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Themes and correlations of participant experience and evaluation of an interactive bioterrorism release exercise – a mixed methods study

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Abstract

Bioterrorism and pandemics pose great risk to the health and safety of our modern world. Pandemic scenario exercises commonly use diseases that are most likely to cause moderate harm in an epidemic scenario, such as influenza. Despite the generalisable nature of most pandemic responses, exercises often fail to take account of the broader impacts of a pandemic scenario. In August 2018, The Exercise Mataika pandemic workshop was conducted by the NHMRC Centre for Research Excellence Integrated Systems for Epidemic Response at the University of New South Wales, Australia. By utilising a high risk, worst case scenario – the deliberate release of Smallpox in Fiji and a much larger Asian country – impacts not often considered in pandemic planning, such as the resiliency of the health system, absenteeism, social cohesion and broader impacts on society, were considered and compared across geographic and social groupings. This study aimed to collect and analyse participant perceptions and evaluation of Exercise Mataika. A mixed methods study collecting participants ratings of experience, value and utility aspects of the scenario coupled with a thematic analysis of qualitative responses was conducted. Quantitative ratings for the activity were overwhelmingly positive, with respondents highlighting that the activity was useful, different in format, identified issues not often explored in pandemic exercises, and was a valuable educational opportunity. Qualitative analysis and combined mixed-methods analysis revealed more nuanced findings. While respondents remained positive about the exercise format, subgroups highlighted potential missed opportunities and areas within the scenario where greater focus could have been directed. Overall, the findings highlighted the value of including a wide range of exercise attendees across sectors and nationalities and addressing a far broader set of considerations across multiple sectors. These findings will guide future development of pandemic response exercises and education.

Introduction

Bioterrorism and pandemics pose great risk to the health and safety of our modern world. Given the rarity in which they occur and the extent to which they have so far been mitigated, training opportunities are key to preparedness. Hypothetical scenario-based training and simulation training have been used in public health and epidemiology to train staff in active epidemics (1) and to assess capability and weaknesses (2). Modelling-based simulation training offers considerable advantages over a live functional exercise in both cost of training and number of participants required (2). Deliberate practice of skills relevant to the performance of expert tasks, such as decision making in pandemics and public health analysis and intervention, is associated with demonstrable improvements in performance (3–5). Workshops can be conducted in a low threat environment, unlike real events, and provide opportunities for practitioners to critically evaluate procedures and strategies without risk to personnel, at considerably lower financial cost and without significant disruption to normal services (6).

Scenario simulations commonly use diseases, such as influenza, that reflect the most concern regarding social and economic impact, but relatively modest mortality and morbidity compared to diseases such as security sensitive bioterrorism agents (7–8). Despite the generalisable nature of most pandemic responses, these often fail to take account of the broader impacts of a pandemic scenario (7, 9) or the potential for an event involving a pathogen of greater transmissibility and severity. Additionally, the considerable logistical challenges likely to be faced in a pandemic, (10) such as impacts on civil infrastructure and society, are often considered superficially (11). Previous studies have focused on smaller scales, such as local public health responses (12), state preparations (13) and in one case
from a transatlantic perspective (14). There have not been any recent workshops of this nature that take into account the unique factors of the Pacific region. Often, pandemic scenario activities are focused at the national level to meet national readiness or training goals but assume away many of the complexities associated with infectious disease events that traverse jurisdictional, national, geographic or social boundaries (11, 15, 16).

In August 2018, The Exercise Mataika pandemic workshop was conducted by the NHMRC Centre for Research Excellence Integrated Systems for Epidemic Response at the University of New South Wales, Australia. The scenario was designed to collect and examine the decision-making processes of participants sampled from a wide variety of occupations, seniority and nationalities in a hypothetical weaponised smallpox release in the Pacific. Representatives from ten Pacific nations attended, alongside representatives from academic, industry and Australian government agencies. By utilising a high risk, worst case scenario – the deliberate release of Smallpox in Fiji and a much larger Asian country – impacts not often considered in pandemic planning, such as the resiliency of the health system, absenteeism, social cohesion and broader impacts on society, were considered and compared across geographic and social groupings.

The scenario was divided into three phases; i) initial release and investigation, ii) national impact and emergency response, and iii) a pandemic scenario with international impacts on civil society, government, health care and the economy. Online supplementary material on smallpox was released to participants midway through Phase 1.

**Aim**
This study aimed to collect and analyse participant perceptions and evaluation of the Exercise Mataika workshop conducted at The University of New South Wales, Sydney, in August 2018.

**Methods**
The workshop utilised a novel design with extensive use of live electronic voting on decisions, inclusion of post-epidemic civil societal impacts as factors for the participants to consider, and was attended by international and cross sectorial participants. The workshop was an event of the NHMRC Centre for Research Excellence, Integrated Systems for Epidemic Response (ISER). Invitations to attend the workshop and the research activity consisted of direct selection of key stakeholders and shortlisted national, state and international organisations who were free to register any number of participants. Participants were required to be either affiliated or sponsored by an academic, government or industry organisation to attend the conference due to the potential sensitivities of the content. In this study the experiences of participants in the Exercise Mataika workshop were evaluated using a mixed quantitative and qualitative research methodology. This research was approved by the University of New South Wales Human Research Ethics Advisory Panel (HREAP) Executive (approval HC180501).

**Data Collection**
The data was collected from a paper-based survey distributed at the conclusion of the exercise (n=46 of 64 consenting participants). The survey consisted of 23 questions divided into three section: Pre-survey demographics, General feedback on the workshop, and About your role in the workshop. The survey used a mixture of categorical questions on demographics and ranking their thoughts on parts of the workshop, as well as text questions to expand on what particularly factored into their categorical responses.

**Quantitative Data Analysis**
Quantitative data were initially transcribed into Microsoft Excel and then analysed using descriptive statistics. Further statistical analysis was conducted using SPSS (IBM Corporation) version 25. Statistical comparisons of the Likert scale responses (17) between groups was conducted using the independent sample Mann Whitney U (18, 19), with significance set at p<0.05, and comparisons considered where group sizes were greater than 5 (detailed statistical results presented in Annex 1).

**Qualitative Data Analysis**
Qualitative data was imported into NVivo Pro Version 12 (20) and analysed for recurring concepts using an inductive approach. Each survey question was reviewed and answers were codified as primary codes searching for underlying concepts (themes) (21). Recurring concepts were grouped together as themes once saturation was achieved. All responses were cross-codified as being positive, negative or neutral. From this data matrix coding and cross coding functions were used to determine weightings of themes by their proportion of positivity.

**Mixed methods analysis**
Major themes were triangulated with predominant findings from the quantitative data collection and analysis (22). Resultant triangulated concepts were then consolidated into major concepts for discussion and reflection.

**Findings**

**Participants**
All workshop participants at the August 2018 Exercise Mataika were invited to complete a post activity survey at the completion of the exercise. From the 76 attendees at the workshop, 64 consented to be recorded for further research, 2 participants withdrew from the workshop, and 10 participants did not consent. All participants who did not consent were removed from transcripts. From the 64 attendees who
gave their consent for further research, 46 completed the survey provided, giving a response rate of 58% of overall workshop attendees. Forty-five surveys were sufficiently completed, and one response stated only nationality of the participant and was not used in further analysis.

The survey respondents comprised of attendees from 13 nations (Australia, Fiji, French Polynesia, Guam, New Caledonia, New Zealand, Papua New Guinea, Tonga, Singapore, The United State of America, Denmark, Malaysia and the United Kingdom), the majority being from Australia (n=29). The respondents were comprised of a diverse range of employer type, representing governments, non-government organizations, industry and academia. Respondents were able to mark multiple occupations applicable to them, which resulted in a wide variety of occupations being recorded as present (11 Policy, 10 General public health, 13 Surveillance, monitoring and control of communicable diseases, 2 Environmental health, 6 Domestic emergency services, 10 International emergency response, 1 Acute care, 7 Defence/Military and 10 Other). The results from the survey showed that whilst all responses were either positive or neutral, there was variation in responses on basis of respondent demographic and this is outlined below. From the questionnaire, the most varied questions related to the themes of group work and discussion, relevance and workshop materials.

Workshop Supplementary Materials
Participants were asked to evaluate the usefulness of the online supplementary material provided to attendees during to the conduct of the exercise. These materials contained information relating to the modeling and simulation data presented during the activity and supporting references. Overall, the material was found to be useful by the majority of attendees, with response ranging from strongly agree (7/43) and agree (26/43) to neutral (10/43).

Internet Based Quiz Usefulness
Participants were asked to evaluate the usefulness of the real-time internet based quiz software. There was a difference in the responses between the National government attendee group and State/Territory government representatives. National government representatives were more positive (12/18 strongly agree) than State representatives who more often responded as agreed (7/9) (p= 0.033).

Group Work and Discussion.
Participants were asked to evaluate the usefulness of the Group Work and Discussion activities conducted during the exercise. The majority of respondents either agreed or strongly agreed to this question (17/41), but there were some neutral responses (7/41), which were equally distributed across participant groups.

Workshop Relevance
Participants were asked to evaluate the relevance of the workshop in their respective professional roles. 27/45 respondents claimed to strongly agree that the workshop was relevant to their situation, with 13 agreeing and 5 respondents claiming neutral. There was a significant difference between those who self-identified as senior decision makers and those who considered themselves mid-career in their responses, with senior decision makers responding more positively (14/18 strongly agree) compared to mid-career (7/16 strongly agree, 6/16 agree, 3/16 neutral) (p= 0.027).

Role in the Scenario
Participants were asked to report on their role in the scenario, and their perceptions of the interactivity and engagement with the exercise. There was a lower response rate on the participant’s role in the scenario (35/45 participants). Overall, respondents were satisfied with their roles in the scenario (24/34), but a large number were unsure (10/34, one no response). There appeared to be clearly distinct groups who felt their contribution to discussion differed within the scenario; the two highest responses were for giving inputs only in important parts of discussion (12/29) and actively participated (11/29). No respondent stated that they led the discussion, but 4 respondents noted they did not participate in the discussion at all. All responses to the question of whether the scenario added to participants understanding of epidemic response were positive (35/35) and the three highest stated categories were in health systems capacity, logistics and supply chain, and vaccination strategy. 24/34 respondents stated they had participated in an epidemic response before, and of them, 7/26 stated that this scenario was similar to others, 14/26 stated it was different and 5/26 stated it was very different.

Thematic Analysis
Primary codes were generated from the survey data using an inductive approach (23). As saturation became apparent, recurrent concepts were recoded as themes (21). Each unique reference was also coded as being a positive, negative or neutral comment. From the resultant 12 themes, four overarching themes were identified; Value of the exercise, Practical and realistic nature of the exercise, the diversity of thought and attendees, and the format of the workshop itself. Themes were tabulated into a code matrix according to codes for positive, negative and neutral responses in Table 1, and the definition of each theme explored in the subsequent analysis.

Table 1. Frequency of thematic response grouped by positivity of comment. (Note: Some comments are coded into multiple values. Only unique references are counted for calculation of overall comments on a theme)

<table>
<thead>
<tr>
<th>Themes</th>
<th>A : Positive</th>
<th>B : Neutral</th>
<th>C : Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 : Value</td>
<td>16</td>
<td>11</td>
<td>6</td>
<td>33</td>
</tr>
<tr>
<td>Priority areas raised</td>
<td>11</td>
<td>8</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>Networking opportunity</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Expert opinions</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2 : Practical and realistic</td>
<td>38</td>
<td>11</td>
<td>6</td>
<td>55</td>
</tr>
<tr>
<td>Novel Scenario</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Focus of the Scenario</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Educational value</td>
<td>27</td>
<td>10</td>
<td>1</td>
<td>38</td>
</tr>
<tr>
<td>3 : Diversity</td>
<td>20</td>
<td>6</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>Diverse attendees</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Different perspectives and experiences</td>
<td>16</td>
<td>4</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>4 : Workshop Format</td>
<td>20</td>
<td>9</td>
<td>19</td>
<td>28</td>
</tr>
<tr>
<td>Use Of Technology</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Workshop Logistics</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Workshop Facilitation</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Participant Interaction</td>
<td>12</td>
<td>7</td>
<td>12</td>
<td>31</td>
</tr>
</tbody>
</table>

**Value of the exercise**

Participants in the workshop made several comments regarding the value of the exercise that could be classified as positive, negative or neutral. There was importance placed on the ability of the workshop to generate areas for further consideration of research or capability development, highlighted by exploitation of current capability gaps and weaknesses in current disaster response strategies throughout the conduct of the exercise. Diversity of thought and approaches to issues were seen as a net benefit to discussions to such an extent that many of the comments made about the format of the workshop itself and level of interaction were linked to increasing their ability to hear these alternative viewpoints.

Identifying and raising priority areas was very important for attendees. Participants remarked that it “increased visibility on all of the various considerations of a pandemic scenario”, and there was “more thorough exploration of scenario and aftermath” when compared to similar workshops. Some neutral comments recognised that this workshop had “more focus on logistics and supply of PPE than the broader pandemic factors”, which made a point of difference with other workshops. Another issue that was criticized was a view that some responses to questions was either “led” or “a little artificial”.

**Practical and Realistic**

The participants commented positively about the realism and practical nature of the exercise itself. Having the scenario include discussion on logistics, such as stockpiling of vaccines, and insights into technical humanitarian, social, ethical and legal system insights was seen as a benefit to the exercise and provided comprehensive coverage of the scenario. This enabled critical thinking and further assessment of capability gaps between the various nations. Other attendees suggested that the specific focus on the Pacific was somewhat negative, as it reduced discussion of the global impacts of such a scenario and that a “Pacific focus was not directly useful and [the] opinion of individuals only”.

The focus on the Pacific and the conduct of the third phase of the exercise were the most controversial aspects. Some commenters found these areas to be irrelevant or not directly useful, whilst others found the inclusion of 2nd-4th order effects (effects on civil infrastructure and society) to be insightful and offered “increased visibility on all the various considerations of a pandemic scenario”. One commenter appeared unsure as to what purpose the post epidemic situation served, stating “Why focus on “post”-epidemic (sic) medicine?”. This highlights a recurring issue amongst some attendees that they either misunderstood the purpose of the workshop itself or expected the
workshop to be similar to others they had attended before. The use of a novel scenario, particularly one that several the participants were unfamiliar with, added a dimension to the exercise that 5/11 of participants commented as being positive with the remainder neutral. Responses focused on the agent used (Smallpox) (“This one is unique - both from the nature (small pox), scope and the details of the steps and challenges”), and the generalisability of the workshop (“Perhaps highlighting the differences in outbreak situations in smaller Pacific Island Countries vs more developed ones and the differences in capacity to identify and response to outbreak situation”; “Knowing how the process was able to be broken down. For example - Media, how, military response, etc”; and “Increased visibility on all of the various considerations of a pandemic scenario”). There were no negative comments raised regarding the novelty of the scenario used. Additionally, some commented that it was good to have an exercise that was not focused on influenza and was not seen as “US-centric” implying that this is often the case.

Participants found the breaks and pauses after voting to discuss issues useful to gain a better understanding of said issues and learn more about the specific topics. This was noted as a particular benefit of assembling such a diverse range of experts and perspectives.

Diversity

Several participants (n=20) commented a number of times about how the exercise enabled them to hear different perspectives and different experiences from other attendees. The participants thought the diversity of attendees representing a broad range of occupations and nationalities enabled a better understanding of the issues particular to those fields and those nations. Multiple comments were made that the plenary format of the workshop didn’t sufficiently capitalise on the presence of these individuals and some attendees would have preferred more smaller group style discussions. This represents a potential missed opportunity for participants to hear more from the different perspectives the various roles and nationalities provided. Some commented that the diversity was perhaps not taken far enough and they would like to see an even wider representation at future workshops, specifically from “civil society organisations who have field experience in outbreak situations in smaller Pacific Island Countries vs more developed ones and the differences in capacity to identify and response to outbreak situation”; “Knowing how the process was able to be broken down. For example - Media, how, military response, etc”; and “Increased visibility on all of the various considerations of a pandemic scenario”).

Mixed Methods Analysis

The addition of factors such as logistics of PPE and vaccines added a level of complexity and educated the audience on issues they had not previously considered, which is supported by the quantitative data showing all respondents selecting that the scenario added to their understanding of epidemic response and that most of these responses were either in capacity of health systems (7/35), logistics (7/35) and/or vaccination strategy (6/35). The participants generally stated the workshop was relevant to their needs, particularly in the higher decision makers demographic. This is perhaps suggestive that the workshop, being a regional level scenario, was most applicable to the more senior attendees.

Positive overall, the largest number of negative free text comments related to the logistics of the exercise and workshop materials. Broadly, the reaction to workshop materials was positive but had the lowest number of the most strongly positive responses. The use of electronic voting and AV aids was beneficial and added to both the educational and realism of the exercise. There were a small number of problems with the internet connectivity and AV technology had more negative comments (7/13) than positive or neutral. Whilst the format was the most criticized portion of the workshop, it was notable that there were no negative responses recorded in any section of the categorical rating of the survey. This suggests that despite feeling that the issue could be improved upon, the issue was not sufficient to negatively impact the conduct of the exercise.
experiences were overall positive, specific constructive criticisms, but not negative concerns, were identified.

**Discussion**

This paper sought to evaluate the responses to a post-activity survey for a hypothetical pandemic scenario conducted at UNSW Sydney in August 2018. The most significant findings related to practicality and realism of the scenario, engagement and interaction of participants, and the value of a diverse range of attendees. Participants mentioned they gained the most from their interactions with other participants by hearing their experiences and different perspectives on issues, which helped them to consider the vulnerabilities of their current strategies in a response to a pandemic event. The inclusion of issues beyond the immediate epidemic event challenged participants to consider broader aspects of pandemic response beyond the initial public health response.

Whilst the quantitative data showed most respondents found the group discussions useful, some qualitative comments suggest that some participants would have preferred smaller group work. Some commenters (n=4) remarked that they found the discussions useful as a means to network and hear alternative viewpoints with regard to the scenario. A theme that emerged amongst some attendees was that they were unsure about the precise purpose of the workshop and the research aims and how the workshop worked towards those objectives. As the purpose of the exercise was to evaluate decision making processes of the individuals and not primarily targeted at either being a training or networking focus, the two most common focuses of research into disaster management table top exercises (11), participants may not have understood fully the underlying purpose of the exercise. This exercise utilised a novel approach to presenting an epidemic scenario and asked participants to explore dimensions to a response not often taken into consideration. An alternative interpretation of this feedback is that the exercise took some participants outside of their expectations of an epidemic scenario resulting in uncertainty regarding the approach.

Previous studies have shown that attendees at preparedness workshops utilize such exercises as a forum to share knowledge and experiences, suggesting an expectation that the purpose and main effort of such exercises is the sharing of experiences (24). Familiarity with previous workshop designs which are standardised (25, 26) may have led local participants to expect a particular format from the workshop that would be conducted along the lines of standardised processes such as the National Communicable Disease Plan (27) or Australian Health Management Plan for Pandemic Influenza (28). However, the exercise was not focused on Australia. Channelling thinking along the lines of standardised plans and procedures may lead to neglecting critically important broader societal issues that are not addressed in national plans. In this exercise, focus was placed on the intersectoral, international and interagency dynamics that are likely to emerge as a major epidemic unfolds. Rather than concentrate on the health system dimensions or business continuity dimensions of epidemic response, participants were challenged to consider dilemmas and problems that could only be solved through cooperative, synchronised and well-orchestrated response. Similar studies that focussed on outcomes from epidemic workshops have shown the importance of highlighting aspects of a response plan participants may not have considered before (6) and a requirement to focus on a single objective of the research (11), resulting in a practical benefits to not just the individual attendees, but also to the organisations they represent (24). By adding a critical infrastructure issue into a public health response scenario, indirect impacts to the resiliency of these vital areas can be assessed and response plans can be developed.

Further research into this area is important to explore the links between organisational resilience and disaster resilience to ensure impacts to critical infrastructure are better understood (29).

This study has limitations, primarily on the sample size used in the study, as only 58% of attendees completed the survey, the majority of whom were Australians. Whilst most workshop attendees were from high income countries, it was nevertheless balanced by including views from low- and middle-income countries on account of support provided to participants to enable their attendance. This study was strengthened by the involvement of the Fiji Ministry of Health which provided assistance in the development of materials used in the exercise, cultural awareness and appropriateness of responses used in the scenario. While coding and thematic analysis were conducted by one investigator (JA) and validated by another (DH) – potentially introducing coding bias – there were no significant areas of difference of opinion between JA and DH during the process. Additionally, codes and themes were triangulated with the quantitative data which showed broad agreement across the study and both investigators assessed that thematic saturation was achieved approximately with around 20 surveys.

This exercise highlighted the value of including a wide range of attendees across both sectors and nationalities and addressing a far broader set of considerations across multiple sectors. While there were comments from participants about the use of a Pacific centred scenario over other options, this did not impact on the reported value of the exercise by the participants. The value of a scenario that drew on the backgrounds of a diverse range of participants was repeatedly highlighted by participants. Evaluation of exercises and scenarios can inform the planning of future exercises for maximal benefit to diverse groups of stakeholders. Participants found the most valuable aspects of exercises were the opportunities to hear from different perspectives, particularly from different nationalities and fields of occupation. Diversity of perspectives and experiences helped participants to challenge and critically assess their own capabilities in
pandemic management and prepare for such high-impact events.

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RESEARCH ARTICLES

Rapid risk assessment for communicable diseases in humanitarian emergencies: validation of a rapid risk assessment tool for communicable disease risk in humanitarian emergencies

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Abstract

Background: Communicable diseases pose a significant risk in humanitarian emergencies. This paper reports on the development and validation of a rapid risk assessment tool for communicable diseases in humanitarian emergencies.

Methods: We developed a tool assessing the 20 most critical risk factors for disease outbreaks in humanitarian emergencies. This paper reports on the development and validation of the tool consisting of face and content validation with key informant interviews (n=25) and a reliability validation (inter-rater reliability test) with groups of volunteer aid workers (n=4 groups).

Findings: Face and content validation confirmed the importance of rapid risk assessment methods and the suitability and usefulness of the developed tool. Participants without prior health protection experience were able fill in the tool with an accuracy of 81·25% (SD 4.08) across both scenarios (82·35% and 80·15% for scenarios 1 and 2 respectively). Errors primarily occurred when judging the severity of risk factors that could not be captured quantitatively. Revisions of the tool have been made based on the validation process.

Conclusion: The tool was successfully validated for the use in different humanitarian emergency settings and is suitable for users with and without experience in health protection.

Keywords: communicable diseases, disasters, epidemiology, health protection, humanitarian emergencies, risk assessment

Introduction

Humanitarian emergencies pose a significant risk to human health. Communicable diseases are one of the primary health concerns in humanitarian emergencies (1-18). The outbreaks of diphtheria and measles among the Rohingya refugees are striking examples of this (19-22).

Early identification of at-risk populations is an important step towards not only a better response but also preparedness and prevention of outbreaks, or at least more serious outbreaks. Rapid risk assessment is therefore a priority research area. The aim of this study was to develop and validate an easy-to-use rapid risk assessment tool for communicable diseases in humanitarian emergencies. The tool was designed as part of a larger project to understand vulnerabilities towards communicable disease outbreaks in humanitarian emergencies other than a disease outbreak. The tool development draws on the existing literature on outbreaks in humanitarian crises, a systematic review of the literature on communicable disease risk factors in complex humanitarian emergencies (23), theoretical-conceptual framework development (24), expert elicitation (25) and the validation phase. The results were used to develop a rapid risk assessment tool for communicable diseases in humanitarian emergencies. An early draft was further refined after reflective practice and deliberations with the research team prior to the validation and testing process described in this paper (see Figure 1). The tool captures data on the 20 most critical risk factors that indicate a heightened risk for communicable disease outbreaks in humanitarian emergencies, which fall into three categories: water, sanitation and hygiene (WASH), health and socio-political. Table 1 gives an overview of the risk factors and their sub-factors. Table 2 gives definitions of the main elements of the tool. The tool is accompanied by a guide. The tool presents the results of the risk assessment both numerically – in the form of weighted risk scores – and visually – using a traffic light system. Ideally, the risk assessment should be completed immediately following the onset of an emergency or the set-up of a response operation, within the first 72
hours to 14 days. Subsequent iterations of the assessment should be repeated at regular intervals throughout the response and recovery phases.

The tool differs considerably from previous tools such as the risk assessment matrix described as part of the World Health Organization’s (WHO) early warning system (EWARN) (26, 27). Our tool does not draw on a qualitative assessment of the riskiness of the individual factors with regard to outbreak risk nor does it provide an overall risk assessment of that, meaning that users are asked to answer questions such as, ‘how many liters of clean water are available per person per day?’ and the tool calculates what the answer means in terms of outbreak risk. Thus, this tool enables responders with little or no health protection experience to input secondary or primary data and obtain an evidence-based and objective assessment based on that data. Subjectivity is thereby eliminated from the risk assessment process and the only level of subjectivity remains in the data collection and evaluation thereof, not in the assessment of the consequences of the factors for outbreak risk. This should also reduce the cognitive bias often inherent in risk assessment processes. As such, this tool serves a different purpose than the WHO EWARN risk assessment matrix. For organisations not involved in health protection, the overall weighted risk score can be used to support their overall risk assessment. For organisations involved in health protection or coordination, the individual weighted risk scores can be used to prioritise response, as can the overall weighted risk score if the tool is done for multiple spatial units (e.g. sections of a refugee camp). Overall, the tool can be useful for smaller organisations that do not have extensive health protection portfolios, as well as a companion for existing well-established mechanisms, such as WHO EWARN or similar mechanisms.

The aim of the research described in this paper – the validation phase – was to test the validity of the content of the tool and its reliability. This was done in a structured process with tiered changes to the tool based on the results of previous work.

Figure 1. Tool development process

Methods
The first part of this study was performed remotely with experts from the fields of humanitarian aid and health protection and the second part of the study was performed in the field with volunteer aid workers. The tool that was tested was in English. The aims of this research were to determine the validity of the content of the tool and its inter-rater reliability when used by aid workers with no or limited expertise in health protection. We used mixed methods to ensure robust testing and optimal fulfilment of the aims.

