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...
Table 1
Comparison of the evaluation criteria of different schemes for prioritisation of infectious diseases (the prioritisation by Réseau National de Santé Publique, 1995, France, is not included as it contained categorisation principles rather than criteria) between 1995 and 2008

<table>
<thead>
<tr>
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</tbody>
</table>

Group of criteria

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

Occurrence
- Not applied

Epidemiologic dynamic
- Potential threat
- Potential spread
- Changing patterns

Potential threat
- Long term effects on communicable diseases
- Outbreak potential
- Trend
- Emerging potential

Burden of disease
- Burden of ill health
- Severity

Disease impact
- Present burden of ill health
- Severity
- Mortality

Health opportunity
- Health gain opportunity
- Preventability

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

Evidence for risk factors/groups
- Validity of epidemiologic information
- Evidence for pathogenesis

Information need
- Not applied

Veterinary public health
- Not applied

Other
- Not applied

Public health attention
- Not applied

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Other
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Public health attention
- Not applied

Figure 1
Work flow for prioritisation, Robert Koch Institute, 2008

Preparation
- Selection of pathogens
- Identification of criteria
- Definition of scores for each criterion
- Definition of weights for each criterion

Identification
- Delphi panel
- Assigning scores to pathogens
- Applying weights
- Ranking by sum of weighted scores

Evaluation
- Publication
- Feedback and response

No need for revision

Methodology needs revision

Assess need for revision

Scoring needs revision

Ranking
- Scoring needs revision

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

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Evaluation
- Publication
- Feedback and response

No need for revision

Methodology needs revision

Assess need for revision

Scoring needs revision

Ranking
- Scoring needs revision
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 of pathogens 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

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Values</th>
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</thead>
<tbody>
<tr>
<td>Burden of disease</td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Severity</td>
<td>0</td>
</tr>
<tr>
<td>Mortality*</td>
<td>1</td>
</tr>
<tr>
<td>Epidemilogic dynamic</td>
<td></td>
</tr>
<tr>
<td>Outbreak potential</td>
<td></td>
</tr>
<tr>
<td>Trend</td>
<td></td>
</tr>
<tr>
<td>Emerging potential</td>
<td></td>
</tr>
<tr>
<td>Information need</td>
<td></td>
</tr>
<tr>
<td>Evidence for risk factors /groups</td>
<td></td>
</tr>
<tr>
<td>Validity of epidemiologic Information</td>
<td></td>
</tr>
<tr>
<td>International duties and public attention</td>
<td></td>
</tr>
<tr>
<td>Evidence for pathogenesis</td>
<td></td>
</tr>
<tr>
<td>Health gain opportunity</td>
<td></td>
</tr>
<tr>
<td>Preventability</td>
<td></td>
</tr>
<tr>
<td>Treatability</td>
<td></td>
</tr>
<tr>
<td>Proposed alternative to mortality</td>
<td></td>
</tr>
<tr>
<td>Case fatality rate*</td>
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</table>

### Table 3

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Values</th>
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<tbody>
<tr>
<td>Burden of disease</td>
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<tr>
<td>Incidence</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Severity</td>
<td>0</td>
</tr>
<tr>
<td>Mortality</td>
<td>1</td>
</tr>
<tr>
<td>Epidemilogic dynamic</td>
<td></td>
</tr>
<tr>
<td>Outbreak potential</td>
<td></td>
</tr>
<tr>
<td>Trend</td>
<td></td>
</tr>
<tr>
<td>Emerging potential</td>
<td></td>
</tr>
<tr>
<td>Information need</td>
<td></td>
</tr>
<tr>
<td>Evidence for risk factors /groups</td>
<td></td>
</tr>
<tr>
<td>Validity of epidemiologic Information</td>
<td></td>
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<tr>
<td>International duties and public attention</td>
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<tr>
<td>Evidence for pathogenesis</td>
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<tr>
<td>Health gain opportunity</td>
<td></td>
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<tr>
<td>Preventability</td>
<td></td>
</tr>
<tr>
<td>Treatability</td>
<td></td>
</tr>
<tr>
<td>Proposed alternative to mortality</td>
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</tr>
<tr>
<td>Case fatality rate*</td>
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</table>
Table 3

