

# How can infectious diseases be prioritized in public health?

A standardized prioritization scheme for discussion

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The prevention and control of infectious diseases involves dealing with numerous pathogens, each of which poses a specific threat to public health. In order to rationally allocate the limited resources for research, surveillance and other activities, it is necessary to prioritize infectious diseases; how to do this is the dilemma that public-health experts face. The scientific literature abounds with examples in which the authors request that one specific disease or health issue be recognized as a priority for research, for surveillance or for funding, often accompanied by plausible arguments. Yet, few publications address the issue of prioritization in a comparative and transparent manner, and even those that do usually refer to research priorities in the fields of nursing, occupational health or public health in low-income countries.

This failure to prioritize effectively is due to many factors, including: an intrinsic difficulty in defining measurable criteria for the importance of disease in terms of public health; a lack of data—in part because of insufficient research in this field—for quantifying or measuring these criteria; a mixture of criteria by which to prioritize, some of which are driven by medical or social factors and others by political and cultural ones; and the difficulty of agreeing on a weighting scheme for those factors.

In any case, any form of prioritization is only useful in the context in which it is conducted. Naturally, it is impractical to compare the relative priority of a wildlife research project with that of a project about bone-marrow transplant. However,

a non-medical research group specializing in disease-transmitting ticks might benefit from the prioritization of its research agenda, and would probably find transparent and comparable criteria in common with purely medical-focused research. Yet, the benefit would be limited to this specific group and, in general, the larger the frame of prioritization, the greater the challenge to agree on universally applicable criteria.

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Even within the area of infectious disease research, various disciplines—clinical research, molecular biology, microbiology, virology, mycology, parasitology, veterinary sciences and epidemiology, to name a few—are involved. Despite this multidisciplinary mix, some efforts have been made to prioritize infectious diseases by using criteria that are applicable to all.

In 1995, British scientists began an ongoing consultation exercise—the ‘Overview of Communicable Diseases’—which has subsequently involved more and more participants, in order to guide rational and transparent service planning and resource allocation (Horby *et al*, 2001; Rushdy & O’Mahony, 1998). So far, the overview has assessed and prioritized 58 diseases and 11 generic disease groups according to five criteria. Also in

1995, the French Government asked a group of experts to revise its national policy on infectious disease surveillance and to sort diseases according to priority, albeit without applying a uniformly systematic set of criteria (Reseau National De Sante Publique, 1995). In 1997, a charter group informed the European Commission about priority areas for European collaboration in the field of communicable disease. The group applied a so-called Likert-type scale in nine specific categories (Weinberg *et al*, 1999). Although the categories were sorted by importance, there was no precise weighting allocated to the criteria. In 1998, the Canadian Advisory Committee on Epidemiology (CACE) used criteria to prioritize 43 communicable diseases for national surveillance (Doherty, 2000). In 2001, another French initiative attempted to prioritize zoonoses and applied a set of criteria that were unfortunately not translated into a quantifiable score (Institut de Veille Sanitaire, 2002). In 2002, as part of the so-called ‘Dubrovnik Pledge’ to coordinate public-health activities, representatives from seven south-east European countries conducted a prioritization exercise for disease surveillance using eight criteria (WHO, 2002), although the different criteria were not weighted and the scores were not defined.

All of these initiatives should be commended for systematically addressing the need to prioritize infectious diseases; they all applied a variable amount of standardization and relied on the judgement of expert groups using, to a certain extent, the Delphi method. However, the method used by the CACE in 1998 seems to be the only one so far that has

published definitions for each score given. This is an important point: if the meanings of individual scores are not clearly defined, the members of a Delphi panel might interpret them differently. Another problem that these prioritization efforts have shared is that there has been no transparent weighting scheme applied to the different criteria, implying that each criterion had equal importance. Although the CACE approach did implicitly use weighting—because different criteria had different scoring scales—it remains unclear how the weights were determined.

In 2004, the Department for Infectious Disease Epidemiology at the Robert Koch Institute (RKI; Berlin, Germany)—the national public-health institute of the German Federal Ministry of Health—initiated its own prioritization exercise to guide its research and surveillance strategies. We developed a methodology to address the issue of defining scores and weights for all criteria used to prioritize infectious diseases. We presented our initial findings at three international scientific conferences and our work also received some interest from the general print media in Germany, the wider public and the general scientific community (Mayer, 2007). As the acceptance of any prioritization scheme can benefit from general debate and eventual agreement about methodology, here we describe a revised categorization scheme for discussion in the scientific community, in order to further improve and consolidate the methodology. Readers are cordially invited to contact the authors to comment on the proposed methodology, and we will take their comments into consideration for further improvement of the prioritization scheme.