Study site, partners and participants
Validity testing was done with key-informant interviews. This was done remotely to include a wide variety of participants from different backgrounds and geographic locations, including persons currently deployed in the field. The reliability testing was done in August 2018 in Thessaloniki, Northern Greece. Thessaloniki remains a hotspot for the response efforts to the European migration crisis and hosts many of the smaller and volunteer-based organisations. We partnered with the InterEuropean...
Human Aid Association (IHA). IHA started as an entirely volunteer-based organisation in 2015 and has since developed professional recognition. The organisation works with Greek and international partners and provides services to refugees in camps in Northern Greece. However, the reliability testing was not done specifically in the context of the migration crisis as the response effort in Greece is considerably different from other humanitarian emergencies. Rather, volunteers from IHA were involved to test whether the tool was reliable for volunteers with a background in humanitarian aid but not necessarily in medicine or health protection.

Table 1. Risk factors and sub-factors (items) in tool.

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Factors</th>
<th>Sub-factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>WASH</td>
<td>Lack of clean water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>WASH</td>
<td>Lack of toilets</td>
<td>Not applicable</td>
</tr>
<tr>
<td>WASH</td>
<td>Inadequate distance between housing and human</td>
<td>Average distance between housing and human waste disposal</td>
</tr>
<tr>
<td></td>
<td>waste disposal</td>
<td>Shortest distance between housing and human waste disposal</td>
</tr>
<tr>
<td>WASH</td>
<td>Flooding (waste water)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>WASH</td>
<td>Lack of waste management</td>
<td>Not applicable</td>
</tr>
<tr>
<td>WASH</td>
<td>Exposure to disease vectors</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Health</td>
<td>Lack of health facilities</td>
<td>Access to health facilities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Availability of clinics and/or health posts (or other primary care facilities)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disease surveillance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hospital beds</td>
</tr>
<tr>
<td>Health</td>
<td>Lack of health workers</td>
<td>Doctors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nurses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Community health care workers</td>
</tr>
<tr>
<td>Health</td>
<td>Insufficient vaccine coverage</td>
<td>Measles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meningococcal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polio</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Health</td>
<td>Poor health status of the population</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Health</td>
<td>Lack of medicines</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Health</td>
<td>Reluctance to follow disease prevention measures</td>
<td>Local health professionals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>General population</td>
</tr>
<tr>
<td>Health</td>
<td>Insufficient nutrient intake</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Health</td>
<td>Lack of health and hygiene education</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Extreme poverty and food insecurity</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Overcrowding</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Ongoing conflict</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Population displacement</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Lack of organisational and political will to</td>
<td>(I)NGOs and donors</td>
</tr>
<tr>
<td></td>
<td>address public health issues</td>
<td>Local and national government</td>
</tr>
<tr>
<td>Socio-political</td>
<td>Breakdown of government and infrastructure</td>
<td>Transport</td>
</tr>
<tr>
<td></td>
<td>services</td>
<td>Communications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electricity</td>
</tr>
</tbody>
</table>
Participants were from various countries in Europe and all had a background in humanitarian aid, specifically in response in formal and informal refugee camps with varying experience. Participants had no prior training in health protection, and informal refugee camps with varying experience.

We reached saturation after 20 interviews and conducted another five interviews to confirm. We interviewed 25 people. We did not determine the study size a priori as we agree with Sim et al. (28) that a priori determination of the sample size for qualitative key-informant interviews is fraught with problematic issues due to the underlying “questionable philosophical and/or methodological assumptions”. We reached saturation after 20 interviews and conducted another five interviews to confirm. We interviewed 17 people with a health background, five academics and three humanitarian generalists (these represent the primary backgrounds of the participants, several participants fell into multiple groups). Specific practitioner backgrounds included expertise in water, sanitation and hygiene, epidemiology, microbiology, health protection, logistics, clinical medicine and nursing. Apart from academics from institutions in Europe and North America, we interviewed participants from Public Health England, the WHO, Doctors Without Borders, the UK Public Health Rapid Support Team, the United Nations Relief and Works Agency in Jordan and several other organisations. Participants were from Europe, Asia, Africa and North America.

For the reliability testing we invited volunteers from IHA and partner organisations to take part. We conducted adapted focus groups with four groups of two participants each. Participants were from various countries in Europe and all had a background in humanitarian aid, specifically in response in formal and informal refugee camps with varying experience. Participants had no prior training in health protection, epidemiology or risk assessment.

Validity testing
Validity testing covered both content validity testing, defined as the usefulness, appropriateness, relevance and suitability of the tool (29), as well as face validity, defined by the level to which the tool actually measures communicable disease risk and hence a measure of accuracy (30). Participants were given access to the tool. They were asked to comment on the design of the tool, specifically the layout and ease of use, the order and inclusion of risk factors, and the amount of information (i.e. the length of the tool). Additionally, risk factors and their measurements were discussed individually regarding their suitability. The interview concluded with a discussion of the colour-coding system and the interpretation of the results given by the tool. The interviews used a mix of open-ended introductory questions and more detailed further queries. If the participants desired, they were provided with details on the development of the tool and the data sources used. Interviews were performed using an open-ended interview guide and responses were recorded on standardised response sheets. Response sheets were reviewed after each interview and key themes and repeated suggestions for improvement were recorded on a running document.

Reliability testing
The tool was designed so that aid workers with little or no experience in health protection would be able to consistently fill in the tool with the right information. This was assessed by a reliability testing with two fictitious scenarios (31). Participants filled in the tool for both scenarios – one a displacement crisis set in a refugee camp and the other a response to an earthquake. They had access to the tool, the tool guide and a scenario description. The tool was completed in pairs and inter-rater reliability testing was done based on the filled-in tool documents provided by the participants. Scenarios were modelled after real emergencies (mainly by combining aspects of different past emergencies) and authentically reflected situations with incomplete information. Scenarios were provided in written form. There was no time limit for participants to complete the tool but times to completion were recorded for each group and scenario. Analysis was done against an answer sheet and agreement with the answer sheet was recorded for the overall weighted risk score as well as line-by-line

Table 2. Main elements of the rapid risk assessment tool (for more detailed descriptions refer to the tool guide in the supplemental files).

<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>Category describes the sphere of the risk factor in question.</td>
</tr>
<tr>
<td>Risk Factor</td>
<td>The risk factor is the factor being measured; it can have multiple sub-factors.</td>
</tr>
<tr>
<td>Measure</td>
<td>The measure defines how this risk factor is measured. Measures can be quantitative or qualitative.</td>
</tr>
<tr>
<td>Answer</td>
<td>The answer is the observed situation, measured either quantitatively or via a selection of options for qualitative factors.</td>
</tr>
<tr>
<td>Score (0-2)</td>
<td>The score is the quantification and standardisation of the answer (with pre-defined categories for scores of 0; 1; and 2)</td>
</tr>
<tr>
<td>Weight in this type of emergency (0-4)</td>
<td>The weight is pre-determined by the selection of the emergency type.</td>
</tr>
<tr>
<td>Weighted Risk Score (0-8)</td>
<td>The weighted risk score is derived from the score reached and the weight of the risk factor in the emergency type (multiplicatory).</td>
</tr>
<tr>
<td>Overall weighted risk score (0-8)</td>
<td>The overall weighted risk score combines the weighted risk scores for all included risk factors. It works on the same scale as the weighted risk scores.</td>
</tr>
</tbody>
</table>
for each individual risk factor and sub-factor. Accuracy was determined as inter-rater reliability when tested against the answer sheet. Any answer that was not in line with the answer sheet was considered a mistake, even if it consisted of a blank. We recognise that there are some answers that could be contested, hence our aim was for 70% agreement with the answer sheet and not higher. Potentially contestable answers were those that required a qualitative judgement of the situation. After completion of the two scenarios, all groups came together as one focus group to discuss the ease of use of the tool. Results of this discussion were recorded in the form of field notes and considered in the final changes made to the tool.

Changes to the tool were made after each phase of the testing. After analysis of the reliability testing, the tool was finalised and is included as Supplementary Files 1 (digital) and 2 (print). The guide is available as Supplementary File 3. The two scenarios are available as Supplementary Files 4 and 5.

**Results**

**Validity testing**

Participants generally found the tool useful, comprehensible and accurate (24/25). Positive feedback was given for the inclusion of both a print and a digital version of the tool. Those who suggested the inclusion of other risk factors agreed that the 20 included were suitable after discussion of the data sources and evidence upon which the design of the tool was based. Suggestions for changes made by the participants included issues regarding the layout and design of the tool, the measurement of qualitative risk factors and the breakdown of risk factors into sub-factors. Changes were incorporated in subsequent iterations of the tool.

Specific changes were made based on the face and content validation. The risk factor ‘health facilities’, which initially only included hospital beds, was extended to include primary care facilities, access to health care and disease surveillance. For several risk factors, responses were broken down by groups. For example, ‘lack of political and organisational will to address public health issues’, was split into the groups ‘local and national government’ and ‘non-governmental organisations and donors’. A risk factor concerning government services was clarified into government and infrastructure services and broken down into roads/transport, communications, electricity and education. Minor changes were made to the wording of some risk factors. Additionally, for the digital version, a tab with a mock filled-in version was added to give users a visual example and risk factors were sorted into clusters based on suggestions from participants. Participants also provided detailed input into issues to be included in the accompanying guide, including the use of a smaller spatial scale where possible and the need to re-do the assessment if significant changes to the situation have occurred.

**Reliability testing**

Inter-rater reliability testing was done based on the completed tools provided by all groups for both scenarios (n=8). The time that the participants needed to complete the tool decreased with the second scenario, with the average time for completion being 33 minutes and 1 second for scenario 1 and 13 minutes and 15 seconds for scenario 2 (see Table 3). This leads to the assumption that the tool is easier to use once participants have some experience with it. Discussions with the participants confirmed this assumption.

The aim of the analysis of the completed tools was to test whether participants with little or no experience with health protection could fill in the tool and reach accuracy levels of 70% or greater. Participants without prior health protection experience were able to fill in the tool with an accuracy of 81.25% (SD 4.08) across both scenarios (82.35% and 80.15% for scenarios 1 and 2 respectively). Answers that required a qualitative judgement of the situation were the most likely to be answered wrongly.

**Table 3. Completion time for both scenarios.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39 min 14 sec</td>
<td>14 min 48 sec</td>
</tr>
<tr>
<td>2</td>
<td>38 min 20 sec</td>
<td>12 min 51 sec</td>
</tr>
<tr>
<td>3</td>
<td>27 min 15 sec</td>
<td>12 min 30 sec</td>
</tr>
<tr>
<td>4</td>
<td>27 min 15 sec</td>
<td>15 min 11 sec</td>
</tr>
<tr>
<td>Average</td>
<td>33 min 01 sec</td>
<td>13 min 50 sec</td>
</tr>
</tbody>
</table>

**Scenario 1 (see Table 4)**

For 50% of the items, 100% of the groups gave the correct answers. For 11 items (out of 34 items in total) three groups gave the correct answer (75%). The final six items were correctly completed by less than three groups (50% or lower). Quantitative items were generally more likely to have been identified correctly (8 completely correct answers out of 14 quantitative items versus 11 completely correct answers out of 20 qualitative items).

**Scenario 2 (see Table 5)**

58.82% of items were correctly answered by 100% of participants. 17.65% were correctly answered by three groups. Half the groups or less answered the remaining 23.52% (eight items) correctly. As in scenario 1, quantitative items were more likely to be answered correctly (92.86% of quantitative items answered correctly by all groups versus 35% of qualitative items answered correctly by all groups).

Additional to the line-by-line and group-by-group analysis, the overall risk scores were compared with the overall risk score ascertained with the answer sheets (see Table 6).
Table 4. Item and group validation for scenario 1 (line-by-line and group-by-group comparison of the answers of all four groups for scenario one in comparison with the answer sheet); for each item a score of 0, 1 or 2 may be given, N/A refers to items with no score assigned (i.e. not answered) by the respective group.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Type</th>
<th>Answer Sheet (score)</th>
<th>Group 1 (score)</th>
<th>Group 2 (score)</th>
<th>Group 3 (score)</th>
<th>Group 4 (score)</th>
<th>Number Correct</th>
<th>% Correct</th>
</tr>
</thead>
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<td>1</td>
<td>quant</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>quant</td>
<td>2</td>
<td>2</td>
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</tr>
<tr>
<td>3a</td>
<td>quant</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
<td>1</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td>3b</td>
<td>quant</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
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<td>3</td>
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<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
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<td>N/A</td>
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<td>N/A</td>
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<tr>
<td>18</td>
<td>qual</td>
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<td>3</td>
<td>75</td>
</tr>
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<td>1</td>
<td>0</td>
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<td>3</td>
<td>75</td>
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</tr>
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<td>1</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>75</td>
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<td>26</td>
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<td>% Correct</td>
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</table>
Table 5. Item and group validation for scenario 2 (line-by-line and group-by-group comparison of the answers of all four groups for scenario two in comparison with the answer sheet); for each item a score of 0, 1 or 2 may be given, N/A refers to items with no score assigned (i.e. not answered) by the respective group.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Type</th>
<th>Answer Sheet (score)</th>
<th>Group 1 (score)</th>
<th>Group 2 (score)</th>
<th>Group 3 (score)</th>
<th>Group 4 (score)</th>
<th>Number correct</th>
<th>% Correct</th>
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for considering the tool reliable in the field, especially if the main source of error was to be qualitative assessments. We acknowledge that some of the qualitative items are open for debate and as such the answer sheet is not as directive for them as it is for the quantitative items. Hence, we consider these results to show the adequateness of the tool.

While the overall weighted risk scores that the participants calculated were higher than those from the answer sheet, they were close enough to consider the tool adequate. In relation to the overall weighted risk scores, we considered adequateness to be achieved if the overall weighted risk score of the answer sheet lay within one standard deviation of the mean overall weighted risk score achieved by the participants. This was the case for both scenarios (see Table 6). Additionally, the scores achieved by the participants were generally higher than the overall weighted risk score assumed based on the answer sheet and, as we consider erring on the side of caution to be advisable, any discrepancies between the answer sheet and the participants’ answers are particularly unproblematic in this context.

Based on the reduction in time for completion from scenario 1 to scenario 2, we assume that repeatedly working with the tool will increase the ease of use and the time needed to complete it. Familiarity with the tool does not seem to increase the accuracy. However, we assume that two scenarios are too few to make any substantial comments on the likelihood that repeated use of the tool makes an individual or group more accurate when using it.

**Limitations**

There are several limitations to this study, as well as to the tool itself. The tool is only suitable for certain emergency types. Due to the conceptual basis of the tool, it is not suitable for any emergency in which an outbreak of an infectious disease constitutes the humanitarian emergency, such as the 2014 West Africa Ebola outbreak. Additionally, the tool does not have a specific emergency type for entrapment crises or displacement crises where most of the displaced population(s) is displaced into urban and non-camp settings. Should such emergencies occur in a situation where one of the other emergency types – most likely conflict – also apply, this is the emergency type that is the most suitable, which will be the case for most if not all entrapment crises. However, should urban/non-camp displacement be too far removed from the original cause of the displacement, this tool is not suitable. The decision to not include such situations was made based on the comparably limited evidence base for such situations and the authors call for more primary research into health needs and communicable diseases in both entrapment crises and displacements into urban/non-camp settings.

As this tool focuses on the 20 most critical risk factors for communicable disease outbreaks in humanitarian emergencies, we expect that some users will feel that important issues are missing. Risk factors

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**Discussion**

This study successfully validated a newly developed tool to rapidly assess communicable disease risks in humanitarian emergencies. The results of the validity and reliability testing suggest that the tool is useful and appropriate for aid workers with and without training in health protection to rapidly assess the risk that communicable diseases pose in the context of their field deployment. While reliability testing was done in Greece, no part of the study was specific to one singular context and the tool is suitable for all types of humanitarian emergencies that are not caused by the outbreak of a communicable disease. This tool can be used in the following settings: conflicts and war zones, floods, tropical storms and other hydro-metereological disasters, geo-disasters such as earthquakes, complex emergencies, famines, tsunamis, protracted crises and displacement crises with displacement into refugee and similar camps.

The participants’ feedback on the tool was positive and reflected both face and content validity. They determined the tool easy to use and remarked that for those risk factors that are not quantitative, an element of subjectivity remains, but that this is limited with the detailed descriptions in the tool guide. Based on the feedback from the participants the tool was modified. This tool can only be as reliable as the data that is used to fill it in. If data is missing the tool can be used with an incomplete data set; however, that can potentially lead to an inaccurate representation of the actual risk. Alternatively, additional data can be collected on the missing factors and sub-factors. While the tool is mainly designed to draw on already existing data, a suitable method for additional data collection would be cross-sectional surveys with random or cluster random sampling.

The results from the evaluation of the completed tools for the two scenarios show that aid workers with little or no experience in health protection, risk assessment or epidemiology can successfully and adequately use this tool to assess the risk of a communicable disease outbreak in different types of emergencies. We agreed prior to field validation that a reliability of 70% or greater was considered suitable for considering the tool reliable in the field, especially if the main source of error was to be qualitative assessments. We acknowledge that some of the qualitative items are open for debate and as such the answer sheet is not as directive for them as it is for the quantitative items. Hence, we consider these results to show the adequateness of the tool.

While the overall weighted risk scores that the participants calculated were higher than those from the answer sheet, they were close enough to consider the tool adequate. In relation to the overall weighted risk scores, we considered adequateness to be achieved if the overall weighted risk score of the answer sheet lay within one standard deviation of the mean overall weighted risk score achieved by the participants. This was the case for both scenarios (see Table 6). Additionally, the scores achieved by the participants were generally higher than the overall weighted risk score assumed based on the answer sheet and, as we consider erring on the side of caution to be advisable, any discrepancies between the answer sheet and the participants’ answers are particularly unproblematic in this context.

Based on the reduction in time for completion from scenario 1 to scenario 2, we assume that repeatedly working with the tool will increase the ease of use and the time needed to complete it. Familiarity with the tool does not seem to increase the accuracy. However, we assume that two scenarios are too few to make any substantial comments on the likelihood that repeated use of the tool makes an individual or group more accurate when using it.

**Limitations**

There are several limitations to this study, as well as to the tool itself. The tool is only suitable for certain emergency types. Due to the conceptual basis of the tool, it is not suitable for any emergency in which an outbreak of an infectious disease constitutes the humanitarian emergency, such as the 2014 West Africa Ebola outbreak. Additionally, the tool does not have a specific emergency type for entrapment crises or displacement crises where most of the displaced population(s) is displaced into urban and non-camp settings. Should such emergencies occur in a situation where one of the other emergency types – most likely conflict – also apply, this is the emergency type that is the most suitable, which will be the case for most if not all entrapment crises. However, should urban/non-camp displacement be too far removed from the original cause of the displacement, this tool is not suitable. The decision to not include such situations was made based on the comparably limited evidence base for such situations and the authors call for more primary research into health needs and communicable diseases in both entrapment crises and displacements into urban/non-camp settings.

As this tool focuses on the 20 most critical risk factors for communicable disease outbreaks in humanitarian emergencies, we expect that some users will feel that important issues are missing. Risk factors
were selected based solely on their ability to be a reliable indicator of risk and not on any other considerations. Issues like sexual and reproductive health, as well as the protection of vulnerable groups, are extremely important in humanitarian emergencies. They are not included in this tool because they are not among the best indicators of disease outbreak risk – not because they are not important.

The scores calculated by the tool will be less reliable in situations of considerable inequity. In such situations, smaller spatial units should be used. If measures are not distributed equitably, their reliability and the reliability of the overall score is questionable.

While the study included systematic validity and reliability testing, the results and hence the suitability and value-added of the tool will only be entirely clear after the tool has been used in the field for a longer time and in multiple occasions. Such a test was not within the scope of this study. We hope that over the next months and years, organisations and individuals involved in the response to humanitarian emergencies will make use of the tool either on its own or alongside other risk assessment procedures and we would welcome any feedback any organisations using the tool would be willing to provide. The small sample size of the inter-rater reliability test is another limitation. However, the consistency of the answers and especially of the qualitative data obtained suggests that despite the small sample size the results are reliable. Finally, the majority of our participants represent (international) response organisations rather than host countries and affected populations.

Conclusion

We attempted to develop a rapid risk assessment tool for communicable diseases in humanitarian emergencies that gave both quantitative and qualitative indications of risk level and could be used by aid workers with little or no training in health protection.

The tool works as an initial assessment tool and is applicable across a large range of different settings. In some cases, specialised organisations might want to have a more focused risk assessment only looking at their own area. Thus, one hurdle is that the tool is interdisciplinary and it may be difficult to convince organisations that the tool is suitable and useful at first instance even if they have their own more detailed and subject-specific assessments. This applies particularly to highly specialised organisations. However, one of the main groups this tool is aimed at are smaller organisations that do not have extensive health protection portfolios. For those organisations, this tool can be empowering when used together with an initial needs assessment to understand priority areas for action both within and beyond their own scope.

In the context of larger – especially country-level – responses, we do not see this tool as a substitute or in competition with well-established mechanisms such as the WHO’s EWARN (26, 27). Rather it is a companion that seeks to quantify outbreak risk (to a degree) and make rapid risk assessment for communicable diseases in humanitarian emergencies possible without the expert knowledge necessary to complete a qualitative risk assessment. Additionally, the results of the tool can shed light on how the wider humanitarian crisis is affecting health outcomes in the context it is completed in.

In addition to the digital and print versions of the tool, it is possible to develop the tool into an app for mobile devices such as tablets and smartphones. The tool can be used as a general rapid risk assessment tool that users can become highly familiar with across different deployments, as well as be adapted for specific circumstances and settings. The tool and the accompanying guide are available in the public domain and the authors are available for any questions regarding the use and adaptation of the tool. We would also welcome any feedback from organisations adopting the tool as part of their rapid risk assessment.

Ethical approval

The research study has been approved under the regulations of the University of East Anglia’s Faculty of Health and Medicine Ethics Committee. All participants provided written informed consent prior to participating.

Competing interest statement

The authors declare no competing interests.

Author’s contributions

All researchers helped design thestudy and provided input for the tool. CH designed the tool and programmed changes based on the testing. CH did the interviews, conducted the field investigation and wrote the draft manuscript. All authors approved the final analysis and manuscript.

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Acknowledgement

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References

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Two clustered cases of confirmed influenza A(H7N9) virus infection, Beijing

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2Yanqing District Centers for Disease Prevention and Control, Yanqing District, Beijing, China

Abstract

During April 1-8, 2017, a cluster of two laboratory-confirmed A(H7N9) influenza virus infections occurred in Yanqing district, Beijing. None of the 10 close contacts developed symptoms during the medical observation period after their last exposure. Throat swabs collected from close contacts all tested negative for influenza virus. Our study showed that the highly pathogenic avian influenza virus has spread to northern China, where the number of reported cases was relatively small, but the virus is not capable of sustained human-to-human transmission yet. In Beijing, informal live poultry trading in rural areas plays an important role in transmitting highly pathogenic H7N9 virus from poultry to human. Enhanced surveillance in ILI and SARI patients is required to strengthen the case detection capabilities during epidemic periods.

Introduction

In 2013, the first human case of avian influenza A(H7N9) virus infection was reported in China. By March 2019, over 1500 laboratory-confirmed human cases had been reported and the overall case fatality ratio was around 39% [1]. To prevent and control avian influenza infection and transmission, live poultry markets have been forbidden in Beijing since 2005 [2]. However, sporadic cases were still reported, and most cases had a history of exposure to poultry. In this study, we report the investigation of two clustered cases infected with A(H7N9) virus. We provide epidemiologic information on the outbreak, including history of poultry exposure, close contacts investigation, source of infection investigation and enhanced surveillance.

Methods

Patients

Between April 1-8, 2017, a cluster of two laboratory-confirmed A(H7N9) influenza virus infections were reported in Yanqing district, Beijing. The two cases were brothers (aged 52 and 66) who had been exposed to poultry together and both developed symptoms on April 1.

Clinical and epidemiological collection

CDC staff collected clinical and epidemiological information by interviewing cases and their household members. The standard questionnaire provided in The Protocol of Human Infection with Avian Influenza A(H7N9) virus Prevention and Control was applied. Information included the demographics of cases, disease clinical course, history of poultry exposure within 10 days of illness onset, history of traveling and history of contact with persons with similar symptoms. Close contacts and other exposed persons were identified. Close contacts were defined as individuals who contacted (< 1 meter) the patient without the use of personal protective equipment from the time of illness onset to the time when the H7N9 case was diagnosed and isolated.

Enhanced surveillance

As per the Protocol of Human Infection with Avian Influenza A(H7N9) virus Prevention and Control, enhanced surveillance was conducted in all secondary level and above medical institutions in the region in which the H7N9 cases were diagnosed. All patients that visited or were admitted to the sentinel hospitals were screened for influenza-like illness (ILI) symptoms and severe acute respiratory infection (SARI). Throat swabs were collected from ILI and SARI patients with their verbal consent and were tested for influenza virus.

Laboratory-testing

Throat swabs collected from cases were tested by PT-PCR according to the Chinese Guideline of Diagnosis and Treatment for Human Infections with the Avian Influenza A (H7N9) Virus, issued by the National Health and Family Planning Commission of China (NHFPCC)(3). Virus genetic sequences were obtained using Ion Torrent Personal Genome Machine sequencer (ThermoFisher, Guilford, CT, USA).

Results

Case descriptions

Case 1 was a 66 year old man who lived in a village in Yanqing district, Beijing. On April 1, 2017, he experienced fever (39°C), chest pain, shortness of breath and cough with sputum. On April 4, he visited...
a local hospital, as the disease had become more severe. Physical examination showed a body temperature of 40°C and a blood pressure of 170/90mmHg. Blood tests revealed a leukocyte count of 4.93x10⁹/L (neutrophils, 88.5%) and a C-reactive protein level of 114.25mg/L. Blood gas analysis revealed a pH of 7.5, a PaCO₂ of 22.8 mmHg and a PaO₂ of 53.0 mmHg. A chest computed tomography scan revealed a ‘frosted glass’ appearance (diffuse infiltrates) in both lungs. He was then diagnosed as a probable case with influenza A(H7N9) virus infection. On the evening of the same day, he was transferred to the intensive care unit of Ditan hospital. On April 5, a throat swab and sputum sample were collected from the patient and both samples tested positive for influenza A(H7N9) virus. On April 8, the 8th day of illness, the patient died.

