Perspectives

PRIORITISATION OF INFECTIOUS DISEASES IN PUBLIC HEALTH - CALL FOR COMMENTS

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In order to allocate rationally resources for research and surveillance of infectious diseases at the level of the German public health institute (RKI), we prioritised pathogens by public health criteria. After screening the relevant literature we developed a standardised methodology including a three-tiered scoring system for selected pathogens. The pathogens were rated in four categories containing a total of 12 criteria: burden of disease including incidence, severity, mortality; epidemiologic dynamic including outbreak potential, trend, emerging potential; information need including evidence on risk factors/groups, validity of epidemiologic information, evidence for pathogenesis; international duties and public attention; health gain opportunity including preventability, treatability. For each criterion a numerical score of +1, 0 or -1 was given and each criterion received a weight by which the numerical score of each criterion was to be multiplied. The total weighted scores ranged from +22.7 (influenza) to - 64.4 (cholera) with the median being -22.9 (rubella). Relevant changes were observed between weighted and unweighted scores. The chosen approach proved to be feasible and the result plausible. However, in order to further improve the methodology we invite experts to give feedback on the methodology via a structured web-based questionnaire at www.rki.de/EN > Prevention of infection > Infectious Disease Surveillance > Pathogen prioritization. Results of this survey will be included in a modification of the methodology.

Background

One of the challenges of public health is that infectious disease control covers a wide range of pathogens requiring diverse methods for prevention and control. Furthermore, infectious diseases vary greatly in occurrence, severity and other factors that make it difficult to compare the public health importance of the underlying pathogens. Resources for research, surveillance and other public health activities are limited; it is therefore of major importance to allocate rationally these resources by using public health criteria. The agendas of institutions in the field of public health and infectious diseases, however, are fragmented and experts are increasingly specialised, making it difficult to find institutions or individuals who would be able to prioritise a broad range of infectious diseases without being biased by individual professional focus on one hand or lack of specific pathogen-related knowledge on the other.

In the past decade a number of efforts have been made to prioritise systematically infectious diseases by public health criteria resulting in different outcomes depending on the objectives and methodology used [1-5]. But even prioritisation schemes with similar objectives have applied different sets of criteria as illustrated in Table 1.

In 2004 the department for infectious disease epidemiology of the Robert Koch Institute (RKI), the national public health institute in the portfolio of the German federal ministry of health, initiated a prioritisation exercise to guide the research and surveillance strategies of the department [6]. Initial findings were presented at three international scientific conferences in 2006 and 2007 [7-9].

After this a publication in a nationwide non-scientific journal [10] elicited considerable and unexpected interest from the general public and the scientific community. Therefore, as part of updating and improving the current prioritisation methodology, we would like to present this methodology also to the broader international public health community outside the RKI and Germany to collect suggestions for improvement. In the following we describe and evaluate the methodology of the prioritisation previously conducted by the RKI to provide the background information necessary for comment on our approach. We cordially invite comments on the proposed methodology via a web-based questionnaire accessible at http://www.rki.de/EN > Prevention of infection > Infectious Disease Surveillance > Pathogen prioritization.

Methodology

While preparing our exercise we analysed prioritisation efforts over the past decade by searching the literature in Medline using the search terms prioritisation OR priority AND (surveillance OR infectious diseases OR public health) and based on presentations from the EAN workshop on "New Tools for early Warning" that took place in Lyon on 6 and 7 February 2004, [1-5,18,19]. A flow chart of our methodology is presented in Figure 1.

A list of pathogens was compiled based on one or more of the following criteria: notifiable according to German law [11], reportable within the European Union according to European regulations [12], listed as chapters in selected established manuals and textbooks on infectious diseases [13-15], causative agent in outbreaks reported to RKI in the past 10 years, agent with potential for deliberate release [16]. In the following we list the pathogens but also refer to the related diseases in humans.

