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The Lancet Infectious Diseases Series on the Modern Landscape of Ebola Disease: Embedding treatment in stronger care systems

Running Head: Modern Landscape of Ebola Disease response

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Abstract

A key lesson from the west Africa (2014-2016) Ebola disease epidemic was that outbreak responses fail when they respond to patients through a narrow clinical lens without considering the broader community and social context of care. In this continuation of *The Lancet Infectious Disease* series on the Modern Landscape of Ebola Disease, we review progress in the last decade to improve patient-centred care. While the biosafety imperatives of treating Ebola Disease remain, recent advances show how to mitigate these so that patients are cared for in a safe and dignified manner that encourages early treatment-seeking behaviour and provides support following return to their communities. We review advances in diagnostics, including the reduction of turnaround times for Ebola disease detection through real-time RT-PCR, improvements in Ebola disease Treatment Unit designs that enhance patient safety and dignity, advancements in care provision such as the integration of palliative care and mobile communication, greater access to research through harmonised clinical trials, and strengthened community engagement and psychosocial programmes that address stigma and provide emotional support for survivors.

Key Points:

1. Integration of social science in outbreak responses improves risk communication and community engagement (RCCE) activities critical for outbreak control.
2. The availability of near-patient diagnostic tests has increased markedly, and future guidelines should incorporate their use for specific use-cases.
3. Facilitating communication between patients and loved ones, integration of palliative care, and improved responsiveness in the practices of safe and dignified burials have been key components of making clinical care more dignified.
4. Improved Ebola Treatment Unit (ETU) designs enhance patient visibility, monitoring, safety, and communication though challenges remain in implementation, cost, and the sustainability of the infrastructure developed.
5. Integrating more efficient trial designs (such as platform adaptive designs, and factorial randomisation) will improve the likelihood that future trials are powered to reach definitive outcomes.
6. Ebola disease stigma hinders both survivor reintegration and outbreak response, necessitating targeted interventions and better assessment tools.

Introduction

This is the second instalment in The Lancet Infectious Diseases series on the Modern Landscape of Ebola Disease. Reflecting upon the ten-year anniversary of the west Africa (2014-2016) epidemic, this series provides an overview of the progress made in improving the clinical care for patients with Ebola disease since then. The first of this series[1] focussed on advances in understanding the epidemiology and clinical manifestations of Ebola Disease, along with developments in treatment and vaccines, care in special populations, and the evolving challenges of Ebola disease sequalae and viral persistence. However, one of the most crucial lessons of the west Africa epidemic was that responding through a restricted

clinical focus without considering the broader context of care, fails patients and communities.

Patients receiving care during the west Africa epidemic faced harrowing experiences. Early on, a lack of community engagement led to fear and a reluctance to seek testing or care.[2] For many reasons, the initial response was slow and complicated.[3] At times, the clinical workload was overwhelming – Médecins Sans Frontières (MSF) reported that during the peak of admissions, clinicians had only one minute per patient per day.[4] Facilities had to turn away sick patients due to lack of capacity to care for them safely.[4] Initially most clinical care was provided in large Ebola disease Treatment Units (ETUs), often located far from affected communities.[5] Typically, these were large tents accessible only by healthcare workers wearing enhanced personal protective equipment (PPE). Healthcare workers had limited time inside treatment areas due to the risk of heat stroke. Some patients reported living amongst corpses and watching helplessly as relatives and friends died of the same illness. Survivors returned home only to be stigmatised and ostracised.[6]

However, improvements in community based[5] and clinical strategies throughout the epidemic led to a greater proportion of patients seeking testing and care, which ultimately contributed to stopping transmission. In this second part of the series, we highlight the continued advances since in developing stronger care systems for Ebola disease at each step of the care pathway. For those at risk of disease, this requires improving the willingness to seek care through developing contextually appropriate systems and access to fast, local, and trustworthy diagnostics. For those infected this demands provision of dignified clinical care in safe, appropriate, and effective treatment facilities and with equitable access to advancing clinical research. And finally, for those who survive Ebola disease, care needs to go beyond managing the biological and virological consequences with active efforts to combat stigma and support the psychosocial welfare of survivors. These advances, along with remaining scientific priorities, are summarised in table 1.

Improving willingness to seek care

Involving communities

Risk communication and community engagement (RCCE) has long been a crucial strategy for containment of disease outbreaks. It is designed to build trust and ensure that the outbreak response is meeting the needs of the community. When trust is lacking, this manifests in both individual-level actions such as hospital avoidance, and more organised community level acts of “resistance” that can meaningfully hamper outbreak control efforts.[10] Conversely, greater trust means patients presenting earlier[10], greater uptake of vaccination efforts[11,12], and better engagement with public health measures[13], allowing for the more effective utilisation of the biomedical advances in therapeutics and vaccines discussed in the first part of this series[1]. However, it is only recently that the systematic

integration of social science into outbreak preparedness and responses has gained prominence.[14]

