of negative controls (almost all UK-based), change in cutoff from previous studies, and imperfect orthogonal corroboration restricted to symptomatic participants (as opposed to those deemed minimally symptomatic) mean that further validation of the assay would be welcome. In our previous study[4] in Sierra Leone, we found—albeit with a different assay—that European and American negative controls provide much less noise and thus prompt lower optical density cutoffs (the threshold for determining whether someone is a case or not) than do controls in west Africa, potentially due to cross-reactivity of our assay with closely related pathogens circulating in the region.

Timothy and colleagues corroborate emerging evidence that suggest minimally symptomatic infections were common in the 2013–16 outbreak in west Africa and that a substantial portion of Ebola transmission events might have been undetected during the outbreak.[4,5] Indeed, even WHO has admitted that the true toll of the epidemic "was certainly greater" than the 28 616 suspected, probable, and confirmed cases of EVD that were reported.[6]

Notwithstanding the minor limitation of recall bias, most will agree that this well designed study yields important insights into the genesis of the 2013–16 Ebola virus outbreak in west Africa; however, we must be wary of leaving epidemics to the epidemiologists. It is important to consider that the real genesis of this preventable outbreak is the combined effect of the legacies of slavery (ie, Maafa[7]), exploitative colonialism, purposeful underdevelopment, structural adjustment, resource extraction, illicit financial flows, poverty, gender violence, and enabled civil war.[8,9] When viewed through this lens, even the revised case fatality of 55·6% is misleading: we estimate the true case fatality of EVD to be less than 10% when patients have access to a high-level intensive care unit—notably, all repatriated Americans infected with Ebola virus survived.[10] In summary, although highly skillful work—like that of Timothy and colleagues—is integral to improved understanding of viral transmission dynamics, such virtuosity should not obscure recognition of the structural determinants of epidemics.[11]

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Endemic Zika virus transmission: implications for travellers

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In 2016, a Zika virus epidemic swept across the Americas and resulted in the declaration of a Public Health Emergency of International Concern because of the potentially devastating consequences of congenital infection.[1,2] Globally, Zika virus transmission occurs at a much lower level today than in 2016; however, cases have been reported in 2017 and 2018 in Africa and India, and serological studies suggest nearly 10% of children

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younger than 5 years in Indonesia have evidence of Zika virus infection.[3-5] Better international surveillance for Zika virus and Zika-associated birth defects is needed to appropriately counsel pregnant women, partners of pregnant women, and reproductive-aged couples living in or travelling to Zika virus-endemic areas.[6] In *The Lancet Infectious Diseases*, Henrik Salje and colleagues[7] compare the age distribution of confirmed Zika virus disease cases in Thailand with that during the Colombian Zika virus outbreak, and with the historical age distribution of dengue virus in Thailand.[8] Although serosurveys typically establish levels of population immunity, cross-reactivity with other flaviviruses limits use of this method for Zika virus. Surveillance of confirmed, symptomatic cases, as presented by Salje and colleagues, can inform levels of population immunity, but might underestimate levels of population immunity from focal outbreaks. In settings with high levels of population immunity, recent cases would predominate in younger, previously unexposed populations, although exposure and health-care seeking can vary with age.[7] Use of confirmed symptomatic cases to draw inferences about population immunity assumes that immunity is long lasting, protective of clinical disease, symptomatic attack rates are similar across age groups, and sufficient numbers in all age groups were tested.

Based on the age distribution of cases, Thailand might not have had sufficient levels of Zika virus transmission to yield widespread durable population immunity. Although the numbers tested in each age group are not clear, 368 symptomatic Zika virus infections in Thailand were confirmed from January 2016 to December 2017, from 29 of the 76 provinces. By contrast with dengue virus, where cases among children younger than 10 years are over-represented, with about four-fold more cases compared with the underlying population in that age group, the proportion of Zika virus cases in children younger than 10 years in Thailand was essentially identical to the underlying population. The age distribution of symptomatic Zika virus cases in Thailand in a setting of endemic transmission was similar to the age distribution observed in Colombia during the Zika virus epidemic, with those aged 21–30 years over-represented in both women and men, suggesting that many individuals of reproductive age in Thailand did not have immunity to Zika virus.[7] This absence of immunity has implications for the risk of Zika-associated birth defects.