Every pathogen was rated according to the 12 criteria listed in Table 2. For each criterion a numerical score of +1, 0 or -1 was given as defined in Table 2. The score of +1 represented high and a score of -1 low importance with respect to a criterion. A score

Comparison of the evaluation criteria of different schemes for prioritisation of infectious diseases (the prioritisation by Reseau National de Santé Publique, 1995, France, is not included as it contained categorisation principles rather than criteria) between 1995 and 2008

Reference	Rushdy & O'Mahony 1998 (3)	Weinberg et al 1999 (20)	Doherty 2000 (1)	Horby et al 2001 (2)	Institute de Veille Sanitaire (InVS) 2001 (5)	World Health Organisation 2003 (4)	Krause et al. 2008 (6)
Country	United Kingdom	European Union	Canada	United Kingdom	France	South East Europe	Germany
Group of criteria	Specific name of criteria (as used in respective publications)						
International aspects and public concern	- public concern - public health laboratory service (PHLS)-added value	- international surveillance programmes	- international consideration - risk perception - potential to drive public health policy - other sector interest	-public concern	- not applied -	- not applied -	- international duties and public attention
Occurrence	- not applied -	- not applied -	- incidence	- not applied -	- epidemiology	- not applied -	- incidence
Epidemiologic dynamic	- potential threat	- not applied -	- potential spread - changing patterns	- potential threat	- not applied -	-potential threat -long term effects on communicable diseases	- outbreak potential - trend - emerging potential
Burden of disease	- burden of ill health	- not applied -	- severity	- burden of ill health	- not applied -	-disease impact -present burden of ill health	- severity - mortality
Health gain opportunity	- health gain opportunity	- not applied -	- preventability	- health gain opportunity	- prevention and control measures	-low incidence only maintained by public health activities - health gain opportunity - necessity for immediate public health response	- preventability - treatability
Socioeconomic aspects	- social/economic impact	- collective economic impact	- socioeconomic burden	- social/economic impact	- not applied -	-social/economic impact	- not applied -
Information need	- not applied -	- not applied -	- not applied -	- not applied -	- not applied -	- not applied -	- evidence for risk factors/groups - validity of epidemiologic information - evidence for pathogenesis
Other	- not applied -	- not applied -	- not applied -	- not applied -	- veterinary public health	- not applied -	- not applied -

Work flow for prioritisation, Robert Koch Institute, 2008
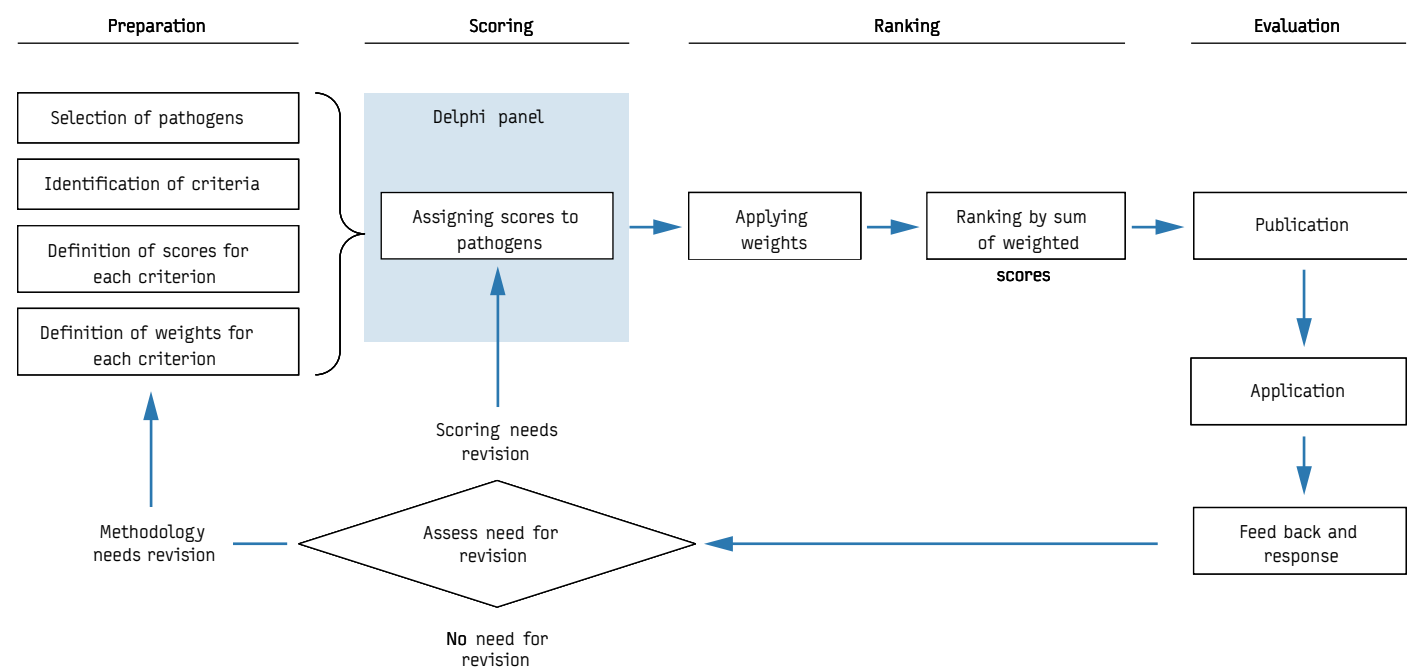
of 0 referred to pathogens with average importance or pathogens, for which lack of knowledge or opinion of the participants in the working group did not allow a decision for one of the other two scores.

