ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid





Impact of infectious disease epidemics on tuberculosis diagnostic, management, and prevention services: experiences and lessons from the 2014–2015 Ebola virus disease outbreak in West Africa



Rashid Ansumana ^{a,b,*}, Samuel Keitell ^b, Gregory M.T. Roberts ^b, Francine Ntoumi ^{c,d}, Eskild Petersen ^{e,f}, Giuseppe Ippolito ^g, Alimuddin Zumla ^h

- ^a Mercy Hospital Research Laboratory, Kulanda Town, Bo, Sierra Leone
- ^b Department of Community Health and Clinical Studies, Njala University, Kowama Campus, Bo, Sierra Leone
- ^c Fondation Congolaise pour la Recherche Médicale, Brazzaville, Republic of Congo
- ^d Institute for Tropical Medicine, University of Tübingen, Tübingen, Germany
- ^e Institute of Clinical Medicine, University of Aarhus, Aarhus, Denmark
- ^f The Royal Hospital Muscat Oman
- g Lazzaro Spallanzani National Institute for Infectious Diseases, IRCCS, Rome, Italy
- h Centre for Clinical Microbiology, Division of Infection and Immunity, University College London, and the National Institute of Health Research Biomedical Research Centre at UCL Hospitals, London, UK

ARTICLE INFO

Article history: Received 9 October 2016 Accepted 17 October 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Epidemics
Ebola
Tuberculosis
Outbreak
Health services

SUMMARY

The World Health Organization (WHO) Global Tuberculosis Report 2015 states that 28% of the world's 9.6 million new tuberculosis (TB) cases are in the WHO Africa Region. The Mano River Union (MRU) countries of West Africa-Guinea, Sierra Leone, and Liberia-have made incremental sustained investments into TB control programmes over the past two decades. The devastating Ebola virus disease (EVD) outbreak of 2014-2015 in West Africa impacted significantly on all sectors of the healthcare systems in the MRU countries, including the TB prevention and control programmes. The EVD outbreak also had an adverse impact on the healthcare workforce and healthcare service delivery. At the height of the EVD outbreak, numerous staff members in all MRU countries contracted EBV at the Ebola treatment units and died. Many healthcare workers were also infected in healthcare facilities that were not Ebola treatment units but were national hospitals and peripheral health units that were unprepared for receiving patients with EVD. In all three MRU countries, the disruption to TB services due to the EVD epidemic will no doubt have increased Mycobacterium tuberculosis transmission, TB morbidity and mortality, and decreased patient adherence to TB treatment, and the likely impact will not be known for several years to come. In this viewpoint, the impact that the EVD outbreak had on TB diagnostic, management, and prevention services is described. Vaccination against TB with BCG in children under 5 years of age was affected adversely by the EVD epidemic. The EVD outbreak was a result of global failure and represents yet another 'wake-up call' to the international community, and particularly to African governments, to reach a consensus on new ways of thinking at the national, regional, and global levels for building healthcare systems that can sustain their function during outbreaks. This is necessary so that other disease control programmes (like those for TB, malaria, and HIV) are not compromised during the emergency measures of a severe epidemic.

Crown Copyright © 2016 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

The World Health Organization (WHO) Global Tuberculosis Report 2015 states that 28% of the world's 9.6 million new

tuberculosis (TB) cases are in the WHO Africa Region, where the annual case detection rates are more than double the global average of 133 per 100 000. TB incidence has continued to fall by an average of 1.5% per year since 2000 and is now 18% lower than the level during the year 2000. Gains made by TB control programmes need to be sustained, and an upward trajectory of investments into activities of TB diagnostic, treatment, and prevention services is required to bring TB under control. To this

^{*} Corresponding author.

E-mail address: rashidansumana@gmail.com (R. Ansumana).

end, the Mano River Union countries (MRU; Guinea, Sierra Leone, and Liberia) and other West African countries have made incremental and sustained investments into TB control programmes over the past two decades. However, the devastating Ebola virus disease (EVD) outbreak of 2014–2015 in Guinea, Liberia, and Sierra Leone, hich claimed an estimated 11 310 lives and affected 28 616 people, impacted significantly on all sectors of the healthcare systems, hick direct and indirect impacts of the EVD outbreak on various aspects of TB diagnostic, management, and prevention services are highlighted.

