

# Spillover or endemic? Reconsidering the origins of Ebola virus disease outbreaks by revisiting local accounts in light of new evidence from Guinea

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## INTRODUCTION

New research finds that the 2021 outbreak of Ebola virus disease (EVD) in Guinea originated in viral resurgence from a persistently infected survivor from the major 2013–2016 epidemic 5–7 years ago<sup>1</sup> prompting an urgent need to re-evaluate whether past EVD epidemics hitherto considered as independent zoonotic spillovers may have had similar origins. Here, we reconsider local accounts from the West African epidemic that trace its origins to people, dismissed until now as implausible. We thus reinterpret existing scientific accounts of other alleged spillovers, finding that several past outbreaks probably originated in persistent infections over even longer latency. By recalibrating the balance between ‘spillover’ and ‘flare-up’, we suggest that EVD manifests less as a series of discrete epidemics and more as an endemic disease in humans over long timescales and wide areas, helping to account for the increasing frequency of episodes.

## LOCAL ACCOUNTS

Epidemiologists identified the index case of the West African epidemic to be an infant in the small village of Meliandou in Guinea’s Forest Region,<sup>2</sup> and a multidisciplinary team suggested he was infected from a *Mops condylurus* bat colony.<sup>3</sup>

During DM’s scoping visits in 2016, however, some villagers, including Meliandou’s community health-worker, explained that a woman named ‘Fanta’ seeking treatment from a noted village healer brought EVD to the village. She had come from the diamond region of Sefadou in nearby Sierra Leone immediately before the outbreak in December 2013, but had first visited several months earlier after being referred to the

## Summary box

- ▶ That the 2021 outbreak of Ebola virus disease (EVD) in Guinea originated in viral resurgence from a survivor infected 5–7 years ago requires local and scientific accounts of past outbreaks to be revisited.
- ▶ Many past EVD epidemics hitherto considered as independent zoonotic spillovers may have originated from similar flare-ups even after decades, prompting reconsideration of EVD more as an endemic disease over long timescales and wide areas than as a series of discrete epidemics, and accounting for increasing outbreak frequency.
- ▶ Key assumptions in analysis of phylogenetics and of the ecology and drivers of Ebola virus (EBOV) spillover from wildlife hosts such as bats need to be reassessed.
- ▶ More collaborative, respectful approaches with local communities are needed to understand the origins of outbreaks, to address them and to support rather than stigmatise sufferers and survivors.

healer by doctors at Gueckedou hospital. The healer said that Fanta suffered from *Gnangafoo* in his Kissi language, for which he was a specialist. Understood usually as a socially caused affliction, this manifests in itchy skin over much of the body and hair loss; Fanta had these symptoms.

Fanta initially lodged with the healer for about 2 months but also befriended the mother and grandmother of the infant ‘index case’. The healer recalled how Fanta and this infant’s mother ‘ate, slept and did everything together’ with Fanta often carrying the infant on her back. After recovering somewhat, Fanta left for Sierra Leone but returned to finish treatment just prior to the outbreak. As the healer was travelling, his wife said that she only stayed 5 days or less and had ‘no symptoms of disease’. The residential community health-worker explained how:

In my humble opinion, it is a certain Fanta ... who brought us this illness. She suffered from a severe skin complaint that she came to treat here. She was healed. She left back to Sierra Leone and then returned for a second time. She slept in the same bed, cooked and ate with [the index case's grandmother]... Several days after she left, [the grandmother] fell ill with joint pains and headaches. She recovered initially. A few days later deaths struck the family. Six died rapidly in the family that welcomed Fanta.

Variants of this narrative circulate in the region (Gbanace *et al*, 2014)<sup>4</sup> describing Fanta's friendship with a former Sierra Leonean soldier who had returned from the Democratic Republic of Congo (DRC). Villagers told DM, too, that Fanta was linked to a diamond dealing or mining family across the border. The virus phylogenetics suggest that the West African outbreak has a common origin with the virus circulating in diamondiferous regions of the Luebo outbreak in DRC in 2007/2008, diverging from it in c.2004.<sup>5</sup>

Researchers who traced EVD to Meliandou heard narratives concerning Fanta but rejected them as she had no Ebola symptoms as then known, and had arrived with *Gnangafou* months before the outbreak, far longer than the EVD incubation and infection period. It was then believed that Ebola patients either died or recovered, clearing active virus from their body. This reasoning cannot now be upheld. First, the symptoms that brought Fanta to Meliandou are now known to be common sequelae of post-Ebola syndrome.<sup>6</sup> Second, flare-ups of EVD have been traced to 'survivors' in at least 13 instances during or within 2 years of the West African epidemic, with the new evidence now extending this to 7.<sup>7,8</sup> Third, oral accounts link Fanta with DRC and despite their ambiguities, they render infection from DRC plausible when combined with evidence of longer-term persistence.