RCCE was not always present or embedded early in the west Africa epidemic response. There were many reasons for this, including the predominance of international rather than local actors, a lack of coordination between different response organisations, overwhelmed organisations prioritising biomedical solutions, and the emergence of Ebola disease in a new region which meant that RCCE activities from other outbreaks were applied without being adapted. In contrast, by the end of the epidemic, social mobilisation programmes were cited as a key factor in ending transmission.[15] Emphasising this is an analysis that related the impact of the major interventions to the epidemic curve in Liberia which concluded that the decline in the number of Ebola disease patients was primarily driven by critical behaviour changes within local communities, rather than international efforts such as expanding ETU capacity.[16]

The largest subsequent Ebola disease outbreak has been the 2018 to 2020 outbreak in North Kivu.[1] This outbreak occurred in the midst of a conflict with a background of significant civilian distress[17,18], seriously complicating response efforts. In addition, the community response to the outbreak, including violence against health care workers and facilities[19], reflected mistrust of government and international responders and profuse misinformation.[20] Again, early failures of RCCE were thought to be due to transplantation of experiences from the west Africa epidemic. However, over time, interventions were contextualised, and a variety of novel social interventions implemented.[20] Some examples of successful programmes included the development of a rapid analysis system for community feedback[20] and a World Bank supported cash-for-work programme rolled out to improve community trust and build local capacity[21]. In addition, large numbers of local community health workers were used, although analysis of the benefits of this intervention has been limited due to challenges in gathering and interpreting data.[22] Shared initiatives, such as embedding social mobilisers in other interventions such as vaccine programmes have demonstrated how RCCE can be integrated so that all pillars[23] of outbreak response can benefit.[7]

A key issue has been improving the integration of social sciences findings in outbreak response structures.[24] Unfamiliarity with data types (such as narrative descriptions) and differences in understanding of terms between social scientists and other outbreak responders has limited the translation of findings into response actions. Guidance supported by WHO, UNICEF, and IFRC has been developed to attempt to address this and support implementation.[25] However, there remains ongoing need to ensure special populations, such as children, are included in outbreak response research and policy development.[26]

Enabling rapid diagnosis

The key clinical benefits of early and definitive Ebola disease diagnosis include allowing non-infected patients to return home, reducing the risk of hospital acquired infection, and in accelerating access to treatment.[27] At a public health level, early diagnosis reduces onward transmission, with some mathematical modelling suggesting the availability of rapid diagnostics testing, in combination with polymerase chain-reaction (PCR) testing, in the west Africa epidemic could have reduced the size of the outbreak by as much as a third.[27]

For decades, countries affected by Ebola disease outbreaks lacked diagnostic capacity to confirm and manage cases. Specimens from suspected cases had to be sent to laboratories in the USA, Europe, or South Africa. The west Africa epidemic was also confirmed by virus isolation and PCR in laboratories in Europe.[28] However, this epidemic was a game changer for the development of regional diagnostic capacity.

The most widely used technique for virus detection during the west African epidemic was real-time RT-PCR.[29] Affected countries and international partners deployed various mobile laboratory units at ETUs to enable rapid confirmation and management of patients and contacts.[30–33] Notably this meant diagnostic capacity was typically centralised around treatment sites. From sample reception to diagnosis took about 6 hours. Most real-time RT-PCR assays are specific for an orthoebolavirus; however, some assays are broadly reactive and detect all human pathogenic species.[34] The former are generally more sensitive and preferable in an outbreak once the etiologic virus has been identified, while the latter are suitable for the diagnosis of cases of unknown aetiology. Real-time PCR assays are commercially available with industry standard features such as internal controls to monitor RNA extraction and reaction efficacy.

One advantage of real-time PCR is the semi-quantitative readout in Cycle Threshold units, which inversely correlate with viral RNA levels. The viral load on admission is an important prognostic marker: the higher the viral load, the poorer the outcome.[35–38] However, real-time PCR testing in the field still requires extensive laboratory infrastructure, special containment needs, and well-trained experts. Therefore, automated commercial real-time RT-PCR tests have been developed that integrate RNA extraction, amplification, and detection and provide results within 2 hours or less.[39,40] These systems can be used near the patient and operated by trained local staff. Another addition to the diagnostic portfolio are lateral flow immunoassays for the detection of orthoebolavirus antigen - so-called rapid diagnostic tests (RDTs) - which provide results within minutes at the bedside.[41,42] The sensitivity and specificity of automated near-patient PCR tests are high, while there remain important concerns about the sensitivity and specificity of RDTs.[43,44] The potential of RDTs for improving surveillance and triage, accelerating access to therapeutics, and

decoupling access to diagnostics from centralised treatment centres should be further explored.

By 2023, 23 African countries have established diagnostic capacity for orthoebolaviruses, up from only five in 2010.[45] While key capacities, including sequencing, are now available in centralised, well-equipped facilities, more and more decentralised laboratory facilities are being established in areas at high risk of Ebola disease occurrence. Due to a lack of resources in the region, 110 days elapsed between the first case and confirmation of the west Africa outbreak, leading to wide spread of the disease. Thanks to improved diagnostic infrastructure the interval between symptom onset in the index patients and the declaration of an outbreak has only exceeded 33 days on two occasions since.[45]

Optimising clinical care

Ensuring clinical care is dignified

Admitting infectious patients to ETUs allows potentially life-saving medical care to be provided as safely as possible. It is also important as it helps reduce transmission within communities. However, in achieving these aims there is a need to strike a balance between best intentions – both clinical and public health – and respecting individual patients' dignity and right to self-determination.