2. Lack of community education and public engagement

Media hype during any epidemic outbreak usually and inadvertently creates stigma and fear-driven responses among the affected communities. The EVD outbreak was no different. 15-17 Right from the onset, due to misconstrued conspiracy theories that were propagated by the local media and community gossip about the perceived origin of Ebola virus (EBV), the EVD outbreak was characterized by community fear, stigma, apprehension, and misunderstanding of the role of healthcare centres operating under prevailing epidemic conditions. 15-17 Where these perceived fears outweighed potential benefits, the creation of Ebola treatment centres further hindered healthcare-seeking behaviour. 16,17 There was widespread reluctance of people with symptoms such as fever to visit healthcare facilities for fear of being diagnosed or suspected of having EVD. People also refrained from visiting healthcare facilities to avoid being infected with EBV. There was also heightened anxiety amongst some healthcare workers (HCWs) to engage with or treat patients, 18 and many healthcare facilities in all three countries were closed during the

Several indicators of poor utilization of healthcare facilities and services during the EVD outbreak have emerged. In Guinea, there was a 50% decrease in outpatient visits and a 54% drop in hospital admissions between August 2013 and August 2014.⁶ In Liberia, 62% of health facilities were closed, and there was a 50% drop in hospital deliveries and a 26% drop in child immunizations.⁶ In Bong County in Liberia, facility-based delivery decreased from over 500 per month to a low of 113 during the EVD outbreak.⁷ In Sierra Leone, only 4% of health facilities were closed, but there was a 39% drop in children treated for malaria and a 23% decrease in facility-based deliveries.⁷ Furthermore, there was an 18% decrease in women accessing postnatal care, and 11% decrease in deliveries at healthcare centres, with a concomitant 30% increase in maternal deaths and 24% increase in newborn deaths.⁸

3. Impact of the EVD outbreak on TB services and management outcomes

The EVD outbreak impacted all sectors of the healthcare systems, decreasing healthcare capacity in all three countries, including the TB prevention and control programmes. Whilst EVD caused an estimated 11 000 deaths in 2014 and 2015, TB claimed about 11 900 lives in all three countries in the year 2014, with Sierra Leone estimated to have had 3500, Liberia 3300, and Guinea 5100 TB-related deaths. Of the deaths from TB, about 2164 (95% confidence interval (CI) 1815–2548) in Sierra Leone, 3463 (95% CI 2808–4349) in Guinea, and 2164 (95% CI 1815–2548) in Liberia were estimated to have been influenced by EVD.

Moreover, the mortality rate for TB from 1990 to 2012 was 23 per 100 000 in Guinea, 143 per 100 000 in Sierra Leone, and 46 per 100 000 in Liberia. In 2014, which formed the learning curve and peak of the EVD outbreak, the mortality rate in Guinea

doubled to 43 per 100 000, and in Liberia it rose to 76 per 100 000 with Sierra Leone having 56 per 100 000. Some of these deaths would have been preventable if routine TB care and prevention efforts had been fully operational during the EVD outbreak.

The three MRU countries combined had over 400 DOTS centres (directly observed treatment services), which ensured testing for new and recurrent cases of TB, provided treatments, and monitored adherence. In Kenema District, Eastern Sierra Leone. for example, the DOTS centre at the Government Hospital in Kenema did routine testing for TB, admitted TB patients for treatment, and provided daily drugs for TB patients who had to come to the hospital daily for their TB regimen, except for those who were adherent. During the EVD outbreak, two HCWs at the DOTS centre contracted EVD and died. Inpatients at the DOTS centre discharged themselves, patients who were on regular chemotherapy avoided the clinic, and prospective TB patients also avoided the healthcare system. Even though the DOTS centre was not closed, its functionality was impaired by the quarantine and patient boycott. The patient boycott in Kenema was related to how Ebola was reported in the District.

In Liberia, DOTS centres were among the 62% of health facilities that were closed during the EVD outbreak. DOTS centres are also typically healthcare facilities that could be peripheral health units or hospitals. While it was difficult to close big hospitals completely during the EVD outbreak, it was easier to close down peripheral health units, some of which were DOTS centres in the MRU, and this hampered TB diagnosis, treatment, and adherence.