**The idea of prioritization is to come up with a relative ranking rather than to define an absolute cut-off beyond which diseases are not considered important**

We compiled a list of pathogens for prioritization based on the criteria shown in Table 1. The criteria assessed the importance of a disease according to whether it is notifiable under German law, reportable within the European Union, listed as a chapter in established manuals and textbooks on infectious diseases (Heymann, 2004; Mandell *et al*, 2005; Murray *et al*, 1999), a causative agent

of an outbreak reported to the RKI in the past 10 years or an agent with the potential for deliberate abuse (Tegnell *et al*, 2006).

Each pathogen identified by these criteria was then rated according to the burden of disease (incidence, severity and mortality), the epidemiological dynamic (outbreak potential, trend and emerging potential), the information requirement (evidence of risk factors/groups, validity of epidemiological information, international duties and public attention, and evidence for pathogenesis), and the opportunities for prevention and treatment. Each of these was weighted as shown in Table 1.

A score of 0 was given to pathogens of average importance, or pathogens for which a lack of knowledge or opinion precluded another score. Each criterion was assigned a weighting by which the numerical score was multiplied. We then generated a sum of unweighted scores and a sum of weighted scores for each pathogen. In addition, all participants reviewed the final results for plausibility, which led to a revised definition of values and some corrections in the categorization.

The weights of each criterion were determined before—and independently of—the categorization for each pathogen: all of the participants were asked to put the 12 criteria in sequential order, with 12 being the most important and 1 being the least important. The weight was then calculated as the average for each criterion. The total weighted score was defined as the sum of the weighted scores of all 12 categories per pathogen. These were finally normalized to the unweighted total scores to allow comparisons. To show the effect of the weighting, we present the data on some selected pathogens with highest, lowest and median ranking in Table 2.

The Working Group on Prioritization involved 11 senior epidemiologists and infectious disease specialists from four different units of the Department for Infectious Disease Epidemiology at the RKI, who together categorized 85 pathogens (Sidebar A). The total weighted scores ranged from +22.7 for influenza to –64.4 for cholera, with a median score of –22.9 for rubella (Fig 1). The range of the total unweighted scores contained 12 possible ranks from +2 to –9. After normalization of the total weighted scores, influenza received a weighted rank of +2 compared to an unweighted rank of +1. Cholera still ranked

last together with two other diseases with a score of –9, and rubella kept its median rank with a score of –4 regardless of whether the score was weighted or not. However, two diseases with similar crude weighted scores to rubella would have received different ranks without weighting: rotavirus moved one rank up from unweighted –5 to a normalized weighted rank of –4; cyclosporiasis moved down from an unweighted –2 to a weighted –4.

**As the acceptance of a prioritization effort can only be as good as the acceptance of the applied methodology, we want to initially put the methodological aspects up for discussion and refine them before updating the prioritization exercise**

The described methodology attempts to establish a systematic and transparent manner of prioritizing pathogens for a German national public-health institute. The result shows a multimodal distribution wherein most pathogens have scores lower than 0, which indicates that the participants tended to assign lower scores more frequently. The idea of prioritization is to come up with a relative ranking rather than to define an absolute cut-off beyond which diseases are not considered important. Therefore, it is not necessary for the median to be close to 0. The outcome among the sample diseases is plausible, considering that in Germany, influenza would be expected to appear on the upper end and cholera on the lower end of the priority list. In countries with endemic cholera this might, of course, be different.

We intentionally do not publish a list of all prioritized diseases, in order to focus the discussion on the methodology. As the acceptance of a prioritization effort can only be as good as the acceptance of the applied methodology, we want to initially put the methodological aspects up for discussion and refine them before updating the prioritization exercise.