While many patients report positive experiences of care during outbreaks, attitudes and behaviours of frontline responders can be negatively influenced by biosafety imperatives, the fear of being infected, harsh working conditions, and the burden of witnessing severe illnesses and deaths.[46,47] There is a risk that this can unintentionally impact on relationships with patients. Many examples exist of effective provision of holistic, compassionate care in outbreaks, as well as the effects on patients and their families when efforts fall short or are absent.[46,48,49] Improving the 'patient experience' of an ETU not only benefits patients directly, but also likely improves the reputation of, and trust in, ETUs and broader outbreak response measures.

The importance of patients having contact with their loved ones is clear. Simple measures include providing ETU patients with mobile phones, mobile phone credit, and an ability to charge the phones. Allowing in-person communication is more challenging, though possible, with improved ETU design (see below).[48] It can be easy to overlook the importance of creating a comfortable environment for patients and deprioritise addressing issues such as poor ventilation, excessive temperatures or poor or excessive lighting. However, the severity of Ebola disease should not prevent efforts to make isolation more tolerable, and such changes may also benefit staff. There is an unmet need to conduct more research into specific patient experiences and how they can be improved, accepting that findings may differ between outbreaks and countries.

Palliative care has been largely neglected for patients in humanitarian crises, including Ebola disease outbreaks. Specific challenges highlighted during the west Africa epidemic included prognostic uncertainty, patient distrust manifesting as a reluctance to receive palliate treatments, poor access to medication, and limited healthcare worker experience with opioids. There were reports of low to no availability of morphine in some ETUs during the west Africa epidemic.[50,51] Patients with Ebola disease especially emphasise the fear of dying alone.[52]

Since this time, provision of palliative care has been included as an essential component of care in international standards for humanitarian response.[51] However, current treatment guidelines and standard operating procedures for Ebola disease have been criticised for a continued lack of recommendations pertaining to palliative care[51] and there remain significant gaps in extending the standardisation of supportive care discussed in the first part of this series[1] to include routine provision of palliative care. There is an increasing awareness of the need to strengthen healthcare worker training, including on palliation for paediatric patients, and improve the availability of equipment.[51] While this will undoubtedly relieve suffering for patients, there may also be benefits in alleviating the trauma experienced by healthcare workers in this setting.

For patients who do survive, most ETUs will ceremonially mark discharge. Interestingly, there appears to be no research focussed on perceptions of these events. While they are clear in their intent as celebration, risks do exist – particularly with regard to patient confidentiality and inadvertent distress to survivors who are grieving or exhausted.[53] Similarly, hearing celebrations could create either hope or distress for other patients whose prognosis remains unclear, or who have recently lost a relative to Ebola disease. Discharge also should not mark the end of care as survivors need support through various social, psychological, and biomedical sequalae (see the *supporting survivors* section and part 1 of this series[1]). In this respect, discharge needs to be thought of as not just a celebration, but as an opportunity to ensure continuity of care, including for patients suspected of, but subsequently confirmed not to have Ebola disease.

For patients who die, ‘safe burials’ have now become ‘safe and dignified burials’[54] (SDBs) to convey explicitly the importance of respect. In brief, SDBs are burials that maintain strict infection control procedures,[55] but are contextually adapted to better meet cultural and spiritual needs of communities.[56] As an example, during the 2018-2020 DRC outbreak, the burial service was continuously refined based on community feedback resulting in adaptations including families being given a say in the burial site, preservation of traditional burial customs, and psychosocial support for grieving relatives.[56] In addition, a community-led emergency burial scheme trained local community members in difficult-to-reach locations to

conduct SDBs using supplies from neighbouring health facilities, so that appropriate burials could be performed in an acceptable timeframe even when locations were inaccessible.[56] In some areas, transparent body bags were introduced to allay fears about bodies being stolen.[57] Overall, there were almost 15,000 requests for SDB during this outbreak, and around 60 percent of these resulted in a successful SDB, with higher levels of uptake thought to be largely inhibited by violence and instability.[56] Early and widespread adoption of SDB is often stated as a key intervention in ending the 2022 SUDV outbreak in Uganda, but quantitative data on transmission reduction are not yet available.