<table>
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<tr>
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<tr>
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<td>European Union</td>
<td>Canada</td>
<td>United Kingdom</td>
<td>France</td>
<td>South East Europe</td>
<td>Germany</td>
</tr>
<tr>
<td>Organisation</td>
<td>Reseau National de Santé Publique (RNSP)</td>
<td>Public health laboratory service (PHLS) Overview of Communicable Diseases Committee</td>
<td>Charter group of European Commission (EC)</td>
<td>Canadian Advisory Committee on Epidemiology</td>
<td>Public health laboratory service (PHLS) Overview of Communicable Diseases Committee</td>
<td>Institute de Veille Sanitaire (InVS)</td>
<td>Dubrovnik Pledge / World Health Organisation</td>
<td>Robert Koch Institute</td>
</tr>
<tr>
<td>Prioritisation objective</td>
<td>select diseases for surveillance</td>
<td>programme initiatives in infectious disease control</td>
<td>select diseases for surveillance</td>
<td>programme initiatives in infectious disease control</td>
<td>programme initiatives in infectious disease control</td>
<td>prevention of non-foodborne zoonotic diseases</td>
<td>select diseases for surveillance</td>
<td>epidemiological, research and surveillance</td>
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<tr>
<td>Type of participants</td>
<td>Interministerial and regional experts</td>
<td>experts in communicable disease control and public health laboratory service (PHLS)</td>
<td>heads of national institutions with responsibilities for communicable diseases surveillance</td>
<td>provincial epidemiologists</td>
<td>different health care professionals</td>
<td>Interministerial and regional experts</td>
<td>participants of World Health Organization workshop (not published)</td>
<td>epidemiologists at national public health institute (IMI)</td>
</tr>
<tr>
<td>Number of diseases</td>
<td>84</td>
<td>33 (+8 generic disease groups)</td>
<td>26</td>
<td>43</td>
<td>58 (+11 generic disease groups)</td>
<td>37</td>
<td>53</td>
<td>85</td>
</tr>
<tr>
<td>Number of criteria</td>
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<td>5 criteria</td>
<td>9 criteria</td>
<td>10 criteria</td>
<td>5 criteria</td>
<td>&gt; 5 criteria</td>
<td>8 criteria</td>
<td>12 criteria</td>
</tr>
<tr>
<td>Scoring system</td>
<td>No</td>
<td>5-tiered</td>
<td>5-tiered</td>
<td>3-, 4-, and 6-tiered</td>
<td>5-tiered</td>
<td>not quantifiable</td>
<td>5-tiered</td>
<td>3-tiered</td>
</tr>
<tr>
<td>Score-specific definition</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Weighting applied</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>implicitly</td>
<td>no</td>
<td>no</td>
<td>systematically</td>
<td></td>
</tr>
<tr>
<td>Methodology of collecting opinion</td>
<td>Delphi</td>
<td>survey</td>
<td>Delphi</td>
<td>survey</td>
<td>working group</td>
<td>Delphi</td>
<td>Delphi</td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>over 50</td>
<td>194</td>
<td>14</td>
<td>6</td>
<td>518</td>
<td>10</td>
<td>not published</td>
<td>11</td>
</tr>
<tr>
<td>Interministerial and regional experts</td>
<td>experts in communicable disease control and public health laboratory service (PHLS)</td>
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Table 4

