Editorial: Multidisciplinary success conceals a missed opportunity

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The 2013–16 Ebola epidemic in West Africa was larger than all previous Ebola outbreaks combined and was unique in the breadth of its geographical dispersion. The size and scope of this epidemic provided the potential to achieve significant advances in understanding the disease and to improve outbreak prevention strategies and public health responses for the future. This special issue gathers together research on key aspects of the disease to ensure that lessons can be learned and improvements made for the benefit of future responses. It is the first compendium compiled addressing the largest Ebola epidemic in history.

The nature of research into neglected tropical diseases, particularly those which only result in occasional outbreaks, is that publication is infrequent. This special issue builds on a comprehensive previous special issue published following the second largest outbreak to date in Kikwit, Democratic Republic of Congo in 1995. This was published in *Journal of Infectious Diseases* (1999) and contains the key body of scientific work underpinning much of what we knew about Ebola prior to the 2013–16 epidemic (1).

This current special issue reflects the multidisciplinary approach required to deal with a global health crisis and offers new research to enhance the biological, epidemiological, clinical and operational Ebola knowledge-base. Due to the unprecedented scale of cross-national virus transmission, we also include dedicated research on the behavioural and socio-political factors that both drove and eventually played a part in halting the epidemic. For example, *Wilkinson et al.* (2) provide detailed accounts of the landscape of local outbreak responses which complements work by *Jalloh et al.* (3): a "Knowledges, Attitudes and Practices" survey conducted through the epidemic in Sierra Leone and Guinea, the first such study related to Ebola. Additionally, *Wenham et al.* (4) and *Ross* (5) detail the high-level architecture of outbreak response management.

The most important step forward during the epidemic was the development of a safe and highly effective vaccine and this publication includes the first review of the vaccine candidates (*Lambe et al.* (6)). In addition, the use of mathematical modelling and computationally intensive statistical techniques has become a mainstay of outbreak control analysis and this work, which has not previously been applied to Ebola outbreaks, is reflected in the current issue: e.g. *Funk et al.* (7) and *Mbala et al.* (8). *Whitty* (9) highlights the crucial role of integrating such diverse disciplines to optimise the outbreak response and he hypothesizes that without this the epidemic would have been significantly worse.

On the other hand a key opportunity was missed: this epidemic provided the potential to collect enough data over a sufficient period of time to develop, test and implement therapeutic, prophylactic and non-pharmaceutical control strategies for Ebola. Previous outbreaks had been over too quickly with too few cases to set up rigorously controlled studies, whereas this epidemic provided a rare opportunity. However, notwithstanding the significant contribution to future disease control of the effective rVSV ZEBOV vaccine that underwent successful phase III clinical trials in Guinea (10), insufficient data was gathered to develop clinical knowledge regarding the basic supportive management and appropriate therapeutic protocols for Ebola patients. This missed opportunity is exemplified by the editors' inability to commission a clinical research article for this special issue. While many factors influencing disease outcome remain elusive, we have included a number of papers focused on clinical aspects of the outbreak: *Rojek et al.* (11) review the developments in pharmaceutical therapeutics that occurred during the epidemic and suggest barriers to regulatory approval; *Garske et al.* (12) conduct comprehensive analyses of line list data to evaluate predictors of case fatality risk; and *Logue et al.* (13) provide a case study of Ebola diagnostics and training in field laboratories during the outbreak.

Unfortunately, the sparsity of data collected also serves to limit our understanding of the effectiveness of different interventions. This in turn restricts our ability to better understand the answers to key public health questions such as: which transmission interventions work best?; and in which order should they be deployed? It is only through indirect and retrospective analysis—e.g. Funk et al. (6), Skrip et al. (13), and Senga et al. (14)—that we can start to address these questions given there were no direct observational studies conducted during the epidemic. The ineffective implementation of interventions, together with the lack of data, not only hampered research efforts but also had a direct effect on the spread of the epidemic. Senga et al. estimate that only a small fraction of new cases reported over the first six months were known contacts of prior cases (documented on contact tracing lists) meaning that contact tracing in the initial stages of the epidemic was highly ineffective. This led to unmonitored, sustained transmission that, in all probability, prevented the epidemic from being contained.

The paucity of data sits in stark contrast to the surge in publications about Ebola that appeared during the first year of the crisis as the epidemic ran uncontrolled (Figure). *Cori et al*. (14) provide a comprehensive description of the data and data management techniques we will need to control future outbreaks, with an important discussion of the need for rapid transfer of useably formatted data to facilitate real time analysis of outbreak control. While resolving this issue was not feasible during the 1995 Kikwit outbreak, technological developments by the 2010s meant this should not have remained a problem.

