Ebola in DRC:
Recommendations for accelerating outbreak control

WHO Scientific and Technical Advisory Group for Infectious Hazards (STAG-IH)*

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The Scientific and Technical Advisory Group for Infectious Hazards (STAG-IH) provides independent advice and analysis to the Health Emergencies Programme of the World Health Organization (WHO) on the infectious hazards that may pose a potential threat to global health security. Their third meeting was convened on 3-4 June 2019, during which members reviewed the interventions and research being conducted to manage and contain the outbreak of Ebola virus disease (EVD) in eastern Democratic Republic of Congo (DRC) and made recommendations[1] for accelerating outbreak control.

Ebola virus transmission has continued for 10 months in areas of high security risk for inhabitants and responders. The case count has now exceeded 2 000, with an estimated overall case-fatality ratio of 66%. Transmission is occurring across a large area of North Kivu and part of Ituri provinces, with outbreaks in multiple sites requiring localised responses. Outbreak control has been severely hindered by the high-risk security environment. The response is layered on decades of conflict and tension in which individuals and communities must rapidly shift allegiances to survive. Political, social/ethnic, and economic complexities, community frustration and mistrust, and security instability have been added to an already challenging operational landscape. Except for the June spill-over event in Uganda,[2] spread has been limited to two provinces possibly due in part to intense efforts at the Points of Entry at which millions of people crossing the borders have been screened to date.

The outbreak is not yet under control, with weekly case counts higher than several months ago. Containment continues to be a challenge despite implementation of multiple control measures. These include case isolation and treatment in six specialised Ebola treatment centres (ETCs); isolation and diagnosis in suspect patient transit centres; contact tracing and follow-up, with more than 110 000 registered contacts to date; daily fever surveillance for approximately 80% of known contacts; and safe burials supported in all affected communities. Seven field laboratories are operational across the epicentres.

Investigational vaccines and therapeutics were deployed at an early stage during the outbreak and are being administered using IRB-approved protocols for 1) administration of the rVSV vaccine to contacts and contacts of contacts (ring vaccination); 2) administration of four experimental

[1] The Independent Oversight and Advisory Committee (IOAC) for the WHO Health Emergencies Programme (WHE) conducted a special investigation into the outbreak and provided its report and recommendations to WHO, part of which was reported to the WHA72 (https://www.who.int/about/governance/world-health-assembly/seventy-second-world-health-assembly) as a statement of the IOAC Chair whilst the comprehensive report is underway. The IOAC covers broader aspects of WHO's response including performance of its Incident Management System at three levels and international partner coordination, whilst the STAG-IH's focus remains the technical aspects of the outbreak response of WHO and all actors.

[2] https://www.who.int/csr/don/13-june-2019-ebola-uganda/en/

therapeutics[3] under a compassionate use programme known as Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI); and 3) a randomised control trial of the same four therapeutics **(**PALM).[4] More than 130 000 individuals (90% of those eligible[5]) have been vaccinated, and an estimate of high vaccine efficacy has been observed from recent analyses.[6] The MEURI trial and the PALM randomised control trial have enrolled 616 and 304 patients, respectively. Both the MEURI and the PALM studies require and provide strengthened hospital support.

Data collected and analysed by the Ministry of Health, WHO and other partners suggest several reasons for prolonged transmission, many of which derive from continuing challenges related to community engagement and trust, and security instability. These include 1) insufficient contact tracing: approximately 50% of new cases identified are not registered as contacts and, although approximately 80% of known contacts have been actively followed up, 40% of cases hospitalised in ETCs are not found on contact lists; 2) extended exposure time in the community or in patient transit centres: the mean time from symptom onset to hospitalisation is 6 days for cases that are not contacts under surveillance or that are in transit centres awaiting diagnosis; 3) non-hospitalisation of patients: approximately 40% of deaths from confirmed EVD are not occurring in ETCs and a substantial proportion of these are diagnosed post-mortem in communities; 4) highly sensitive case definition that results in exposure of many non-infected persons to Ebola in transit centres: current data suggest that 16% of suspected cases are laboratory confirmed; 5) non-compliance to basic infection prevention & control (IPC) in health facilities: up to 18% of new patients have a history of exposure to a traditional or other type of health facility as their only suspected source of infection; and 6) the large number of paediatric patients (<5yrs) is also suggestive of healthcare-associated infection. In addition, the fragile security situation has forced a total cessation of response activities for up to 10 days on several occasions resulting in the substantial drop of contact tracing activities. Between 1 January and 22 May 2019, 175 health facilities were attacked, with 6 healthcare workers killed and more than 50 injured; each such event results in a cessation or decrease in activities that impedes the momentum of the response.[7]

Recognising that there have been tremendous efforts to achieve a successful response, and that many of them are ongoing, the STAG-IH provides the following specific technical recommendations with the aim of supporting the public health advice[8] of the IHR(2005) Emergency Committee for this outbreak convened on 14 June.

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[3] ZMapp, developed by Mapp Biopharmaceutical, Inc.; mAb114, developed by NIAID, with early support from the INRB; remdesivir (also known as GS-5734), an antiviral drug developed by Gilead Sciences, Inc.; and REGN-EB3 (also known as REGN3470-3471-3479), developed by Regeneron Pharmaceuticals, Inc.

[4] The PAmoja TuLinde Maisha (PALM) clinical trial, a large collaborative effort that the World Health Organization is coordinating. See https://www.niaid.nih.gov/news-events/clinical-trial-investigational-ebola-treatments-begins-democratic-republic-congo

[5] Defined in the ring vaccination protocol.