In Guinea, in the forested region of Macenta, a 40% drop in primary healthcare outpatient enrolment and a correlated 53% decrease in TB diagnosis rate was reported in one study. Decrease in TB diagnosis rate was reported in one study. Decrease in Conakry, Ortuno-Gutierrez and colleagues reported a stable TB prevalence rate of 13% in both 2013 (when there was no documented EVD in Guinea) and 2014 (when there was an ongoing EVD outbreak in Guinea). The two datasets, one from a more rural region with typically less access to healthcare and smaller facilities and the other from a very urban setting, demonstrate that the impact of EVD on the healthcare system was not symmetrical. Facilities that were far from the capital cities experienced much more reduced care during the outbreak.

4. Effect of EVD on routine childhood BCG vaccination

The EVD epidemic disrupted healthcare services, including routine childhood vaccination programmes. ¹⁹ The WHO guidelines for immunization programmes during the Ebola outbreak advised against vaccination campaigns because of the threat of EBV transmission.²⁰ Vaccination against TB with BCG in children under 5 years of age was affected adversely by the EVD epidemic. Many parents were gripped with fear, wary of the healthcare centres and possibility of EBV transmission, and avoided vaccination clinics and hospitals. Reasons for boycotting the clinics were varied and included: (1) that children were weighed using the same scales without these being disinfected in-between children, and (2) HCWs had died after contracting EVD in the clinics and hospitals. Others believed the conspiracy theories about EBV transmission that 'the injections received at hospitals contained EBV for killing patients' or that 'when you visit the hospital, they will diagnose you with Ebola'. As a consequence, over 3000 children missed essential vaccinations for TB and other diseases such as measles, which resulted in an outbreak of measles post-Ebola 19 and a rise in new TB cases post-Ebola.

5. Effect of EVD on access to, and delivery of healthcare services

The EVD epidemic generated disruptive collateral damage to all ongoing healthcare services.^{4–14} A large proportion of available

healthcare resources in the MRU countries were diverted to the fight against EVD. This included manpower, vehicles, buildings, and financial resources. Even though the global funds for TB increased by 2.3% (USD 13 million) in 2014, the amount available to Liberia and Sierra Leone was low (although Guinea had sustained TB funding). As a consequence, there was a failure to bring in drugs that were adequate for TB control in some parts of the MRU (Liberia and Sierra Leone) and this created the conditions for the development of drug-resistant TB . In all three MRU countries, the disruption to TB services due to the EVD epidemic will no doubt have increased *Mycobacterium tuberculosis* transmission (both drug-resistant and drug-sensitive strains), TB morbidity and mortality, and patient adherence to TB treatment, although the likely impact will not be known for several years to come.

6. Effect of EVD on the healthcare workforce

The EVD outbreak adversely impacted all HCWs involved in healthcare service delivery.^{8,18,21-24} At the height of the EVD outbreak in all MRU countries, numerous staff members contracted EBV at the Ebola treatment units and many died; these included doctors, nurses, ambulance drivers, porters, and other ancillary staff who received, examined, treated, nursed, and/or moved patients with symptoms. Furthermore, many HCWs were infected in healthcare facilities that were not Ebola treatment units but were national hospitals and peripheral health units that were unprepared for receiving patients with EVD. According to a WHO report, there were 815 confirmed and probable EVD cases among the HCWs spanning January 2014 to March 2015, with 328 in Sierra Leone, 288 in Liberia, and 199 in Guinea. Importantly, the deaths of HCWs deprived the weak healthcare systems of much needed human resources. For example in Sierra Leone, a nation of just over seven million people, there are less than 1500 HCWs in the entire country. Following the EVD epidemic, HCWs conveyed a feeling of loss of trust within and across health facilities, and between HCWs and communities.²⁵ Providers described feeling lonely, ostracized, unloved, afraid, saddened, and no longer respected. They also discussed restrictions on behaviours that enhance coping, including attending burials and engaging in physical touch (hugging, handshaking, sitting near, or eating with colleagues, patients, and family members). Providers described infection prevention measures as necessary but divisive because screening booths and protective equipment inhibited bonding or 'suffering with' patients. The EVD epidemic leaves a smaller workforce, which is trying to deal with the ongoing TB epidemic, and this too will have its toll on the TB care and control services in West Africa.