Each criterion received a weight by which the numerical score of each criterion was to be multiplied. Hence for each pathogen a sum of the unweighted and a sum of the weighted scores was generated. The weight of each criterion was determined before and independently of the categorisation for each pathogen: all participants were asked to put the 12 criteria in a sequential order with 12 being the most important and one being the least important criterion. An average was computed for each criterion, defining its weight. The total weighted score was defined as the sum of the weighted scores of all 12 categories per pathogen. These were finally normalised to the spectrum of the unweighted total scores to allow comparisons. We demonstrate the effect of weighting by presenting detailed data on the highest, lowest and median ranking pathogen as well as for the two pathogens with adjacent ranks to the median rank.

Results

The overview of prioritisation exercises in Table 3 shows that objectives, methodological approaches and especially the level of standardisation differed considerably in these efforts. Partly due to different objectives of the prioritisation, also the number and type of criteria varied. Categories used by most groups are incidence, burden of disease and opportunity for health gain [1-5], which are included in our exercise.

The working group on prioritisation consisted of eleven senior epidemiologists and infectious disease specialists at the department for infectious disease epidemiology at RKI. They categorised a list of 85 pathogens shown in Table 4.

The distribution of the normalised ranks is presented in Figure 2 and detailed scores for selected diseases are shown in Table 5. The total weighted scores ranged from +22.7 (influenza) to - 64.4 (cholera) with the median being -22.9 (rubella). The spectrum found in the total unweighted scores contained 12 possible ranks ranging from +2 to -9. Table 5 demonstrates the differences obtained from weighting for some selected pathogens.

TABLE 2

Criteria and definition of the respective scores for the prioritisation of pathogens, Robert Koch Institute, 2008