Case 2 was the younger brother of case 1. He was a 52-year-old man. On April 1, he ran a fever (39.6°C) and developed respiratory distress, shortness of breath and fatigue. He visited a local community health service center and received symptomatic treatment. On April 4, day four of illness, he visited the infectious disease department of the district hospital. Physical examination showed a temperature of 38.3°C and a blood pressure of 111/88mmHg. Rales were not heard in the lungs. Blood tests revealed a leukocyte count of 5.85x10⁹/L (neutrophils, 63.4%). A chest computed tomography ray revealed two increased lung markings and high-density shadows in left lung. A throat swab tested negative by rapid influenza detection test. The patient density shadows in left lung. A throat swab tested negative by rapid influenza detection test. The patient was administered Cefmetazole and aspirin-dl-lysine. The patient was diagnosed as probable case with A(H7N9) virus infection. On April 5, the patient was transferred to the intensive care unit of Ditan hospital. On April 4, day four of illness, he visited the infectious disease department of the district hospital. Physical examination showed a temperature of 38.3°C and a blood pressure of 111/88mmHg. Rales were not heard in the lungs. Blood tests revealed a leukocyte count of 5.85x10⁹/L (neutrophils, 63.4%). A chest X-ray revealed two increased lung markings and high-density shadows in left lung. A throat swab tested negative by rapid influenza detection test. The patient was administered Cefmetazole and aspirin-dl-lysine. The patient was diagnosed as probable case with A(H7N9) virus infection. On April 5, the patient was transferred to the intensive care unit of Ditan hospital. On April 6, the patient was diagnosed as laboratory-confirmed case of influenza A(H7N9) virus infection. On day 15 of illness, the patient was discharged from hospital. On April 26, the patient was discharged from hospital.

**Epidemiologic Links and Exposure History**

Between March 20 and April 4, case 1 stayed in his brother’s (case 2) home in a village of Yanqing district, Beijing. Case 2 raised chickens in his backyard. On March 27, case 1 and case 2 bought over 70 chickens from a street peddler. Starting April 1, the newly bought chickens became sick and more than 10 of them died. Case 2 disposed of the dead chickens in a small brook nearby. Case 1 and case 2 had no other contact with live poultry or with patients with respiratory symptoms in the 10 days before illness onset. The street peddler was said to be from Hebei province and came to the town where the cases lived occasionally to sell poultry.

**Close contact and co-exposed person investigation**

A total of 9 close contacts were identified. Five were household contacts and four were neighbors of cases. They all had close contact with the cases but not with poultry. Another brother of the cases was identified as a co-exposed person because he had fed the chickens. None of these 10 persons developed symptoms during the 10 day medical observation period after their last exposure. Throat swabs were collected from the 10 persons and all were negative for influenza virus.

**Enhanced surveillance**

From April 7 to April 20, a total of 173 ILI and 79 SARI patients were identified and 215 throat swabs were collected from them. All samples were tested for influenza virus by RT-PCR and one tested positive for influenza A(H7N9) virus (case 3). Case 3 was investigated and environmental samples from his home backyard were collected and tested.

**Source of infection investigation**

On April 6 and 7, 39 environmental samples were collected from the backyard of case 3. Of these, 11 tested positive for influenza A(H7N9) virus.

Genome sequence analysis demonstrated that the sequences from the virus isolated from case 1 were identical to those from case 2. The gene sequences of virus isolated from case 2 and the environment samples from case 3 showed that they shared 99.8% and 100.0% nucleic acid sequence. All isolated virus belonged to Yangtze River Delta evolution branch. The virus contained the Q226L substitution at the receptor binding sites in the HA, which is known to enhance the binding to mammalian α₂, 6-linked sialic acid receptors. Phylogenetic analysis in NA have not detected resistant mutations, and thus the virus should be sensitive to NA inhibitors.

**Discussion**

Since the first report of a human case of influenza A(H7N9) infection, human cases have spread across China, with most cases in Yangtze River Delta Region and Pearl River Delta Region (4). Sporadic human infections have been reported in Beijing, but less frequently than in South Eastern China. In this study, we report two clustered human cases caused by highly pathogenic H7N9 viruses.

Epidemiologic investigation showed that all three cases had contact with dead poultry before illness onset. Genome sequencing analysis showed that they were infected with highly pathogenic (HP) avian influenza virus. This is consistent with findings in other regions of China during the same period, which showed HP H7N9 virus emerged in poultry and caused human infections (5). Unlike H5N1, in many human cases of H7N9, there is no history of close contact with poultry (6). In February 2013, two human cases with HP A(H7N9) virus were identified in Guangdong, a city in southern China (7,8). Soon thereafter, additional human cases of HP virus infection were reported in other southern China cities (9). Our study shows that HP virus has spread to northern China, where the number of reported cases has been relatively small.

Through investigation, we found that the two clustered cases shared common exposure to poultry...
and they developed symptoms on the same day as each other. Therefore, the infections were most likely caused via poultry exposure rather than human-to-human transmission. In addition, none of the close contacts got infected, suggesting the HP virus was not capable of sustained human-to-human transmission (10).

Previous studies have showed that live poultry trade plays an important role in H7N9 virus transmission, although much less than H5N1 (11). Although poultry markets have been banned in Beijing, informal live poultry trading continues (12). Poultry sellers move from wet market to streets and lanes in rural areas that are outside the scope of monitoring and surveillance. The epidemiological investigation and genome sequencing analysis of the isolated virus revealed that the two cases got infected from chickens bought from a street peddler. In addition, from interviews and genome analysis of samples from the case identified through enhanced surveillance (case 3), we found that case 3 had been exposed to dead chickens that were bought from a street peddler before illness onset and the genome sequences were highly similar with each other (99.95%-100%). This suggests that case 3 acquired his infection from the chickens he bought. Moreover, we found that there was 99.95%-100% similarity between viruses isolated from case 3 and case 2 (99.76%-100%). This suggests that the chickens might have been bought from the same street peddler, as case 3 and case 2 lived in different villages and they had no contact with each other. Our study demonstrates the role of illegal trading activities in transmitting viruses in Beijing, where formal LPMs have been completely prohibited. However, we failed to find the street peddler who transported and sold the chickens that carried H7N9 viruses. Most of them are cross-border sellers, whose activities are irregular. Our study demonstrates that illegal trade contributes to H7N9 virus infection in Beijing. According to a sampling investigation of adults in Beijing, 6.0% of them purchased live poultry within a year (13). This suggests that new approaches are necessary to manage informal live poultry trading in Beijing.

Although ILI and SARI surveillance are regularly performed in Beijing, their limited sampling rates might miss cases. Enhanced surveillance requires all ILI and SARI patients be sampled and tested with their consent, enhancing case detection capabilities. To conclude, the study reveals no evidence of human-to-human transmission of HP H7N9 virus in two related human cases. Illegal poultry trading played an important role in zoonotic H7N9 transmission.

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RESEARCH ARTICLES

Laboratory-based influenza surveillance system evaluation in Pakistan, 2017

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Abstract

Background: Influenza is a common respiratory disease in Pakistan. However, the absence of a robust surveillance system makes it difficult to estimate the burden of disease.

Purpose: We conducted this study to identify key strengths and weaknesses of the laboratory-based influenza surveillance system in Pakistan and to make recommendations for improvement.

Methods: We conducted an evaluative descriptive study of the national laboratory-based influenza surveillance system from April to July 2017. We conducted this assessment using the updated guidelines for evaluating public health surveillance systems issued by CDC in 2011.

Findings: The system was found to be simple and easy to operate, but with little flexibility to integrate with other pathogens and diseases. Data quality was good, given that 80% of observed forms were completed. Timeliness was good, as it takes only 24-48 hours from sample collection to report a submission to the central level. Acceptability was good, since both private and public sector hospitals and labs are involved. Sensitivity was 62% and positive predictive value (PPV) was 37.2%. The representativeness of lab based influenza surveillance system was poor, since it is a sentinel surveillance system with specific, strategically placed reporting sites.

Conclusions: The system meets its objectives. Sustainability and stability of the system needs to be improved by allocation of public funds. Coverage of the system should be expanded to improve representativeness. Regular capacity building with staff at reporting sites will ensure continued quality of reporting.

Keywords: Lab based Influenza Surveillance System, Sentinel sites, Pakistan

Introduction

Public health surveillance is the systematic collection, analysis and interpretation of health-related data that is required for the planning, implementation and evaluation of public health practice. It can:

1) Function as an early warning system for imminent public health emergencies;
2) Provide evidence of the impact of an intervention by tracking the progress towards specified goals; and
3) Monitor the epidemiology of health problems to help prioritize and inform public health policy and strategies (1)(2).

Influenza is an infectious respiratory illness that ranges from mild to severe and sometimes fatal illness (3). Influenza affects 5-10% of adults and 20-30% of children worldwide each year, causing 3-5 million cases and 650,000 deaths annually. Influenza A (H1N1) virus caused the last global influenza pandemic in 2009 (4).

WHO conducts global influenza surveillance through the Global Influenza Surveillance and Response System (GISRS), which consists of 143 institutions in 113 WHO member states, including national influenza centres, 6 WHO collaborating centres and 13 WHO H5 reference laboratories. GISRS is primarily responsible for monitoring the mutations and trends in influenza viruses, providing updated recommendations for laboratory diagnostics, vaccines and antiviral susceptibility, risk assessment, and serving as a platform for the global alert of the emergence of influenza viruses with pandemic potential. (5)

Pakistan has the sixth largest population in the world and is in south Asia, with a tropical to temperate climate. Influenza is a common illness; it has as high as a 20%–30% attack rate in preschool children. Since
2004, influenza surveillance in Pakistan has been conducted by the Pakistan National Institutes of Health (NIH) in conjunction with the US Centers for Disease Control and Prevention (CDC). Sporadic influenza surveillance is done by the National Influenza Centre (NIC) based at NIH, Islamabad. In 2007, with the support of CDC, a national database was established for tracking influenza and hepatitis activity. This aimed to strengthen the national preparedness plans, training, and capacity building (6).

In 2008, a sentinel laboratory-based influenza surveillance system was established in collaboration with CDC to assess influenza-like-illness (ILI) and severe acute respiratory illness (SARI) trends, monitor the predominant circulating strains of influenza viruses, characterize the clinical manifestations of influenza, and identify vulnerable high-risk population groups. Lab-based surveillance systems conduct weekly sampling and reporting, using real-time RT-PCR assay to type and sub-type samples. Previously, Pakistan lacked the laboratory capacity for performing influenza diagnostics. However, the National Influenza Lab Based Surveillance Project (NILSP) now provides conventional and advanced diagnostic facilities for influenza and contributes influenza virus isolates to the Global Influenza Surveillance Network for influenza vaccine strain selection. Surveillance for ILI and SARI cases is done at the designated provincial sentinel sites (Figure 1). Influenza specimens from outbreaks are also received from both public and private major hospitals in all cities. The lab-based influenza surveillance system is comprised of seven sentinel sites located in tertiary health facilities in provincial headquarters. Sentinel site location is based on tertiary healthcare facilities, geographic distribution, population density, catchment area, patient turnover, technical expertise, commitment, and motivation of staff. Fully equipped labs are available at each sentinel site for PCR testing. A microbiologist, one lab technician, and a medical technologist are available at each sentinel site. Staff at sentinel sites are provincial government employees working on the surveillance system on a monthly incentive basis.

We conducted this evaluative study to obtain a comprehensive summary of the operational working of the system through information provided by system representatives and to identify the key strengths, weaknesses, and limitations of the system.

**Aims**
To evaluate the influenza sentinel surveillance system in Pakistan.

**Methods**
We conducted this evaluation study from April to July 2017 at NIC, with the aim to evaluate the influenza surveillance system at the national level according to the updated guidelines developed by the CDC for the evaluation of public health surveillance systems (7). We adhered to the following steps:
1. Defining the purpose of the evaluation.
2. Identification & engagement of stakeholders in the evaluation process.
3. Description of the system in terms of
   a. Purpose of the system.
   b. Operational arrangements.
   c. Resources used to operate the system.
4. Gather reliable evidence regarding the performance of the system and describe the system in terms of standard attributes with the CDC guidelines.
5. Conclusions and recommendations.
**Evaluation procedure**

We developed a semi-structured questionnaire addressing purpose, objectives, performance and indicators accessing the system attributes in accordance with CDC guidelines (7). Ten attributes, as described in the updated guidelines, were evaluated in the system: usefulness, simplicity, flexibility, data quality, predictive value, sensitivity, timeliness, acceptability, representativeness and stability. Qualitative and quantitative system attributes were evaluated as per the framework provided by the Updated CDC Guidelines for Evaluation on Public Health Surveillance Systems, 2001 (7).

We reviewed documents related to the system (strategic plan, guidelines, manuals, annual reports and databases) and conducted consultations and interviews with stakeholders. In addition, we interviewed key informants, including microbiologists, lab technician pathologists, virologists and data entry officers from each sentinel site.

We conducted a desk review of relevant system records before interviewing managers. We approached the heads of virology and immunology departments to obtain the necessary information. We also interviewed the operational managers of other relevant departments, such as public health laboratories, field epidemiology and disease surveillance division, and all sentinel sites. We calculated selected indices such as case definition uniformity, data flow and data quality, as described in the guidelines [5].

We used the following formulas to calculate sensitivity and positive predictive value.

\[
\text{Sensitivity} = \frac{\text{No of Reported Cases}}{\text{No. of Expected Cases}*} \times 100\%
\]

*Expected cases include those cases which are not picked by the surveillance system

\[
PVP = \frac{\text{No. of positive cases}}{\text{No. of reported cases}**} \times 100\%
\]

**Reported cases are all the cases from whom samples are collected

**Description of surveillance system**

**Public health importance**

Community influenza surveillance is a key mechanism for defining the beginning and end of the influenza season, estimating the burden of disease in the community and identifying unusual epidemiologic trends. This surveillance data is used for planning at federal level. The benefit of the system is two-fold: epidemiological in terms of trends identified, and clinical, as the laboratory component helps in timely diagnosis of influenza.

**Objectives of surveillance system**

The objectives of the program are to assess the disease burden, monitor trends of ILL and SARI cases, determine the predominant circulating virus strain, serotype circulating influenza strains, and detect any potential pandemic variant. Other objectives include contributing to global surveillance, providing scientific evidence for preventive measures, strengthening emergency preparedness/response and updating regional strains for vaccine development.

**Case definitions**

Case definitions used are simple, uniform and consistent throughout the program. They are adapted from WHO case definitions. *Influenza like illness (ILI)* was defined as an acute respiratory infection with measured fever of ≥ 38 °C and cough (onset within the last 10 days). *Severe Acute Respiratory Infection (SARI)* was defined as: an acute respiratory infection with measured fever of ≥ 38°C and cough (onset within the last 10 days) requiring hospitalization.

**Operations of Surveillance System**

- Standard forms, including history of patient, are filled at sentinel sites and various health facilities in the catchment area of sentinel sites.
- Samples from suspected cases are collected from the outpatient departments and inpatient wards of most public and private health facilities. In peak season, over 30 samples per week are collected. The minimum number of samples is 10 per week. Then samples are transferred to and processed at sentinel site labs. Shipments are sent biweekly or monthly.
- Follow up is done by mail and email. If responses are not received weekly, sites are followed up by phone.
- Data collected through standardized forms are entered into SPSS software by trained staff. Incomplete forms are filled in by staff in the central lab from hard copies of forms. Any missing information is obtained from staff at sentinel sites or from patients by phone call. Data analysis is done in SPSS. Annual reports are generated and shared with CDC.
- All reported cases are confirmed by laboratories at sentinel sites using real-time PCR and viral culture. Positive samples are sent to the central lab for quality control. The total numbers of received samples and influenza positive samples by subtype are recorded.
  - The system identifies circulating influenza strains to help develop seasonal vaccine formulations.
  - There is a backup mechanism for storing data and records. Records are stored in both hard copy and electronic format. The security of the labs was enhanced by restricted access.
  - Private sector engagement with sentinel sites and the central lab is good. Diagnostic tests are performed free of charge for both the public and private sectors.
  - Changes in case definitions can occur in some situations, such as pandemics. Standard data...
forms for case definitions are used from sources such as the WHO.
- Data is shared with partners, including WHO, sentinel sites, and provincial and executive district health offices (EDHO)
- The catchment population of surveillance is the population living in the catchment area of tertiary care hospitals.
- The surveillance system is 100% donor funded (CDC funding).

**Findings**

Results of this evaluation were based on system attributes according to the CDC guidelines for evaluating surveillance systems. The system attributes were evaluated quantitatively as well as qualitatively.

**Simplicity (good)**

Case definitions were adopted from WHO and were simple, uniform, and consistent. The system was simple and easy to understand. Staff were trained in data collection, management of data and dissemination of findings to authorities. Data from sentinel sites includes hard copies of forms and samples from reported cases. The system collects information on demographics, clinical diagnosis, signs and symptoms, comorbidities and risk information for influenza cases. The flow of data and information from sentinel sites to the national lab is efficient. Information is shared with WHO, CDC, and district and provincial officials if action is required. There are regular staff trainings for use of the information and data collection tools. The system is not difficult to operate and uses standard data formats provided by WHO/CDC. Analysis is done in SPSS, which is a user-friendly software. The level of integration with other organizations like NARC is minimal, making it easy to operate and manage.

**Flexibility (average)**

The system has limited flexibility to integrate with other systems. The system has the capacity to be expanded to accommodate new health-related events and other respiratory viruses, but additional time and resources would be required.

**Data Quality (good)**

Forms were randomly selected from two sentinel sites, and 80% were fully completed. About 20% of forms have missing information on radiology, comorbidities, admission details and/or outcomes. Data was assessed as complete and accurate. Samples were collected from persons based on their clinical features, and test results of RT-PCR and viral culture are reported. Paper copies, as well as electronic-based data management system (SPSS), are present. Completeness and validity of recorded data reflect good data quality. Data analysis is done at federal/central levels on weekly and monthly basis and the results are uploaded on Flu Net. Data management processes regarding data collection, entry, editing, analysis and feedback were good.

**Acceptability (good)**

Private hospitals and private labs have good participation in the lab-based influenza surveillance system. All stakeholders participate in the system, but contribution from different stakeholders is not equal. There is a high rate of samples and case reports from private health facilities directly to the central lab. The system is readily accepted by all affiliated healthcare providers.

*Figure 2. Flow chart of lab-based influenza surveillance system, Pakistan*

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*NIH-National institute of health, WHO-World Health Organization, GISRS- Global Influenza Surveillance and Response System, CDC-Centre for Disease Control Peshawar-Hayatabad Medical Complex, DHQ Gilgit-District Headquarter hospital, FGPC-Federal Government polyclinic Islamabad, AMIC-Abbas Institute and Medical Centre Muzzafarabad, BMC-Bolan Medical College Quetta*
Sensitivity (low)

Sensitivity is defined as the ability of the surveillance system to identify the true cases of influenza in the country (sensitivity = positive cases/expected cases × 100%). The case definition used for reporting suspected influenza cases can identify almost all the true positive cases by lab detection. Sensitivity is supposed to be low, as the system is sentinel-based and therefore not representative of the true population. People not visiting these sites are not reported and therefore missed. The measurement of the sensitivity of the surveillance system requires the true frequency of the disease in the population under surveillance, and as it is a sentinel site-based surveillance, it is beyond the scope of this evaluative study.

All respiratory swab samples (n = 1497) were tested by real-time RT-PCR assay according to CDC protocol. Of these, 30.4% were positive for influenza viruses. Out of positive samples, only a few representative samples were grown on MDCK cell lines (virus cultivation) to have isolates for further testing. The performance of both assays cannot be compared as all samples are not cultivated.

Figures for existing cases were shared by the data records of central lab Incharge. In total, 1497 samples were received in 2016, and 455 positive cases were detected by the system.

Positive Predictive Value (PVP)

\[
\text{PVP} = \frac{\text{total samples received}}{\text{total samples positive}} \times 100\% = \frac{455}{1497} \times 100\% = 30.39\%
\]

Representativeness (poor)

The representativeness of the lab-based influenza surveillance system is poor because it is sentinel surveillance, not country wide, thus only covering a limited catchment population. People not visiting these sites are therefore not reported and missed. Among reported cases, males accounted for 54%, people aged at 1-12 years accounted for 66%.

Timeliness (good)

The timeliness of the system is good. It was quantified by measuring the time required for sample collection and transfer, the processing of forms, and the availability of laboratory results. Data is generated on a weekly and monthly basis. The analyzed data/reports are shared at provincial and federal level within the required time and submitted to CDC and WHO (Flu Net). CDC influenza experts visit the reference lab twice a year. Outbreak detection and response was observed to be timely and accurate.

Stability (average)

The system is donor funded. Labs were well equipped with computers and other logistics were available at sentinel sites. The system responds to cases in time and is reliable. The system is available when needed and is stable. Uninterrupted working electronic instruments are available. The system can collect and manage data without failure. Monitoring and evaluation of the system is done on a yearly basis. All resources are dependent on CDC funding.

Usefulness (good)

Data from all sentinel sites are analyzed at a national reference lab. The system provides data to the country influenza database. All virological and epidemiology data is updated on WHO GISRS website on a weekly basis (Flu Net). The system provides data on risk factors, and thus helps to make strategic decisions on prevention and control of disease. In addition, serial data can show seasonal and yearly trends of influenza. The system also provides support for outbreaks by timely reporting and continuous feedback from the national lab. Major activities of the system include development of surveillance, laboratory protocols and management guidelines, submission of representative/un-typable samples to WHO for vaccine strain selection, capacity building of human resources through training, quality assurance, laboratory management, enhanced biosafety & biosecurity, improved data entry & management capability.

Discussion

The results of this study show that the influenza surveillance system provides timely information through weekly and quarterly reporting. A similar evaluative study conducted in tropical countries of Asia and Africa in coordination with CDC and WHO emphasized the importance and necessity of influenza surveillance systems and influenza laboratories to address the challenges and pandemic threat posed by influenza (8). A study conducted in 2015 describing the Australian influenza surveillance system illustrated the importance of timely syndromic and laboratory surveillance of influenza in decreasing the burden of influenza in the Australian community. This allows decision makers to have access to the best available and timely information on circulating strains in relation to vaccine effectiveness (9). In our study, we found that the timeliness of the influenza surveillance system was good. Information shared by surveillance system is used for policy and planning decisions at national and international level. The system has a high degree of acceptability among stakeholders. The public health impact of the surveillance system on community is twofold; both epidemiological and clinical. The lab-based system has a very strong lab component, helps in timely diagnosis, and contributes to vaccine formulation by providing information on circulating strains. Laboratory-confirmed surveillance is beneficial and an effective way to monitor influenza transmission and seasonality. A similar study conducted in China to
evaluate influenza surveillance emphasized laboratory-confirmed surveillance as a tool for developing influenza early warning systems (10).

Surveillance data is used for planning at the provincial and federal levels. The provincial coordination network with ownership from federal government is a key feature of the surveillance system. The system contributes to the web-based reporting system Flu Net (northern hemisphere), which is used as a basis for the composition of influenza vaccine. In a study conducted in Alaska, electronic health records were utilized for effective influenza surveillance after the 2009 influenza Pandemic (11).

The surveillance project is primarily foreign funded by CDC, thus having poor sustainability. Sentinel surveillance is not representative of the whole population, as sentinel sites are in major cities of Pakistan. An evaluation study of the surveillance system in South Africa found that a major weakness of the system was that sentinel sites were inaccessible to a proportion of the population (12).

Conclusions
Community influenza surveillance serves as key mechanism for defining the beginning and end of influenza season, estimating the burden of disease in the community, identifying unusual epidemiologic trends, and assisting with vaccine formulation. Given that the system conducts sentinel surveillance covering specific catchment areas, it is not representative of the total population. Sustainability of funds for running the laboratories is an issue. For example, supply of reagents is not reliable or regular, and is totally donor funded. Provincial ownership is lacking. Retention of qualified & trained staff is an issue due to lack of financial incentives.

Recommendations
The surveillance system needs expansion, with inclusion of all the public and private health care facilities to make it truly representative of the entire population. Ownership by provincial government to manage sentinel sites’ laboratories is needed. Strengthening of public-private partnership and involving private sector data into surveillance systems will increase participation and representativeness of the system. Financial and career incentives need to be introduced to improve motivation and retention of trained staff. Capacity building and enhancement of skills can be achieved by regular training of staff and frequent quality checks through field visits. More efforts are required to ensure the sustainability and stability of system.

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Epidemiological and Entomological Investigation of Chikungunya Outbreak, in Serdang Bedagai District, North Sumatera Province, Indonesia, 2013

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Abstract

Background: Chikungunya is a serious emerging arbovirus in Indonesia. On 12 October 2013, an outbreak of chikungunya was reported in Serdang Bedagai District, North Sumatera, Indonesia.

Objective: An epidemiological investigation was conducted to identify the risk factors for the outbreak and recommend control measures.

Methods: A 1:1 matched case-control study was conducted. A case of chikungunya was defined as a previously well resident of Sei Suka Subdistrict who had clinical symptoms of chikungunya fever such as fever, arthralgia, myalgia, rash and headache of at least two days duration between 8 August and 17 November 2013. Cases were identified by active case finding through the affected area; a control was defined as a neighbor of a case that did not have clinical signs and symptoms of chikungunya, matched for age and gender. Blood samples were tested using ELISA assay to confirm the presence of anti-CHIKV specific IgM antibody.

Results: Total of 94 cases and 94 controls were included in the case control study. Age ranged from 1 year to 76 years (median 35 years) and 57% were female. In multivariate analyses, being a household contact of a chikungunya case (adjusted OR=11.4, 95%CI=4.69-27.55) and lack of routinely eliminating mosquito breeding sites were risk factors (adjusted OR=3.3, 95%CI=1.50-7.05). Six out of ten cases were positive for CHIKV IgM antibody.