Zika virus infection during pregnancy can cause serious defects of the brain and eye, and has been linked to neurodevelopmental disabilities.[9,10] The findings from Thailand underscore the ongoing risk to men and women of reproductive age living in endemic settings, and have important implications for travellers to areas with any Zika virus transmission. Although immunity to Zika virus is anticipated after infection, the duration of immunity is unknown. Reliable tests for immunity with high sensitivity and specificity are not yet readily available. Counselling about the risk of infection for residents and travellers is fraught with uncertainty. Lessons can be learned from the successful prevention of congenital rubella syndrome, achieved through widespread availability of an effective vaccine, universal immunisation of young children, and implementation of systems to identify and vaccinate adults without evidence of immunity.[11] Zika virus will remain a threat to healthy pregnancies until an effective Zika virus vaccine and reliable tests of immunity are readily available. Until then, we expect to continue to see increased numbers of adverse birth outcomes in countries with Zika virus transmission.

Monitoring for adverse birth outcomes requires robust birth defects surveillance. The same serious birth defects of the brain and eye that can be caused by Zika virus affected about 0·16% of liveborn infants in the USA before the introduction of Zika virus to the Americas, but there was a more than 30-fold increased risk of these birth defects among pregnancies with laboratory evidence of possible Zika virus infections.[9] Infants with congenital Zika syndrome have been reported from Thailand both among pregnancies with laboratory-confirmed Zika virus infection and when diagnosis did not occur until after delivery. Most of the countries and territories affected by Zika virus are without adequate birth defects surveillance necessary to identify and monitor cases of Zika-associated birth defects, limiting international understanding of the full effect of Zika virus.

Pregnant women should carefully consider the risk for Zika virus when planning travel, because decisions about travel are one effective strategy to prevent mosquito-borne transmission of Zika virus. However, determining the risk posed by Zika virus can be hampered by delays in identifying and reporting Zika virus cases—an infection that often occurs with mild or

no symptoms. Travellers, particularly pregnant women or their partners, should be counselled about possible risks and should be aware that we often do not have real-time regional epidemiological data on Zika virus transmission, and travel guidance should consider the limitations of available epidemiological data. Thailand, and presumably many countries in southeast Asia, have experienced variable transmission across many regions. The findings from Salje and colleagues regarding the distribution of symptomatic persons in Thailand heighten concerns there might be lower levels of population immunity than expected and therefore an ongoing risk to pregnant women travelling to or living in endemic settings.[7]

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The STREAM trial: missed opportunities and lessons for future clinical trials

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Final results of the STREAM trial were presented at the 2018, 49th Union World Conference on Lung Health, held in The Hague, The Netherlands. STREAM is a randomised controlled trial comparing the 18–24 month WHO-recommended multidrug-resistant tuberculosis (MDR-TB) treatment regimen with a 9–12 month regimen similar to that first described in Bangladesh.[1] Under programmatic conditions, the longer regimen results in treatment success for approximately 50% of patients,[2] whereas the shorter 9–12 month regimen improved treatment success to 80% or higher in selected countries.[3,4] Because these countries had relatively low HIV prevalence and relatively high percentages of treatment success with the longer regimens, questions around generalisability were raised.[4] STREAM was a multi-million dollar undertaking that took almost 10 years from the time of study design until the release of final results. Given the time and costs involved it is essential to reflect on lessons learned, and what the trial results tell us to inform how we accumulate future evidence to guide MDR-TB treatment.

STREAM found that both the longer and shorter regimens performed well, with 80% and 79% favourable outcomes, respectively. In routine programmatic settings, loss to follow-up with the longer regimen is a major contributor to poor patient outcomes.[2] By contrast, previous studies of the shorter regimen documented reduced loss to follow-up, contributing to overall improved treatment success.[3,4] However, because of the patient support provided in STREAM, as in most randomised controlled trials, the potential real-world effect of the shorter regimen on loss to follow-up could not be fully assessed. We must consider whether randomised controlled trials are the best way of evaluating the effect of a regimen on adherence and loss to follow-up. STREAM shows that improved patient support and encouragement during treatment improves