Criteria	Values		
	-1	0	1
Burden of disease			
Incidence	<1/100.000	1/100.000-20/100.000	>20/100.000
Severity	hospitalisation is very rare, work loss less than 2 days, no persisting handicaps	hospitalisation is rare, work loss of more than 5 days is rare, very rarely persisting handicaps	hospitalisation is frequent, work loss of more than 5 days is frequent, persisting handicaps do occur
Mortality*	<50 deaths/year in Germany	between 50 und 500 deaths /year in Germany	more than 500 deaths /year in Germany
Epidemiologic dynamic			
Outbreak potential	outbreaks are very rare	outbreaks with 5 or more cases are rare	outbreaks with 5 or more cases are frequent
Trend	diminishing incidence rates	stable incidence rates	increasing incidence rates
Emerging potential	disease already endemic or very unlikely to be introduced to Germany	disease has the potential to be introduced to Germany sporadically	disease is likely to emerge in Germany in a relevant way
Information need			
Evidence for risk factors /groups	risk factors and risk groups are identified based on scientific evidence	risk factors and risk groups are basically known but scientific evidence is missing	risk factors and risk groups are not known
Validity of epidemiologic information	epidemiologic situation is well known and scientifically valid	epidemiologic information exists but is scientifically not very valid	epidemiologic information is insufficient
International duties and public attention	no international duties or political agenda, minor public attention	no international duties but informal political expectations, moderate public attention	international duties or explicit political agendas, high public attention
Evidence for pathogenesis	information on pathogenesis and transmission routes is available and well supported by scientific evidence	information on pathogenesis and transmission routes is basically available but not well supported by scientific evidence	information on pathogenesis and transmission routes is hardly available
Health gain opportunity			
Preventability	there are hardly any possibilities for prevention or there is no need for prevention	concepts for prevention are established but there is need for further research to improve its effectiveness	strong need for further research on preventive measures because need for prevention is clear but concepts for prevention are missing
Treatability	medical treatment is rarely necessary or effective treatments are available to positively influence the burden of disease or the prognosis	medical treatment is frequently indicated but medical treatments only have a limited influence on the burden of a disease or the prognosis	medical treatment is desirable but currently there is no treatment available that positively influences the burden of disease or the prognosis
Proposed alternative to mortality			
Case fatality rate*	<0,01%	0,01- 1%	> 1%

Distribution of pathogens by total weighted and un-weighted scores during prioritisation, Robert Koch Institute, 2008

Reference	Anonymous 1995 (19)	Rushdy & O'Mahony 1998 (3)	Weinberg *et al* 1999 (20)	Doherty 2000 (1)	Horby *et al* 2001 (2)	Institute de Veille Sanitaire (InVS) 2001 (5)	World Health Organisation 2003 (4)	Krause et al. 2008
Year	1995	1997	1997	1998	1999	2000-2001	2002	2005
Country	France	United Kingdom	European Union	Canada	United Kingdom	France	South East Europe	Germany
Organisation	Reseau National de Santé Publique (RNSP)	Public health laboratory service (PHLS) Overview of Communicable Diseases Committee	Charter group of European Commission (EC)	Canadian Advisory Committee on Epidemiology	Public health laboratory service (PHLS) Overview of Communicable Diseases Committee	Institute de Veille Sanitaire (InVS)	Dubrovnik Pledge / World Health Organisation	Robert Koch Institute
Prioritisation objective	select diseases for surveillance	programme initiatives in infectious disease control	select diseases for surveillance in	select diseases for surveillance	programme initiatives in infectious disease control	prevention of non-food-borne zoonotic diseases	select diseases for surveillance	epidemiological research and surveillance
Number of diseases	84	33 (+8 generic disease groups)	26	43	58 (+11 generic disease groups)	37	53	85
Number of criteria	3 principles	5 criteria	9 criteria	10 criteria	5 criteria	> 5 criteria	8 criteria	12 criteria
Scoring system	No	5-tiered	5-tiered	3-, 4-, and 6-tiered	5-tiered	not quantifiable	5-tiered	3-tiered
Score-specific definition	no	no	no	yes	no	no	no	yes
Weighting applied	no	no	no	implicitly	no	no	no	systematically
Methodology of collecting opinion	Delphi	survey	Delphi	Delphi	survey	working group	Delphi	Delphi
Number of participants	over 50	194	14	6	518	10	not published	11
Type of participants	interministerial and regional experts	experts in communicable disease control and public health laboratory service (PHLS)	heads of national institutions with responsibilities for communicable diseases surveillance	provincial epidemiologists	different health care professionals	interministerial and regional experts	participants of World Health Organisation workshop (not published)	epidemiologists at national public health institute (RKI)