Conclusions: In this confirmed outbreak of chikungunya, using anti mosquito measures were protective, reinforcing the need for routine elimination of mosquito breeding sites as well as control measures in affected households and communities.

Introduction

Chikungunya fever is a viral illness caused by an arbovirus of the family Togaviridae and genus Alphavirus and can transmit to people through the bite of Aedes mosquito (1, 2). Aedes aegypti and Aedes albopictus are the main vector of the disease (3, 4). The incubation period of the disease ranges from 2-12 days (5, 6). The United Republic of Tanzania, Africa was the first country that reported the disease in 1952 (6-8). The name chikungunya was derived from Kimakonde dialect of Makonde people, which translates to “that which bends up”, indicating the stooped appearance of patient with severe joint pain and a syndrome typically characterized by fever, headache, myalgia, and rash.

Chikungunya fever is one of the most common emerging vector-borne diseases with a high morbidity rate, prolonged polyarthritis in some cases and substantial socioeconomic impact (4, 9). It causes a large public health impact in countries in Africa and Southeast Asia. Indonesia has some of the greatest chikungunya burden in Southeast Asia. Samarinda city, East Kalimantan was the first area that reported chikungunya cases based on clinical symptoms in 1973, with the first virologically confirmed cases reported in Jambi in 1982 (10, 11). The disease rapidly moved to other provinces in Indonesia, and since 1985 all provinces have reported chikungunya outbreaks (6). Many chikungunya outbreaks have been reported in North Sumatera, West Java, Central Java, West Kalimantan, Bali, and other parts of the country (11-14). The main risk factors of these outbreaks were failure to routinely eliminate mosquitoes breeding sites (15-17), lack of use of personal protective measures against mosquitoes (12, 17), hanging out worn clothes (6, 17), and having a household contact with chikungunya (17).

On 12 October 2013, the District Health Office of Serdang Bedagai reported an outbreak of chikungunya in Sei Suka Subdistrict. Surveillance officers from North Sumatera Provincial Health Office and Serdang Bedagai District Health Office jointly conducted an investigation from 13 to 17 November 2013 to identify the risk factors and recommend control measures.
Methods

Study design and setting
This was a matched case-control with a ratio of 1:1 cases/controls. A case of chikungunya was defined as a previously well resident of Sei Suka Subdistrict who had major clinical symptoms of chikungunya fever such as fever, arthralgia, myalgia, rash and headache of at least two days duration between 8 August and 17 November 2013, identified by active case finding through the affected area. The study period was based on the first reported case until the end of the chikungunya outbreak. The criteria for declaring the end of the outbreak was two times of incubation period (3-7 days) of chikungunya cases. A control was a neighbor of the cases, who did not have clinical symptoms of chikungunya during the study period. Medical reports from health facilities were reviewed to make sure that cases and controls were correctly classified. To control confounding variables, cases and controls were matched for age and gender.

Data collection
A house-to-house investigation was carried out to identify cases and controls in Sei Suka Subdistrict. The standard chikungunya outbreak investigation questionnaire from the Ministry of Health (MoH) of Republic of Indonesia, including data on demographic profiles, sanitation practices, clinical symptoms, and all potential risk factors was administered to all cases and controls.

Data and statistical analysis
Age and gender specific attack rates (AR) and case fatality rates (CFR) during the study period were calculated to evaluate severity of the outbreak. AR was calculated as the proportion of those who became ill divided by the number of population at risk for the infection. The highest AR defined the most affected group. CFR was calculated as the proportion of deaths associated with infection divided by the total number of cases. The AR and CFR were expressed as percentages (%).

To assess the risk factors associated with the chikungunya outbreak, a two-step logistic regression model was employed. In the first step, all variables were analyzed in an unadjusted analysis. Then, all variables with p-value < 0.25 were included in the multivariate model. The 95% confidence interval (CI) is used to estimate the precision of the OR. The estimated crude OR was used in the univariate analysis, and the adjusted OR was used in the multivariate analysis. Risk factors examined included having a household contact with chikungunya, routine elimination of mosquito breeding sites, hanging out of worn clothes and use of personal protective measures (long sleeved clothing and insect repellent) against mosquitoes.

Laboratory investigation
Venous blood samples were collected from ten chikungunya cases, selected at random, that presented with fever, rash, myalgia and arthralgia after three days of fever. Samples were tested to confirm the cause of the outbreak. The samples were transferred to the National Institute of Health Research and Development of Ministry of Health of Indonesia to confirm the diagnosis. The blood samples were tested using enzyme-linked immunosorbent (ELISA) assay to confirm the present of anti-CHIKV specific IgM antibody.

Entomological investigation
Entomological investigation was conducted by entomologists from the District Health Office of Serdang Bedagai by observing water containers in and surrounding each selected house, recording whether larvae were observed, and collecting larvae if present. The entomologist determined the species of mosquito larvae and calculated the entomology indices as below: house index (HI), container index (CI) and Breteau index (BI) (6).

HI = \[
\frac{\text{Number of houses infested}}{\text{Number of houses inspected}} \times 100
\]

CI = \[
\frac{\text{Number of positive containers}}{\text{Number of containers inspected}} \times 100
\]

BI = \[
\frac{\text{Number of positive containers}}{\text{Number of houses inspected}} \times 100
\]

Ethics
Ethics clearance was not required as this investigation was part of an emergency response to an outbreak. However, participants provided verbal informed consent prior to interviews and blood sample collection.

Results

Case characteristics
The total number of chikungunya cases identified in Sei Suka Subdistrict was 94. The age ranged from 1 year to 76 years (median 35 years) and 57% were female. All cases presented with fever, rash and arthralgia (100%) and other associated common symptoms such as headache (34%), and red eyes (15%).

The epidemiological investigation was conducted on 13 October - 17 November 2013. From the investigation, the team determined that the first chikungunya case was reported on 8 August 2013. The outbreak occurred for more than ten weeks, peaked between 15 August 2013 and 2 October 2013, and the last case was identified on 24 October 2013 (Figure 1). The most affected age group was 15-44 year (AR: 4.94%) and gender was female (AR: 4.28%). The total attack rate (AR) in this area was 3.82%. There were no deaths reported, so the case fatality rate was 0% (Table 1).
Figure 1. Chikungunya fever cases by date of onset in Sei Suka Subdistrict, Serdang Bedagai District, North Sumatera, Indonesia, from 8 August to 17 November 2013 (n=94)

Table 1. Number of cases and deaths, attack rates, and case fatality rates of chikungunya fever outbreak in Sei Suka Subdistrict, Serdang Bedagai District, North Sumatera, Indonesia, 8 August-17 November 2013 (n=94)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Population at risk (n=2462)</th>
<th>Number of case (n=94)</th>
<th>Number of death</th>
<th>Attack rate (%)</th>
<th>Case fatality rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>90</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1-4</td>
<td>281</td>
<td>7</td>
<td>-</td>
<td>2.49</td>
<td>-</td>
</tr>
<tr>
<td>5-14</td>
<td>339</td>
<td>8</td>
<td>-</td>
<td>2.36</td>
<td>-</td>
</tr>
<tr>
<td>15-44</td>
<td>1153</td>
<td>57</td>
<td>2</td>
<td>4.94</td>
<td>-</td>
</tr>
<tr>
<td>&gt;44</td>
<td>599</td>
<td>22</td>
<td>-</td>
<td>3.67</td>
<td>-</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1200</td>
<td>40</td>
<td>-</td>
<td>3.33</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>1262</td>
<td>54</td>
<td>-</td>
<td>4.28</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2. Characteristics of cases (n=94) and controls (n=94) of chikungunya outbreak in Sei Suka Subdistrict, Serdang Bedagai, North Sumatera, Indonesia, 8 August-17 November 2013

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of cases (%)</th>
<th>Number of controls (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (year)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-4</td>
<td>7 (7.4)</td>
<td>7 (7.4)</td>
</tr>
<tr>
<td>5-14</td>
<td>8 (8.5)</td>
<td>8 (8.5)</td>
</tr>
<tr>
<td>15-44</td>
<td>57 (60.7)</td>
<td>57 (60.7)</td>
</tr>
<tr>
<td>&gt;44</td>
<td>22 (23.4)</td>
<td>22 (23.4)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40 (42.6)</td>
<td>40 (42.6)</td>
</tr>
<tr>
<td>Female</td>
<td>54 (57.4)</td>
<td>54 (57.4)</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7 (7.4)</td>
<td>8 (8.5)</td>
</tr>
<tr>
<td>Primary</td>
<td>13 (13.8)</td>
<td>15 (16.0)</td>
</tr>
<tr>
<td>Secondary</td>
<td>70 (74.5)</td>
<td>65 (69.1)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>4 (4.3)</td>
<td>6 (6.4)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>9 (9.6)</td>
<td>10 (10.7)</td>
</tr>
<tr>
<td>Student</td>
<td>28 (29.8)</td>
<td>30 (31.9)</td>
</tr>
<tr>
<td>Businessman</td>
<td>8 (8.5)</td>
<td>5 (5.3)</td>
</tr>
<tr>
<td>Employee</td>
<td>9 (9.6)</td>
<td>13 (13.8)</td>
</tr>
<tr>
<td>Farmer</td>
<td>30 (31.9)</td>
<td>25 (26.6)</td>
</tr>
<tr>
<td>Housewife</td>
<td>10 (10.6)</td>
<td>11 (11.7)</td>
</tr>
</tbody>
</table>

There were 75 cases before the outbreak was detected. For more than two months before it was detected, there was already 94 cases and 94 controls included in the case control study. There was no significant difference between cases and controls (Table 1). In the bivariate analyses, being a household contact with a chikungunya case was the strongest risk factor (OR=11.9, 95%CI=4.99-28.42). Other statistically significant risk factors included lack of use of personal protective measures against mosquitoes (OR=3.5, 95%CI=1.76-7.17), lack of routinely eliminating mosquito breeding sites (OR=2.8, 95%CI=1.38-5.73) and hanging out worn clothes (OR=2.6, 95%CI=1.29-5.22).

The findings in the multivariate analyses showed that being a household contact of a chikungunya case (adjusted OR=11.4, 95%CI=4.99-27.55) and lack of routinely eliminating mosquito breeding sites (adjusted OR=3.3, 95%CI=1.50-7.05) were significantly associated as risk factors for chikungunya (Table 3).

### Entomological investigation

During the entomological investigation, the team observed an abundance of breeding sites of Aedes in the backyards and surroundings of the chikungunya cases’ houses. The majority of the cases of chikungunya had improper waste disposal in their homes. The entomologist confirmed that the mosquito larvae that were collected were Aedes albopictus and Aedes aegypti. The result of entomology indices were above the national standard indices of less than 5% for HI, 38% for CI, and 25% for BI, while all were above the national standard indices of less than 5%.

### Laboratory investigation

During the epidemiological investigation, ten blood samples were collected from cases who were willing to be tested to confirm the present of anti-CHIKV-specific IgM antibody. The test confirmed that six were positive for CHIKV confirming the outbreak of chikungunya.

### Discussion

This outbreak of chikungunya had been occurring for more than two months before it was detected. There were already 75 cases before the outbreak was reported. The delay between the emergence of the outbreak’s index case and the detection of the outbreak by public health authorities was due to the lack of routine elimination of mosquito breeding sites and low sensitivity of public health surveillance and lack of resources (18-21). Public health surveillance should have high sensitivity to detect and respond rapidly to the public health problems in the community (4, 18-20).

The epidemiological investigation revealed an outbreak of chikungunya fever in Sei Suka Subdistrict, Serdang Bedagai District, North Sumatera from 8 August to 17 November 2013. The last reported chikungunya case was on 24 October 2013. The District Health Office of Serdang Bedagai declared the end of the outbreak on 17 November 2013, after 24 days from the last reported case. The main risk factors of the outbreak were being a household contact of a chikungunya case and lack of routine elimination of mosquito breeding sites.

Being a household contact of a chikungunya case was the strongest risk factor of the chikungunya outbreak. The CHIKV is transmitted through the bite of infected female mosquito, so this suggests that household contacts are at risk of the same exposure as cases. Patients infected with chikungunya can be the reservoir of infection for others in the household (22). Therefore, to minimize this risk of infection in the household, the vector population and vector contact must be minimized. When there is a chikungunya case it can increase risk of chikungunya to other members of the household (7, 8, 23). It has been previously noted that there is an increased risk of chikungunya in other member of the household (24). All chikungunya fever cases should sleep under bed nets during the viremic phase to limit the spread of infection (9). Our results are consistent with other outbreaks of chikungunya fever in the Philippines and Puerto Rico which showed that sharing a household with a chikungunya case was the main risk factor (22, 25).

Lack of routine elimination of mosquito breeding sites was found to be another risk factor of chikungunya fever. During the environmental investigation, we observed multiple breeding sites in the backyards such as discarded tires, plastic bottles, coconut-shells, vehicular tyres, pots and other water containers. Aedes mosquito use natural and artificial water containers to lay their eggs on the sides of the containers. After hatching, larvae grow and develop into pupae in about a week and into adult mosquitoes in two days. The breeding sites can contribute to high entomological indices (HI, CI, and BI). High entomological indices indicate a high risk for dengue.
and chikungunya outbreaks (26-28). Without the existence of breeding sites, the lifecycle of *Aedes* can be interrupted and the mosquitoes will have less opportunities to lay eggs and cannot develop through their aquatic life stages (5, 6). Eliminating mosquito breeding sites should be conducted routinely in high risk areas (4). The greater the number of mosquito breeding sites, the more sensitive and vulnerable the area is to chikungunya transmission (3, 7, 13).

The most effective method of controlling *Aedes* larvae is by removing or treating open containers that can serve as larval habitats in the environment (6, 13). Breeding sites, the more sensitive and vulnerable the area is to chikungunya transmission (3, 7, 13).

### Strengths and limitations

This epidemiological investigation used neighbourhood controls. It can represent the exposure in the neighbourhood that produced each case, and therefore tends to control for known and unknown confounding factors that exist in the population. There was limited testing of clinical specimens in this study. Since not all chikungunya cases were laboratory confirmed, some of them might be affected by other illnesses with similar manifestations.

### Conclusion

An outbreak of chikungunya fever was confirmed in Sei Suka Subdistrict, Serdang Bedagai, North Sumatera. Being a household contact of a chikungunya case and not routinely eliminating mosquito breeding sites were the strongest risk factors associated with the outbreak.

### Recommendations

During the outbreak, vector control activities against larvae and adult mosquitoes and intensive information, education and communication (IEC) campaigns to take measures to avoid mosquito bites were performed in the affected communities. Strict surveillance of chikungunya fever should be conducted for early detection, prevention and control of chikungunya fever in the future.

### Competing Interests

The authors have no competing interests to declare.

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Use of Mobile Apps for epidemic surveillance and response – availability and gaps

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1 University of New South Wales, Sydney, Australia

Abstract

Background: Early detection of disease outbreaks, using appropriate surveillance methods, is a basic principle for effective control of epidemics. Indicator-based surveillance methods, such as comprehensive surveillance, sentinel surveillance and syndromic surveillance, have been routinely utilized for early epidemic detection to minimize mortality and morbidity related to emerging infectious disease threats. In addition, event-based surveillance uses unstructured data sources to detect and monitor outbreaks such as media reports, social media and websites. The use of mobile phone technology is growing in many low and middle-income countries, which has made mHealth an efficient means of health communication in such countries for epidemic surveillance, mitigation and response. Mobile Apps may draw data from validated health sources or unvalidated public sources and convey information to responders. The aim of this study was to review mobile Apps used for epidemic surveillance and response.

Methods: A review of Google Play and the App Store was conducted from June 2018 to August 2018 for Apps containing the words “epidemic”, “outbreak”, “pandemic”, “public health”, “infectious diseases”, “infection”, “bioterrorism” or “CBRNE”, “surveillance”. Available Apps were analysed by the intended user, purpose, platform, functions and number of downloads.

Results: We found a total of 106 Apps in an initial search, and of those 80 Apps did not meet the selection criteria and were excluded. Finally, 26 relevant surveillance Apps, including 21 free of charge and 5 paid Apps, were included in this review. Of these, 17 Apps are for single disease surveillance, 7 Apps for multiple disease surveillance and 2 Apps provides information on possible bioterrorism agents. The intended user varied from the general public (18 Apps) to health practitioners (4 Apps) and remaining 4 Apps intended for both general public and health practitioners. The Apps included real-time tracking in an interactive map (10 Apps), daily notification alerts (3 Apps), user function to report diseases/outbreaks (4 Apps) and multiple disease tracking options (7 Apps). The most downloaded Apps were Sickweather with 100,000+ downloads and HealthMap with 10,000+ downloads. Only 4 Apps were available on both Android and iOS platforms.

Conclusion: There are at least 26 mobile Apps for surveillance of epidemics, mostly free of charge and mostly for laypeople. Among them, HealthMap is the most comprehensive, but by far the greatest number of downloads was for a consumer App, Sickweather. Some Apps can provide real-time tracking and interactive maps. However, limitations included unavailability of Apps suitable for general public or surveillance of potential bioterrorism incidents, limited geographic or disease relevance, and high cost for some Apps. There is great potential to utilize existing Apps and develop new ones, especially which meet the needs of health professionals and public health authorities for real-time disease surveillance.

Introduction

Early detection of disease outbreaks, using appropriate surveillance methods such as indicator-based surveillance (IBS) and event-based surveillance (EBS), is a basic principle for effective reduction and control of epidemics (1). IBS is comprehensive surveillance, using structured, validated reports of specific diseases from laboratories and the health system to public health officials (2). Sentinel surveillance involves detecting specific diseases or syndromes in sentinel geographic sites to gain early warnings (3). Syndromic surveillance involves detection of clinical syndromes as a signal of severe infections (2, 4) and is utilized when high-quality data is required for a specific disease (5). EBS is the use of unstructured data such as media reports, rumors, stories, social media and websites to detect and monitor outbreaks. EBS is community-based and utilises reports of health events on news, social media, blogs or messaging systems (6). The development of automated intelligence methods is of growing interest (15), including Open-source intelligence (OSINT) (16). The availability of information technology (IT) for electronic data collection and execution has given support to Web-based surveillance methods which can notify rapid epidemic intelligence on public health.
incidents (7). Web-based sources provide more timely information for identifying infectious disease outbreaks, such as detecting cases of disease-relevant keywords in social media like Twitter, Instagram or published reports of news (8). Several web-based surveillance systems like ProMed-mail, HealthMap and Global Public Health Information Network (GPHIN) have been utilized to monitor disease trends across the globe (2). The use of mHealth technology and mobile Apps are of interest due to high usage of mobile phones and internet in many low and middle-income countries, where other surveillance systems may be weak (9). Mobile health or mHealth is defined as medical and public health services supported by mobile devices such as smartphones, tablets, personal digital assistants (PDAs), patient monitoring devices and wireless devices (10, 11). It provides immediate access to information for effective decision making and supports better communication between healthcare workers and patients (10). Mobile Apps and online portals can link patients to their health providers and their health data to establish high-quality care (10). A mobile phone's key utilities such as voice and short messaging service (SMS) and other essential functionalities including GPRS (general packet radio service), 3G and 4G mobile telecommunications, GPS (global positioning system) and Bluetooth technology can be harnessed through mHealth (11). Common m-health initiatives include health call centers, emergency phone services, managing emergencies and disasters, and mobile telemedicine. However, there are many barriers to mHealth such as technical limitations, lack of knowledge among health staff, high operating cost and infrastructure.

The use of mobile phone technology is growing in many low and middle-income countries, making mHealth an efficient means of health communication in such countries. In countries such as India, for example, mobile phone ownership and usage is almost universal, and much higher than computer ownership, making mHealth a suitable tool for improving healthcare (12, 13). Many governments have shown their interest in mHealth as a tool for strengthening health systems toward attaining the United Nations Sustainable Development Goals in those countries (14-16).

Most of the mobile Apps in health have been designed to be used by patients for individual clinical care, and mostly in chronic disease management (17). Other Apps are used to educate patients about health (18). Apps may receive or convey information from or to a patient or a health professional (19). There is increasing interest in the use of mHealth for epidemic surveillance, mitigation and response (20). In this case Apps may draw data from validated health sources or unvalidated public sources and also convey information to responders (21). The aim of this study was to identify available mobile Apps for epidemic surveillance, review their utility in public health and identify any gaps in need.

**Methods**

A review of Google Play and the App Store was conducted from June 2018 to August 2018 for Apps containing the words “epidemic,” “outbreak,” “pandemic,” “public health,” “infectious diseases,” “infection,” “bioterrorism” or “CBRNE,” “surveillance.” In addition, major sites for public health response to outbreaks such as the US Centers for Diseases Control and Prevention (CDC), World Health Organizations (WHO), United Nations and Australian Department of Health, were searched for relevant Apps. Apps were searched on 20th June 2018 from Google Play and the App Store. In cases where Apps were not available in Google Play, they were searched in google search engine using keyword “App name (XYZ) apk” and downloaded from third party android websites such as Apkpure (22).

Available Apps were analysed by the intended user, purpose, platform, functions and number of downloads. Apps were reviewed for platform (Android or iOS), relevance, purpose, intended users, cost and the number of downloads. We excluded apps related to games, health education for members of the public, or not relevant for public health. All the surveillance apps were compared based on the following criteria: features available in the App, the types of diseases they track, surveillance regions, sources of disease reports, release and last updated date, device compatibility, languages available, number of downloads, ratings, and price (free or paid). In addition, we identified the underlying models or digital technology used to detect the disease epidemics and compared among the reviewed apps. The Apps found from the review of Android and iOS stores were categorized by multiple diseases and single disease surveillance App. Furthermore, the apps were categorized based on user-friendliness of their features.

**Results**

A total of 106 Apps were found in the initial search. Of those, 80 did not meet the selection criteria and were excluded (Figure 1). Finally, 26 relevant surveillance Apps were included in this review, which are summarised in Table 1. Of 26 relevant surveillance Apps, 21 were free of charge and 5 were paid Apps. Of these, 17 Apps are for single disease surveillance, 7 Apps for multiple disease surveillance and 2 Apps provided information on possible bioterrorism agents. The intended user varied from the general public (18 Apps) to health professionals (4 Apps). A further 4 Apps were intended for both the general public and health professionals. Features included real-time tracking using an interactive map (10 Apps), daily notifications (3 Apps), user ability to report diseases/outbreaks (4 Apps), and multiple disease tracking options (7 Apps). The most downloaded Apps were Sickweather with 100,000+ downloads, followed...
by HealthMap with 10,000+ downloads. Other Apps were far less frequently downloaded (17 Apps have downloads less than 10,000, and number of downloads is not available for seven Apps), and 4 Apps were downloaded less than 100 times (Figure 2). The maximum downloads were of Apps available in the Android platform. Only 4 Apps were available on both Android and iOS platforms, while, 16 Apps were available on the Android platform and 6 Apps in iOS platform.

Seven Apps had multiple-disease surveillance (including HealthMap and ProMed-mail); another 17 Apps were for single-disease surveillance, and two Apps provided information on possible bioterrorism agents (Figure 3). Of single disease Apps, 8 were on influenza only, 3 on dengue, 3 on Ebola, 2 on Zika virus and 1 on malaria (Figure 4). Some Apps are country-specific, such as the CDC FluView and Flu-near-you applications, which used for surveillance of influenza-like illness (ILI) activity in the United States. Some were designed to track a geolocation such as Mo-Buzz, which uses hotspot maps to track dengue outbreaks in Colombo city, Sri Lanka. The ECDC Threat Reports App gives reports on communicable disease threats only in the European region. Dengue Map monitors dengue outbreaks in Brazil.

A few Apps can only be accessed from Google play in selected countries, such as MoBuzz and Flutrack (Table 1). Almost all the Apps were in the English language; however, some Apps were available in different languages such as Dengue Map App in Portuguese. Paid Apps had fewer downloads compared to free Apps. Some unique features of these Apps include: the Outbreak App has offline access to incoming updates and pinpoints the exact location of the outbreak; the HealthMap App can give users customised alerts on outbreaks occurring in a specified region; ProMed-mail App allows users to submit reports about disease outbreaks; and the MoBuzz App uses hotspot maps to track dengue affected areas. Of 26 available Apps, 13 Apps had a user rating of 3.5 or higher out of 5, 4 Apps had ratings <3.5 and no rating was available for the rest of the Apps.

**Mathematical models and digital technologies used**

The following Apps use complex mathematical models or digital technology for surveillance of outbreaks.

1. **HealthMap-** uses models such as Fisher-Robinson Bayesian filtering, and also relies on Google Maps, Google Map API, Google Translate API for disease tracking (23).

2. **Sickweather-** uses Advanced machine learning models, Artificial intelligence (AI) and cognitive APIs to forecast the rate of illnesses up to 15 weeks in advance with more than 90% accuracy (24).

Other apps use simple mathematical models or digital technology for the surveillance using various informal networks such as public, twitter, and social media reports, and formal reports from health organisations, government and humanitarian organizations, clinical data and simple technologies such as Reliefweb API, twitter API, and crowdsourcing technology. Examples include Fluview App, which only uses data collected by CDC in a visualized format of influenza activity. CDC gets data from Influenza-like Illness Surveillance Network (ILInet), U.S. World Health Organization (WHO) Collaborating Laboratories System and National Respiratory, and Enteric Virus Surveillance System (NREVSS) collaborating laboratories. Some other apps which use data from CDC are Flu tracker, Field facts, LRN Rule-Out Refer, Swine Flu 101.

Further examples of simple model surveillance Apps are Flu near you 2, ViralMap, Flutrack, ECDC Thread Reports, Mo-Buzz, Epidemic Tracker, ProMED-mail, LA - Malaria Case Surveillance, FluTracker NTU, Appdemia, DengueWatch, Flu Map Tracker, Zika Tracker.