Improving care infrastructure

Patients with Ebola disease are usually treated in dedicated units (ETUs) to manage transmission risk.[58] Historically, these were enclosed temporary tent structures with open wards. The benefit of this design is they are rapidly transportable and easy to erect. The critical issues with this design are poor visibility of patients, difficulties in limiting transmission risk between patients awaiting diagnosis, lack of dignity and privacy for patients, and isolation of patients from their loved ones. Since the west Africa epidemic, improvements in the design of ETUs have occurred that address some of these limitations and allow easier access to patients, improved monitoring, better safety, and more communication between patients have family.[59,60]

Several organisations now provide technical briefing papers describing best practice in constructing and decommissioning ETUs, including those from Oxfam[61] and MSF[62]. In particular, a coordinated approach led by WHO has resulted in a multi-sectorial investment into guidance that involves new health, spatial, and technical requirements to advance the design of facilities.[63] However, at the beginning of an outbreak, as occurred in Uganda in 2022, the urgency to establish ETUs and the need for complex inter-agency coordination can result in these requirements not being fully implemented.[64] During that recent outbreak, patients were often managed in repurposed existing buildings while more specialist facilities were being erected[64], suggesting there is room for global improvement in preparedness. Even when facilities exist, uptake may be challenging. For example, during the outbreaks in North Kivu and Ituri provinces, home-isolation was used as an alternative care model where access to treatment units was impossible due to violence or where communities were too fearful or distrustful of the response effort to consent to admission.[18,65]

At the forefront of modern ETU design is an increased emphasis on selecting the best site and taking that decision in partnership with affected communities. Important to the consideration is data that suggest that decentralising care leads to benefits such as increased community ownership, improved reporting times, more local staff, and increased family involvement in care (such as cooking for the ill).[66] However, these

advantages must be balanced against leveraging existing health care facilities, including national isolation units, and the advantages of concentrating resources. The design must also recognise the life cycle of an ETU from initial implementation through to decommissioning, whilst also having capacity for expansion if required. Finally, the challenges of managing special populations such as children, newborns, and pregnant women need to be considered.

The most critical recent ETU design innovation has been in increasing observation of patients in the high-risk zone (HRZ; the area enclosing potentially infectious patients and equipment) from a low-risk zone (LRZ; an area where healthcare workers are not required to wear PPE).[63] This is especially essential for paediatric and critically ill patients. LRZ observation can be facilitated by peninsula-shape corridors into HRZs where transparent screens allow maximum visibility without staff having to wear PPE.[63] Reducing the need for hot and cumbersome PPE has benefits for healthcare workers[67] and is less foreign and impersonal for patients. Additional recent innovations involve methods of providing care across the barrier separating the HRZ. Prefabricated isolation units have been developed (e.g. ALIMA Cube[68] – figure 1) that are an autonomous structure with transparent walls and external arms, unique for their rapid set-up time and low-risk access to the patient.[60] They improve the patient experience, as the family can be in contact with the patient, and they provide the opportunity for body viewings for loved ones. However, such set-ups are power-dependent and consequently not always suitable for a rural context. Other important considerations are cost, with an ALIMA Cube costing around €16000 per unit in 2018[60], and the practical challenges associated with large-scale implementation of these more modern designs.

Further developments in patient visibility and HRZ accessibility, such as using cameras mobiles, and wearables, have also improved observation of, and communication with, patients, as well as improving data flow.[70] The standardisation of supportive care[1] including routine rehydration as well as the empiric use of antibiotics and antimalarials in suspected cases prior to definitive diagnosis has also become a key feature of care in ETUs. Indeed, a key criticism of ETUs is their implicit prioritisation of Ebola disease in communities where there are often significant ongoing health disparities and lack of access – leading to distrust regarding the motivations of response organisations.[48] This is particularly the case because they are decommissioned and usually demolished following use.

Integrating research into clinical management.

The west Africa epidemic saw greater emphasis on providing evidence-based prevention, diagnosis and treatment for patients. Vaccine and treatment trials were launched for the first time and there were improvements in standardised clinical data capture[1]; however, the research response was criticised for generally failing to produce robust findings that improved patient outcomes.[71,72] The reasons for this were

multifaceted but included the operational complexities of trying to conduct regulatory compliant trials in ETUs, a lack of preparation, a propensity for non-randomised studies, regulatory delays, and a lack of coordination or harmonisation between studies.[73–76] Subsequent innovations to optimise clinical research to provide robust and reliable results in this setting have led to successes, including approved vaccines and treatments for orthoebolavirus infection.[1,38] In this way, research innovations in Ebola disease are a good exemplar for other outbreak prone infectious diseases.

To date, clinical treatment trials have still been relatively slow to open to recruitment. In an attempt to provide potentially promising treatments to patients, Monitored Emergency Use of Unregistered Investigational Interventions[77] (MEURI) has been used. This is an ethical framework that aims to give access to unproven clinical interventions outside of clinical trials during international public health emergencies and may be considered when initiating research immediately is impossible.[78] MEURI does not provide research evidence to evaluate safety and efficacy of investigational products, but importantly this framework can be used to improve operational capacity and sensitise communities ahead of clinical trials.[78] The risks with MEURI include causing delays to trials where operations are stretched, and increasing reluctance to do randomised trials, due to perceived benefit or harm based on compassionate use experience. The MEURI framework was used in the DRC, and recently in Uganda and Equatorial Guinea but specific results have not yet been published.