List of pathogens selected for prioritisation, Robert Koch Institute, 2008

Adenovirus	*Escherischia coli*, shigella toxin producing (STEC/HUS)	*Leishmania* spp.	*Salmonella* typhi
Babesia microti	*Echinococcus granulosus*	*Leptospira interrogans*	*Shigella* spp.
Bacillus anthracis	*Echinococcus multilocularis*	*Listeria monocytogenes*	*Staphylococcus aureus*, methicillin resistant (MRSA)
Bartonella spp.	*Ehrlichia chaffeensis*	Measles virus	*Staphylococcus aureus*, toxigenic
Bordetella pertussis	*Entamoeba histolytica*	*Microsporum* spp.	*Streptococcus* spp. other than *Str. pneumoniae*
Borrelia burgdorferi	Epstein-Barr virus	Molluscipoxvirus	*Streptococcus pneumoniae*
Brucella abortus	*Francisella tularensis*	Mumps virus	*Toxoplasma gondii*
Bovine Spongioform Encephalitis (BSE)/ variant Creutzfeldt Jakob Disease (vCJD)	*Giardia lamblia*	*Mycobacterium* Leprae	*Treponema pallidum*
Campylobacter jejuni	*Haemophilus influenzae*	*Mycobacterium tuberculosis*	*Trichinella spiralis*
Central European tickborne encephalitis virus	Hanta virus	*Mycobacterium*, other (non-tuberculous)	*Trichomonas vaginalis*
Chlamydophila pneumoniae	*Helicobacter pylori*	*Mycoplasma* spp.	Varicella virus
Chlamydophila psittaci	Hepatitis A virus	*Neisseria gonorrhoeae*	Variola virus
Chlamydia trachomatis	Hepatitis B virus	*Neisseria meningitidis*	*Vibrio cholerae*
Clostridium botulinum	Hepatitis C virus	Norovirus	Viruses, others causing hemorrhagic fevers
Clostridium tetani	Hepatitis D virus	Parvovirus B 19	West Nile virus
Corynebacterium diphtheria	Hepatitis E virus	*Plasmodium* spp.	Yellow fever virus
Coxiella burnetii	Herpes simplex virus (HSV)	Polio virus	*Yersinia enterocolitica*
Cryptosporidium parvum	Human immunodeficiency virus (HIV)	Rabiesvirus	*Yersinia pestis*
Cyclospora cayetanensis	Human papilloma virus (HPV)	Rota virus	*Yersinia pseudotuberculosis*
Cytomegalovirus	Human T-cell lymphotrophic virus (HTLV)	Rubellavirus	
Dengue virus	Influenza virus	*Salmonella* spp. (non typhi non paratyphi)	
Escherichia coli, enteropathogenic (non STEC/HUS)	*Legionella pneumophila*	*Salmonella* paratyphy	

Discussion and conclusions

The described methodology builds on the experiences of similar efforts [1-5,18, 19] and attempts to increase the level of standardisation and transparency in prioritising pathogens based on public health criteria. In comparison to the cited prioritisation efforts, our approach may appear overly standardised. We believe, however, this ensures transparency and reproducibility, which are important, especially as prioritisation may easily affect funding and policy issues. Furthermore, our methodology allows for adaptations if certain conditions change e.g. if a vaccine becomes available or if the incidence changes significantly.

The result of the prioritisation at RKI shows a multi-modal distribution with the majority of scores below 0 indicating that, with a given definition of scores and a list of diseases to prioritise, participants tended to opt more frequently for lower scores. Therefore, we propose to replace the criterion of mortality by case fatality, as presented in Table 2, because mortality is implicitly dependant on incidence, whereas case fatality is another criterion for burden of disease complementing the criterion of severity. Among the selected diseases presented, the proposed exchange would somewhat lower the score for influenza but it does not seem to result in a relevant change of ranking.

A five-tiered scoring system as used in the overview of communicable diseases or in the Dubrovnik pledge could allow for a more differentiated scoring than the three-tiered system we used [2-4]. However, the challenge to generate clear definitions for each score increases with the number of scores. For many diseases

and criteria information may not be available in the detail needed to permit such a differentiated approach.