For other Apps such as Ebola tracker, Outbreak app, Dengue Map, Ebola Map Global Ebola Tracker, and Global Zika Tracker, the methods are unknown/undisclosed.
Figure 1. Search strategy Diagram containing procedure followed to find out disease surveillance Apps from Google Play and the App store
**Figure 2.** Number of Apps according to the number of downloads in Google Play and the App Store

**Figure 3.** Availability of Apps based on surveillance of single disease, multiple diseases and bioterrorism events

**Figure 4.** Disease-specific tracking of Apps
<table>
<thead>
<tr>
<th>Sl No.</th>
<th>App name</th>
<th>Features or Description</th>
<th>Diseases tracked</th>
<th>Intended Users</th>
<th>No. of Downloads</th>
<th>Copyright / Offered by</th>
<th>Source of information</th>
<th>Category</th>
<th>Intended Users</th>
<th>Price</th>
<th>Compati bility</th>
<th>Rating</th>
<th>Release date</th>
<th>Language</th>
<th>Cons</th>
<th>Reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HealthMap: Outbreaks near me</td>
<td>Latest real-time disease outbreak information</td>
<td>All outbreaks</td>
<td>Health &amp; Fitness, General Public</td>
<td>10,000+ (Google Play)</td>
<td>HealthMap</td>
<td>ProMED Mail, WHO, GeoSentinel, OIE - World, Organisation for Animal Health, Food and Agriculture Organization of the United Nations (FAO), EuroSurveillance, Google News, Moreover - A news feed aggregation service by VeriSign, Wildlife Data Integration Network, Baidu News, Soso Info.</td>
<td>Health &amp; Fitness</td>
<td>General Public</td>
<td>Free</td>
<td>Android platform 2.3 or up; Requires iOS 7.1 or later. (iOS Universal)</td>
<td>3.6/5 (Google play); 3.9/5 (Apple store)</td>
<td>April 04, 2012 (Android); Aug 31, 2009 (iOS)</td>
<td>English</td>
<td>No. of downloads not available in Apple store</td>
<td>“This App is a great service, but could you consider no longer gathering a list of the Apps on my phone. My security program is complaining that this App is gathering that info.”</td>
</tr>
<tr>
<td>2</td>
<td>FluView</td>
<td>Explore Influenza-Like Illness (ILI) Activity Levels across the US</td>
<td>Influenza</td>
<td>Medical Health Practitioner</td>
<td>N/A</td>
<td>CDC</td>
<td>Influenza-like Illness Surveillance Network (ILINet)</td>
<td>Medical</td>
<td>Health Practitioner</td>
<td>Free</td>
<td>iOS 4.0 or later. (iOS Universal)</td>
<td>1.8/5</td>
<td>Mar 27, 2012</td>
<td>Mar 27, 2012</td>
<td>English</td>
<td>No. of downloads not available</td>
</tr>
<tr>
<td>3</td>
<td>Flu tracker</td>
<td>Get flu-related news updates. A map feature shows weekly state by state influenza activity in the US.</td>
<td>Influenza</td>
<td>Medical General Public</td>
<td>N/A</td>
<td>Anoush Srin, M.D.</td>
<td>CDC</td>
<td>Medical</td>
<td>General Public</td>
<td>Free</td>
<td>Requires iOS 10.0 or later. Compatible with iPhone, iPad and iPod touch.</td>
<td>N/A</td>
<td>May 13, 2011</td>
<td>Dec 04, 2016</td>
<td>English</td>
<td>No. of downloads not available</td>
</tr>
<tr>
<td>4</td>
<td>LRN Rule-Out Refer</td>
<td>Obtains essential information regarding six potential bioterrorism agents</td>
<td>Bacillus anthracis, Brucella species, Yersinia pestis, Francisella tularensis, Burkholderia pseudomallei, and Burkholde ria mallei</td>
<td>Medical</td>
<td>Health Practitioner s</td>
<td>CDC</td>
<td>U.S. laboratories</td>
<td>Medical</td>
<td>Health Practitioner s</td>
<td>Free</td>
<td>iOS 7.0 or later (iPad)</td>
<td>N/A</td>
<td>Feb 25, 2015</td>
<td>Sep 13, 2015</td>
<td>English, Korean</td>
<td>Not useful for surveillance of potential bioterrorism incidents; No. of downloads and user ratings not available</td>
</tr>
<tr>
<td>5</td>
<td>Field Facts</td>
<td>It provides helpful information to first responders for implementation in the initial few hours or moments during a potential bioterrorism incident.</td>
<td>Medical Health Practitioner(s)</td>
<td>500+ (Google Play)</td>
<td>CDC</td>
<td>CDC</td>
<td>U.S.</td>
<td>Free</td>
<td>Android platform 4.0 or up; iOS 8.0 or later (iOS Universal)</td>
<td>Ratings: 3.7/5 (Google Play)</td>
<td>Dec 18, 2017 (Android); June 07, 2018 (iOS)</td>
<td>Dec 18, 2017 (Android); June 07, 2018 (iOS)</td>
<td>English, Korean</td>
<td>Not useful for surveillance of potential bioterrorism incidents.; No. of downloads not available in Apple Store</td>
<td>“I like in this time we need to be aware of everything. Also, we should know where the bacteria viruses and plague come from and what to do in case of emergency. Is a proved information. Connected with the CDC even better.”</td>
<td>“It’s a good App very informative.”</td>
</tr>
<tr>
<td>6</td>
<td>Flu near you 2</td>
<td>Get real-time updates about the onset of flu in your area. Provides real-time, trending information about influenza-like illness in your immediate vicinity.</td>
<td>Influenza Unknown</td>
<td>General Public</td>
<td>HealthMap</td>
<td>Individuals reports, Voluntary Participation, Crowdsourced Data, Visualized Data</td>
<td>U.S.</td>
<td>Free</td>
<td>Android 4.1 or above</td>
<td>3.0</td>
<td>N/A</td>
<td>March 02, 2018</td>
<td>English</td>
<td>This App is currently not available in all locations on Google Play</td>
<td>“If Flu Near You worked properly, it’d be a great solution for people who want to avoid getting sick especially during flu season. Unfortunately, numerous bugs with signing in, and a general lack of crowdsourcing data points these days, greatly hamper its effectiveness at most locations.”</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>ViralMap</td>
<td>Monitors tweets related to personal reports involving flu or influenza all around the world.</td>
<td>Influenza Health &amp; Fitness</td>
<td>General Public</td>
<td>Ricardo Mansilla</td>
<td>tweets related with personal reports</td>
<td>Global</td>
<td>Free</td>
<td>Requires Android 2.2 and up (third party App)</td>
<td>5/5</td>
<td>June 25, 2014</td>
<td>July 1, 2014</td>
<td>English</td>
<td>“Wow Information overload!”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Flutrack</td>
<td>Detects flu symptoms using Twitter.</td>
<td>Influenza Health &amp; Fitness</td>
<td>General public and health practitioner(s)</td>
<td>alex199568</td>
<td>Flu-related tweets using Twitter API</td>
<td>Global</td>
<td>Free</td>
<td>Requires Android 4.1 and up (third party App)</td>
<td>N/A</td>
<td>April 4, 2018</td>
<td>April 10, 2018</td>
<td>English</td>
<td>Rating not available; Not available in all locations on Google Play</td>
<td>N/A</td>
<td></td>
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<tr>
<td>9</td>
<td>Sickweather</td>
<td>It provides real-time alerts from social media whenever you enter a Sick Zone. Provides alerts for Flu, Norovirus, Pink Eye, Whooping Cough, and 19 other illnesses. Allows users to enter symptoms when they are ill.</td>
<td>Influenza, Norovirus, Pink Eye, Whooping Cough</td>
<td>Social</td>
<td>Global Media monitoring, crowdsourcing, forecasting and output, Population, Sales &amp; Clinical Data</td>
<td>Global</td>
<td>Paid (U.S. $2.99)</td>
<td>Requires Android 4.4 and up; Requires iOS 9.1 or later. Compatible with iPhone, iPad, and iPod touch</td>
<td>September 30, 2014</td>
<td>April 24, 2018</td>
<td>English</td>
<td>Uses your location even when it is not open, which can decrease smartphone battery life.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>ECDC Thread Reports</td>
<td>Provides direct access to key updates and reports on communicable disease threats of concern to the EU.</td>
<td>Communicable diseases</td>
<td>Medical</td>
<td>European Centre for Disease Prevention and Control</td>
<td>Europe</td>
<td>Free</td>
<td>Requires Android 4.1 and up</td>
<td>December 21, 2016</td>
<td>August 25, 2017</td>
<td>English</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Ebola tracker</td>
<td>Up to date mapping Application of the Ebola outbreak currently spreading throughout the world. Shows Number of new cases in the last 24 hours.</td>
<td>Ebola</td>
<td>Medical</td>
<td>Ebola Tracker</td>
<td>Unknown</td>
<td>Global</td>
<td>Paid U.S. $3.99</td>
<td>Requires iOS 10.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>Sep 13, 2014</td>
<td>Aug 10, 2017</td>
<td>English</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Mo-Buzz</td>
<td>Use hotspot maps to keep track of those parts of your city that are most affected by dengue.</td>
<td>Dengue</td>
<td>Free tools</td>
<td>Cosmic Centre NTU</td>
<td>Crowdsourcing technology and health education</td>
<td>Colombia city, Sri Lanka</td>
<td>Free</td>
<td>Requires iOS 10.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>Dec 15th, 2015</td>
<td>August 17, 2017</td>
<td>English</td>
<td>Not available in all locations on google play</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Outbreak</td>
<td>Posts global disease outbreaks such as H1N1, Ebola, Anthrax and Malaria.</td>
<td>H1N1, Ebola, Anthrax, Malaria</td>
<td>News &amp; Magazines</td>
<td>Unknown</td>
<td>Global</td>
<td>Free</td>
<td>Android 5.0 and up</td>
<td>July 7th, 2015</td>
<td>May 21, 2018</td>
<td>English</td>
<td>Not able to access the App after being downloaded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

“Helpful and useful App! I recommend to download this App, gives us latest updates of all Hazardous epidemics in our world.”; “Nice App Very helpful App”

“So at first this App was really cool, now its constantly saying there’s constantly a 98% chance of getting sick, and head lice is being the only thing reported, last week allergies. Way to get it together sickweather.”; “Can’t figure out how to remove a location.”
<p>| 14 | Epidemic Tracker | Helps users follow reports of major current diseases being tracked. | Cholera, Dengue, Ebola, Polio, Malaria, Measles, MERS-CoV, Zika, Chikungunya, Dengue, Zika, dengue, influenza | Tools | General Public | 100+ | Emerging Infections | Ref: ReleWeb API, ET, government and humanitarian organizations | Global | Free | Android 4.2 and up | 4.0 | December 28, 2016 | February 18, 2017 | English | N/A |
| 15 | ProMED-mail | The global electronic reporting system for outbreaks of emerging infectious diseases &amp; toxins, open to all sources. | Outbreaks of emerging infectious diseases | Medical | General Public and Health Practitioners | 500+ | ProMED-mail, International Society for Infectious Diseases | media reports, official reports, online summaries, local observers | Global | Free | Requires Android 3.3 and up; Requires iOS 6.0 or later. Compatible with iPhone, iPad and iPod touch. | 4.0 | November 30, 2015 | August 24, 2016 | English | &quot;Handy if you want to review promed when out and about. Standard text quite small but can be enlarged on each article. Would be useful to have a setting to keep text larger. Great idea to increase ease of reporting. Thanks for making it available.&quot; |
| 16 | LA - Malaria Case Surveillance | Tracks and reports positive cases of malaria in near real-time using District Health Information Software 2 (DHIS2) | Malaria, dengue, Zika virus, dengue, chikungunya | Tools | Health &amp; Fitness | Health Practitioners | 500+ | PSI GRS | PSI’s District Health Information Software 2 (DHIS2) | Global | Free | Requires Android 4.0.3 and up | 5.0 | August 30, 2017 | September 22, 2017 | English | &quot;Not available in all locations in Google Play&quot; |
| 17 | FluTrack-NTU | Provides notification of potential influenza outbreaks in Singapore | Influenza | Tools | General Public | 100+ | SMISPH, National University of Singapore, NUS, TSIM, CDC | Singapore | Free | Requires Android 5.1 and up | 5.0 | April 27, 2018 | May 10, 2018 | English | N/A |
| 18 | AppDemia | Anyone can track the more relevant health occurrences in their region | Fever; diarrhea, Zika virus, dengue, chikungunya | Tools | Health &amp; Fitness | General Public and Health Practitioners | 100+ | Prosperi Tecnologia | Public reports | Global | Free | Requires Android 4.0.3 and up | 4.8 | July 20, 2016 | October 14, 2016 | English | &quot;Very useful! &quot;Good Very good, I especially enjoyed the &quot;design.&quot; |
| 19 | Dengue Map/ Mappada Dengue | Monitors dengue outbreaks in your region. | Dengue | Tools | Health &amp; Fitness | General Public | 1,000+ | Web Fantastico | Unknown | Brazil | Free | Requires Android 1.6 and up | 3.5 | November 29, 2015 | December 13, 2015 | Portuguese | N/A |
| 20 | DengueWatch | Online alerts and notifications of dengue cases reported by users or authorities; near their homes and/or workplace. | Dengue | Tools | Health &amp; Fitness | General Public | 5+ | ISMEUS | Users or authorities report | Global | Free | Requires Android 4.1 and up | Not rated | January 30, 2018 | January 30, 2018 | English | N/A |
| 21 | Flu Map Tracker | Tracks TwitFed flu all over the world and showing them on the mobile phone’s Google Map. | Influenza | Tools | Health &amp; Fitness | General Public | 100+ | Devlin Duldulao | Twitted flu reports | Global | Free | Requires Android 6.0 and up | N/A | January 14, 2018 | January 14, 2018 | English | Rating not available | N/A |</p>
<table>
<thead>
<tr>
<th>No.</th>
<th>App Name</th>
<th>Description</th>
<th>Category</th>
<th>Access</th>
<th>Price</th>
<th>Requirements</th>
<th>Rating</th>
<th>Release Date</th>
<th>Review</th>
<th>Rating</th>
<th>No. of Downloads</th>
<th>Price</th>
<th>Requirements</th>
<th>Rating</th>
<th>Release Date</th>
<th>Review</th>
<th>Rating</th>
<th>No. of Downloads</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>Ebola Map</td>
<td>Tracks the Ebola outbreak and get up to the minute Ebola locations and status.</td>
<td>Ebola Health &amp; Fitness General Public</td>
<td>1,000+</td>
<td>Real IT Experts</td>
<td>Unknown</td>
<td>Global</td>
<td>Free</td>
<td>Requires Android 2.3 and up</td>
<td>3.9</td>
<td>October 18, 2014</td>
<td>November 20, 2014</td>
<td>English</td>
<td>Free</td>
<td>Requires Android 2.3 and up</td>
<td>3.9</td>
<td>October 18, 2014</td>
<td>November 20, 2014</td>
</tr>
<tr>
<td>23</td>
<td>Swine Flu 101</td>
<td>Tracks influenza cases around the world. Map of all outbreak cases and corresponding information updated to the minute</td>
<td>influenza News General Public</td>
<td>N/A</td>
<td>TapFactory Apps</td>
<td>CDC</td>
<td>Global</td>
<td>Free</td>
<td>Requires iOS 4.1.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>2.5</td>
<td>May 08, 2009</td>
<td>May 10, 2009</td>
<td>English</td>
<td>Free</td>
<td>Requires iOS 4.1.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>2.5</td>
<td>May 08, 2009</td>
<td>May 10, 2009</td>
</tr>
<tr>
<td>24</td>
<td>Zika Tracker</td>
<td>Daily updated mapping application of the Zika outbreak.</td>
<td>Zika Medical General Public</td>
<td>N/A</td>
<td>Zika Tracker</td>
<td>Individuals posts and reports</td>
<td>Global</td>
<td>$1.99</td>
<td>Requires iOS 9.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>Not rated</td>
<td>Sep 30, 2016</td>
<td>Aug 09, 2017</td>
<td>English</td>
<td>Not rated</td>
<td>Requires iOS 9.1 or later. Compatible with iPhone, iPad, and iPod touch.</td>
<td>Not rated</td>
<td>Sep 30, 2016</td>
<td>Aug 09, 2017</td>
</tr>
<tr>
<td>25</td>
<td>Global Ebola Tracker</td>
<td>Scans the world continent maps for reported Ebola cases from 2014 to the present, Reported and Confirmed Ebola Locations</td>
<td>Ebola Health &amp; Fitness General Public</td>
<td>1+</td>
<td>Garden State Software</td>
<td>Unknown</td>
<td>Global</td>
<td>Paid $1.27</td>
<td>Requires Android 4.0 and up</td>
<td>Not rated</td>
<td>March 20, 2015</td>
<td>March 3, 2016</td>
<td>English</td>
<td>Paid $1.27</td>
<td>Requires Android 4.0 and up</td>
<td>Not rated</td>
<td>March 20, 2015</td>
<td>March 3, 2016</td>
</tr>
<tr>
<td>26</td>
<td>Global Zika Tracker</td>
<td>Scans the world for reported Zika cases from 2015 to the present.</td>
<td>Zika Health &amp; Fitness General Public</td>
<td>1+</td>
<td>Garden State Software</td>
<td>Unknown</td>
<td>Global</td>
<td>Paid $1.39</td>
<td>Requires Android 4.0 and up</td>
<td>Not rated</td>
<td>February 26, 2016</td>
<td>February 26, 2016</td>
<td>English</td>
<td>Paid $1.39</td>
<td>Requires Android 4.0 and up</td>
<td>Not rated</td>
<td>February 26, 2016</td>
<td>February 26, 2016</td>
</tr>
</tbody>
</table>
Discussion

For epidemic surveillance, mitigation and response, implementation of mHealth technologies are potential enablers (20), and there are several options available. We found 26 Apps relevant to epidemic surveillance, mostly free of charge, the majority for the Android platform and single diseases, particularly influenza. Some Apps were country- and language-specific and had narrow applicability. Some Apps can provide real-time tracking and interactive maps. HealthMap was the most useful for epidemic surveillance, but a consumer App, Sickweather, was downloaded over 10 times more frequently. However, download statistics suggest that surveillance Apps are not widely used, with only 2 Apps (Sickweather and HealthMap) downloaded more than 10,000 times.

The Apps for the general public and health professionals have different needs and should be tailored accordingly, but there were relatively few Apps for health professionals. Use by general consumers is much more common than by health authorities or health professionals, with only a minority of Apps designed for the health sector. This indicates the potential for more widespread uptake of Apps for epidemic surveillance in public health. This is also an area where more products could be developed to assist disease surveillance. For increased uptake, ideally, apps should be free of cost and available on both the iOS and Android platforms to make them accessible for a larger set of users. The Apps should be accessible in different locations in multi-languages for maximal functionality. By creating awareness among users through several techniques such as Digital marketing, advertisements may also increase the utilization of Apps for disease surveillance.

Existing solutions are inherently prone to many biases (such as the language of reporting) which can affect the validity and reliability of the data due to background noise and lack of representativeness. For example, the HealthMap App had limitations in detecting the outbreaks near some specific geographic locations. Another example is that the Sickweather App uses social media data and validate it against CDC data to forecast the illness instead of directly taking data from CDC, WHO and other official sources. Hence, the results may not always be 100% reliable. The use of rigorous mathematical models and digital technologies such as advanced machine learning models, Artificial intelligence (AI) and cognitive APIs, Google Maps, Google Map API, Google Translate API could improve the user experience and efficiency of Apps by providing more accurate, up to date and meaningful information to users (25). Moreover, the use of crowdsourcing technology, efficient algorithms for social media (e.g. Twitter API) monitoring, techniques to identify affected populations and factors responsible for the health event, and data validation techniques could provide more relevant and validated information for the health professionals. Other limitations included unavailability of Apps suitable for general public or surveillance of potential bioterrorism incidents and limited geographic or disease relevance.

There is great potential to utilize existing Apps and develop new ones, especially those which meet the needs of health professionals and public health authorities for real-time disease surveillance. In general, mobile Apps can harness vast amounts of open-source data and potentially can provide more timely information to detect signals for infectious disease epidemics, especially if they allow users to submit data. The benefits of these Apps include low logistical burden, easy implementation and improved accessibility to previously inaccessible groups. This type of surveillance cannot replace traditional surveillance but may be a useful adjunct for more timely identification of epidemics. They can also be useful in low-income settings where traditional surveillance systems are weak.

Acknowledgements

The research was conducted under the direction of Prof. CR MacIntyre and funded by the NHMRC Centre for Research Excellence Integrated Systems for Epidemic Response (ISER) and her NHMRC Principal Research Fellowship. Copyright for the App review is vested in Prof. CR MacIntyre, UNSW.

References

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PERSPECTIVES FROM THE FIELD

Antimicrobial resistance in developing Asian countries: a challenge to global health security demanding tailored, local approaches

Rajesh Bhatia

1Former Director Communicable Diseases, WHO Regional Office for South-East Asia, New Delhi, India

Abstract

Antimicrobial resistance (AMR) has been globally recognized as one of the largest and harshest challenges to global health security and economic development. Factors responsible for rising rates of AMR are well known. In developing countries, including India, antimicrobial agents are extensively and often irrationally used in human health, veterinary and fisheries sectors. The main reasons for such widespread usage are inadequate awareness, weak regulatory mechanisms, inadequate diagnostic services and a conducive environment. Possible avenues for rapid containment of AMR have been articulated. Huge resources, both financial and technical, are needed by developing countries. In the absence of these, innovative cost-effective approaches are needed. Universal health coverage and a One Health approach that brings together human health, animal health and environmental sectors may be considered by resource-limited countries. While universal health coverage, which is already high on national political agendas, can improve access to and rational use of antimicrobial agents, a One Health approach may facilitate comprehensive and multipronged actions to contain antimicrobial resistance. These approaches need to be adopted in local contexts and implemented efficiently and effectively.

Despite rapid advances in medical innovations, the treatment of infectious diseases is becoming more difficult due to widespread emergence of antimicrobial resistance (AMR) in major pathogens, which makes antibiotics ineffective and results in treatment failure, prolonged illness, disability, greater risk of death and economic loss [1]. Furthermore, due to slowed development of new antimicrobials, very few antimicrobials are left to effectively treat infections caused by multidrug-resistant pathogens, and still fewer that are affordable in the developing world [2]. Containment of AMR is complex. Many developing countries may not be able to garner adequate resources to combat AMR. Clearly innovative approaches that are result-oriented and cost-effective are needed. Two of these approaches are described in this article.

Several studies in the current millennium have documented international spread of resistant pathogens originating from Asia [3,4]. An example is the swift spread of the New Delhi metallo-beta-lactamase-1 (NDM-1) producing Escherichia coli from India to the UK, Sweden, Austria, Belgium, France, Netherlands, Germany, the United States, Canada, Japan, China, Malaysia, Australia and Korea [3]. Colistin-resistant Enterobacteriaceae emerged in China in 2016 and spread rapidly to more than 30 countries [4].

The future implications of AMR are a serious risk to global health security. Immense gains of antimicrobial agents in the past eight decades may be negated by the emergence and spread of resistant malaria and common bacterial infections, including healthcare-associated infections, which account for high morbidity, mortality and economic loss in resource-limited countries with weak infection control practices [5]. Antimicrobial resistant pathogens currently cause about 700,000 deaths worldwide every year. If no serious action is initiated now, this number is estimated to rise to 10 million by 2050 [6], with most of these deaths in low income countries in Asia and Africa. It is estimated that by 2050, AMR will cause a global loss of US$100 trillion and a decrease of global gross domestic product by 3.5% [6]. Livestock production may decrease due to infections in food producing animals, thus impacting food security and disproportionately affecting the poor [7]. The past few years have seen immense global concern and political dialogue on combating AMR. In an unprecedented move in 2016, the United Nations General Assembly [8] deliberated on AMR and called for urgent implementation of global, coordinated efforts adopting a One Health approach to address AMR.

Few Asian countries have efficient surveillance systems to detect and monitor trends in antimicrobial resistance or antimicrobial use across human, animal and food production sectors. The Asian Network for Surveillance of Resistant Pathogens, with members spread over 14 countries (Saudi Arabia, Sri Lanka, India, China, South Korea, Japan, Hong Kong, Taiwan, Thailand, Vietnam, the Philippines, Malaysia, Singapore and Indonesia), has demonstrated increasing trends in AMR in these nations [10]. Thailand has estimated that antibiotic resistant pathogens are killing more than 38,000 people every year and an annual economic loss of US $1.3 billion [9].

Methicillin resistant Staphylococcus aureus (MRSA) is widely prevalent in almost all Asian countries. In China, Indonesia, Korea, Japan, Thailand and Vietnam
the rates of this pathogen exceed 50% in several healthcare facilities [11]. The Indian Network for Surveillance of Antimicrobial Resistance found an MRSA prevalence rate of 41% [12]. The same Indian network detected resistance to nalidixic acid in 83% of the S. enterica serovar Typhi, and 93% of S. enterica serovar Paratyphi A strains [13].

More than 70% of bacteria were resistant to erythromycin in several countries, including Sri Lanka, India, China, South Korea, Japan, Hong Kong, Taiwan, Thailand, Vietnam, the Philippines, Malaysia, Singapore and Indonesia [14]. Carbapenem-resistance in Acinetobacter spp. and Pseudomonas aeruginosa are highly prevalent in Asian economies [15]. In Thailand, between 2000 and 2014, the prevalence of imipenem resistant P aeruginosa and Acinetobacter spp increased from 10% to 22% and from 14% to 65%, respectively [16]. NDM-producing Enterobacteriaceae that were first detected in India [17] have been frequently isolated from several geographical locations in India, Pakistan, Europe and Bangladesh [18,19,20].

Data from India during 1996-2008 reveals the alarming trend of swift increases in ciprofloxacin and penicillin resistance in Neisseria gonorrhoeae (Figure 1). Rising trends of resistance to several affordable antibiotics were observed. All the isolates were sensitive to spectinomycin except one strain in 2002. Of the total isolates analysed in this study [21], 23.3% were resistant to multiple antibiotics.