Due to the relatively small and short-lived nature of most outbreaks, clinical trials in Ebola disease require innovative approaches to generate sufficient data. WHO is leading a collaborative network of filovirus researchers in "at risk" countries in a framework for clinical research preparedness to ensure clinical research is promptly integrated into future outbreak responses. The team of experts, led by Ministries of Health and national research teams, have developed the collaborative multi-country multi-site SOLIDARITY PARTNERS vaccine and therapeutics adaptive pan-filovirus protocols.[79] These will undergo joint ethical and scientific review in preparation for future filovirus outbreaks. These trials have key features, many of them recent innovations, designed to overcome previous challenges in Ebola disease research (table 2). Special populations, including pregnant women and children, are intentionally included within these trial protocols.[79]

Some work has been done to understand patient perceptions of participating in Ebola disease clinical research, but this is an understudied area. In general, patients have been motivated to participate as an opportunity to survive and regain their health but also by a desire to help others.[83,84] Participants' fears were sometimes based on circulating rumours.[84] Common difficulties include facing stigma as a result of

participation, and a lack of confidentiality (for example due to researcher home visits).[83] Remaining key questions, such as how to improve informed consent procedures for patients who are often critically unwell or have limited healthcare literacy may draw from trials in other disease outcomes.[85,86]

Despite the improved yield from research, a critical ongoing challenge is ensuring that patients in the most affected countries benefit from this. The two licensed treatments for EBOV are not registered or generally available in countries most at risk for Ebola disease outbreaks.[87] Furthermore, unaffordability and lack of supply are likely to be issues even if registration is successful[88], with much further work needed on improving post-regulatory access.[87,89]

Supporting survivors

Reducing Ebola disease stigma

Survivors and their families can be profoundly affected by stigma associated with Ebola disease.[90–92] While it is thought to be a common phenomenon, estimates of the proportion of survivors affected vary widely and are limited by sampling strategy, small sample sizes, and lack of validated tools to measure stigma. The consequences can be severe.[90,91,93] As an example, separate cohorts from Sierra Leone and Liberia reported job or income loss in over a third of survivors.[92,94] as well as forced evictions and forced relocations.[95] What places an Ebola disease survivor at increased risk of experiencing stigma is not well understood, but data suggest an association with visible ongoing symptoms or requirements for ongoing medical care, presumably because these invoke a fear of contagion.[96]

Long term follow up studies of Ebola disease survivors show that stigma decreases over time but continues to affect the social integration, mental health, and economic opportunities for survivors, and other community members associated with Ebola disease up to 8 years after an outbreak.[8,92,97–103] The news that the 2021 outbreak in Guinea was linked to sexual transmission involving a survivor of the 2014-2016 west Africa epidemic resulted in a resurgence in stigmatisation of survivors.[99,104]

At a community level, Ebola disease stigma disrupts social cohesion.[105] The stigmatisation of response workers evident during the west Africa epidemic has also been a feature of subsequent outbreaks.[106,107] In 2019 at least 20 healthcare workers were killed in DRC during an Ebola disease outbreak, and another 16 abducted.[108] Forty-three health facilities were subject to arson attacks during this period, including an Ebola disease treatment centre in North Kivu, resulting in the destruction of medical wards and vehicles. Four patients with confirmed Ebola disease diagnoses fled the hospital.[109] The discrimination and attacks targeted at healthcare

workers severely affect the availability and willingness of response personnel.[91]

The impact of stigma on healthcare worker availability exemplifies how Ebola disease stigma hinders outbreak response and contributes to ongoing transmission (Figure 2). Other pathways include concealment of symptoms and sick relatives, delayed healthcare seeking (or preferential use of traditional healers), and migration from high-incidence communities, contributing to the spread of Ebola disease.[93] For this reason, stigma reduction is now considered a critical policy priority in Ebola disease strategic response.[110,111]

However, public health interventions may also inadvertently exacerbate stigma (Figure 2), for example, being quarantined was associated with reported or perceived stigma in some studies.[102] "No-touch' public messaging contributed to children's perceptions of anyone associated with Ebola disease in Sierra Leone, and another study[112] found those exposed to messaging aimed at preventing Ebola disease related stigma showed paradoxically higher level of stigmatising attitudes toward survivors.[8]

Stigma reduction interventions are usually embedded in a broader suite of community engagement and mobilisation activities including education and myth busting campaigns. Specific examples of stigma directed interventions include replacing terminology, for example avoiding the term 'isolation centre' in preference for 'treatment unit', use of community protection bylaws that fine individuals found to mistreat survivors,[113] and reintegration programmes for survivors and patients with suspected, but non-confirmed Ebola disease returning home.[53] Along with psychological support, these programmes need to address the socioeconomic impact of Ebola disease on affected communities. The 2022 Ugandan outbreak saw the rapid introduction of psychosocial teams and survivor support groups, to proactively address stigma from the start of the outbreak.[114]

Despite the clear consequences of stigma on individual and community wellbeing, and on outbreak control, there is an absence of best-practice guidelines for stigma reduction, or guidelines to ensure that response interventions do not inadvertently worsen stigma. Furthermore, there are no well validated tools to measure the impact of stigma interventions when they are implemented.[115] This re-emphasises the need for further integrating social science research into outbreak response, as previously discussed.