The examples in Table 5 demonstrate that some diseases that were far apart in the unweighted scaling moved close together after weighting had been applied. This makes it obvious that weighting is important and that it may result in changes in both directions. There is reason to believe that the objectiveness of the procedure is increased if weighting is done independently of, and prior to,

FIGURE 2

Distribution of pathogens by total weighted and unweighted scores during prioritisation, Robert Koch Institute, 2008
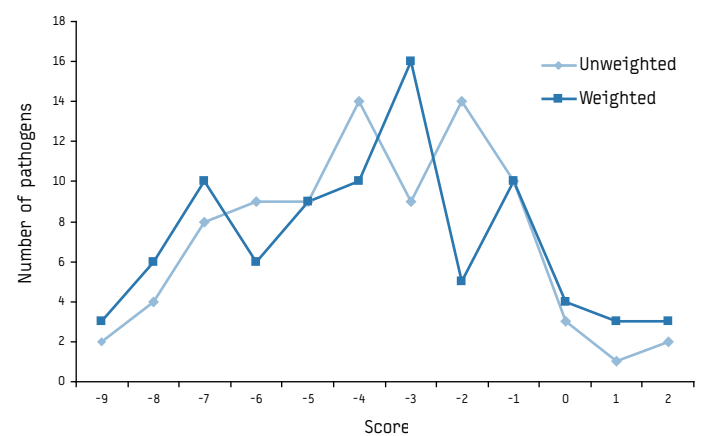

TABLE 5

Prioritisation scores for five selected pathogens out of 85, Robert Koch Institute, 2008

Disease	Weight	Crude weighted scores				
		Maximum		Median		Minimum
		Influenza	Rotavirus	Rubella	Cyclosporiasis	Cholera
Burden of disease						
Incidence	10.7	10.7	10.7	0	-10.7	-10.7
Severity	10.3	0	-10.3	-10.3	-10.3	0
Mortality	8.4	8.4	0	-8.4	-8.4	-8.4
Epidemiologic dynamic						
Outbreak potential	10.1	10.1	10.1	10.1	0	-10.1
Epidemiologic trend	7.7	0	0	0	0	-7.7
Emerging potential	5.4	-5.4	-5.4	-5.4	0	0
Information need						
Evidence for risk factors /groups	5.5	-5.5	-5.5	-5.5	5.5	-5.5
Validity of epidemiologic information	5.4	-5.4	-5.4	0	5.4	-5.4
Political agendas, public awareness	5.2	5.2	0	-5.2	-5.2	0
Evidence for pathogenesis	3.4	-3.4	-3.4	-3.4	0	-3.4
Health gain opportunity						
Preventability	8.0	8	-8	0	0	-8
Treatability	5.2	0	-5.2	5.2	0	-5.2
Total weighted score (crude)		22.7	-22.8	-22.9	-23.7	-64.4
Total unweighted score		1	-5	-4	-2	-9
Total weighted score (normalised to a scale from +2 to -9)		2	-4	-4	-4	-9

scoring. This is a way to avoid individual preferences of participants biasing the process. The advantage of quantitatively determining the weight for each individual criterion is that other institutions may choose to apply different weights to adapt the ranking to their respective mission. This increases the flexibility of the system and allows it to be used for different applications. For example the Eurostat task force on human health issues related to food safety has recently adopted a number of our criteria and also our concept of weighting in an attempt to identify the top 20 diseases from the inventory of food safety related diseases in Europe. (Ana Martinez, Eurostat, personal communication)

Call for comments

For an upcoming update of our prioritisation methodology we plan to include the views from experts from various fields and institutions outside the RKI.

While suggesting that a structured prioritisation approach similar to the one presented here is useful, there are still a number of questions that we plan to re-assess before going through such a procedure again:
- Does the list contain all relevant pathogens?
- Do the 12 criteria cover the relevant characteristics for prioritisation and are they not redundant or strongly dependant on each other? If other categories are missing, would the available information suffice to allow scoring based on defined scores?
- For which categories would a five-tiered scaling be a major improvement and if so would it be feasible to generate clear definitions for each scale?
- Are the existing definitions for the three scores for each criterion clear and plausible? Can they be applied? Are they valid to detect differences?
- Is the weighting of the criteria plausible?
- How large should the group of participating experts be and how should it be composed?