Access to diagnostic services to determine rational management and self-medication are serious issues for Asia. In China, 78% of hospital inpatients were treated with antibiotics in 2002 while only 3.8% of these had laboratory-based evidence of bacterial infections [22]. In Indonesia, antibiotics were prescribed for 84% of inpatients, of which only 21% had laboratory evidence of bacterial infection [23]. Upper respiratory tract infections (URTI) accounted for almost half of the prescriptions for antibiotics, in spite of URTI being often of viral aetiology [24].

Contrary to common beliefs, more antibiotics are used in livestock production than in humans. It is estimated that in the USA, veterinary sector consumes almost 80% of all antibiotics [25]. In 2013, the global consumption of antimicrobials in food-producing animals was estimated at 131,109 tons and is projected to reach 200,235 tons by 2030 [26]. Between 2000 and 2015, antibiotic consumption in India doubled, making it the world’s biggest consumer of antibiotics [27].

According to the World Organisation for Animal Health (OIE), only 27% of its member countries collect quantitative data on antimicrobial use in livestock production [28]. Economic prosperity and population growth have increased demand for animal protein and have resulted in a substantial increase in per capita consumption of animal protein in many Asian countries in recent years [29]. Fish production systems have become more intensive to meet this growing demand [30]. China, India and Vietnam are currently the three largest producers of aquaculture products globally [31] and also large consumers of antibiotics. Most developing countries use antimicrobials as growth promoters to prevent, rather than to treat, infections in poultry and pig production systems [32,33]. The United Nations Food and Agriculture Organization (FAO) has determined that all classes of antimicrobials important for human medicine are used in animals in Southeast Asia [33]. Several European countries and Thailand have discontinued use of antibiotics as growth promoters without any adverse impact on food production [34,35].

Weak enforcement of regulations facilitates the availability of almost all antimicrobials ‘over the counter’ in all Asian countries. Self-medication and prescription for antibiotics by unauthorized health professionals is widely reported [36]. The quality of antimicrobials available in Asia is also questionable. An estimated 78% of all counterfeit drugs are manufactured in Asia and 44% are used also in Asia [37]. The magnitude of counterfeit drugs can be seen by the fact that global value of these drugs is estimated to be about $75 billion a year [37]. The counterfeit drugs usually carry suboptimal quantity of antimicrobials, thus giving an advantage to pathogens in their interaction with antimicrobial agent.
The health sectors in developing countries have been devising various strategies to combat AMR. Under the WHO Global Action Plan against AMR, more than 60 countries have developed their respective National Action Plans (NAP) [38]. However, implementation of these NAPs is difficult. It is neither technically nor financially feasible to have a stand-alone national AMR programme in many Asian countries. The NAPs in developing countries suffer from waning advocacy, inadequate availability of financial and technical resources, inadequate engagement from the private sector, and poor coordination and collaboration amongst different stakeholders [39]. Nevertheless, immediate actions can be initiated through a few other operational vehicles or platforms, including universal health coverage (UHC) and a One Health approach.

Innovative approaches

UHC means that all individuals and communities receive the health services they need without suffering financial hardship [40]. UHC provides expanded coverage in activities such as vaccination, preventative care and hygiene measures that reduce disease burden, thus bringing about a proportionate reduction of antimicrobial resistance [41]. All UN Member States have agreed to try to achieve UHC by 2030 [40]. UHC with appropriate amendments can support various AMR-specific and AMR-sensitive interventions. One of the components of the Global Action Plan on AMR is to improve access to affordable antibiotics, and UHC can facilitate implementation of this component efficiently [42]. Access to quality antibiotics and their rational use are common features of both UHC and Global Action Plan on AMR. AMR Programmes can also draw financial resources provided by international development partners for UHC.

One Health is a simple and powerful transdisciplinary approach, yet its implementation is complex and its adoption in Asia is slow. It must overcome currently practised and well-established silo approaches towards health in all countries wherein there is inadequate collaboration between all sectors that influence animal and human health. It is imperative to bring about a change in national narratives to zoonoses. This change can be catalysed by political leadership. Strong, continuous advocacy is important, especially by international development partners such as WHO, FAO and OIE through sharing of evidence-based outcomes, expected economic gains and global best practices. The Sustainable Development Goals offer a unique opportunity for advocacy, as well as an integrated methodology in which several sectors work together with a common objective of preserving efficacy of antimicrobial agents [43,44].

The framework for effective implementation of One Health would involve incorporation of political commitments, policy formulation, sustainable financing, programme development, knowledge sharing, institutional collaboration, capacity enhancement, engagement of civil society and active participation of the communities [41].

While AMR has increased, the discovery and development of new classes of antimicrobial medicines have drastically slowed because of the high cost of discovery and low return on investment. The inappropriate use of antibiotics in humans, animals and food production must be curbed. In human health, both prescribers and users must consider the potential risks of indiscriminate use of antimicrobial agents. In animal health, the use of antibiotics as growth promoters must be discontinued and replaced with good animal husbandry practices in Asia. The global battle against AMR must ensure engagement of Asian countries.

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RAPID REPORTS

Outbreak investigation of sheep pox in District Barkhan, Balochistan, Pakistan

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2Livestock and Dairy Development Department, Balochistan, Pakistan

Abstract
During mid-January 2018, a significant number of suspected sheep pox cases were reported from the district of Barkhan, Balochistan to the Director of Animal Health. An investigation team was deployed after an unusually high mortality rate and complaints of skin lesions accompanied by lacrimal & nasal discharge were reported. The aim of this investigation was to estimate the magnitude of the disease, identify risk factors and implement preventive measures to stop further spread of disease. We defined a sheep pox confirmed case as a sheep with fever >40˚C and necrotic skin lesions along with one or more of the following: papules or nodules anywhere on the body, mucopurulent nasal discharge, hyperemia, oedema (generalized), swollen eyelids and enlarged prescapular lymph node. Using a pre-tested questionnaire, rates and frequencies were calculated using Epi Info™ 7 Software. A case-control study was conducted in March 2018. During active case finding, 43 farms were suspected for sheep pox infection, with a total of 4050 infected animals. Of these, infected adult sheep comprised 76% (3081), followed by 24% (969) lambs. The case fatality rate was 33% (1337/4050) with an overall attack rate of 55% (4050/7438). Almost half the farms (21/43) responded that wool shearing within a flock was done, 42% (18/43) introduced new animals into a flock without prior quarantine, but only 5% (2/43) were aware of isolation and only 21% (9/43) vaccinated the animals. New animals within flocks (OR: 3.7, CI 1.34 – 10.2, P-value 0.008) and wool-shearing (OR: 3.15, Cl 1.24 – 7.9, P-value 0.01) were statistically associated with disease spread. This outbreak of sheep pox is much larger than those previously reported. The outbreak occurred in an area with new animal arrival, low vaccine coverage, and poor biosecurity and sanitary measures. Standard biosecurity and sanitary prophylaxis measures were recommended to control the outbreak.

Introduction
Sheep pox is a devastating viral disease of sheep; it is highly contagious and widely distributed in some parts of the world [1]. In recent years it has mainly been reported from Asia and Africa. The virus belongs to the genus Capripox, sub-family Chordopoxvirinae of the Poxviridae family. The transmission of virus is either by close contact, aerosols, or indirectly by feed and water [2]. The virus can remain viable for months on wool or dried scabs.

The incubation period ranges from 8 to 13 days, with a maximum incubation of 21 days. It is one of the major viral diseases of ovines and caprines, with high morbidity and considerable mortality of 70-90% [3], which can sometimes approach 100% [4]. The sheep is the primary host and all age groups are equally affected. However, young lambs are at higher risk of death [5]. Severe economic losses occur from the high mortality, abortions, skin damage and loss of wool and mutton [6]. The disease appears on the World Organization for Animal Health (OIE) list as a notifiable disease [7-8].

During mid-January 2018, 1500 suspected sheep pox cases were reported by local field veterinarians in the district of Barkhan, Balochistan. The cases presented with skin lesions accompanied by lacrimal & nasal discharge and unusually high mortality. The investigation team was assigned on 28th February to visit District Barkhan to investigate the situation and recommend control measures for future prevention of ongoing outbreak. The district Barkhan has a total sheep population of 413,840 and shares a border with Punjab province. The aim of this investigation was to conduct an outbreak investigation and control the disease through preventive measures to stop further spread of disease.

Methods
After literature review on sheep pox, the investigation team visited the affected areas of district Barkhan on March 1st, 2018. To understand the outbreak and the perspective of the community, a combined meeting session with farmers & administrators in the area was conducted. There were very few veterinary dispensaries or hospitals in the area with records; therefore, interviews of the farmers were conducted for data collection. The investigation was carried out from the 1st to 3rd March 2018 and a descriptive followed by case-control study was conducted. By using standard case definition, a case was defined as a sheep with fever >40˚C, necrotic skin lesions and one or more of the following: papules or nodules anywhere on the body, mucopurulent nasal discharge, hyperemia, oedema (generalized), swollen eyelids and enlarged prescapular lymph node, between January 10th to March 10th, 2018 in...
Barkhan. Using a semi-structured questionnaire, demographic, clinical, and risk factor data were collected. Risk factors included vaccination status, biosecurity practices and waste disposal methods. All flock owners were interviewed and animals were examined for infection.

Data Collection

To find the risk factors associated with sheep pox, flock to flock investigation was carried out in the district. The information associated with sheep pox cases was collected from farm owners or workers by using the semi-structured questionnaire. Data was collected about the mortality patterns of the flocks, total mortality in the last 50 days, and status of vaccination against sheep pox virus (SPV). Vaccination was recorded as no vaccination, single or two shots of SPV vaccine. The animal history included being a newly introduced animal, isolation and wool shearing. The history and reasons for not getting vaccine were asked in detail.

Data Analysis

Frequencies were calculated and tables and graphs were generated by using Epi InfoTM 7 and discussed with relevant stakeholders. Risk factors were analysed by calculating odds ratios for infection. The odds of getting disease in newly introduced animals versus unintroduced animals, isolation versus no isolation, and wool shearing versus no wool shearing were calculated. All significance was reported at confidence interval of 95% and p-value less than 0.05.

Active case finding was conducted in the area. A case-control study of affected and unaffected farms was conducted. The farms were selected as cases if they had sheep pox, based on our case definition and inclusion criteria. Control farms were those that were disease-free. The risk factors were coded as 0= No and 1= Yes. The controls were taken from the same and adjoining union councils of the district in a 1:1 ratio. The inclusion criteria for controls were flocks of same village or adjoining area that did not have sheep pox at that time. For comparison, a total of 43 controls were randomly selected. Vaccination practices were documented for case and control farms.

The attack rate (AR) was defined as proportion of animals that develop disease / total no. of animals at risk. We considered the at-risk population as the total population in the affected farms. We calculated the AR in the affected farms. Vaccine effectiveness among infected flocks was calculated by using the formula [Attack rate in unvaccinated - attack rate in the vaccinated] / attack rate in the vaccinated), or [VE = [ARU – ARV] / ARU].

Results

Active Case Finding Results

For active case finding, clinical examinations were conducted. A total of 47 farms in the affected area were investigated and 43 of them were suspected for sheep pox infection as per the case definition. A total of 43 farmers were interviewed, having 7,438 animals. These farmers had a population that comprised 80.5% (5988) adult sheep, and 19.5% (1450) lambs.

There were 4050 animals with active clinical infection or suffering from the same clinical signs as our case definition. Of these, infected adult sheep comprised 76% (3081), followed by 24% (969) lambs. The attack rate in adult sheep was 52% and 66% in lambs. The attack rate for animals is also given in Table 1 below. The overall attack rate was 55% (4050/7438).

A similar pattern was observed for the case fatality rate. The case fatality rate (CFR) is given in Table 2 below. The overall case fatality rate was 33% (1337/4050).

Infected animals from a single flock were considered as 1 unit. Fever was reported in 88% (38/43) of flocks, along with nasal discharge in 74% (32/43) and swollen eyelids in 58% (25/43). 49% (21/43) exhibited oedema while 40% (17/43) had hyperemia (Figure 1). Necrotic skin lesions were reported in almost all infected flocks. However, 63% (27/43) of flocks had skin lesions around the face, 58% (25/43) had around ear and udder, 51% (22/43) had lesions around the mouth, and 30% (13/43) reported lesions all over the body (Figure 2).

The distribution of suspected sheep pox flocks regarding the onset of symptoms was also recorded. The first suspected infected flock (index) was reported on 17th January 2018 after new animals were introduced into a flock. Infected flocks started being reported from 20th January 2018, with the first and second peak observed on 31st January and 8th February, respectively. Then it began to decline in magnitude but remained prevalent and peaked again on 2nd March 2018. Afterwards the cases reduced significantly, and the last case was reported on 7th March.

The team found that most flocks were not vaccinated. Out of a total of 43 flocks, 34 flocks were non-vaccinated, three were fully vaccinated and six were partially vaccinated. The majority 62% (21/34) - responded that vaccine was not available in the area, 26% (9/34) faced the problem of inaccessibility to a veterinary hospital and 12% (4/34) said the vaccine was unaffordable.

Half of the case farms, 49% (21/43), responded that wool shearing within a flock was done twice a year. 42% (18/43) reported that new animals were introduced in a flock without prior quarantine. Only 5% (2/43) were aware of isolation and 21% (9/43) vaccinate the animals.

Among controls, 23% (10/43) responded that wool shearing within a flock was done twice a year, 16% (07/43) introduced new animals in a flock and 19% (8/43) were aware of isolation and 53% (23/43) vaccinated the animals. Table 3 shows the univariate analysis. The risk of disease was significantly associated with the introduction of new animals (OR: 3.7, CI 1.34 – 10, P-value 0.008) and wool shearing (OR: 3.15, CI 1.24 – 7.9, P-value 0.01).

Vaccine effectiveness among infected flocks was 0.55, or 55% in preventing infection.
Table 1. Attack rates for the infected animals

<table>
<thead>
<tr>
<th>Animals</th>
<th>Infected Animals</th>
<th>Total Population</th>
<th>Attack Rates</th>
<th>Odds ratio (OR)</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamb</td>
<td>969</td>
<td>1450</td>
<td>66%</td>
<td>1.9</td>
<td>1.6 - 2.1</td>
<td>0.000</td>
</tr>
<tr>
<td>Adult</td>
<td>3081</td>
<td>5988</td>
<td>52%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. The case fatality rates of the animals

<table>
<thead>
<tr>
<th>Animals</th>
<th>No. of fatal cases</th>
<th>No. of infected animals</th>
<th>Total no. of animals</th>
<th>CFR %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>776</td>
<td>3081</td>
<td>5988</td>
<td>25%</td>
</tr>
<tr>
<td>Lamb</td>
<td>561</td>
<td>969</td>
<td>1450</td>
<td>58%</td>
</tr>
<tr>
<td>Total</td>
<td>1337</td>
<td>4050</td>
<td>7438</td>
<td>33%</td>
</tr>
</tbody>
</table>

Figure 1. Symptoms among affected flocks during sheep pox outbreak in District Barkhan

Figure 2. Skin lesions among affected flocks during sheep pox outbreak in District Barkhan
Figure 3. Suspected sheep pox cases reported from District Barkhan from January to March 2018 (n=4050)

Table 3. Risk factors for sheep pox outbreaks.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Risk Factor</th>
<th>Cases (n %)</th>
<th>Controls (n %)</th>
<th>OR</th>
<th>95% Cl</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduced new animals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>18 (72%)</td>
<td>7 (28%)</td>
<td>3.7</td>
<td>1.34-10.2</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>25 (41%)</td>
<td>36 (59%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Isolation of infected animals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2 (20%)</td>
<td>8 (80%)</td>
<td>0.21</td>
<td>0.04-1.07</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>41 (54%)</td>
<td>35 (46%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Wool shearing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>21 (68%)</td>
<td>10 (32%)</td>
<td>3.45</td>
<td>1.24-7.9</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22 (40%)</td>
<td>33 (60%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Vaccination status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>9 (28%)</td>
<td>23 (72%)</td>
<td>0.23</td>
<td>0.08-0.59</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>34 (63%)</td>
<td>20 (37%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Case-control analysis of affected and unaffected farms

<table>
<thead>
<tr>
<th>Vaccination of sheep</th>
<th>Case farms</th>
<th>Controls</th>
<th>Total</th>
<th>Risk/attack rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>9</td>
<td>23</td>
<td>32</td>
<td>0.28</td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>20</td>
<td>54</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Conclusion of outbreak investigation

The outbreak was attributed to the introduction of new animals into the flocks. The index flock farmer introduced new animals without prior quarantine. Other factors included wool shearing and low vaccination rates. That led the disease to spread to entire region and other Union councils. There was no scheduled vaccination in the area and a lack of awareness about safe disposal of deceased animals. The deceased animals were discarded openly, anywhere, which allowed consumption by stray dogs and wild birds.

Discussion

We describe a large propagated outbreak of sheep pox which progressed rapidly, with a vaccine effectiveness of 55%. As far as we are aware, there are no other available estimates of field vaccine effectiveness. However, Boumart et al. [9] compared live and attenuated vaccine efficacy in 2016. They found inactivated Romanian SPPV has the potential to control and prevent disease in endemic areas. A breach in biosecurity contributed to the outbreak, specifically allowing introduction of new animals without screening. This was exacerbated by shearing and low vaccination rates. Our findings are similar to
the results reported by Hamouda et al. [10]. GB Manjunathareddy et al. [11] reported disease spread mainly through close contact, introduction of new animals and transportation. In our study, the morbidity rate was high in young lambs compared to adult animals (OR: 1.9, CI 1.6 – 2.1, P 0.000). A study conducted in Ethiopia reported high seropositivity in young age (OR 2.2, CI: 1.46 - 3.4, P 0.01) and ewes (OR: 1.99, CI: 1.96 – 3.40, P 0.008) as compared to adults and rams. The low level of immunity in young animals explained the higher seropositivity [12]. In our study, by taking history we found that sheep pox remains endemic in the whole belt of the district and cases arise during the winter season. Most studies show that disease is more prevalent during the winter and autumn season [13]. Mixing of animals and animal movement for grazing were also potential sources of direct transmission of disease. The indirect spread of disease may have occurred through open air disposal of deceased animals. Authie E et al. [13] reported an outbreak in Greece during 2013- 2014. Greece shares borders with Bulgaria and Turkey, resulting in spread of sheep pox between the countries through direct contact with sick and dead animals. In 2014, an outbreak among unvaccinated sheep occurred in Turkey. With further investigation they found new animals had been introduced to farm recently [14]. Similar findings were reported by several other authors [2, 15, 16, 17]. Low vaccine coverage also contributed to the spread of disease. Lack of awareness, lack of access and cost all contributed to low vaccine coverage.

**Actions taken and recommendations**

A public awareness session was conducted in union councils where farmers were briefed about the vaccine and the significance of vaccination. The farmers were provided with free vaccination. The farms in the surrounding area of a 3 km radius were screened for sheep pox and advised accordingly. Active surveillance was conducted to detect unvaccinated infected flocks and monitoring in vaccinated flocks was started in the affected area.

The study had limitations, as age-specific and gender distribution of cases within flocks were difficult to assess. The farmers did not have the accurate birth or age records of the animals. Moreover, there was continuous purchase and sale of animals during the outbreak period. On the basis of these findings it is highly recommended that farming community should be educated about the importance of vaccination and sanitary precautions. Media and livestock workers should play a role in advocacy and communication about vaccinations to limit economic losses. More research is required to investigate field vaccine effectiveness, the variation of the strain, and to estimate the economic losses due to such outbreaks.

**References**


Feedback from operational stakeholders who manage or respond to outbreaks is that they are often too busy to review literature or obtain relevant background information to assist them with acute response. Unlike a traditional analytical outbreak investigation report, Watching Briefs are intended as a rapid resource for public health or other first responders in the field on topical, serious or current outbreaks, and provide a digest of relevant information including key features of an outbreak, comparison with past outbreaks and a literature review. They can be completed by responders to an outbreak, or by anyone interested in or following an outbreak using public or open source data, including news reports.

Keywords: Ebola; Ebola virus disease, outbreak; epidemiology; Democratic Republic of Congo; DRC; North Kivu; Bas-Uele; Equateur; viral persistence; zSVS-ZEBOV

<table>
<thead>
<tr>
<th>Watching brief</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
</tr>
<tr>
<td><strong>Author(s)</strong></td>
</tr>
<tr>
<td><strong>Date of first report of the outbreak</strong></td>
</tr>
<tr>
<td><strong>Disease or outbreak</strong></td>
</tr>
<tr>
<td><strong>Origin (country, city, region)</strong></td>
</tr>
<tr>
<td><strong>Suspected Source (specify food source, zoonotic or human origin or other)</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Date of outbreak beginning</strong></td>
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</table>
On 9 May 2017, the World Health Organization (WHO) was informed of a cluster of undiagnosed illness and deaths with haemorrhagic symptoms from 22 April 2017 in Likati health zone, Bas-Uélé province, northern DRC (near the Central African Republic border). Five blood samples were sent to the Institut National de Recherché Biomédicale (INRB) laboratory in Kinshasa, two of which tested positive for EBOV using RT-PCR. On 11 May 2017, WHO declared the start of the outbreak after being notified by the Ministry of Health (MOH) of DRC of the first two confirmed EVD cases. By then, 9 suspected cases, including 3 deaths, have been reported [1].

2018 Équateur province outbreak

From 4 April to 9 May 2018, 32 EVD cases (including 18 deaths) were reported from Bikoro health zone, Équateur province, northwest DRC (near the Congo border), approximately 800km southwest of Likati, Bas-Uélé [5]. Five samples were sent to the INRB, two of which tested positive for EBOV using RT-PCR. On 8 May 2018, WHO declared the start of the outbreak, after being notified by the MOH of DRC of two confirmed EVD cases [6].

2018 North Kivu province outbreak

On 28 July 2018, the MOH of DRC was informed of a cluster of haemorrhagic fever cases by the North Kivu health division, eastern DRC (near the Uganda border). Mangina, the epicentre of the outbreak [7], is approximately 700km southeast of Likati, Bas-Uélé and 1,300km east of Bikoro, Équateur [5]. Six blood samples were sent to the INRB laboratory, four of which tested positive for EBOV using GeneXpert-automated PCR. On 1 August 2018, WHO declared the start of the outbreak after being notified by the Ministry of Health (MOH) of DRC of the four confirmed EVD cases. By 3 August 2018, 43 EVD cases (13 confirmed and 30 probable), including 33 deaths, had been reported in North Kivu province and the neighbouring Ituri province [8].

<table>
<thead>
<tr>
<th>Date outbreak declared over</th>
<th>For EVD, the end of an outbreak will be declared 42 days (two 21-day incubation cycles of EBOV) after the last confirmed patient of the affected area tested negative for the disease for the second time.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017 Bas-Uélé province outbreak</td>
<td></td>
</tr>
<tr>
<td>Affected countries &amp; regions</td>
<td>2017 Bas-Uélé province outbreak</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td></td>
<td>Because of the remote and isolated nature of Likati district, the outbreak was contained within the boundary of Bas-Uélé province. Cases were reported from four health areas:</td>
</tr>
<tr>
<td></td>
<td>• Nambwa (3 confirmed and 2 probable, including 3 deaths);</td>
</tr>
<tr>
<td></td>
<td>• Muma (1 confirmed, no death);</td>
</tr>
<tr>
<td></td>
<td>• Ngayi (1 probable, including 1 death);</td>
</tr>
<tr>
<td></td>
<td>• Mabongo (1 confirmed, no death) [11].</td>
</tr>
<tr>
<td></td>
<td>2018 Équateur province outbreak</td>
</tr>
<tr>
<td></td>
<td>Cases were reported from three health areas in Équateur province:</td>
</tr>
<tr>
<td></td>
<td>• Bikoro (10 confirmed and 11 probable, including 18 deaths);</td>
</tr>
<tr>
<td></td>
<td>• Iboko (24 confirmed and 5 probable, including 12 deaths);</td>
</tr>
<tr>
<td></td>
<td>• Wangata (4 confirmed, 3 deaths) [10].</td>
</tr>
<tr>
<td></td>
<td>2018 North Kivu province outbreak</td>
</tr>
<tr>
<td></td>
<td>As of 12 May 2019, cases were reported from the following 21 health zones:</td>
</tr>
<tr>
<td></td>
<td>• North Kivu province: Beni, Biena, Butembo, Kalunguta, Katwa, Kayna, Kyondo, Lubero, Mabalako, Manguredjipa, Masereka, Musienene, Mutwanga, Oicha, Vuhovi (1,465 confirmed and 76 probable, including 1,024 deaths);</td>
</tr>
<tr>
<td></td>
<td>• Ituri: Bunia, Komanda, Mandima, Nyakunde, Rwampara, Tchomia (152 confirmed and 12 probable, including 100 deaths) [12].</td>
</tr>
</tbody>
</table>
Initial presentation of EVD is non-specific and can be misdiagnosed as other diseases such as malaria, typhoid, and other viral haemorrhagic fevers (including dengue or Lassa fever) [13].

According to WHO’s case definition, an EVD case is classified as “suspected” if either of the following symptoms applies:

- a sudden onset of high fever (39-40°C) and at least three of the following symptoms: headaches, anorexia, stomach pain, vomiting, diarrhoea, lethargy, aching muscles or joints, difficulty swallowing, difficulty breathing, hiccups; or
- inexplicable bleeding; or
- sudden, inexplicable death.
A case is classified as “probable” if it is evaluated by a clinician, or if a diseased patient has an epidemiological link with a confirmed case.

A case is classified as “laboratory confirmed” if a blood sample is tested positive for virus antigen via reverse transcriptase-polymerase chain reaction (RT-PCR) or detection of IgM antibodies directed against EBOV [14].

For the three outbreaks, cases were alerted to the MOH of DRC by the referral health centre upon showing symptoms of acute haemorrhagic fever. The common symptoms for most of the early cases were high fever and intense fatigue [15,16,17]. No detailed description was given for any haemorrhagic symptom that accompanies fever (e.g. conjunctival bleeding, gastrointestinal bleeding or bleeding from venipuncture site).