Providing psychosocial care

Psychological distress is common amongst survivors and affected communities.[116]

A study assessing the prevalence of psychological distress amongst villages and cities recently affected by Ebola disease in the DRC found just

under half of participants experienced severe psychological distress associated with the outbreak, but was limited by a lack of control population given the difficult to access environment.[117] Increasing exposure to Ebola disease, stigmatisation, and living in a village compared to a city were all associated with severe psychological distress.[117] Degree of exposure has also featured in other studies where knowing someone quarantined for Ebola disease was independently associated with anxiety-depression and post-traumatic stress disorder symptoms.[118] A meta-analysis found that one in five individuals exposed to Ebola disease—including survivors, families, communities, healthcare workers, and SDB teams—were diagnosed with depression.[119] Structural impacts such as business and industry disruptions, the closure of markets and schools, and reduced access to health and support services, have been shown exacerbate the long-term psychosocial effects of the outbreak.[105,120]

Over the course of the west Africa epidemic and in following years, several programmes were created to respond to the psychosocial needs of the survivors and their families. Exemplars include the Comprehensive Programme for Ebola Survivors (CPES) and Ebola Survivor Corps (ESC) in Sierra Leone, founded in 2015. CPES was supported by WHO and aimed to ensure that survivors could access necessary health and social welfare services, counselling, sexual health advice, and semen testing.[94] ESC was developed to address Ebola disease survivor concerns and employs Ebola disease survivors as advocates to provide health education and facilitate access to health care.[121] The Social Rehabilitation and Payment to Ebola disease Survivors (a joint project by the United Nations and Government of Sierra Leone) aimed to address social marginalisation through discharge packages to survivors and socio-economic support.[122] Ebola disease survivors were represented by the civil society organisation Sierra Leone Association of Ebola Survivors (SLAES) who worked with established government networks and implementing partners to advocate for the needs of survivors.[123]

Limitations

It is essential to recognise that delivering Ebola disease care is closely linked to addressing broader structural challenges and vulnerabilities within healthcare systems. In turn, it is important to acknowledge some of the biggest challenges in outbreaks, such as maintaining critical routine care and economic activity, are not discussed in this review. In addition, significant progress has also been made in key areas of public health – such as surveillance and contact tracing – and basic scientific research, including molecular epidemiology and outbreak modelling. While these are crucial elements of outbreak response pillars, they have not been discussed in this manuscript due to the focus on advancements in clinical care. However, these aspects of the response are fundamental to successful control of future outbreaks, and it will remain crucial that these pillars receiving due attention in future research.

Conclusions

Improvements in Ebola disease patient care during the last decade have benefitted from a more holistic approach and have extended to innovations in the care environment and community partnership approaches (table 2). Social sciences work to improve patient willingness to engage with care systems has been complimented by faster diagnostic testing. Advances in clinical care[1] have been enabled by improvements in ETU design and commitments to enable access to clinical research. Recognition of viral sequestration and survivor syndrome[1] has made clear that clinical care should extend beyond discharge, and foremost for survivors are measures to reduce stigma and provide psychosocial care. All of these efforts can help optimise medical care of patients with Ebola disease and this ultimately can benefit overall outbreak control.

There have been continued Ebola disease outbreaks since the west Africa epidemic – but none as large. It is hoped that the scientific advancements since this time, along with clear priorities for action moving forward, will ensure that it was a tragedy not repeated.

Author contributions

AR, JD, PH contributed to conception and design of the study. All authors contributed to writing of the manuscript and reviewed the final draft. AR and PH were responsible for the decision to submit the manuscript for publication.

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Conflicts of interest:

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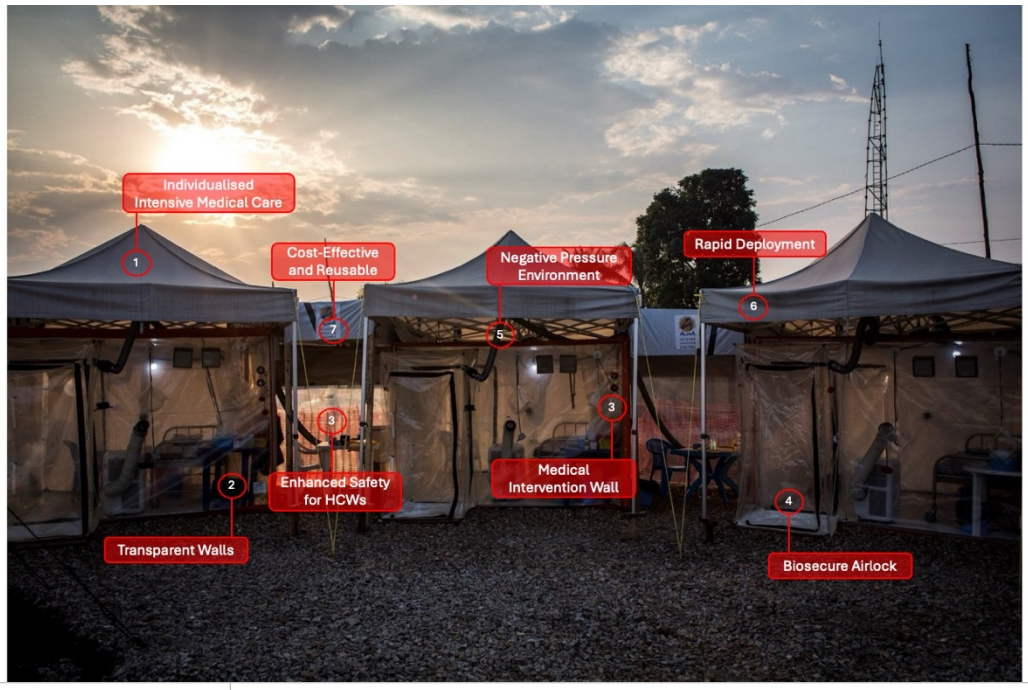
Table 1: Summary of important advances in caring for Ebola disease patients since the west Africa epidemic with ongoing scientific priorities.