We invite suggestions, feedback and answers to the questions above through a structured web-based questionnaire available from http://www.rki.de/EN > Prevention of infection > Infectious Disease Surveillance > Pathogen prioritization. This may initiate a fruitful discussion in the scientific community and provide some guidance on how to improve our prioritisation scheme and maybe that of other institutions. Ultimately, we hope this will in return contribute to rational allocation of attention and resources in the control and prevention of infectious diseases.

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References

1. Doherty J-A. Establishing priorities for national communicable disease surveillance. Can J Infect Dis. 2000;11(1):21-4.
2. Horby P, Rushdy A, Graham C, O'Mahony M, PHLS Overview of Communicable Diseases Committee. PHLS overview of communicable diseases 1999. Commun Dis Public Health. 2001;4(1):8-17.
3. Rushdy A, O'Mahony M. PHLS overview of communicable diseases 1997: results of a priority setting exercise. Commun Dis Rep CDR Suppl. 1998;8(5):S1-12.
4. World Health Organization (WHO). The Dubrovnik pledge on surveillance and prioritization of infectious diseases. Report on a WHO Meeting, Bucharest, Romania, 21–23 November 2002. Copenhagen: WHO; 2003. Available from: http://www.euro.who.int/document/e78888.pdf
5. Institut de Veille Sanitaire (InVS). Definition of priorities in the area of non-food-borne zoonoses 2000-2001. [In French]. St. Maurice: InVS; 2002. Available from: http://www.invs.sante.fr/publications/2002/def_priorite_zoonoses/index.html
6. Krause G, Working Group on Prioritization at Robert Koch Institute. How can infectious diseases be prioritized in public health? A standardized prioritization scheme for discussion. EMBO Rep. 2008;9 Suppl 1:S22-7.
7. Krause G, Alpers K, Benzler J, Bremer V, Claus H, Haas W, et al. Prioritising infectious diseases in Germany [Poster]; International Meeting on Emerging Diseases and Surveillance, 23.-25.02.2007 Vienna, Austria.
8. Krause G, Alpers K, Benzler J, Bremer V, Claus H, Haas W, et al. Standardised Delphi Method for Prioritising Foodborne and Zoonotic Diseases in Germany [Poster]; Priority Setting of Foodborne and Zoonotic Pathogens; 19.-21.07.2006 Berlin, Germany.
9. Krause G. Prioritization of Infectious Diseases by Public Health Criteria, 8th EMBO/EMBL Joint Conference on Science and Society; 2.-3.11.2007 Heidelberg, Germany.
10. Mayer K-M. Parade der Keime - Deutschlands Seuchenexperten reihen erstmal Infektionserreger nach deren Gefährlichkeit. Focus 2007 Mar 5;44.
11. Gesetz zur Neuordnung seuchenrechtlicher Vorschriften - (Seuchenrechtsneuordnungsgesetz - SeuchRNeuG vom 20. Juli 2000). Bundesgesetzblatt 2000;33(Teil I - G5702):1045-77.
12. Decision No 2119/98/EC of the European Parliament and of the Council. European Commission Communicable Disease Network Committee; 1998.
13. Heymann D. Control of Communicable Diseases Manual. Washington: American Public Health Association; 2004.
14. Murray P, Baron EJ, Pfaller MA, Tenover FC, Yolken RH. Manual of Clinical Microbiology. Washington: American Society for Microbiology; 1999.
15. Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases. Washington: American Society for Microbiology; 2005.
16. Tegnell A, Van Loock F, Baka A, Wallyn S, Hendriks J, Werner A, et al. Development of a matrix to evaluate the threat of biological agents used for bioterrorism. Cell Mol Life Sci. 2006;63(19-20):2223-8.
17. Jones J, Hunter D. Qualitative research: Consensus methods for medical and health services research. BMJ. 1995 5;311(7001):376-80.
18. Reseau National De Sante Publique (Saint-Maurice). Revision de la politique de Surveillance des Maladies infectieuses. 1995 Oct 24.
19. Weinberg J, Grimaud O, Newton L, On behalf of the Charter Group. Establishing priorities for European collaboration in communicable disease surveillance. Eur J Public Health. 1999;9(3):236-40.