<table>
<thead>
<tr>
<th>Mode of transmission (dominant mode and other documented modes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bodily fluids contact</strong></td>
</tr>
</tbody>
</table>
| Initial transmission of EBOV occurs through contact with an infected animal, such as a fruit bat or a primate. After that, EBOV can be transmitted from human to human via direct contact with blood or bodily fluids (urine, saliva, sweat, faeces, vomit, breast milk and semen) of an infected or deceased person [18].

The virus can remain in bodily fluids secreted from immunologically privileged sites, including semen, breast milk, ocular fluid and spinal column fluid, even after the infected person has recovered from EVD [19]. However, the amount of viral shedding in each type of fluid is not well quantified [18].

An infected person can only transmit EBOV once he or she develops signs and symptoms [18]. The incubation period is approximately 2-21 days [21]. Healthcare workers (HCWs) and burial personnel are at high risk of contracting EVD because of close contacts with the infected person and handling of instruments (needles and syringes) containing bodily fluids [22,23]. Hence, infectious control measures in hospitals and safe burial practices are critical in transmission control.

**Fomite transmission**

Theoretically, fomite transmission is possible because EBOV was detected in visible dried blood stains [20] and could persist on glass surface and in the dark for 6 days in a laboratory-controlled setting [24]. However, EBOV does not remain infectious if allowed to dry on environmental surfaces, especially in routinely disinfected wards [20].
Airborne transmission (aerosol or large droplets)

Experiments have demonstrated transmission of EBOV without direct contact among animals [25,26], suggesting the possibility of transmission via aerosol or large droplets secreted by the infected animal. In mechanically produced aerosols, EBOV was found at sufficient levels to cause lethal infections in primates [27,28]. However, airborne transmission from human to human is uncertain in previous outbreaks [29]. In pathology specimens of the lung, abundant Ebola virus is found [30], and the Kikwit outbreak in 1995 suggests airborne transmission in at least five cases [31].

Others

EBOV cannot be transmitted by food (except for consumption of bushmeat in certain parts of the world), mosquito bites, or casual contact with a survivor [18]. However, sexual transmission from recovered survivors and vertical transmission from mother to baby have been documented [32].

Demographics of cases

Demographic details were not available for the 2017 Bas-Uélé province outbreak.

2018 Équateur province outbreak

7 out of 54 reported cases (13%) were HCWs [10]. The median age was 40 years (range 8-80) and 40% were females. 71% of confirmed cases had contact with infected patients, and 58% of confirmed cases attended funerals before the onset of disease [16].

2018 North Kivu province outbreak

As of 12 May 2019, among 1,705 reported cases, 56% were female, and 29% were children aged less than 18 years. 101 cases (6%) were HCWs [12].

Case fatality rate (CFR)

2017 Bas-Uélé province outbreak

By 2 July 2017, 4 out of 8 reported cases were fatal. The overall CFR is 50%. The number of fatalities among confirmed cases was not published [11].

2018 Équateur province outbreak

By 24 July 2018, 33 out of 54 reported cases (17 out of 38 confirmed cases) were fatal. The overall CFR was 61%; the CFR among confirmed cases is 45% [10].
| Complications | **2018 North Kivu province outbreak**  
As of 12 May 2019, 1,124 out of 1,705 reported cases (1,036 out of 1,617 confirmed cases) were fatal. The overall CFR is 65.9%; the CFR among confirmed cases is 64.1% [12]. |
| **Complications** | The initial non-specific presentation of the disease is followed with abdominal pain, severe vomiting and diarrhoea, leading to fluid loss and hypovolemic shock [13]. Patients are also prone to systemic inflammatory response syndrome, characterised by symptoms commonly associated with bacterial sepsis (fever, tachycardia, hyperventilation and leukopenia). Haemorrhage is only observed in a minority of patients [33].  
The combination of hypovolemia, septic shock and haemorrhage eventually results in multi-organ dysfunction, particularly the renal, hepatic and coagulation systems. This happens typically by the second week of the disease and rapidly leads to organ failure and death [33].  
Ebola survivors may develop ocular complications such as uveitis, which can lead to vision loss [34]. |
| **Available prevention** | Wearing of personal protective equipment (PPE) can reduce the risk of EBOV transmission by introducing a physical barrier against the infected person’s bodily fluids [35]. However, emphasis on proper donning and doffing technique and double gloving [36,37] is crucial to minimise the risk of self-contamination during removal of PPE [38].  
Several vaccines for EVD are being evaluated in clinical trials [39,40,41,42]. One vaccine, called rVSV-ZEBOV, has been demonstrated in phase I-III clinical trials to be safe and immunogenic in humans [43]. This vaccine consists of recombinant vesicular stomatitis virus (VSV) vector expressing a surface glycoprotein from the Zaire Kikwit 1995 strain [44].  
rSVS-ZEBOV is recommended by the Strategic Advisory Group of Experts on Immunization (SAGE) for use against subtype Zaire if no licensed vaccine is available [45]. It was approved for compassionate use by the DRC's Ethics Committee during the early stage of the 2018 Équateur province and 2018 North Kivu province outbreaks [46,47] based on the genomic analysis of early cases' pathogen samples [48].  
In May 2019, SAGE recommended an additional vaccine alternative for lower risk individuals, for whom the Ad26.ZEBOV/MVA-BN is being considered [49]. The |
Ad26.ZEBOV/MVA-BN is a two-dose, multivalent vaccine consisting of an adenovirus-26 vector (Ad26.ZEBOV) and a modified vaccinia Ankara vector (MVA-BN) encoded with Ebola glycoproteins, which have been demonstrated in phase I-II randomised controlled trials (RCT) to be safe and immunogenic for human volunteers [50,51].

**Available treatment**

Current treatment for EVD is limited to supportive care and symptomatic treatment only. Rehydration via oral or IV route is routinely encouraged to prevent hypovolemic shock. Transfusion of whole blood or coagulation regulators (e.g. clotting factors, fibrinolysis inhibitors, etc.) is administered to counteract haemorrhage. Some patients require anticoagulants to reduce risk of thrombosis and disseminated intravascular coagulation following haemorrhage. Intensive care, including dialysis, hemofiltration, intubation, and mechanical ventilation, is required for patients with multi-organ system failures, but is limited to developed-country settings [52].

Several experimental therapies are under development, including antivirals, interferons, antibodies and interfering RNA [53], although none have successfully completed human RCT. There is increasing interest in convalescent therapy, in which patients receive whole blood or plasma from Ebola survivors, which has improved survival rates in past outbreaks [54]. It is recommended by WHO as an interim empirical treatment during outbreaks [55].

A cocktail of three chimeric monoclonal antibodies, named ZMapp, demonstrated strong antiviral activity in preliminary studies and prevented death even when administered in the late stage of the disease. However, the human RCT (PREVAIL II) only succeeded in demonstrating safety, not efficacy, due to insufficient enrolment [56].

A phase II-III RCT is underway in the DRC to compare the safety and effectiveness of 3 new therapies against Zmapp: mAb114 (a single monoclonal antibody), remdesivir (an antiviral) and REGN-EB3 (a monoclonal antibody cocktail). The trial is enrolling EBOV patients in Beni, with plans to include patients from other Ebola treatment units [57].

**Comparison with past outbreaks**

Case fatality rate

The 2018 Équateur province outbreak reported CFR of 61%, which is comparable to previous outbreaks of the same scale,
such as the 2014 outbreak (69 cases, CFR 71%) or the 2008 outbreak (32 cases, 47%) [58].

The 2018 North Kivu province outbreak was the most severe outbreak in the history of the DRC, with 1,705 cases and CFR of 65.9%, which is comparable to other large outbreaks such as the 2007 outbreak (264 cases, 71%) or the 1995 outbreak (315 cases, 79%) [59].

The 2012 outbreak reported a lower CFR (36 cases, 36%). However, it was caused by a different virus, Bundibugyo ebolavirus [48].

Causative agents

All three outbreaks were caused by Zaire ebolavirus, which is the causative agent behind the 2014-2016 outbreak in West Africa and all previous outbreaks in the DRC except for the 2012 outbreak [58,60]. Phylogenetic analysis shows that the EBOV strains behind the 2018 Équateur outbreak are genetically linked to the 2014 outbreak, which occurred at the neighbouring Tshuapa province [61].

Geographic footprint

Like most previous outbreaks, the Bas-Uélé and Équateur outbreaks were geographically contained due to the remote nature of their epicentres. The Bas-Uélé outbreak’s epicentre is a forested region of Likati health zone, with a population density of only 7 people/km² [62]. The Équateur outbreak’s epicentre is Bikoro health zone, which is 280km by road from the provincial capital, Mbandaka [6].

In contrast, the North Kivu outbreak has extended to urban locations, including Beni (population 420,000) and Butembo (population 1 million) [7,63]. It is comparable to the 1995 outbreak in Kikwik (population 500,000) [64].

Impact on HCWs

The proportion of HCWs among total EVD cases are lower (6-13%) [10,12] compared to previous Ebola outbreaks (25-31%) [22].

Vaccination

This is the first time a vaccination strategy was adopted in the DRC for Ebola response [65]. An extensive ring vaccination campaign with rSVS-ZEBOV has been carried out since August 2018, covering more than 120,000 high-risk individuals, including
children, contacts and front-line HCWs. 80% of identified cases (776) had their rings defined and their contacts gave consent for vaccination. 90% of consented contacts were vaccinated, indicating high coverage [66]. Acceptance of vaccination among families and HCWs is high [67].

To date, Merck & Co. has shipped 100,000 rSVS-ZEBOV doses to the DRC and agreed to maintain a global emergency stockpile of 300,000 doses. However, in view of the scale of recent Ebola outbreaks, an option to increase the stockpile may be revisited in the future [68].

### Unusual features

By 12 May 2019, over 93,400 contacts have been registered, 14,459 were under surveillance, and 114,498 contacts have been vaccinated with rSVS-ZEBOV [12]. In April 2019, WHO published preliminary results from the observational study of this campaign, claiming an overall vaccine efficacy of 97.5% (95% CI 95.8-98.5%). Out of all vaccinated contacts, 71 contracted EBOV (0.076%). The report concludes that ring vaccination with rSVS-ZEBOV demonstrates protective effects on secondary degree contacts and lowers fatality rate among those contracting EBOV (CFR was 16% among those contracting within 9 days post-vaccination and 0% among those contracting 10 days or more post-vaccination) [66].

However, despite unprecedented advancements in vaccines, diagnostics, experimental treatment and accumulated institutional experience, the response strategies that were successful in containing the Équateur outbreak failed to replicate the same result in the North Kivu outbreak. Since October 2018, new clusters continue to emerge in multiple health zones [7].

### Critical analysis

#### Phylogenetic analysis

Genome sequencing confirmed that the two EBOV strains behind the outbreaks in Équateur and North Kivu provinces are genetically distinct. The 2018 Équateur strain is genetically closer to the 2014 outbreak that hit the neighbouring Tshuapa province [61]. On the other hand, samples from Mangina and Beni (2018-2019 North Kivu outbreak) are genetically closer to the sample from Likati (2017 Bas Uélé outbreak) [69].

The three EBOV strains seem to be independent lineages diverging from a single clade in 1976-1977 (the first Ebola outbreak in the DRC) [61]. This raises the possibility of a single origin reservoir that has been propagating EVD across
geographic distances in the DRC, either through habitat fragmentation or migration. A similar hypothesis emerged for the 2014 outbreak, in which bats were identified as the main zoonotic reservoir of EBOV and their spatial-temporal migration patterns were said to correlate with hot spots of EVD outbreaks in West Africa [70].

Persistence of the outbreak

The current North Kivu-Ituri outbreak is characterised as a complex humanitarian emergency because efforts to contain the outbreak were hampered by a multitude of interlinked issues.

- **Security deterioration & community resistance**
  Unlike the other two, the North Kivu outbreak occurred in a war zone – the Kivu province is the stronghold of the opposition, with over 100 active armed groups in conflict for over 25 years [71]. Ebola treatment centres (ETCs) and HCWs have been repeatedly attacked by militants [71,72,73].
  Besides armed groups, HCWs have frequently encountered community resistance in multiple locations, especially in Beni [74,75]. The tension between HCWs and the civilians stems from frustration over unmet health needs, postponement of presidential elections due to the Ebola outbreak and the resulting suspicion of the Ebola response as a political ploy by the incumbent government [76]. In rural areas, residents are generally distrustful of health personnel because of past violent acts by outsiders and the perceived high death rates at ETCs [73].
  These incidents were disruptive to contact tracing, safe burials and vaccination – the three pillars of Ebola prevention.

- **Ineffective contact tracing**
  More than half of reported EVD cases were not on existing lists of identified contacts, suggesting a potential weakness in contact tracing, or that the source of infection was not an identified case [73,77]. The reported barriers to identifying and monitoring contacts were low engagement of community health workers, particularly traditional healers, and heightened insecurity [74].
  In addition, continuous movement of more than a million refugees and internally displaced people (IDP) in and out of North Kivu and Ituri provinces [78] creates barriers to effective contact tracing. The towns of Beni and Butembo, in particular,
see constant traffic, often unreported, across the DRC-Uganda border for micro-commerce activities, family visits and trafficking [71].

- **Suboptimal infection prevention and control (IPC) measures**
  
  IPC practices – wearing gloves, washing hands, disinfecting infected wards and quarantining – remain inadequate in public and private health centres, as reflected in a high incidence of EVD among HCWs [12,79]. Infected but undiagnosed HCWs might be an important focal point that transmit EVD to community cases, who visit health facilities for other illnesses [74,80]. Supplies of PPE may also be short.

  Another important source of infection is informal clinics belonging to traditional healers, which serve a majority of hard-to-reach communities. Their large number and unregistered nature demands multiple supervisory visits to ensure compliance with IPC standards. On the other hand, these traditional healers can be potentially engaged as CHWs for community education on sanitation and hygiene [74].

**Viral persistence – A possible mechanism for perpetual flare-ups?**

Despite having declared the end of the Ebola outbreak in March 2015, Liberia still faced several flare-ups throughout 2015 that were from persistently infected survivors, instead of an active reservoir [81]. Another phylogenetic investigation showed that a female EVD survivor from the 2014 Liberia outbreak might have transmitted EBOV to her son one year later [82]. These examples raised the question of whether persistently affected survivors are a source of unidentified transmission chains in the DRC outbreaks. However, this hypothesis is challenged by the fact that the DRC was not the main affected area in 2014 and does not have a large number of survivors present, compared to Sierra Leone, Liberia and Guinea.

One important link to consider is sexual transmission. Several flare-ups from Liberia, Guinea and Sierra Leone were attributed to sexual intercourse with persistently infected male survivors [83,84]. Serological and genomic data from EVD male survivors demonstrated persistence of viral RNA in semen [85,86] that lasted beyond the WHO-defined waiting period for declaring a country to be free from EVD [84]. This opens up another avenue for community health education: safe sex practices such as sexual abstinence or condom use must be included in the community education package for contacts of EVD survivors [84].
Key questions

Why have multiple, genetically distinct outbreaks arisen in the DRC within a period of 24 months?

Figure 2: Geographical locations and timeline of all Ebola outbreaks in the DRC since 1970s, adapted with permission from comersis.com [5] using data from CDC [18].

How can socio-political barriers to disease control be best addressed?

How effective are vaccination campaigns in reducing the spread of the disease in the 2018 North Kivu outbreak, and have cases occurred in vaccinated contacts?

How long will the immunity last among vaccinated people?

How should vaccines be given in view of heightened risk of outbreak expansion? Should the current ring vaccination strategy be replaced by geographical vaccination, covering areas of high population density?
Have persistently infected survivors played a role in the North Kivu outbreak?
What health promotion strategies are needed regarding prevention of sexual transmission among survivors?

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EDITORIALS

The risk of selective investment in downstream pandemic planning

C Raina Macintyre

Introduction

Whilst we recognize an increase in emerging infections and serious epidemics in recent years(1), there has been a lack of investment in upstream prevention and mitigation (2). There has been investment in development of diagnostics, drugs and vaccines, with formation of important organisations such as the Coalition for Epidemic Preparedness Innovations (3). If drugs and vaccines are available, they are important tools for epidemic control but come into play when an epidemic is already established. Equally important are the abilities to prevent epidemics altogether, to identify epidemics early, to ensure effective triage and hospital infection control, surge capacity of space, and resources and personnel within health systems. Failures in any of these could cause health system failure and blow out of epidemics. Recognising the genesis of epidemics and all points where prevention or mitigation can be achieved is critical. Currently, investment is heavily focused on diagnostic tests, drugs and vaccines, which come into play well after an epidemic has occurred, but these are late in the timeline of epidemic emergence (Figure 1). Our ability to prevent and mitigate serious epidemics will be improved by ensuring an equal focus on governance, preparedness planning, surveillance and early diagnosis.

Many failures of epidemic control have been due to delayed or poor surveillance, lack of physical or human resources, weak health systems, failures in diagnosis and triage, poor coordination of response or breakdown in vaccination programs. Measles, for example, can be controlled with an effective vaccine, but is causing epidemics in the Asia-Pacific region, Africa, Europe and North America (4). Conversely, epidemics such as Ebola, MERS Coronavirus and SARS have been controlled with non-pharmaceutical measures such as infection control, isolation and contact tracing and quarantine (5).

The nature of true epidemics

Epidemics have an impact which is immediate, acutely disruptive and requires surge capacity in health systems and human resources. Whilst the term “epidemic” is widely misused, it refers to a specific pattern of exponential growth over a short timeframe, over and above the expected incidence (6). Epidemic control can be achieved at many points along the timeline of emergence, including prevention, surveillance and early detection (7), clinical diagnosis and triage, rapid diagnostics, patient isolation, hospital infection control, contact tracing and social distancing, treatment and vaccination programs. An epidemic detected early using good surveillance is much easier to control, because case numbers are less. Epidemics are defined by an exponential rise in cases over a short period (days to weeks) and characterised mathematically by the reproductive number, R0(6). The epidemic threshold is defined as R equals 1, and any infection with an R0>1 has epidemic potential. Ebola, for example, was estimated to have a Ro of about 2 during the 2014 West African epidemic (8). Diseases such as smallpox and Ebola are epidemic in nature and a delay in response of even weeks can be critical because of the exponential growth in case numbers. This rapid surge in case numbers differentiates true epidemic diseases from endemic infectious diseases such as malaria or HIV. For example, the Ebola epidemic of 2014, was recognized in March of that year, when it was still small in scale. Within the 5 months of delay in response the epidemic grew exponentially, as predicted by a Ro of approximately 2 (9), to an unprecedented scale of over 25,000 cases, most of which could have been prevented if the response had occurred immediately in March (Figure 2).

Governance

Governance, legislation and regulation can influence the risk of emergence of epidemics, particularly those which may arise in the era of genetic engineering and synthetic biology (10). Technology has advanced at a more rapid pace than legal or regulatory frameworks and the risks posed by technologies such as synthetic biology and dual-use engineering and synthetic biology (10) are not fully understood. The risk of emergence of engineered or synthetic epidemics has increased due to increasing accessibility and reducing cost of CRISPR Cas 9 technology and synthetic biology. Gene synthesis has dropped in cost by more than 250-fold in a decade (11). The synthesis of an extinct orthopox virus called horsepox in 2017 (12), whether wise (12) or not (13), proves that variola, the virus that caused smallpox, could equally be created in a lab. Preparedness planning must include regulation of synthetic biology, which is presently unregulated and subject to a voluntary code of conduct. Do it yourself (DIY) biology, too, is expanding rapidly and self-regulated (14). The popularity of DIY biology means lab-in-a-box and other equipment are readily available for purchase online, along with open access scientific publications. The potential for a small group of actors to acquire all the necessary means to produce and then deploy a biological weapon is real.
There is also the recognized threat of highly skilled insiders colluding with terrorist groups or hostile states within regulated laboratories, not just in the highest security laboratories (BSL 4) but in BSL 2 and 3 laboratories, which are far more numerous and less stringently regulated. Currently, most countries do not have adequate legislation to urgently remove a suspected rogue scientist from a lab. In terms of other laws and regulations, such as the Biological Weapons Convention (BWC), the Cartegena Protocol, local gene regulation laws and the International Health Regulations (IHR), none adequately address the need arising from the rapid expansion of genetic engineering and synthetic biology. The BWC focuses on nation states as actors rather than rogue, small group non-state actors and differs from the Chemical Weapons Convention in that it is not enforceable or auditable. The Global Health Security Agenda (GHSA) Action Package touches on some relevant aspects, but is more attuned to response than prevention and is a
voluntary framework that remains health-centric in scope. The IHR are relevant only after a full blown epidemic is apparent and was last fully revised in 2005. It is well understood that many countries cannot comply with the IHR, and the IHR has not made any apparent difference to recent serious epidemics, such as Ebola in 2014. It would seem timely to revise the IHR to better meet the needs of a very different landscape than when it was last revised 15 years ago. The role of legislation, regulation and governance on epidemic control is more important than ever, but finding enforceable, global mechanisms to assist disease prevention and control is a priority.

**Surveillance and early detection of epidemics**

If we could have detected and acted on the 2014 Ebola epidemic earlier, it would be even easier to prevent a large-scale epidemic. Epidemic control depends on surveillance, which in turn requires human resources, systems, capacity, communication and strong networks, which are often inadequate in low income countries. Traditional public health surveillance relies on data from the health system or laboratories, which is validated but may be significantly delayed. In some instances, official surveillance data from countries may be absent altogether due to fear of adverse impacts on tourism or trade. Surveillance data provide insights into trends over time, allow comparison between time periods, and can signal an unusual rise in a disease incidence. Enhanced rapid surveillance and intelligence using novel methods to complement (not replace) traditional surveillance can improve health security. There is a vast array of open source data, including social media and news reports, which capture the concerns and discussions of the community and can provide early signals of epidemics, prior to official detection by health authorities (15, 16). Public health has been slow to adopt this capability, which is particularly useful in low income countries because automated rapid epidemic intelligence systems mitigate the lack of human resources for surveillance. An automated system could reduce the required human resources and increase the efficiency of existing resources by providing early signals for public health investigation. Rapid epidemic intelligence can be developed using data algorithms for mining social media (15), and epidemics can be detected months earlier than by using traditional laboratory or hospital based surveillance (17). To further enable rapid response, risk analysis tools which take into account country-specific, disease specific and other predictors of risk, can be used to flag the need for urgent intervention (18).

**Recognition, triage and diagnostics**

The focus of investment is on diagnostics tests, rapid point of care tests and other novel diagnostic aids. Point of care tests that can be used in the field or at the bedside will improve infection control by providing rapid diagnosis. However, if POCT are not available, suspected contagious cases should be isolated while waiting for a confirmatory laboratory test. In practice, this often does not occur, with outbreaks of measles commonly resulting from undiagnosed cases waiting for prolonged periods in the emergency room (19).

With low probability, high impact cases in an emergency department, such as Ebola, MERS Coronavirus or monkeypox, triage protocols and clinical decision aids, including travel history, are critical. However, failure of triage and missed diagnosis occurs repeatedly, from Ebola in Dallas, USA (20) and Nigeria (21) to MERS Coronavirus in South Korea (22) and smallpox in Yugoslavia (23). There is a need to invest in mandated decision aids and triage protocols to avoid the missed diagnosis of high-consequence infections. Without a clinical suspicion of a disease, the best diagnostic tests are useless because the prompt to using a diagnostic test is awareness of the possibility of the diagnosis – which appears to be the most consistent shortcoming in nosocomial epidemics.

**Health systems, surge capacity and first responder protection**

Many descriptive publications on the magnitude and mortality of the Ebola epidemic were generated in 2014, whilst concerted research efforts began for development of a drug or a vaccine against Ebola. Yet while waiting for drugs and vaccines, no concrete disease control goals were expressed in the first six months of the epidemic. One of the pressing problems in all three affected countries was a lack of hospital beds and isolation facilities for cases of Ebola. It was estimated only 15-20% of Ebola patients were in treatment units at the peak of the epidemic, because of a lack of both hospital beds and health workers (24), which contributed to uncontrolled transmission of infection in communities. Case isolation is an exceptional infection control intervention and can stop transmission of infection effectively. A modelling study published in September 2014 showed that in the absence of any pharmaceutical interventions, isolating 70% of patients could control the epidemic (25). A concerted public health response by local governments and responding military forces expanded the capacity to isolate infectious patients by building of field hospitals. This and other non-pharmaceutical efforts such as improved infection control, burial practices and waste management resulted in eventual control of the epidemic. The lessons of the 2014 Ebola epidemic were very much about understanding the importance of non-pharmaceutical measures, infection control and health system capacity in epidemic control. The Ebola epidemic of 2014 was further characterized by conflict over PPE protocols for health workers (26). The root of the problem is that hospital infection control as a discipline developed around patient safety and...
remains focused on patient safety. The occupational health and safety of health workers is the domain of occupational safety experts, but infection control guidelines are generally written by infection control experts. It is essential that we give the highest priority to the safety and protection of health workers and other essential first responders such as paramedics, police, military and emergency services workers. In addition to the occupational health and safety obligations to first responders, any emergency response will be seriously compromised if first responders are not adequately protected – not only because they may succumb to illness, but because they may refuse to work under conditions of poor occupational safety.