[6] See: Preliminary results on the efficacy of rVSV-ZEBOV-GP Ebola vaccine using the ring vaccination strategy in the control of an Ebola outbreak in the Democratic Republic of the Congo: an example of integration of research into epidemic response. https://www.who.int/csr/resources/publications/ebola/ebola-ring-vaccination-results-12-april-2019.pdf?ua=1

[7] More detailed information on the current Ebola outbreak -- the accomplishments and challenges of current control efforts -- are available in Disease Outbreak News or Situation Reports.
See https://www.who.int/ebola/en/

[8] See https://www.who.int/news-room/detail/14-06-2019-statement-on-the-meeting-of-the-international-health-regulations-(2005)-emergency-committee-for-ebola-virus-disease-in-the-democratic-republic-of-the-congo

1. To complement and help ongoing efforts for the timely identification of EVD patients and their contacts and to understand the true extent and evolution of the outbreak by unveiling hidden spread, there is an urgent need to use Ebola virus genome sequence data from specimens obtained from patients and deaths for real-time analysis, particularly from those for whom epidemiological links are unknown. Where possible, sequencing should be increased at diagnostic laboratories at outbreak sites and it must be ensured that critical information (e.g., time of sample collection and case location) are linked.
2. Continue to evaluate the use of rapid diagnostic tests (RDTs) for Ebola virus antigen detection in communities and remote healthcare facilities to rule out patients with non-Ebola virus infection in a timely manner and to determine whether cause of death in the community is from Ebola virus infection. This should be followed by the development of testing algorithms for expanded use.
3. While maintaining or adjusting the ongoing EVD-focused interventions, other infections that cause fever, including malaria and vaccine-preventable diseases such as measles, should also be diagnosed rapidly and their control measures rolled out in a timely manner (e.g. mass anti-malarial administration with bed nets distribution; vaccination campaigns etc.). Two benefits – the opportunities to directly access people and households and to decrease non-Ebola fevers -- are expected from these interventions.[9]
4. Continue to assess and support implementation of basic or appropriate levels of IPC at healthcare facilities and laboratories. Consider innovative and user-friendly approaches by incorporating the values and preferences of and comfort and ease of use for frontline workers (e.g. the introduction of innovative personal protective equipment [PPE]).
5. Continue to build and strengthen community engagement and participation. A successful response must be anchored in community trust. Ongoing efforts to maximise community engagement and mitigate mistrust should be supported while implementing ways to advance these efforts toward 'community ownership' in affected and high-risk areas, and in preparedness initiatives.
    - Incorporate community-based suggestions and community-led initiatives into the operational response as appropriate. Ensure rapid course-correction in response to community feedback.
    - Implement/support community engagement strategies that address specific operational issues, such as timely identification and referral of cases.
    - Conduct more robust assessments to determine which community engagement interventions work well, when, with whom, and why.
    - Coordinate risk communication policies and messages among response teams and partners.
6. Continue to evaluate the sensitivity and specificity of case definitions and adjust to updated epidemiology.
7. Improve data sharing.
    - Consider developing a single, unified data-sharing platform to facilitate interaction among responders by providing rapid access to data on epidemiology, laboratory testing, clinical outcomes, community socio-behavioural actions, and vaccination, including ethically cleared processes that guarantee confidentiality of patient information and data protection.
    - Consider establishing a mechanism for secure and timely sharing of information by requesting the three data safety monitoring boards to increase understanding of clinical features and disease and transmission dynamics, thereby contributing to the optimisation of

[9] A malaria MDA together with bednets distribution was successfully conducted in Beni and contributed to reduce malaria-associated fever from 50% of fever cases at triage centres to less than 10% (unpublished data, WHO Global Malaria Programme).

care, improved case definition and preliminary analysis of interventions without compromising integrity of the primary and secondary outcomes.

8. Recommend to the Strategic Advisory Group of Experts (SAGE) on Immunization an evaluation of the potential added value of mass vaccination at the sites of most intense transmission; guidance on measures to conserve vaccine stocks in view of the limited supply available; and assessment of the comparative advantage that vaccination adds to other containment activities, including an assessment of vaccine effectiveness as well as that of vaccine efficacy**.**

Strong overall and multi-partner coordination mechanisms to support WHO and public health partners' response activities are welcomed.

Given that this is the tenth Ebola outbreak in the DRC, and unlikely to be the last, this EVD outbreak provides an opportunity for the DRC to rapidly build capabilities in surveillance, data management and information sharing, reference laboratory services, emergency preparedness and response, IPC, risk communication and community engagement, and public health research. It should also be an opportunity to advance ongoing health system strengthening with a diverse set of partners. The intensity of the current response activities in these areas over the last year has inevitably built a cadre of colleagues with some expertise in these areas. This is the time to ensure that these skills remain and are strengthened in DRC for years to come.

Effective outbreak leadership also requires appropriate delegation of authority from the Minister of Health to incident managers in a well-structured, flexible and inclusive incident management system, best located in the emergency operations centre of a national public health institute (NPHI). The role of such an institution would be to regularly analyse the situation on the outbreak and make operational decisions while providing the Minister with the information needed to make strategic decisions. A competent and confident NPHI communicating directly to the population is likely to increase public confidence and improve compliance. NPHIs provide a stable locus of expertise, continuity of experience, scientific knowledge, and appropriate human, technical, and financial resources to tackle public health challenges both within and across countries. Such an organization would support the government in making some of the difficult decisions required in challenging contexts such as the current DRC Ebola outbreak.

Acknowledgement

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[*] Bedford J, Enria D, Giesecke J, Heymann DL, Ihekweazu C, Kobinger G, Lane C, Memish Z, Oh MD, Sall A, Schuchat A, Ungchusak K, and Wieler L.