Towards a coordinated strategy for intercepting human disease emergence in Africa

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Emerging zoonotic viruses are one of the greatest threats to human health and security, as evidenced by the increasing frequency of disease outbreaks.[1] To date, the main pre-emptive response to these outbreaks has been extensive, cost-heavy efforts to document virus diversity in wildlife (eg, PREDICT and the Global Virome Projects).[2,3] Although these efforts have resulted in the identification of thousands of novel viruses, fewer than 1% are described to date, substantial challenges remain around access and benefit sharing from viral discovery programmes, and—perhaps most problematic for public health application—the spillover hazard of these viruses can only be coarsely inferred at present.[4–6]

Our ability to control and restrict the spread of infectious diseases is critically dependent on early detection. This vigilance should include viruses that might not pose immediate or widespread public health threats, but where repeated spillover or persistent, unchecked transmission chains in humans provides latitude for the evolution of increased pathogenicity, host immune evasion mechanisms, and efficient human-to-human transmission.[7] Building on existing research, here we emphasise the importance of a coordinated and targeted strategy for early detection of virus spillover and emergence in humans. This model is based on inter-related study or evidence types and is a collaborative framework geared towards African and other low-income and middle-income countries where risk of disease emergence is often great, infectious disease-related morbidity and mortality are over-represented compared with in high-income regions, undescribed virus diversity is high, and resources are constrained.

For this strategy we highlight four complementary study or evidence types indicative of past or current unknown infection: procurement and screening of diagnostic samples from undiagnosed patients, analysis of samples from suspicious fatalities of unknown cause, serosurveys of high-risk or sentinel groups, and analysis of archived samples (appendix p 1). Approaches might overlap (eg, death and post-mortem analysis of undiagnosed patients) but are independently capable of detecting separate evidence for pathogen spillover and novel disease emergence. Their concurrent implementation heightens detectability.

Collecting and screening samples from patients with undiagnosed febrile illness provides an efficient means to target the subset of populations most likely to have novel infectious diseases. With properly trained staff and systems, sample collections can be implemented at the point of care for continuous monitoring. When possible, collecting and screening samples from people with an unknown cause of death can identify cases of severe disease that might not remain in hospitals sufficiently long for inclusion in a monitoring strategy, present with unusual symptoms, or develop severe disease but not present to a hospital or clinic, as is likely to occur in low-income and middle-income countries where traditional medicine is practiced. Although new technologies such as next-generation sequencing are increasingly available for detection of unknown viruses, linking clinical findings to disease aetiology can be a challenge. Due consideration must also be given to sample types for collection and their appropriate storage.

By contrast, serosurveys or screening of sentinel groups are proactive studies implemented by researchers to collect blood samples from individuals at greatest risk of exposure to zoonotic viruses. Such individuals include pastoralists, agriculture workers, game hunters, traders, or others working in close contact with wildlife. Studies can detect antibodies indicative of spillover events, including asymptomatic cases, and use increasingly efficient and cost-effective screening methods. Likewise, archived samples provide varied, potentially copious, and readily available sample sources that are appropriate for detection of viruses and antibodies indicative of spillover across longer timescales. Like focused serosurveys, archived samples can be especially powerful for identifying viruses that are silently circulating among humans or rare spillover events that could have future implications. These samples also provide important datapoints for efforts to track the effect of global environmental changes on virus spillover, given that most forecasting efforts do not have empirical real-time validation. An important limitation of antibody surveillance is the inability to

See Online for appendix

identify active infections or specific viruses. But these approaches can prompt and guide focused investigation and are integral to a comprehensive strategy.

None of the methods or evidence types that we describe here are novel tools and each has limitations;[8–10] however, we highlight the value of a cohesive, targeted, and widespread approach for maximising the likelihood of detecting novel infections (appendix p 1). We acknowledge that in some settings or situations some of the proposed approaches might not be appropriate or might need to be adapted.

Ongoing research aims to develop predictive tools so that we might be able to infer the zoonotic potential of the ever-increasing number of newly identified wildlife viruses from their genetic sequence. Meanwhile, comprehensive systems for early detection and containment of wildlife virus spillover and emergence remain one of our strongest responses against the threat posed by zoonotic viruses.

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For the **Verena consortium website** see https://www.viralemergence.org/

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