Preparing for high-consequence epidemics

Smallpox was eradicated in 1980, but it is a renewed concern because of new methods which make it possible to create the virus in a lab (13). In contrast to Ebola, we have effective vaccines against smallpox, yet health systems capacity and planning are equally important, even in high income settings. A new study we published in 2019 (27) looked at the impact of a hypothetical bioterrorism attack with smallpox in Sydney, Australia, on the health system. Using a mathematical model of smallpox transmission, we determined requirements for hospital beds, contact tracing and health workers (HCWs) in Sydney, Australia, during an epidemic of smallpox. We found that every day of delay in response increases the epidemic size. The public health response should commence within about a week after the first case of smallpox becomes symptomatic, or a severe epidemic may result. This relies on rapid diagnosis, but many outbreaks of smallpox have not been recognised until second generation cases occurred (23), which means that in practice, delays in response are likely. In terms of surge capacity, the requirement for extra hospital beds could range from 4% to 100% of all available beds in best and worst-case scenarios (27). This means that care of other urgent patients, such as people with heart attacks or strokes, may be affected due to shortage of beds and staff (27). The surge in beds requires a corresponding surge in doctors and nurses to treat smallpox-infected patients, as well as adequate PPE for these clinicians. Most stockpiling provides short-term supplies, but an epidemic could go on for months or years, in which case standard stockpiles (which typically provide a few weeks supply) will be rapidly depleted. Vaccination is critical for epidemic control (28), but the process of vaccination requires more than the vaccine. Smallpox control using ring vaccination (finding and vaccinating close contacts of each case of smallpox) requires contact tracing, with the number of contacts expected to be an order of magnitude greater than cases (27) – yet the public health workforce available to conduct contact tracing is much smaller than the clinical workforce. We estimated that there are about 100,000 clinical HCWs in Sydney, but only about 300 public health workers. Even worse, trained public health workers are not registered as health practitioners in Australia, which means identifying the available pool of qualified workers is difficult. In our modelled smallpox epidemic, it is likely that community volunteers would be required to assist with contact tracing, as was the case during eradication of smallpox. Countries without civil preparedness programs or national service would be more vulnerable if surge capacity needs require community volunteers. There is a strong case for offering civil preparedness courses, training and certification to enable rapid community surge capacity.

In the case of a large-scale epidemic of a serious emerging infection, it is important to have back up plans for pop-up treatment centres (rather than treating cases in general hospitals). This not only reduces the risk of nosocomial infection but can reduce the number of staff exposed to infection and enable better cohorting of patients and rostering of staff. Failure to diagnose Ebola in Nigeria in 2014 during the height of the West African epidemic resulted in a nosocomial epidemic which caused the deaths of several HCWs. After making the diagnosis, Nigeria did this well to control the outbreak, drawing on extensive experience with polio control campaigns (29). They immediately established a separate designated Ebola treatment centre in an abandoned building and moved patients out of the general hospital environment. One surviving doctor, Ada Igonoh, wrote an account of the management of the epidemic in Nigeria through her personal experience of becoming infected and being taken to a makeshift facility for Ebola care. She detailed the meticulous infection control measures taken, including on exit from the facility (30). Aside from the initial missed diagnosis, Nigeria did an exceptional job of containing and stopping the nosocomial epidemic and preventing a larger scale epidemic in the community. A large-scale epidemic in the capital city of the most populous country in Africa would have been a disaster.

In summary, a holistic view of epidemic control from prevention at one end to pharmaceutical interventions at the other is ideal. Forethought, legislation, surveillance, planning, capacity building, training and the ability to effect rapid surge capacity in physical space and human resources can prevent or control an epidemic. Planning should focus on identifying influential factors we can control to mitigate epidemics (31), which are present along the entire spectrum depicted in Figure 1. There is much we can do to prevent and mitigate epidemics, and all opportunities for prevention are equally important. Improving global governance, legislation and regulation, use of rapid epidemic intelligence and risk analysis tools, health systems planning, and systematic triage and diagnosis protocols, can all be achieved. Within health systems, this includes plans for rapid establishment of “pop-up” dedicated...
treatment facilities, rostering plans, surge capacity for staff and volunteers, infection control plans and ensuring health workers are protected with vaccination and adequate PPE. Together with availability of diagnostics, drugs and vaccines, these are the full repertoire of strategies for epidemic control.

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The explosion at Vector: hoping for the best while preparing for the worst

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Abstract

This commentary reviews the implications of the gas explosion at the Russian State Research Centre of Virology and Biotechnology building (Vector) on September 16th, 2019. Public health and engineering perspectives are provided on the implications of the explosion causing a physical breach of the building, and the potential for dispersion of pathogens in the surrounding area. A global public health and risk analysis perspective is taken in discussing preparedness planning around this event.

On September 16th, 2019, an explosion occurred at the State Research Centre of Virology and Biotechnology building (Vector) in the city of Koltsovo, in the Novosiberisk region of Siberia, Russia (1). The affected building was a BSL 4 virology research centre, and one of only two known sites housing variola virus, the cause of smallpox. The facility has one of the largest collections of dangerous pathogens in the world. Whilst laboratory safety breaches are common and do not usually result in epidemics, explosions are rare. Unlike a needlestick injury or an accidental shipping of live anthrax, an explosion of this magnitude is likely to lead to a physical breach of the laboratory, possibly affecting multiple parts of the structure and equipment within. An explosion is sudden, uncontrolled and unpredictable, and involves force which may result in pathogen release into the surrounding environment. An epidemic which arises in close proximity to the explosion could spread beyond the affected region or even globally, which makes this event a concern for global public health.

The explosion was allegedly caused by a gas cylinder or gas tank, according to reports, and was followed by a fire. The fire reportedly spread through the ventilation system of the building and affected an area of 30 square meters before it was extinguished. The explosion on the fifth floor was reported to have shattered the glass in the six-storey building. According to Russian authorities, no biological agents were housed in the affected area. We do not know if this is the case, but it is in the global interest to understand the risks if there were pathogens released. The affected facility was a virology research centre, so we may assume that viruses (rather than bacteria) were present in the building but cannot exclude non-viral pathogens being present. Neither can we exclude theft of pathogens during the chaos and aftermath of the explosion, or that the explosion itself was deliberate to enable theft.

From a risk analysis perspective, an explosion at a BSL 4 facility for dangerous, contagious pathogens is a risk for global health. Despite the Russian government assertion that there is no risk to public health, it would be wise to assess the risk as objectively as possible, given the global community is a stakeholder if an epidemic arises from this accident. In the best-case scenario, there were no pathogens in the affected part of the building, no pathogens released, the situation has been contained and there is no risk to local or global public health. In the worst-case scenario, there were pathogens present at the time, which were aerosolised and propagated outside the building as a result of the explosion. The principle of pandemic and preparedness planning considers the worst-case scenario, rather than hoping for the best-case scenario. So, we need to consider what a worst-case scenario would look like and how best to be prepared and mitigate it.

A gas explosion of this scale can result in propagation of a detonation/shock wave at speeds of 1500-2000 metres/second. The flame on the other hand propagates at a slower speed (typically 20-25 m/second and up to several 100 m/second) (2). In a deflagration, the commonest way a flame propagates in a gas explosion, unburned gas is propagated ahead of the flame. Therefore, in this instance, if any biological material were present, it could have been propagated and aerosolised well ahead of the fire and before the fire was widespread. The reports of shattered glass across multiple floors in the building is indicative of a sufficiently strong explosion that could lead to the dispersion of contagious pathogens to surrounding areas. An explosion interacting with a vial of liquid or frozen pathogen will quickly and completely rupture the contents, creating tiny droplets or particles in the order of microns that could,
conceivably, be projected well clear of the building and resulting fire by the shock wave. Pathogens present in liquid or solid media, even frozen pathogens, could be at risk of dispersion during an explosion. A blast that shatters the windows in a building would equally be expected to shatter freezers, fridges, biosafety cabinets and incubators. We do not have adequate research data on the effect of explosions on pathogen dispersion to make confident assertions about the safety to the public following this incident. BSL 4 laboratories are generally not designed to withstand explosions, so we should assume that secure structures, equipment and workspaces were affected.

The factors which may affect risk include the weather conditions at the time, the force and heat of the blast, the height of the building and affected floor, the structure, quantity, contents and type of laboratory equipment present, the extent of the breach of windows in the building, the type of pathogens present (and their propensity for aerosolization and viability in the environment), the number of people potentially exposed inside the building and the population density in the surrounding areas. It also depends on transmissibility of any pathogens present. Certain pathogens such as anthrax and variola are easily dispersed by aerosolization. Others, such as Ebola, are not primarily spread by the airborne route, but aerosol transmission is also possible (3). If hybrid, synthetic or engineered pathogens were present, this probably increases the risk because such agents may have been designed with enhanced pathogenicity or to be vaccine escape mutants or drug resistant.

Whilst anthrax was purportedly not in the building, dispersion of anthrax spores has been well studied and serve as illustrative of the potential dispersion of pathogens. The spores are less than 3 μm in diameter and can be easily aerosolised and dispersed, especially if weaponised with the use of silica nanoparticles (4). In the real example of the Sverdlovsk anthrax accident in 1979, anthrax spores were pumped out of a Soviet bioweapons facility through an air vent, at a velocity that would have been many orders of magnitude less than a gas explosion. The high-risk zone for inhalational anthrax in Sverdlovsk was up to 4 km from the building, but cases also occurred well beyond this zone (5). Modelled distances of dispersion in an aerosol attack vary from 12 to over 35 km (6). Whilst these data suggest that an explosion could propagate particles to great distances, anthrax is not transmissible from person to person, so the public health impact is limited geospatially. Within the affected area, decontamination would be a challenge because of the resilience of anthrax spores and risk of secondary aerosolization (7).

If a respiratory-transmissible pathogen such as variola were aerosolised as a result of the blast, the risk includes first generation cases among people in the building and in the immediate vicinity, but also second-generation cases in others far beyond the area of initial contamination due to transmission from person-to-person. The infectious dose of variola is very small, so large quantities of virus are not required to cause infection. Local travel could see second and third generation cases occurring beyond the affected area, in neighbouring Kazakhstan, Mongolia and China, as well as further afield globally due to air travel. Failure of diagnosis of initial cases is likely, given the remoteness of the area and the unfamiliarity of clinicians with diseases such as smallpox. We have shown that even a 1-week delay in commencing vaccination and other measures for controlling smallpox can result in a more severe epidemic, and that timely response is critical (9). Failure of diagnosis in travel-related cases has been seen recurrently with emerging infections such Ebola and MERS coronavirus, and in the last European outbreak of smallpox (8). With the long incubation periods of smallpox (12 days) and Ebola (21 days), a missed diagnosis of an index case could result in a lag period of several weeks before secondary cases become symptomatic. Through international travel and trade, this could result in cases occurring far from the accident site. A mitigating factor in this instance is that Koltsovo is in a remote part of Russia and has a small population (approximately 16,000 people), and the wider Novosibirsk District has a population of about 120,000.

Relevant to the explosion in Koltsovo is the unique propensity of variola to spread over long distances, further than can be explained by direct respiratory transmission from person-to-person. This together with the low infectious dose is a serious concern. During the final 100 years of smallpox endemicity in the world, the phenomenon of “aerial convection” was observed in many different countries and settings (10). This period, approaching eradication, had a low enough incidence of smallpox to observe unusual transmissions. Long distance transmission over distances of a mile or more was observed, in the absence of other cases of smallpox in the community in Fulham (10), England (10,11), Salonika, Greece (11), Gravesend, UK (11) and Purfleet, UK (10) as well as several other settings. In 1971, a 400g smallpox “bomb” was exploded on Vozrozhdieny Island, a Soviet bioweapons testing site. A crew member on the Lev Berg ship, which was sailing in the Aral Sea at least 15 km from the island, became infected with smallpox (12). This suggests that an explosion could disperse variola virus at least 15 km.

We do not have the evidence or experience to dismiss the risk of this event. An explosion in a BSL 4 laboratory cannot be classified in the same risk category as misplaced biological samples, needlestick injuries or shipping errors, and the lack of epidemics arising from the latter examples is not grounds to dismiss the risk from this unique event. The building was physically breached by an explosion which would have resulted in propagation of aerosols at subsonic speeds. We do not know what equipment and
materials within the building were breached. Preparedness planning principles can be applied to this event, starting with environmental testing, screening, surveillance and containment. Other considerations would be stockpiling of countermeasures for pathogens known to be housed in the building and planning for human resources and physical space for isolation of cases and quarantine of contacts (9).

Steps which need to be taken include:

1. Accounting for all pathogen samples and stocks in the building, and securing them while the building is breached (broken windows).
2. Perimeter security.
3. PPE and vaccination for all first responders at the scene.
4. Environmental testing for contamination inside and outside the building, including along the likely trajectory of propagation of the shockwave.
5. If any evidence of a breach of pathogens is present, depending on the pathogen, vaccination and/or chemoprophylaxis of staff in the building and the surrounding population should be considered. Smallpox vaccine, for example, is still effective post-exposure.
6. Quarantine of any potentially exposed people.
7. Fever screening and serial interval testing (for example by serology or throat swabs) of people in the building and surrounding area for exposure.
8. Stockpiling of medical countermeasures (drugs, vaccines, PPE, immunoglobulin) informed by the findings in 1-6 above, and plans for rapid deployment of stockpiles which are held far from the site.
9. Enhanced disease surveillance in the local area and beyond, for at least 6 months after the event.
10. Plans for physical space for case isolation and human resources capacity (for treatment of cases and contact tracing and vaccination) in the event of an epidemic.

Only the Russian government has the specific information required to inform preparedness around this event, and the rest of the world relies on prompt communication of any disease cases or clusters from Russia to prevent a pandemic arising. If classified biological research was occurring at Vector, there may be a powerful disincentive for the government to disclose disease occurrence. Other countries, especially surrounding countries, can use disease surveillance for early warning. Surveillance for disease events in the affected area and beyond is important, and there is a strong case for using sentinel syndromic surveillance and open source intelligence for sensitive, rapid detection.13 Syndromic surveillance should look for the most likely clinical syndromes arising from an emerging infection: severe acute respiratory syndrome; rash and fever (including haemorrhage); neurological syndromes (meningitis, encephalitis, acute flaccid myelitis, Guillain Barre Syndrome and neuropathy); and gastrointestinal syndromes; and unexplained deaths. Such surveillance should be commenced immediately to allow baseline data for comparison of any signals occurring in the coming weeks or months in Siberia, the rest of Russia, and neighbouring countries such as Mongolia, Kazakhstan and China. In the case of theft of biological materials, an index case may occur anywhere in the world, and in the case of engineered or synthetic pathogens, previously unknown disease syndromes may occur. The incubation periods of known diseases such as influenza, smallpox and Ebola provide a range of time periods within which first disease clusters may occur, if there has been a pathogen breach. It could be days in the case of influenza, or weeks in the case of smallpox or Ebola. A caveat to this is the dose-response relationship, as known incubation periods relate to doses of natural exposures. If abnormally high dose exposures occur, incubation periods can be substantially shorter. Any signals from syndromic surveillance should be investigated promptly. Epidemic diseases with a Ro >1 can grow exponentially, within weeks to months. Whilst we hope for the best-case scenario, and we may indeed see a best-case scenario eventuate, we must be prepared for the worst. In the event of a worst-case scenario, the earlier a breach of pathogens or an epidemic is detected, the greater the potential for mitigation and control with pharmaceutical and non-pharmaceutical measures.8

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Book review of “Pandemics and Polarization: Implications of Partisan Budgeting for Responding to Public Health Emergencies”

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Budgeting for public health emergencies in the United States (US) is on the decline. This is largely due to funding standoffs between the two dominant parties, republicans and democrats, in the US Congress. The author, Nathan Myers, takes a deep dive to explore how these budgetary decisions have become increasingly partisan over time. He examined differences in party votes and provided compelling examples with recent disease outbreaks where partisan bickering created delays and reduced funding, which contributed to unnecessary deaths and suffering. This book sheds light on how these political feuds are detrimental to the public health system by limiting its ability to respond quickly and effectively to infectious outbreaks.

Myers begins by re-enacting a public health emergency exercise with all the panic and confusion that typically goes into the fear of a possible worldwide pandemic. He paints a realistic picture to discuss some of the key issues that emerge when a virus has been discovered with no known vaccine to protect against it. Immediately, attempts to institute the three major components of public health preparedness: surveillance, countermeasures, and coordination between different levels of government and countries surfaced. Myers’ stressed how each of these activities needs access to funding at the outset of an outbreak in order to readily deploy a health care workforce, begin rapid diagnostics to detect the spread of a virus or infection, as well as the ability to expedite development and distribution of the newly created vaccines.

Overall, Myers makes a persuasive argument by taking the reader step-by-step through different public health emergencies in recent history and how they were poorly addressed with delayed timing and insufficient funds largely due to partisan related issues. The essential components of public health preparedness – surveillance, countermeasures, and coordination – were consistently not optimally conducted due to a slow response from the US government. He highlighted that even in the midst of a clearly recognizable public health emergency, the funding could still come too late and be minimal compared to the request and need.

Myers primarily focused on the appalling handling of the Zika virus and what could happen in future epidemics if no action is taken to address partisan federal budgeting for public health emergencies. In this example, he identified serious gaps in the US public health emergency infrastructure, which has implications for the world. The initial outbreak of the Zika virus occurred during a US government funding showdown, which have become longer and more prevalent events. This shutdown led to months of stagnation in the US Congress before $1.1 billion in funding was finally passed for a Zika response, but this was “too little, too late” (p. 18).

Another notable example is the perception of underestimation, and Myers credited the H1N1 influenza with inadvertently contributing to this belief. Essentially, the virus did not prove to be as severe as predicted and had a successful response by developing, producing, and distributing 126.9 million doses of vaccine to 81 million people (p. 47). Myers suggested that because the H1N1 virus did not result in the projected harm, then it had cultivated an air of underestimation by the public and legislators, which could lead to a false sense of security, and fewer overall dollars to respond to future public health emergencies. Voters are less likely to advocate for public health emergency funding if they don’t feel it is a problem “[they] sense that money is being spent on something that may never happen... it is an issue that continues not to poll very highly” (p. 88). If voters are indifferent to public health emergencies, then legislators may not be as inclined to prioritize this type of funding.

A third major concern that Myers identified is with the current US political system and legislators is the trend to pander to the voting base, especially if it is in an election year. This influence has implications for public health emergencies in that legislators may pass controversial travel bans and quarantines to appear decisive for their base. However, the Centers for Disease Control and Prevention and the National Institutes of Health strongly recommend not passing these problematic measures, which could unduly harm basic human rights. Instead, there should be increase surveillance, such as a fever watch, as one example of an effective, but less dramatic response.

Myers provided additional recommendations that all circle back to overcoming partisan budgeting by creating stronger incentives for better communication, surveillance, and care in cases of public health emergencies. His thoughtful critique highlights significant gaps in how dangerously intertwined partisan politics are with responding to epidemics, which could result in a devastating loss of life for America and worldwide. Hopefully, this book will spark an overdue debate on this topic, which goes beyond party lines and provide needed protection against foreseeable emergencies.
EDITORIAL

CBRN News: Emerging challenges for Risk Management in Chemical, Biological and Radiological Research and Development

David J Heslop

The challenges associated with effective risk management, and the risks of proliferation and developing offensive and defensive capability when working with Chemical, Biological and Radiological agents have recently been highlighted on the world stage. Work in any of the primary dimensions of CBRNE research and production carries a myriad of potential and actual risks that require careful control, and to avoid individual through to population impacts. Failures in risk controls can result not only in personal injury but also expose the wider population to significant and persistent risks.

In 2019 it has been alleged that a new class of missile – codenamed Skyfall in Western countries – suffered a critical accident during testing in the Archangelsk region in Russia. Of most importance is the belief that the new class of missile may rely on a miniaturised form of nuclear propulsion to give it effectively unlimited range and special manoeuvring capabilities. The accident and setback was reported as an accident by the Russian Ministry of Defence and resulted in the deaths of a number of research scientists (1). However, nearby radiological monitoring stations reported a brief burst of gamma radiation, and in the subsequent days surrounding villages were evacuated and officials alerted to potential consequences of radiological contamination (2). Outside of Russia the event has generated much debate and concern regarding the consequences of the weapons design, and implications if a larger accident were to occur. This kind of weaponry has the potential to cause accidental contamination of neutral territories that it overflies, such as if the weapon malfunctioned or crash landed. Despite not necessarily being designed to carry a nuclear payload, the destruction of a nuclear propulsion source on attack could lead to secondary atmospheric fallout and terrain contamination from radiological materials of the target and surrounding area. The handling of a nuclear propulsion system during testing of weaponry is also of concern – in this instance some sources have suggested that the accident occurred during a recovery operation for the weapon system (3). Extensive testing of such a propulsion system is a feature of weapons development, and how the risks associated with working with nuclear powered propulsion in the context of its use in weaponry are mitigated are not clear.

Recent reporting has emerged of a previously unknown and large airborne release of Ruthenium-106 in Central Asia in 2017. Initially identified as an increase in radio-isotope concentration in air, causation for the release was not previously admitted by any facility or organisation known to handle this hazard. Subsequent analyses have shown that the most likely cause for the incident was a large release from the Mayak reprocessing facility in Russia in late September 2017 (4) probably as a consequence of preparation of another large radiological source for scientific experimentation. It has been predicted between 100 and 300 teraBequerels of Ruthenium-106 was released in this incident (5). Atmospheric dispersion modeling and particle pathway back-propagation identified likely release from Mayak over a short period of time, followed by spread throughout Russia, through Southern Eastern Europe and subsequently into parts of Western Europe and Central Asia. While the nature of an event capable of producing such radio-isotopes is unclear, and the public health consequences of the release of relatively short-lived Ruthenium-106 deemed to be not significant, the event has highlighted the potential for regional and global effects from a single release event. Other recent events in the biological domain are also of concern. The recent explosion and fire at the Vector facility in Siberia (6, 7) highlight the potential for accidents to occur in critical facilities. According to accounts provided by Vector, and subsequent reporting around the world, a gas cylinder inside a facility undergoing repairs and maintenance exploded causing a significant fire, blowing out many
windows, and resulting in one casualty sustaining severe burns. While assurances have been provided that biological agents were not present in the facility in the time, the Vector facility routinely conducts research into high risk biological hazards such as Ebola virus, and is one of two official repositories for Smallpox in the world. Were such an accident to occur in the facility where research involving high risk pathogens was being conducted, the exposure of workers to pathogens or the dissemination of pathogens outside of the facility is a possibility due to blast effects, carriage of the pathogen outside of the facility, or loss of pathogen control (8). The implications of highly transmissible agents such as Smallpox spread in the global population are much more significant than in the pre-eradication era due to the lack of general population immunity, rapid and cheap international travel, geopolitical environment, and challenges in providing adequate preventive and medical care to the exposed or affected in a timely way (9). Accidents within high risk pathogen research and development facilities occur more frequently than realised by decision makers and by the broader public health community. Reports of numerous work, health and safety events occurring in major hazard biological research facilities (10-13), or the mishandling of anthrax specimens prior to transport between research facilities in the US and elsewhere in the world (14), are examples. Of significance for risk management, these events have occurred despite stringent and detailed policies and procedures in place. The difficulties of attempting to control a laboratory release of pandemic influenza in various major cities in the world was recently modelled, the results indicating the extreme challenges involved in managing such events (12). This highlights a persistent challenge in capturing potential hazard and risk causal pathways that lead to catastrophic events well prior to events occurring, be they due to failure to adhere to policies or due to the emergence of unexpected safety system fail states.

No safety system is infallible or risk free. By increasing the types and intensities of exposure of complex safety systems to hazards, the rate in which failures of risk controls and safety systems will occur, in parallel, increases. Where the consequences of such a failure is catastrophic to individuals and to populations, the argument for safely increasing work intensity involving such hazards is arguably unjustifiable or should prompt risk management system redesign and improvements. Equally, operational and design assumptions in many legacy systems are now beginning to be challenged (e.g. temperature, weather and population demands) leading to modes of utilisation that exceed design and operational limits of safety systems, often unknowingly to the end user. Many major safety systems for CBRNE facilities were designed and built when funding, maintenance and supporting systems were substantively different. How the Chemical, Biological and Radiological research and development facilities around the world manage both legacy and new and emerging risks is becoming more and more important. Competition between nation states is adding pressure to proliferate, innovate and match perceived and actual balances of capability. This is often in areas of trans-disciplinary research where safety data is necessarily limited in the initial phases of work. This also appears to be driving activity in domains and locations where risk control systems are not necessarily adequate, modern or suited to the task at hand.
About the author

I am an Associate Professor at the School of Public Health and Community Medicine at UNSW and retain military responsibilities as Staff Officer Grade 1 in Public Health, Occupational Medicine and CBRNE to Army Headquarters. I am a practicing vocationally registered General Practitioner, an Occupational and Environmental Medicine Physician, and a fellowship candidate for the Academy of Wilderness Medicine.

My doctoral research focussed on the central autonomic anatomy and integrative neurophysiology relating to the cardiovascular response to noxious inescapable physiological stimuli such as severe haemorrhage and visceral pain. Utilising my research background and subsequent clinical training, through the ADF I have been fortunate to have extensively deployed into a variety of complex and austere combat environments and have gone on to undertake advanced training in Chemical, Biological, Radiological, Nuclear and Explosive (CBRNE) Medicine and Senior Medical Officer training. Consequently, I was appointed as Senior Medical Officer for Special Operations Command for 2014 and was the Officer Commanding and Senior Medical Officer to the ADF CBRNE medical incident response element at Special Operations Engineer Regiment from 2012-2015.

I have extensive experience in the conception, design, planning, delivery and operations of health support systems and capability in remote and austere contexts; incorporating the management of exotic or novel hazards and risks. Extensive actual experience in planning for and management of major disasters, mass casualty and multiple casualty situations. I also have extensive overseas and domestic operational experience in command, personnel management, force protection, health protection systems, resilient systems design and test and evaluation. Direct responsibility and experience with leading deployable expeditionary medical support.

I am regularly consulted and participate in the development and review of national and international clinical and operational CBRNE policy and doctrine. I am additionally a peer reviewer for the journals Military Medicine (AMSUS) and Journal and Military and Veterans Health (AMMA). I also continue to conduct CBRNE medical, and general medical education and ADF GP Registar training within my military capacity, along with civilian instruction of the Major Incident Medical Management System (MIMMS) framework with MIMMS Australia.

My interests lie in health and medical systems innovation and research. I retain linkages with key national civilian and military education, research and development organisations and retain an active involvement in a wide variety of projects and initiatives supporting national public health preparedness goals. My current research effort and interests touch on complexity science, agent based and deterministic modelling, emergent complex adaptive systems phenomena, test and evaluation of systems, policy research, epidemic modelling, exotic and emerging infections, disaster preparedness and response, organisational resilience in health care, development of robust socio-technical systems in health care, and the modelling, simulation and investigation of public health interventions and systems.

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