be the goal. Rather, we need to offer everyone access to the best diagnostic services possible—including high-quality drug susceptibility testing—and treat them with individualised regimens containing the strongest and safest drugs to which their strains are susceptible and avoiding drugs to which there is resistance. Wishful thinking about a scenario in which drug susceptibility testing is not necessary for tuberculosis treatment has no place in the modern approach to tuberculosis. Universal access to drug susceptibility testing will, no doubt, require substantial work, but we must commit ourselves fully to achieving this goal. As the study by Zürcher and colleagues shows, people's lives depend upon it.

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Unrecognised Ebola virus infection in contact persons: what can we learn from it?

The epidemic of Ebola virus disease in west Africa in 2014–16 was the largest and most complex the world has ever seen. The four pillars of Ebola response include: case management, case finding and contact tracing, safe and dignified burial, and social mobilisation and community engagement. These four pillars are being implemented in the current outbreak in the Democratic Republic of the Congo (DRC), which is further complicated by its location in a conflict zone.[1] Increased understanding of disease pathogenesis and the evaluation of novel therapeutics and vaccine candidates has informed current control measures, while access to survivors and their contacts in west Africa has also provided a unique opportunity to research filovirus transmission.

In *The Lancet Infectious Diseases*, Mamadou Diallo and colleagues[2] report data from a large cross-sectional study of contact persons of an established survivor cohort in Guinea. They aimed to estimate the frequency of unrecognised Ebola virus infection in contact persons after excluding individuals who were vaccinated, and to identify risk factors for infection. Using a novel and previously validated Luminex assay[3] on dried blood spots and detailed retrospective exposure histories, they identified 57 Ebola virus infections among 1390 contact persons.

The authors showed increased seropositivity in contact persons who reported any symptom associated with Ebola virus disease (8·33%, 95% CI 5·01–12·80, described as paucisymptomatic contact persons) compared with Ebola virus infection in asymptomatic contact persons (3·32%, 95% CI 2·37–4·51; p=0·0002). Participation in burial rituals and contact with blood or vomit were independent significant risk factors for Ebola virus infection in asymptomatic contact persons in multivariate analysis, while older age and participation in burial practices were risk factors in paucisymptomatic individuals. Their findings concur with a recent meta-analysis of seroprevalence surveys[4] and the results of a study in Sierra Leone of 486 household members of Ebola virus disease survivors, which identified Ebola virus infection in


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12% (95% CI 6·1–20·4) of those with symptoms compared with 3% (95% CI 1·2–4·8) of asymptomatic household members.[5] The same study also showed that burial contact and older age were risk factors for Ebola virus infection.[6]

The conclusions drawn by Diallo and colleagues[2] reaffirm the challenges and failures in case finding and contact tracing highlighted by others in Guinea;[7] evidenced by the 73% of paucisymptomatic contact persons who, in reporting a history of fever, met the WHO definitions for suspected cases requiring isolation and further evaluation.[8,9] Furthermore, they highlight that 30 (14%) of 216 paucisymptomatic contact persons met the Ebola virus disease suspect case definition without contact but were not diagnosed acutely, of whom 20% were seropositive. These results are timely as in the DRC, as of Jan 14, 2019, 4634 contacts remain under surveillance, with follow-up rates ranging from 80–93%.[10] The data from Diallo and colleagues highlight the varying spectrum of Ebola virus disease severity, consistent with early clinical reports in west Africa,[11] and again challenge our perceptions of the roles and balance of viral infective dose and host immune response in clinical phenotypes. Studies like that of Diallo and colleagues could be unique, and impossible to replicate, because of the scale of the west African outbreak and the now established practice of ring vaccination.

Care should also be taken in the interpretation and extrapolation of these results. As the authors acknowledge, there is risk of recall bias: it is challenging to remember clinical symptoms, exposure, and exact timing more than 2 years after the event. The key question is whether these unidentified Ebola virus infection contact persons had any role in transmission chains. This issue was highlighted by Dokubo and colleagues,[12] who reported a familial cluster occurring in Liberia 1 year after an undiagnosed Ebola virus infection in a female contact, probably due to viral persistence. This potential transmission risk should be balanced against the risk of further stigmatisation of both survivors and household contacts.

This study reinforces the importance of robust and detailed contact tracing as a control measure and highlights the high risk posed by burial practices and direct contact with infected fluids. What is also notable is how few contacts who reported high risk exposures were infected. Greater understanding is needed about the mechanisms of Ebola virus transmission to improve the targeting of interventions as part of a coordinated response. Epidemics of Ebola virus disease remain a major risk to health-care workers and populations in endemic regions, and a global threat to health security.

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