Our methodology builds on the experiences of similar efforts, which were presented above. Depending on the main purpose of prioritization, the number and content of the categories in these published efforts vary considerably. Most groups used categories

**Table 1** | Criteria and definition of their scores for the prioritization of pathogens

Criteria	Values		
	-1	0	1
<i>Burden of disease</i>			
Incidence	< 1/100,000	1–20/100,000	> 20/100,000
Severity	Hospitalization is rare, work loss is < 2 days, no persisting handicaps	Hospitalization is rare, work loss of > 5 days is rare, few persisting handicaps	Hospitalization is frequent, work loss of > 5 days is frequent, persisting handicaps occur
Mortality	< 50 deaths/year in Germany	50–500 deaths /year in Germany	> 500 deaths/year in Germany
<i>Epidemiological dynamic</i>			
Outbreak potential	Outbreaks are rare	Outbreaks with five or more cases are rare	Outbreaks with five or more cases are frequent
Trend	Diminishing incidence rates	Stable incidence rates	Increasing incidence rates
Emerging potential	Disease already endemic or 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
<i>Information need</i>			
Evidence for risk factors/groups	Risk factors and risk groups are identified based on scientific evidence	Risk factors and risk groups are known but scientific evidence is missing	Risk factors and risk groups are not known
Validity of epidemiological information	Epidemiological situation is well known and scientifically valid	Epidemiological information exists but is not scientifically valid	Epidemiological 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 available but not well supported by scientific evidence	Information on pathogenesis and transmission routes is rarely available
<i>Health-gain opportunity</i>			
Preventability	There are few possibilities, or there is no need, for prevention	Concepts for prevention are established but there is a need for further research to improve effectiveness	Strong need for further research on preventive measures because they are required 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 treatments are frequently indicated but have a limited influence on the burden of 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
<i>Proposed alternative to mortality</i>			
Case-fatality rate	< 0.01%	0.01–1%	> 1%

including incidence, burden of disease and the opportunity for public-health interventions (Doherty, 2000; Horby *et al*, 2001; Institut de Veille Sanitaire, 2002; Rushdy & O’Mahony, 1998; WHO, 2002). Other criteria reflect the demands of specific groups, such as veterinary-health factors being used to prioritize zoonoses, or international aspects for prioritization efforts involving European collaboration (Institut de Veille Sanitaire, 2002; Weinberg *et al*,

1999). As the main purpose of our work is to guide surveillance and research activities in the field of infectious-disease control and epidemiology in Germany, it is not surprising that most of our categories relate strongly to public health in general and to epidemiology in particular. On the basis of the experience of our exercise, we propose to replace the criterion of mortality with a criterion of case fatality, as presented in Table 1. Mortality implicitly depends on

incidence, whereas case fatality is another criterion for burden of disease, which complements the criterion of severity. Among the selected diseases shown here, the proposed exchange of criterion would lower the score for influenza, but would not significantly change the ranking itself.

In comparison to the cited prioritization efforts, our approach makes the scoring more transparent and reproducible by explicitly defining each score. Although

Table 2 | Prioritization scores for 5 out of 85 pathogens

Disease	Crude weighted scores					
	Weight	Influenza (maximum)	Rotavirus	Rubella (median)	Cyclosporiasis	Cholera (minimum)
<i>Burden of disease</i>						
Incidence	10.7	10.7	10.7	0.0	-10.7	-10.7
Severity	10.3	0.0	-10.3	-10.3	-10.3	0.0
Mortality	8.4	8.4	0.0	-8.4	-8.4	-8.4
<i>Epidemiological dynamic</i>						
Outbreak potential	10.1	10.1	10.1	10.1	0.0	-10.1
Epidemiological trend	7.7	0.0	0.0	0.0	0.0	-7.7
Emerging potential	5.4	-5.4	-5.4	-5.4	0.0	0.0
<i>Information need</i>						
Evidence for risk factors/groups	5.5	-5.5	-5.5	-5.5	5.5	-5.5
Validity of epidemiological information	5.4	-5.4	-5.4	0.0	5.4	-5.4
Political agendas and public awareness	5.2	5.2	0.0	-5.2	-5.2	0.0
Evidence for pathogenesis	3.4	-3.4	-3.4	-3.4	0.0	-3.4
<i>Health-gain opportunity</i>						
Preventability	8.0	8.0	-8.0	0.0	0.0	-8.0
Treatability	5.2	0.0	-5.2	5.2	0.0	-5.2
Total weighted score (crude)	-	22.7	-22.8	-22.9	-23.7	-64.4
Total unweighted score	-	1.0	-5.0	-4.0	-2.0	-9.0
Total weighted score (normalized to a scale from +2 to -9)	-	2.0	-4.0	-4.0	-4.0	-9.0

complete standardization is not possible, published definitions of the scores allow erroneous scoring to be identified, discussed and corrected. This presents the possibility of making adjustments if certain conditions change; for example, if a vaccine becomes available or if the incidence changes significantly. The scoring must, of course, be applied within the given framework, which in our case is public health in Germany. The case-fatality rate for rotavirus, for example, is likely to be much lower in Germany than in many countries in the Southern Hemisphere.