Over 20 years after publication of the Kikwit Ebola special issue, woefully little progress has been made in controlling and treating Ebola. As *Coltart et al.* (15) highlight, many of the same concerns and conclusions documented in the 1990s by Heymann et al. pursuant to the Kikwit outbreak remain relevant now and match the recommendations made by the expert panels reviewing the recent epidemic. This is reinforced by *Piot et al*. (16) who detail examples of recommendations common to both the 1995 and 2013–16 outbreaks including the need for stronger infectious disease surveillance (both national and global), improved international preparedness to provide support when similar outbreaks occur, more broad-based international health regulations, and continued and coordinated Ebola research (diagnostics, patient management, and identification of the natural reservoir).

The impact of this epidemic on individuals, healthcare, societies, and economies was profound and will last many years beyond the end of the outbreak. Had the lessons of previous outbreaks been heeded by the global community, thousands of deaths could have been prevented. Looking forward, we sincerely hope that recommendations will be enacted and translated into tangible solutions. Although Ebola outbreaks remain inevitable, this can and should prevent future outbreaks from reaching the same size and scale as the devastating 2013–16 epidemic.

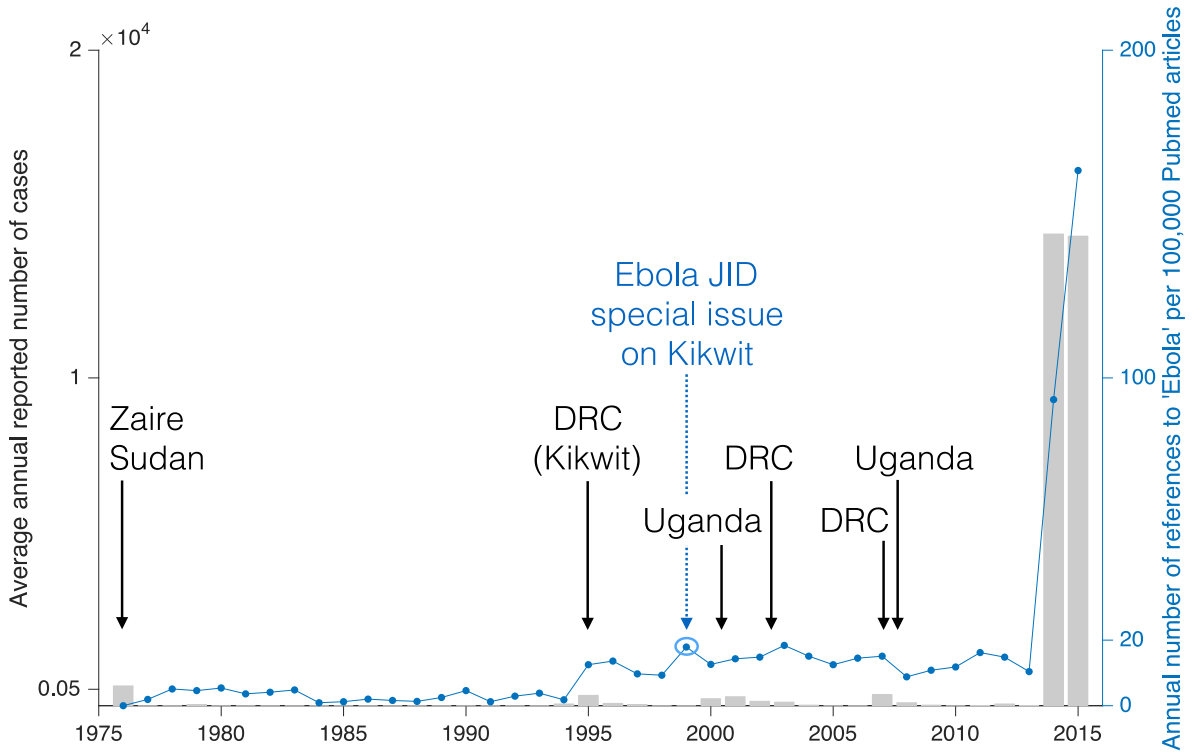

Fig 1: Number of Ebolavirus cases reported by year (bars) and number of published articles containing the word "ebola" by year (points). Labels (black) correspond to previous outbreaks where more than 100 cases were reported. Previous special issue documenting the outbreak in Kikwit in the Democratic Republic of the Congo (DRC, formerly Zaire) time in blue.

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