Research priorities for characterising Bundibugyo virus

Much of what is known about Ebola virus disease comes from outbreaks of *Orthoebolavirus zairense* and *Orthoebolavirus sudanense*. Although these provide important lessons for the current response, Bundibugyo virus (BDBV) differs substantially, with meaningful distinctions at the genomic, epidemiological, clinical, and immunological levels.[1,2] How far findings from other Ebola virus diseases generalise to BDBV is therefore uncertain.

Current knowledge of BDBV derives from fewer than 200 laboratory-confirmed cases and 16 sequenced isolates from 12 cases across all previously documented outbreaks.[1,3] The published epidemiological evidence base illustrates the limits of current understanding. Comparison across parameters described in the available studies is complicated by differences in case definitions, denominators, stratification methods, and analytical approaches used (appendix).[4–8]

To inform the response and future preparedness, we propose a connected set of priority research questions, developed with operational teams on the ground, that span epidemiology, diagnosis, clinical care, and viral ecology. First, how do the distinct symptom-evolution kinetics and incubation period distribution of BDBV infection shape undetected transmission? Second, how do these features—together with an early presentation that overlaps with endemic febrile illnesses such as malaria, arboviral infection, typhoid fever, and cholera—affect the sensitivity of diagnostic-triage algorithms? Third, how might mapping informal socioeconomic and transit corridors with localised mobility data optimise the placement of decentralised diagnostic laboratories compared with static, facility-based screening? Fourth, how do disease severity and outcomes differ among pregnant women, children, and people living with HIV, tuberculosis, malaria, or other co-infections common in affected regions, and how can the cytokine dysregulation driving late-stage sepsis and multiorgan failure inform treatment guidelines for health systems with insufficient intensive care, diagnostic capacity, and access to specialised therapeutics? Fifth, how can minimally invasive post-mortem approaches elucidate a pathophysiology still poorly characterised across filoviruses, where autopsy safety constraints and a reliance on animal models restrict insight? And sixth, do the genomic divergence and mutations seen in preliminary analyses signal viral adaptation through successive circulation in an as yet elusive reservoir? These questions are interdependent; progress on transmission, diagnosis, clinical management, and viral ecology will reinforce one another, and none can be answered well in isolation.

Generating this evidence requires operational research embedded within the response and co-designed with field teams, national and international experts, authorities, and affected communities. Study designs, data-collection tools (eg, case report forms and line lists), methods, and community-engagement approaches must be adapted to the context of this epidemic, which is unfolding in an exceptionally complex setting: a province of seven million people affected by chronic insecurity, nearly one million internally displaced people, informal cross-border movement, and long-standing mistrust of outside interventions.[9] The effort must be led locally, by those who best understand these dynamics. We call on response coordinators, national authorities, funders, and operational research partners to embed evidence generation within the response now. Failure to do so risks leaving the next BDBV response constrained by the same knowledge gaps that are affecting this one.

We declare no competing interests.

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