The high level of standardization allows for the individual and anonymous collection of the judgements of participants. This is an essential component of the Delphi methodology to avoid group dynamics that would bias the judgement of individual participants (Jones & Hunter, 1995). However, it implies that all of the Delphi panel members have a common understanding of the

scoring criteria, which is another reason for the importance of clear definitions.

A five-tiered scaling system—as used in the overview of communicable diseases or in the Dubrovnik Pledge—could provide a more differentiated scale than the three-tiered system that we used (Horby *et al*, 2001; Rushdy & O'Mahony, 1998; WHO, 2002). However, the challenge to generate clear definitions for each scale increases with the number of scales, and there might not be sufficient detailed information available for many diseases and criteria to allow such a differentiated approach.

We think it is important that the weighting of the criteria be transparent; it increases the objectiveness of the procedure if the weighting is done independently from, and preferably before, the scoring, in order to avoid bias from the individual preferences of participants. In our exercise, three diseases that were originally far apart in the unweighted scaling moved closely together

after the weighting. This shows that weighting is important and that it might result in changes in both directions.

The advantage of quantitatively determining the weight for each criterion is that other institutions might choose to apply different weights in order to adapt the ranking to their individual mission. For example, a ministry of health might wish to increase the weight of the category on international duties and public attention, whereas an institution specialized in developing treatments might increase the weight of treatability. The Eurostat Task Force on Human Health Issues Related to Food Safety has recently adopted several of our criteria and our concept of weighting to identify the top 20 diseases from the inventory of food safety-related diseases in Europe.

Our Working Group on Prioritization consisted of scientists who specialized in various areas of infectious disease, and were members of the Department for Infectious

Sidebar A | Pathogens selected for prioritization, listed in alphabetical order

Adenovirus	<i>Escherichia coli</i> , enteropathogenic (non STEC/HUS)	Influenza virus	<i>Salmonella paratyphi</i>
<i>Babesia microti</i>	<i>Escherichia coli</i> , shigella toxin producing (STEC/HUS)	<i>Legionella pneumophila</i>	<i>Salmonella typhi</i>
<i>Bacillus anthracis</i>	<i>Echinococcus alveolaris</i>	<i>Leishmania</i>	<i>Shigella</i>
<i>Bartonella bacilliformis</i>	<i>Echinococcus multilocularis</i>	<i>Leptospira interrogans</i>	<i>Staphylococcus aureus</i> , methicillin-resistant (MRSA)
<i>Bordetella pertussis</i>	<i>Ehrlichia chaffeensis</i>	<i>Listeria monocytogenes</i>	<i>Staphylococcus aureus</i> , toxigenic
<i>Borrelia burgdorferi</i>	<i>Entamoeba histolytica</i>	Measles virus	<i>Streptococcus</i>
<i>Brucella abortus</i>	Epstein–Barr virus	<i>Microsporium</i>	<i>Streptococcus pneumoniae</i>
Bovine spongiform encephalopathy (BSE)/variant Creutzfeldt–Jakob disease (vCJD)	<i>Francisella tularensis</i>	Molluscipoxvirus	<i>Toxoplasma gondii</i>
<i>Campylobacter jejuni</i>	<i>Giardia lamblia</i>	Mumps virus	<i>Treponema pallidum</i>
Central European tick-borne encephalitis (TBE) virus	<i>Haemophilus influenzae</i>	<i>Mycobacterium leprae</i>	<i>Trichinella spiralis</i>
<i>Chlamydia pneumoniae</i>	Hantavirus	<i>Mycobacterium tuberculosis</i>	<i>Trichomonas vaginalis</i>
<i>Chlamydia psittaci</i>	<i>Helicobacter pylori</i>	<i>Mycobacterium</i> , other (non-tuberculous)	<i>Varicella virus</i>
<i>Chlamydia trachomatis</i>	Hepatitis A virus	<i>Mycoplasma</i>	<i>Variola virus</i>
<i>Clostridium botulinum</i>	Hepatitis B virus	<i>Neisseria gonorrhoeae</i>	<i>Vibrio cholera</i>
<i>Clostridium tetani</i>	Hepatitis C virus	<i>Neisseria meningitidis</i>	Viruses, others causing haemorrhagic fevers
<i>Corynebacterium diphtheria</i>	Hepatitis D virus	Norovirus	West Nile virus
<i>Coxiella burnetii</i>	Hepatitis E virus	Parvovirus B 19	Yellow fever virus
<i>Cryptosporidium parvum</i>	Herpes simplex virus	<i>Plasmodium</i>	<i>Yersinia enterocolitica</i>
<i>Cyclospora cayentanensis</i>	Human immunodeficiency virus	Polio virus	<i>Yersinia pestis</i>
Cytomegalovirus	Human papilloma virus	Rabies virus	<i>Yersinia pseudotuberculosis</i>
Dengue fever virus	Human T-cell lymphotropic virus (HTLV)	Rotavirus	
		Rubella virus	
		<i>Salmonella</i> (non-typhi non-paratyphi)	