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Reference</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td></td>
<td>Echovirus coli, shigella toxin producing (STECHUS)</td>
</tr>
<tr>
<td>Babesia microti</td>
<td></td>
<td>Leptospira interrogans, Shigella spp.</td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td></td>
<td>Echinococcus multilocularis, Listeria monocytogenes, Staphylococcus aureus, methicillin resistant (MRSA)</td>
</tr>
<tr>
<td>Bartonella spp.</td>
<td></td>
<td>Measles virus</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
<td></td>
<td>Staphylococcus aureus, toxigenic</td>
</tr>
<tr>
<td>Borellia burgdorferi</td>
<td></td>
<td>Entamoeba histolytica, Microsporum spp., Streptococcus spp. other than Str. pneumoniae</td>
</tr>
<tr>
<td>Brucella abortus</td>
<td></td>
<td>Francisella tularensis, Mumps virus</td>
</tr>
<tr>
<td>Brucella suis</td>
<td></td>
<td>Francisella tularensis, Mumps virus</td>
</tr>
<tr>
<td>Brucella suis suis</td>
<td></td>
<td>Francisella tularensis, Mumps virus</td>
</tr>
<tr>
<td>Campylobacter jejuni</td>
<td></td>
<td>Haemophilus influenza, Mycobacterium tuberculosis, Trichinella spiralis</td>
</tr>
<tr>
<td>Central European tickborne encephalitis virus</td>
<td></td>
<td>Hanta virus, Mycobacterium, other (non-tuberculous), Trichomonas vaginalis</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td></td>
<td>Nelicobacter pylori, Mycoplasma spp., Varicella virus</td>
</tr>
<tr>
<td>Chlamydia psittaci</td>
<td></td>
<td>Nelicobacter pylori, Mycoplasma spp., Varicella virus</td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td></td>
<td>Nelicobacter pylori, Mycoplasma spp., Varicella virus</td>
</tr>
<tr>
<td>Clostridium botulinum</td>
<td></td>
<td>Hepatitis A virus, Helicobacter pylori, Helicobacter pylori, Trichinella spiralis</td>
</tr>
<tr>
<td>Clostridium tetani</td>
<td></td>
<td>Helicobacter pylori, Parvovirus B 19, West Nile virus</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td></td>
<td>Human T-cell lymphophotic virus (HTLV), Rubella virus, Yellow fever virus</td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
<td></td>
<td>Human Immunodeficiency virus (HIV), Rabies virus, Yersinia enterocolitica</td>
</tr>
<tr>
<td>Cyclospora cayetanensis</td>
<td></td>
<td>Human papillomavirus (HPV), Rota virus, Yersinia pseudotuberculosis</td>
</tr>
<tr>
<td>Cytophagovirus</td>
<td></td>
<td>Human T-cell lymphophotic virus (HTLV), Rubella virus</td>
</tr>
<tr>
<td>Dengue virus</td>
<td></td>
<td>Influenza virus, Salmonella spp. (non typhi non paratyphi)</td>
</tr>
<tr>
<td>Escherichia coli, enteropathogenic (non STECHUS)</td>
<td></td>
<td>Legionella pneumophila, Salmonella paratyphi</td>
</tr>
</tbody>
</table>
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,

<table>
<thead>
<tr>
<th>Disease</th>
<th>Weight</th>
<th>Maximum</th>
<th>Median</th>
<th>Minimum</th>
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</thead>
<tbody>
<tr>
<td><strong>Burden of disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>10.7</td>
<td>10.7</td>
<td>10.7</td>
<td>-10.7</td>
</tr>
<tr>
<td>Severity</td>
<td>10.3</td>
<td>0</td>
<td>-10.3</td>
<td>-10.3</td>
</tr>
<tr>
<td>Mortality</td>
<td>8.4</td>
<td>8.4</td>
<td>0</td>
<td>-8.4</td>
</tr>
<tr>
<td><strong>Epidemiologic dynamic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outbreak potential</td>
<td>10.1</td>
<td>10.1</td>
<td>10.1</td>
<td>0</td>
</tr>
<tr>
<td>Epidemiologic trend</td>
<td>7.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Emerging potential</td>
<td>5.4</td>
<td>-5.4</td>
<td>-5.4</td>
<td>-5.4</td>
</tr>
<tr>
<td><strong>Information need</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence for risk factors /groups</td>
<td>5.5</td>
<td>-5.5</td>
<td>-5.5</td>
<td>-5.5</td>
</tr>
<tr>
<td>Validity of epidemiologic information</td>
<td>5.4</td>
<td>-5.4</td>
<td>-5.4</td>
<td>0</td>
</tr>
<tr>
<td>Political agendas, public awareness</td>
<td>5.2</td>
<td>5.2</td>
<td>0</td>
<td>-5.2</td>
</tr>
<tr>
<td>Evidence for pathogenesis</td>
<td>3.4</td>
<td>-3.4</td>
<td>-3.4</td>
<td>-3.4</td>
</tr>
<tr>
<td><strong>Health gain opportunity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preventability</td>
<td>8.0</td>
<td>8</td>
<td>-8</td>
<td>0</td>
</tr>
<tr>
<td>Treatability</td>
<td>5.2</td>
<td>5.2</td>
<td>-5.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Total weighted score (crude)</td>
<td>22.7</td>
<td>-22.8</td>
<td>-22.0</td>
<td>-23.7</td>
</tr>
<tr>
<td>Total unweighted score</td>
<td>1</td>
<td>-5</td>
<td>-4</td>
<td>-2</td>
</tr>
<tr>
<td>Total weighted score (normalised to a scale from +2 to -9)</td>
<td>2</td>
<td>-4</td>
<td>-4</td>
<td>-9</td>
</tr>
</tbody>
</table>
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 dependent 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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