
Giradiasis	0.00	0.00	22
Shigelosis	0.00	0.00	22

The second categorization and prioritization were conducted by the FVA (2019 and 2020). For each disease in the List of the 4 criteria the value

from 0 to 3 is determined. After assigning the values for each disease the total numerical value is determined, which can range from 0 to 3. After obtaining the total numerical value, diseases are sorted in order of the total numerical value from the highest to the lowest value. The zoonoses are extracted from the list and their order is given in Table 2.

Table 2. List of ranked zoonoses in veterinary health according to FVA

Zoonosis	A1	B2	C3	G4	Total score
Bovine Brucellosis	3	3	3	3	12
Bovine Tuberculosis	3	3	3	3	12
Brucellosis in goats and sheep (with the exception of Brucella ovis)	3	3	3	3	12
Salmonellosis (zoonotic salmonella) of importance in public veterinary health	3	3	3	3	12
Avian Influenza (HPAI and LPAI)	2	3	3	3	11
West Nile Virus Fever	0	3	2	2	7
Verotoxigenic E. coli	0	3	2	2	7
Rabies virus infection	0	3	0	3	6
Echinococcosis	3	3	0	0	6
Campylobacteriosis	3	3	0	0	6
Listeriosis	3	3	0	0	6
Trichinellosis	3	3	0	0	6
Anthrax	2	3	0	0	5
Equine Encephalomyelitis	2	0	2	0	4
Glanders	0	3	0	0	3

Table 3. List of zoonoses and vector borne diseases that are subject to mandatory reporting as diseases or microbiologically proven causes of disease in humans, and annual incidence of occurrence in North Macedonia in the period 2013-2019

	CAI	IPH	FVA
Hemorrhagic fevers with renal syndrome	0	0.69	0.250
Leishmaniasis	0.7	0.94	1.000
Tularemia	0	0.57	0.250
Brucellosis	1	0.8	0.500
Listeriosis	0.1	0.97	0.000
West Nile Virus Infections	0	0.54	0.000
Salmonellosis	0.2	0.68	0.000
Leptospirosis	0	0.47	0.000
Tetanus	0	0.82	0.000
Echinococcosis	0	0.74	0.500

Verotoxigenic E. coli infection	0	0.82	0.000
Trichinellosis	0.1	0.97	0.000
Avian Influenza (HPAI, LPAI)	0	0.43	0.000
Anthrax	n.d	0.86	1.000
Lyme fever	n.d	0.77	0.000
Rabies	n.d	0	0.000
Q Fever	n.d	0.91	0.500
Prion diseases	n.d	0.38	0.500
Pestis	n.d	0	0.000
Encephalitis (arthoborne)	n.d	0.9	0.583
Campylobacteriosis	n.d	0	0.000
Rift Valey Fever	n.d	0	1.000
Japanese encephalitis	n.d	0.74	0.917
Glanders	n.d	0	0.250
Encephalitis Arboborne	n.d	0.41	0.000

Phase 3

A total of 21 zoonoses that are important for the human and veterinary sector were selected. These diseases were ranked according to the stated criteria of the two previously prioritized and their comparison was performed.

With the prioritization conducted by IPH and FVA (semi-quantitative method Rist CDC) the first ranked 5 zoonoses were: hemorrhagic fevers with renal syndrome, leishmaniasis, tularemia, brucellosis and listeriosis.

With the prioritization carried out by the FVA (quantitative method modification of OIE), the first 5 ranked zoonoses were: bovine brucellosis, bovine tuberculosis, salmonellosis, avian influenza and West Nile fever.

A Cumulative Annual Incidence was taken as a control parameter. In the cumulative annual incidence, the first 5 ranked zoonoses were: echinococcosis, brucellosis, Lyme fever, leishmaniasis and tularemia.

A comparative overview of the ranked zoonoses from the two prioritizations compared to CAI is given in Table 4.

Table 4. Comparative analysis of the top five ranked zoonoses with CAI.

Ranking	IPH	FVA	Cumulative Annual Incidence
1	Hemorrhagic fevers with renal syndrome	Bovine Brucellosis Brucellosis in goats and sheep	Echinococcosis
2	Leishmaniasis	Bovine Tuberculosis	Brucellosis
3	Tularemia	Salmonellosis (zoonotic salmonella) of importance in public veterinary health	Lyme fever
4	Brucellosis	Avian Influenza (HPAI and LPAI)	Leishmaniasis
5	Listeriosis	West Nile Virus Infections	Tularemia

Discussion

A certain number of countries are prioritizing infectious diseases: the Netherlands[11], Germany[12]; Canada [13,14]. Prioritization is also carried out by international organizations (WHO, OIE) or government agencies (ECDC) (EFSA) [15-19].

In Macedonia until 2019 there was no formalized and official prioritization of zoonoses. Establishing a system of scientifically based prioritization of zoonoses enables policy makers as well as risk managers to make evidence-based decisions (Cardoen 2009) and to develop targeted programs and interventions. To date, a number of different models have been developed, using different approaches and techniques.

Selecting or developing an appropriate method is a crucial step in implementing prioritization. Rist (2014) emphasizes the fact that the initial step in joint activities is the identification of diseases and / or pathogens that are of the greatest importance, so that limited financial and human resources can be effectively directed. Cardoen (2009) emphasizes the semiquantitative method as a method that overcomes the problems that arise with quantitative methods - lack of data and the problems that arise in qualitative methods as subjectivity. The choice of a national method is conditioned by the available data, their uniformity and the level of legislative and regulatory regulation of zoonoses at a given moment. An important factor in determining the methodology is the ultimate goal of prioritization.