7. Lessons from the EVD epidemic

The EVD outbreak was a result of collective regional and international failure to act swiftly and effectively, 26,27 and provided yet another 'wake-up call' to the international community, and particularly to African governments, for improving health systems preparedness for infectious disease outbreaks.²⁸ It illustrated the weaknesses and vulnerabilities of the current healthcare infrastructure in African countries, the inability to respond effectively to any new emerging or re-emerging infectious disease with epidemic potential, and the actions required to improve and preserve health services. The initial efforts to deal with the EVD outbreaks were left to international charities and non-governmental organizations (NGOs)^{27,29} with extensive experience in dealing with famine, refugee, and humanitarian emergencies, but not in dealing with public health and the clinical management of major infectious disease outbreaks. The opportunity to work together was not fully taken up by NGOs and the mortality rate was high, most likely due to inexperience with intravenous therapy, ³⁰ clinical management, and infection control issues. ³¹

Since the next epidemic cannot be predicted with any level of certainty, TB and other health programmes will be under constant threat. Will Zika virus return to Africa in epidemic form?³² Will the Middle East respiratory syndrome coronavirus (MERS-CoV) evolve and increase its human-to-human transmission rate potential and spread across Africa and other continents?³³ Will the monkeypox outbreak in the Democratic Republic of the Congo³⁴ suddenly reemerge as a threat, or will it be avian influenza?³⁵ This uncertainty makes planning for future outbreaks very difficult.

An important lesson from the EVD epidemic is that long-term planning should be based on a holistic approach for strengthening and building health systems and services, moving away from disease-specific national programmes. New ways of thinking at the national, regional, and global levels are required to strengthen healthcare systems. This is required not only to improve the ability of countries and regions to deal effectively with epidemic infectious disease threats, but also to sustain functioning health systems during outbreaks so that other disease control programmes (like those for TB, malaria, and HIV) are not compromised during the emergency measures of a severe epidemic. This will require skilled and trained staff at the national level, and such staff are scarce in most low-income countries. It has previously been argued that central or regional laboratories, able to perform rapid advanced diagnostics on samples from patients with alarming symptoms but without a clear diagnosis, are urgently needed for early outbreak detection.³²

8. The way forward?

There are important global leadership issues that need to be considered. The role of the WHO in the EVD outbreak and its capability to prevent and control epidemics in developing countries has been criticized and questioned.³⁶ So who should take the lead in the proactive surveillance, coordination, and emergency response to future outbreaks? Apart from the WHO, which has advisory and data surveillance functions but cannot act as a funding agency, a suitable choice could be The Global Fund to Fight AIDS, Tuberculosis and Malaria, 37 which provides substantial funds for national programmes for all three diseases, especially in Sub-Saharan Africa. The Global Fund is a public-private partnership founded in 2001 and has invested over \$10 billion in interventions for HIV/AIDS, TB, and malaria in over 130 countries. The Global Fund could work with national and regional authorities to ensure cross-collaboration between the three diseases and close alignment with the rest of the healthcare programme. The Global Fund could also broaden its remit and support training, diagnostic, and operational research activities for all three diseases. For TB there are other funder initiatives that have arisen post-EVD that provide opportunities for synergistic alignment of capacity building and training across all African regions³⁸ and for a 'One Health' approach³⁹ to controlling emerging infections.

Conflict of interest: The authors declare no conflicts of interest.

References

- World Health Organization. Global tuberculosis report 2015. WHO/HTM/TB/ 2015.22. Geneva, Switzerland: WHO; 2015, Available at: http://who.int/tb/ publications/global_report/en/(accessed October 6, 2016)..
- Zumla A, Oliver M, Sharma V, Masham S, Herbert N, World TB. Day 2016 advancing global tuberculosis control efforts. Lancet Infect Dis 2016;16:396–8.
- 3. World Health Organization. Ebola virus disease outbreak. Geneva, Switzerland: WHO; 2016, Available at: http://www.who.int/csr/disease/ebola/en/(accessed May 23, 2016).
- Ansumana R, Bonwitt J, Stenger DA, Jacobsen KH. Ebola in Sierra Leone: a call for action. Lancet 2014;384:303.

