

# Considerations for randomised controlled trials during future filovirus outbreaks

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Dear Editor,

We agree with S Ellenberg and colleagues' assertion that an important opportunity was lost during the 2013-2016 West African Ebola virus outbreak in the evaluation of potentially life-saving treatments for Ebola virus disease (EVD) (1). Among the five therapeutic trials conducted, none of them evaluated the efficacy of an optimised supportive treatment (OST) backbone. Though one RCT aimed to evaluate the efficacy of ZMapp and OST compared to OST alone, the trial results are difficult to interpret given the paucity of data describing the comparability of OST delivery across study arms (2). Importantly, the improved survival (18.5%) among persons with EVD treated in the United States and Europe is less attributable to experimental treatment (less than 50% of patients received a completed course of an experimental therapeutic) and more attributable to OST, namely close monitoring and aggressive supportive care including intravenous fluid hydration, correction of electrolyte abnormalities, nutritional support, and critical care management for respiratory and renal failure (6). We acknowledge that many challenges to delivering OST exist in settings such as those most affected by the West Africa outbreak including treatment centres overwhelmed by patients, lack of adequate health care infrastructure, lack of trained health care workers, and duration of time to deliver care constrained by personal protective equipment (3). These challenges, however, should not impede including the provision and evaluation

of OST in a well-resourced clinical trial. While others have previously stated that “conventional care offers little benefit” despite lack of evidence to support this claim (5), better attempts to incorporate evaluation of OST in a clinical trial might have provided pragmatic evidence (e.g., on fluid resuscitation and monitoring) to help guide frontline clinicians on how best to manage EVD patients in light of resource constraints.

Ultimately, while “consensus about trial design and conduct in inter-epidemic periods” is important, strengthening the local infrastructure and training local health care workers to deliver evidence-based OST should also be prioritised. This approach is important not only to address future filovirus outbreaks but also to prepare for other epidemics with highly infectious and deadly pathogens.

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## References

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