	Advances	**Scientific priorities**
Involving communities	Improved integration of social sciences research into outbreak response activities Social interventions such as rapid community feedback systems and programmes like cash-for-work to build trust have been used successfully	Systematic evaluation of RCCE programmes to identify best practices and areas for improvement Undertaking rapid assessments earlier during outbreaks to establish baseline context[7] Ongoing efforts are required to include marginalised groups, such as children, in outbreak response research and policies
Diagnostics	Improved diagnostic capacity with at least 23 African countries now able to diagnose orthoebolaviruses Automated PCR tests and lateral flow immunoassays (RDTs) have been developed, allowing for quicker, near-patient testing Improved diagnostic infrastructure has led to a general trend of reduced outbreak confirmation time	Upscaling and decentralising capacity for diagnostic testing in risk-prone areas Addressing concerns regarding the sensitivity and specificity of rapid diagnostic tests RDTs, and determining their use-cases during outbreaks
Providing safe and dignified care	Safe and dignified burial has become more routine Palliative care is increasingly recognised as a vital part of Ebola care Better continuity of care for survivors' psychological, social, and biomedical needs after discharge	Understanding clinical and ethical arguments regarding advanced cardiac life support Strengthening palliative care including for children through training for healthcare workers and ensuring access to necessary medications Improving working conditions for healthcare workers Improving the continuity of care and environment for patients with suspected Ebola disease
Ebola disease treatment unit (ETU) design	Availability of technical standards for treatment centre design, construction and decommission ETUs now include transparent-walled designs that prioritise patient visibility, family involvement, and infection control	Understanding patient perceptions and priorities for improved ETU design, especially for special populations Determining best harm-minimisation options for when access to ETUs is impossible Simplifying construction to enable faster commissioning during outbreaks

	Designs enable remote visualisation and/or monitoring of patients by healthcare workers not in PPE Decentralising care and engaging communities in site selection has led to faster reporting, more local staffing, and greater family involvement in care	Explore sustainable ways to transition ETUs into long-term healthcare assets Addressing concerns that ETUs focus solely on Ebola disease at the expense of other pressing health disparities, especially in regions with limited healthcare access
Integrating clinical research into management	Development of harmonised pan-Ebola disease trials Improved global coordination and collaboration Improvements in standardisation of data and data sharing Inclusion of special populations in recent research	Understanding the benefits and ethical risks of MEURI Improving community involvement and co-design of research Addressing challenges in informed consent for critically ill patients, drawing insights from other disease settings Ensuring post-regulatory access is a core part of clinical research
Reducing stigma	Understanding of psychosocial impact on affected individuals, families, and communities Recognition of stigma as a priority for outbreak control Involvement of survivors in advocacy and health education	Designing and evaluating a suite of stigma reduction interventions Determining best methods to address misinformation and emergent rumours Understanding population burden of stigma in affected communities and characterisation of types of stigma experienced Identifying risk factors for experiencing stigmatisation amongst survivors Identifying individual, community, and outbreak characteristics that predict stigma[8] Validation of stigma assessment tools[9] Piloting and evaluating adaptations to traditional outbreak control measures to minimise stigmatisation
Psychosocial support	Long term cohort studies that follow up survivors and include psychological assessments Initiatives to provide survivors with access to healthcare, social services, and psychosocial support and provide advocacy	Understanding population burden of psychosocial distress in affected communities Addressing the need for mental health support for affected populations, including long-term psychosocial services for survivors, healthcare workers, and communities

	Recognition of the need to provide socio-economic support to affected communities	



Feature	Details
1. Individualised Intensive Medical Care	Each CUBE provides a self-contained treatment unit for individual patients. Ensures high-quality care while minimising contamination risks.
2. Transparent Walls	Four plastic, transparent walls allow for continuous patient monitoring. Relatives can see and communicate with patients, improving psychosocial care.
3. Medical Intervention Wall	Equipped with glove boxes and intra-wall passage devices. Medical staff can perform up to 80% of procedures from outside[69], reducing the need for full protective gear. Notably access to the patient's airways is still limited with the current design.
4. Biosecure Airlock Entry	Entry and exit through a secure airlock to maintain biosecurity. Reduces the risk of contamination when entering or leaving the CUBE.
5. Negative Pressure Environment	Maintains a minimum negative pressure of -15 Pa includes HEPA H14 filtration. While arguably of limited need in Ebola disease this makes it possible to repurpose the unit for other diseases.
6. Rapid Deployment	Can be set up in 90 minutes by four people. Easily transportable and can be used indoors or outdoors, however this is dependent on a solid floor and covering structure.
7. Cost-Effective and Reusable	CUBEs can be cost-effective, reducing intervention costs by 75% compared to traditional ETUs. They are reusable and adaptable to various epidemic contexts.
8. Enhanced Safety for Health Workers	The design reduces the need for cumbersome protective clothing and allows a single healthcare worker to manage multiple patients simultaneously. However, integration of wireless monitoring could further improve this.