- 5. Piot P, Muyembe JJ, Edmunds WJ. Ebola in West Africa: from disease outbreak to humanitarian crisis. *Lancet Infect Dis* 2014;**14**:1034–5.
- World Health Organization. Health systems situation in Guinea, Liberia and Sierra Leone. Geneva, Switzerland: WHO; 2014, Available at: http:// www.who.int/csr/disease/ebola/health-systems/health-systems-ppt1.pdf (accessed September 15, 2016).
- Lori JR, Rominski SD, Perosky JE, Munro ML, Williams G, Bell SA, et al. A case series study on the effect of Ebola on facility-based deliveries in rural Liberia. BMC Pregnancy Childbirth 2015;15:254. http://dx.doi.org/10.1186/s12884-015-0694-x
- Voluntary Service Overseas. Exploring the impact of the Ebola outbreak on routine maternal health services in Sierra Leone. VSO; 2015, Available at: https://www.vsointernational.org/sites/default/files/VSO Sierra Leone-Impact of Ebola.pdf (accessed September 15, 2016).
- Parpia AS, Ndeffo-Mbah ML, Wenzel NS, Galvani AP. Effects of response to 2014-2015 Ebola outbreak on deaths from malaria, HIV/AIDS, and tuberculosis, West Africa. Emerg Infect Dis 2016;22:433–41.
- Leuenberger D, Hebelamou J, Strahm S, De Rekeneire N, Balestre E, Wandeler G, et al. Impact of the Ebola epidemic on general and HIV care in Macenta, Forest Guinea, 2014. AIDS 2015;29:1883–7.
- Ortuno-Gutierrez N, Zachariah R, Woldeyohannes D, Bangoura A, Chérif GF, Loua F, et al. Upholding tuberculosis services during the 2014 Ebola storm: an encouraging experience from Conakry, Guinea. *PLoS One* 2016;**11**:e0157296. http://dx.doi.org/10.1371/journal.pone.0157296
- World Health Organization. Health worker Ebola infections in Guinea, Liberia and Sierra Leone. Geneva, Switzerland: WHO; 2015, Available at: http:// www.who.int/hrh/documents/21may2015_web_final.pdf (accessed October 5, 2016).
- Knight GM, Houben RM, Lalli M, Whire RG. Ebola: the hidden toll of tuberculosis. Public Health Action 2016;6:2.
- Bolkan HA, Bash-Taqi DA, Samai M, Gerdin M, von Schreeb J. Ebola and indirect effects on health service function in Sierra Leone. PLoS Curr 2014;6. http:// dx.doi.org/10.1371/currents.outbreaks. pii: ecurrents.outbreaks.0307d588df 619f9c9447f8ead5b72b2d.
- Kpanake L, Gossou K, Sorum PC, Mullet E. Misconceptions about Ebola virus disease among lay people in Guinea: lessons for community education. J Public Health Policy 2016;37:160–72.
- Thiam S, Delamou A, Camara S, Carter J, Lama EK, Ndiaye B, et al. Challenges in controlling the Ebola outbreak in two prefectures in Guinea: why did communities continue to resist? *Pan Afr Med J* 2015;22(Suppl 1):22.
- Kobayashi M, Beer KD, Bjork A, Chatham-Stephens K, Cherry CC, Arzoaquoi S, et al. Community knowledge, attitudes, and practices regarding Ebola virus disease—five counties, Liberia, September–October, 2014. MMWR Morb Mortal Wkly Rep 2015;64:714–8.
- Dynes MM, Miller L, Sam T, Vandi MA, Tomczyk B. Centers for Disease Control and Prevention (CDC). Perceptions of the risk for Ebola and health facility use among health workers and pregnant and lactating women—Kenema District, Sierra Leone, September 2014. MMWR Morb Mortal Wkly Rep 2015;63:1226-7.
- Takahashi S, Metcalf CJ, Ferrari MJ, Moss WJ, Truelove SA, Tatem AJ, et al. Reduced vaccination and the risk of measles and other childhood infections post-Ebola. Science 2015;347:1240-2.
- United Nations Children's Fund. In Sierra Leone, vaccinations another casualty
 of Ebola. UNICEF; 2014, Available at: http://www.unicef.org/infobycountry/
 sierraleone_76892.html (accessed October 5, 2016).
- World Health Organization. Ebola healthcare worker infections. Geneva, Switzerland: WHO; 2015, Available at: http://www.who.int/features/ebola/health-care-worker/en/(accessed October 4, 2016).