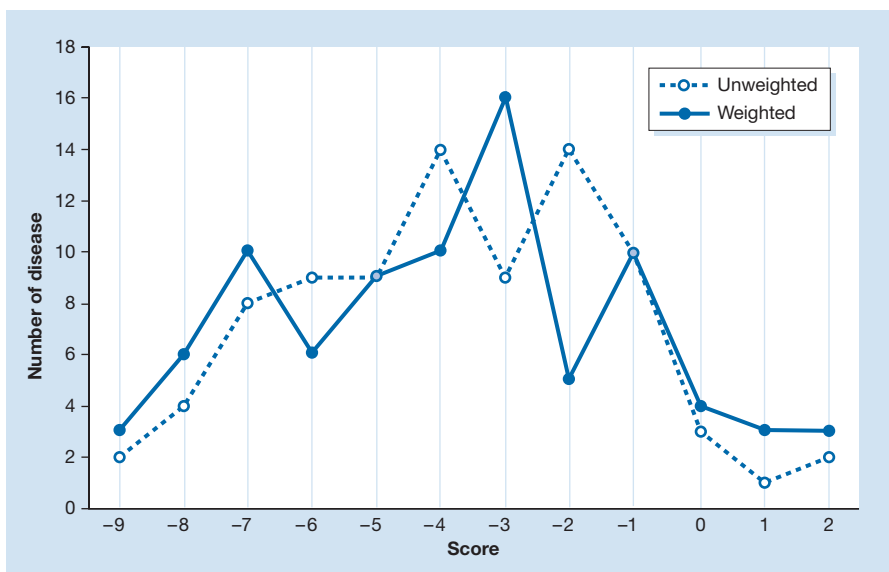


Fig 1 | Distribution of pathogens by total weighted and unweighted scores during prioritization.

Disease Epidemiology at the RKI. The group was relatively small and homogeneous, and external clients or collaborators might therefore not easily accept our prioritizations. Therefore, we plan to invite external experts onto the Delphi panel for the next round of prioritization. Yet, scoring 85 diseases for 12 categories each is a major

effort for every participant. For the next prioritization with a larger number of panelists, we are therefore considering limiting the diseases to those in the upper half of the initial list. This is justified by the likelihood that diseases that initially received a low rank are unlikely to be given a high rank in a second attempt.

One main characteristic of the procedure described is that it addresses the prioritization task pathogen-by-pathogen. However, the field of infectious diseases has numerous other aspects—such as antibiotic resistance or emergency preparedness—which need to be addressed more comprehensively. Some groups have therefore performed prioritization exercises focused on general public-health issues rather than on individual pathogens, or have included those aspects in their ranking (Horby *et al*, 2001; Lynch *et al*, 2000). If all prioritization were to follow a strict pathogen-focused approach, the original purpose of any public-health activity would be severely constrained and it would result in the undesirable competition of vertical programmes. However, individual diseases often do require individual methodological approaches; therefore, a disease priority list might still be beneficial if decision makers keep in mind the operational commonalities among the high-priority diseases.

There are still various questions that should be assessed carefully before going through such a procedure. Does the list contain all of the relevant pathogens? Do the 12 criteria cover the relevant characteristics for prioritization? Are any criteria redundant or do any have a significant dependency on

each other? If other categories were missing, would the available information be sufficient to allow scoring based on defined scores? Would a five-tiered scaling be an improvement for any category and, if so, would it be feasible to generate clear definitions for each scale? Are the existing definitions of the three scores for each criterion clear and plausible, can they be applied and 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?

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Comments on these questions can be submitted through a web-based questionnaire at <http://prio.rki.de>. We hope to receive constructive feedback, which we will take into account before we repeat the prioritization. By doing so, we hope that our prioritizations will create a fruitful discussion in the scientific community, and will ultimately provide some guidance on how to allocate attention and resources in the control and prevention of infectious diseases, which will be crucial for the future of our species.

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