Second, the selection of criteria on the basis of which the prioritization would be carried out is the most sensitive point, although it is the basic determinant for the performance of the method. It should be borne in mind that the choice of criteria is largely conditioned by both the context and the ultimate goal of prioritization. Quantitative methods are less arbitrary; real values are used, and the disadvantage is that they are extensive and require detailed processing of large amounts of data, and there can always be a problem that certain data may be missing.

Allocation of limited resources is a continuous problem of state institutions in charge of prevention and control of zoonotic agents and alimentary infections and intoxications[1]. The results from qualitative and semi-quantitative approaches are highly dependent on the perception of individual experts, which requires further validation of the methodology and comparative analysis with other types of methodologies. Having in mind that the selection of categorization and prioritization criteria is a crucial element in the validity of the process itself, public health decisions should take into account all factors, including social values, public perception and opinion, as well as opinion of professional circles, actual policy and economic factors.

Regarding the comparative prioritizations, it can be seen that there are differences in the results. The results of the prioritization conducted only from the aspect of veterinary medicine do not correspond to the occurrence and incidence of zoonotic diseases in the human population and the prioritization conducted to the IPH.

According to CAI, the diseases with the highest incidence are echinococcosis, brucellosis, Lyme fever, leishmaniasis and tularemia per 100,000

inhabitants. The mentioned CAI also differ from the list of prioritization of IPH and FVA.

Only one disease (brucellosis) has been identified in all three lists. Tularemia and leishmaniasis have been identified in two lists, the other zoonoses are present only on individual lists.

If the most realistic data is taken, the actual occurrence of zoonoses in the human population, i.e. the cumulative annual incidence, it follows that the results of the prioritization of the two institutions do not overlap, and furthermore, they also differ from the actual situation on the ground.

The different ranking of individual zoonoses and the inability to provide a correlation with the values of the cumulative incidence indicate the need for a uniform integrated method of prioritization of zoonoses and the need to focus on zoonoses that have the most significant load.

In the context of the prioritization of zoonoses in the Republic of North Macedonia, two main factors are imposed in the development of the method.

The first factor and the main obstacle in this approach is the lack of an appropriate officially recognized methodology for the two segments of zoonoses (human medicine and veterinary medicine) as well as their insufficient integration and in some cases compatibility. This in turn results in an uncoordinated and therefore not always effective response to public health challenges and threats. It is necessary to provide a unique and flexible methodology that would be recognized and accepted by both sectors and which would simultaneously meet the needs of both sectors, taking into account their different priorities, opportunities and resources.

The second factor is that at the moment there is no uniformity of presentation of data between sectors at the national level and also at the international level. Therefore, the data from the EU institutions are used (in cases when there is data for North Macedonia), or international institutions when such data are not available at EU level. In all aspects, the prioritization method should be efficient in ranking, standardization, reproducibility and transparency.

The selection of criteria was made in accordance with the recommendations or methodologies of other authors. Efforts have been made to ensure a balanced share of the criteria in terms of human health and veterinary health. The findings are not analyzed in terms of their epidemiological and epizootic criteria, given that the main goal is to determine the different outcomes of prioritization when applying certain different methodologies, and display the results of the ranking.

The presented methodology has to be reproducible, standardized and transparently based on publicly available data, which allows its application to continue.

The first important point is that the medical and socio-economic impact, as well as the burden on public health is largely conditioned by the geographical and time period of occurrence2, which requires the prioritization to take place at the national level and in certain time periods. The second important point is enabling and using a unique and integrated methodology for the human and veterinary sector. The different ranking of individual zoonoses and the inability to provide

a justified correlation with the values of the cumulative incidence indicate the need for a uniform integrated method of prioritization of zoonoses and the need to focus on the zoonoses that have the highest burden, and not the zoonoses for which there is greater awareness.

Continuous implementation over a period of time, with subsequent new inputs as a result of changes in prevalence and values of other criteria would allow obtaining a real picture. The development and implementation of an appropriate effective and applicable method for prioritizing diseases is imposed as a priority. A strong contribution to the common prioritization methodologies is the provision of a common position for effective and efficient supervision, coordinated and integrated laboratory capacity, multi-sectoral projections and forecasting, the construction of joint control and prevention strategies.

endemic character, but also a more pronounced risk of new emergent diseases, determines the need to provide consensus on the methodology of prioritization of zoonotic diseases, and its formalization and institutionalization, as a crucial step towards identification and prioritization of zoonoses that would be the subject of joint programs and interventions.

Determination of uniform model can be an initial step in the formal identification and prioritization of zoonoses and pathogens that are of utmost importance to the state and with effective directing of financial resources. The method, based on the internationally recognized methodology, provides a process in which a priority list of zoonoses is prepared on a quantitative method, which allows to reduce the subjective approach to the lowest possible level, given that decisions are based on data, and not on estimation and opinions.

Conclusion

The result of the prioritization process is a ranked list of zoonoses of equal importance to the human and veterinary sectors. Prioritization is an effective tool in creating and implementing health policies, especially in the parts where there is an overlap of sectors with different priorities (zoonoses, human and veterinary medicine).

A comparative analysis of the separate lists of priorities for human and veterinary medicine shows that only a certain percentage overlap. Zoonoses, and especially emergent and re-emerging diseases, pose a serious threat to both humans and animals. This presupposes an equal integrated response in both the human and veterinary sectors. Also, the presence of a number of zoonoses with

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