Figure 1: Three active CUBE units at the ALIMA treatment centre in Beni, Democratic Republic of Congo, with features and advantages of the design highlighted. Adapted from JOHN WESSELS/ALIMA

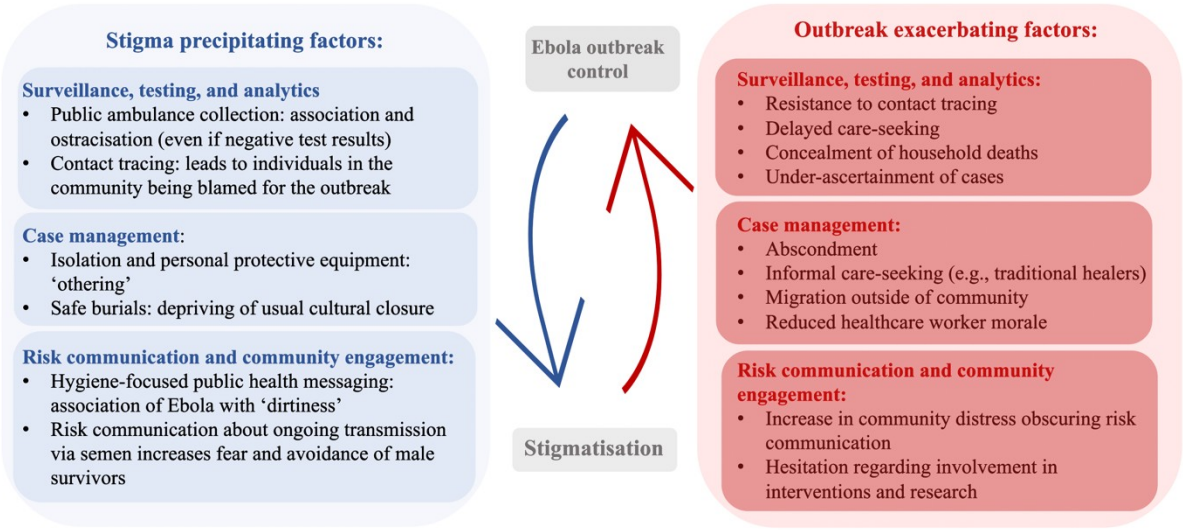


Figure 2: Interplay between outbreak control and stigmatisation (based on Paterson A, Olliaro P, Rojek A, 2023[9])

Table 2. Key features of clinical trials for Ebola disease countermeasures under the SOLIDAIRTY PARTNERS protocols.[79]

Feature	Challenge being addressed	Approach	Planned impact
Independent expert-driven selection of interventions for evaluation	Competing groups may wish to test different therapies of varying promise	WHO R&D platform[80] convenes multidisciplinary Technical Advisory Committees involving diverse stakeholders.	Facilitate detailed and unbiased evaluation of evidence to triage and select most promising candidate vaccines and treatments
Pre-positioned	Trials are too late to start	Trials prepared in advance with regulatory approval, governance and operations in place before outbreaks.	Quick trial initiation during outbreaks, improving likelihood of reaching sample size.
Harmonised	Trials are slowed down by repeating governance and approvals processes in each country	Trials operate regionally.	Benefit from regional initiatives (e.g. African Vaccine Regulatory Forum[81]) and capacity sharing to increase efficiency
Conserved across viruses	Different trials for each virus strain	Single protocol, with virus specific appendices.	Enables assessment of pan-filovirus vaccines or treatments, or host-directed therapies.
Conserved across outbreaks	New trials for each outbreak, data from previous outbreaks not used if sample size not reached.	Enrolment across multiple outbreaks, combining data for robust analysis.	Improves likelihood of recruiting enough participants.
Adaptive platform design	New trials for each candidate vaccine or treatment. Single vaccine or treatment tested at one time.	Roll interventions in and out, and update the standard of care.	Increased efficiency. Able to test combination therapies.
Streamlined[82]	Onerous data collection schedules are infeasible in ETUs.	Focus on critical questions in real settings, minimising administrative burdens.	Improves efficiency and limits impact on routine care without risking patient safety or trial integrity.
Quality by design	Builds safeguards in at every stage of trial development and conduct.	Optimised trial design from the beginning to prevent mistakes and minimise waste.	Reliable results, reduced errors and inefficiencies.
Transparent	Research can be a source of community fear	Freely available trial documents and findings.	Promotes openness, trust, and collaboration.
Respectful of communities	Researchers and community priorities might differ	Trials designed with leadership from affected communities.	Improved relevance, trust, and engagement.
Regulatory	Low-quality trials	Adherence to	Maintains trial integrity

compliant	risks patients and community trust	principles of good clinical practice and approvals from relevant authorities.	and participant safety.

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