- Ulrich CM. Ebola is causing moral distress among African healthcare workers. BMJ 2014;349:g6672.
- Delamou A, Beavogui AH, Konde MK, van Griensven J, De Brouwere V. Ebola: better protection needed for Guinean health care workers. *Lancet* 2015;385:503-4.
- World Health Organization. Health worker Ebola infections in Guinea, Liberia and Sierra Leone: a preliminary report. Geneva, Switzerland: WHO; 2015, Available at: http://www.who.int/csr/resources/publications/ebola/health-worker-infections/en/(accessed October 5, 2016).
- 25. McMahon SA, Ho LS, Brown H, Miller L, Ansumana R, Kennedy CE. Healthcare providers on the frontlines: a qualitative investigation of the social and emotional impact of delivering health services during Sierra Leone's Ebola epidemic. *Health Policy Plan* 2016;31:1232–9.
- Philips M, Markham A. Ebola: a failure of international collective action. Lancet 2014;384:1181.
- 27. Cancedda C, Davis SM, Dierberg KL, Lascher J, Kelly JD, Barrie MB, et al. Strengthening health systems while responding to a health crisis: lessons learned by a nongovernmental organization during the Ebola virus disease epidemic in Sierra Leone. *J Infect Dis* 2016;214(Suppl 3):S153–63.
- Edelstein M, Angelides P, Heymann DL. Ebola: the challenging road to recovery. Lancet 2015;385:2234–5.
- Gursky EA. Rising to the challenge: the Ebola outbreak in Sierra Leone and how
 insights into one nongovernmental organization's response can inform future
 core competencies. Disaster Med Public Health Prep 2015;9:554–7.
- 30. Petersen E, Maiga B. Guidelines for treatment of patients with Ebola virus diseases are urgently needed. *Int J Infect Dis* 2015;30:85–6.
- 31. Walker NF, Whitty CJ. Tackling emerging infections: clinical and public health lessons from the West African Ebola virus disease outbreak, 2014-2015. *Clin Med (Lond)* 2015;15:457-60.
- **32.** Zumla A, Goodfellow I, Kasolo F, Ntoumi F, Buchy P, Bates M, et al. Zika virus outbreak and the case for building effective and sustainable rapid diagnostics laboratory capacity globally. *Int J Infect Dis* 2016;**45**:92–4.
- 33. Zumla A, Rustomjee R, Ntoumi F, Mwaba P, Bates M, Maeurer M, et al. Middle East respiratory syndrome—need for increased vigilance and watchful surveillance for MERS-CoV in Sub-Saharan Africa. *Int J Infect Dis* 2015;37:77–9.
- Kantele A, Chickering K, Vapalahti O, Rimoin AW. Emerging diseases—the monkeypox epidemic in the Democratic Republic of the Congo. Clin Microbiol Infect 2016;22:658–9.
- Monne I, Fusaro A, Nelson MI, Bonfanti L, Mulatti P, Hughes J, et al. Emergence of a highly pathogenic avian influenza virus from a low-pathogenic progenitor. J Virol 2014;88:4375–88.
- Kekulé AS. Learning from Ebola virus: how to prevent future epidemics. Viruses 2015;7:3789–97.
- Global Fund. Annual report 2015. Board Report 2015: annual report on the activities of the Office of the Inspector General. GF/B35/10. Global Fund; 2016. Available at: http://www.theglobalfund.org/en/search/?q=annual+report+2015 (accessed October 7, 2016).
- Ntoumi F, Kaleebu P, Macete E, Mfinanga S, Chakaya J, Yeboah-Manu D, et al. Taking forward the World TB Day 2016 theme 'Unite to End Tuberculosis' for the WHO Africa Region. Int J Infect Dis 2016;46:34–7.
- 39. Zumla A, Dar O, Kock R, Muturi M, Ntoumi F, Kaleebu P, et al. Taking forward a 'One Health' approach for turning the tide against the Middle East respiratory syndrome coronavirus and other zoonotic pathogens with epidemic potential. *Int J Infect Dis* 2016;47:5–9.