How best to test Ebola treatment

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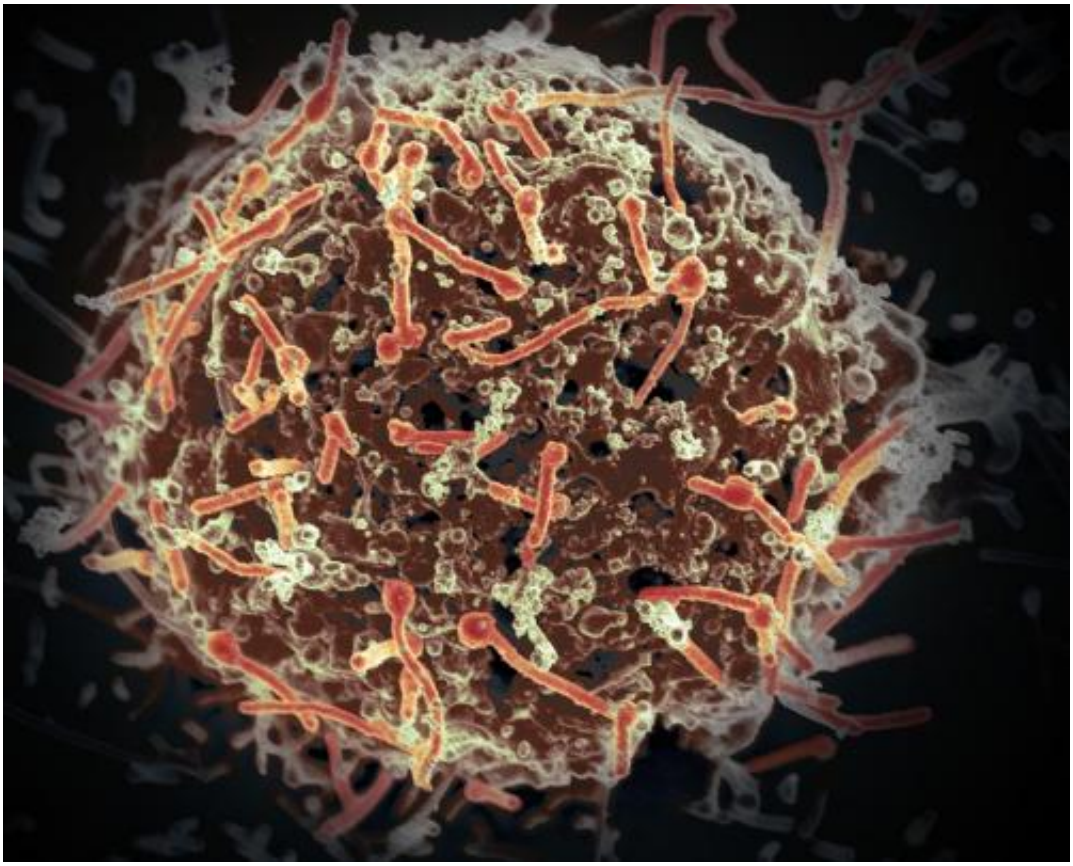

The Ebola virus, isolated in November 2014 from patient blood samples obtained in Mali. The virus was isolated on Vero cells in a BSL-4 suite at Rocky Mountain Laboratories. Credit: NIAID

An unconventional clinical trial design might have advantages over classical trials for testing treatments for Ebola virus disease (EVD), suggests a study published this week in *PLOS Medicine*. The work of an

international team led by John Whitehead of Lancaster University, UK and Ben Cooper of Oxford University, UK, provides much-needed data to inform a debate on the scientific and ethical justification for non-randomized EVD trials that has taken place in the editorial pages of a number of medical journals in past months.

The researchers compared three different scenarios using analytic methods and computer simulations and report that, compared with two different approaches using all randomized trials, a multi-stage approach (MSA) that includes a component without randomization has the potential under certain circumstances to reduce patient harm and the time to roll-out of an effective treatment for EVD.

Although alternative evaluation designs are possible, the researchers suggest that beginning with a non-randomized phase II stage can be the quickest way to triage potential treatments and to decide how to test them further. For treatments that show strong evidence of benefit, it might even be possible to recommend the treatment without undertaking an RCT, they suggest.

While stressing that "RCTs are usually the best method for evaluating interventions", the researchers argue that "the current Ebola epidemic in west Africa is an unprecedented situation where there is substantial uncertainty that RCTs can be conducted successfully and safely". "Given these operational concerns and the results of our analysis", they say, "the MSA—which begins with a less operationally challenging design and yet retains the ability to provide robust and informative results—must be considered."

More information: Cooper BS, Boni MF, Pan-ngum W, Day NPJ, Horby PW, Olliaro P, et al. (2015) Evaluating Clinical Trial Designs for Investigational Treatments of Ebola Virus Disease. *PLoS Med* 12(4): e1001815. DOI: 10.1371/journal.pmed.1001815