Modes of Ebola virus (EBOV) persistence and latency are inadequately known but are associated with immunoprivileged organs. Published research on persistence in women and children is lacking but EBOV genomic material in semen can correlate with eye and joint pain<sup>9</sup> and has also been detected in asymptomatic survivors and even following multiple prior negative samples.<sup>10</sup> Resurgence may be associated with immunocompromised states, including pregnancy, poverty and poor nutrition, and co-infections such as with HIV.<sup>11</sup> The epidemiological team speculated that Fanta may have been suffering AIDS but had no reason to contemplate co-infection with EBOV. Transmission from resurgence can occur from men's sperm and from mother to baby through breastfeeding.<sup>12</sup> The potential for congenital infection has not been considered.

### WERE EARLIER SPILLOVERS ACTUALLY FLARE-UPS?

Given the new Guinea evidence of flare-up over much longer timescales, it is important to reassess whether some past outbreaks once deemed spillovers are better explained as flare-ups. Ebola has often returned to the

same locations after 1 year or 2 years. The Sudan Ebola virus variant struck the same cotton factory in South Sudan twice in 1976 and 1979 and the received view of two separate spillovers now seems unlikely,<sup>13</sup> although the phylogenetic evidence needed to confirm this is not available. In the two outbreaks in Luebo in DRC in 2007 and 2008, the virus was almost identical and must have remained persistent or latent in some way. To explain this as spillover, Leroy and colleagues speculated that the very same migratory fruit bat that they claimed had brought the virus in 2007 must have infected a bat of another non-migratory species which then infected the 'patient zero' a year later.<sup>14,15</sup> Given what we now know, however, this second case would unquestionably be investigated as a flare-up.

While these paired outbreaks were in the same place and within short timescales, an aptly titled paper on the '*Puzzling origins of the Ebola outbreak in the Democratic Republic of the Congo, 2014*'<sup>16</sup> also suggested the significance of longer-term persistence linking outbreaks across regions. The 2014 outbreak was phylogenetically close to outbreaks in equatorial Africa in 1994, a similarity far greater than expected given mutation rates linked to viral replication. Baffled, the researchers speculated that the virus was maintained as latent or persistent in an animal host but did not contemplate long-term viral persistence in people.

Among the recent outbreaks, one in 2018 in Équateur (DRC) was related to this same 2014 outbreak, yet explanations have still been sought only in latency within animal reservoirs and subsequent spillover.<sup>17</sup> Another outbreak in Équateur in 2020 was composed of two distinct viral variants, one of which was so similar to the 2018 outbreak that persistence in people had to be considered, but again researchers still preferred to hypothesise persistence in an animal reservoir.<sup>18</sup> The outbreak in North Kivu in 2021 is accepted as a flare-up from the outbreak there in 2018–2020; this, in turn, was so close to an outbreak in Likati (DRC) in 2017 that latency has had to be invoked, but again is being projected to have been in an animal reservoir.<sup>19</sup>

### CONCLUSIONS

There are wide-ranging implications for science and policy. That many outbreaks may originate in flare-ups does not negate the possible origins of EVD epidemics in spillover from animal reservoirs, but does demand questioning of the balance between these explanations. While some outbreaks may be new spillovers, and the circulation of multiple EBOV variants in diverse animal reservoirs with potential to spillover as claimed by researchers in 2004<sup>20</sup> suggests this, it is increasingly clear that other outbreaks are from latency. And whereas most research effort to date infers latency in animal reservoirs, the new evidence from Guinea demands a refocusing on the significance and mechanisms of latency in people.

Tilting the balance towards flare-ups, including those at the decadal timescale, suggests that EVD should be reconceived less as a series of discrete epidemics, but more as an already endemic disease (although usually in latent form) from which outbreaks occur linked to resurgence, some of which become epidemics.

Further research will need to take local accounts and their social underpinnings far more seriously, triangulating with advances in phylogenetic and ecological analysis. There are new challenges for phylogenetic analysis to explore the implications of latency in people, including the possibility of resurgence after many decades or even across generations. Ecological analysis mapping environmental and demographic drivers of spillover by associating outbreaks with deforestation and encroachment on wildlife must be revisited. That spillover from bats has been incorrectly pinpointed in at least some instances requires attention to how representations of EVD's origins in nature are being over-determined by existing expert discursive formations, and under-determined by local knowledge. Narrative closure among scientists around locally untenable explanations only fuels distrust.

The implications for global health are enormous. EVD outbreaks are rapidly increasing in frequency; a frequency which we can now speculate self-multiplies with the growing number of survivors and thus possible generation of flare-ups, exacerbated by conditions for resurgence that might include co-infections and poverty. All this has gone 'under the radar' amid predominant attention to zoonotic spillover. These new findings will worry and may further stigmatise EVD sufferers, so reaffirm the need to support them, their families and communities over much longer timescales, and through destigmatising approaches that treat them as people with dignity affected by a disease, rather than seeing them through the lens of the disease and as a global public health risk. Experience needs to be drawn from other illnesses where those infected remain a long-term source of human infection, and have then been subjected to counterproductive and repressive social and public health reactions.

Finally, it is all the more imperative to reduce the number of sufferers and future survivors and spot and curtail EVD outbreaks at an early stage. More attention needs to be paid to collaborative, respectful approaches with local communities both to understand the origins of outbreaks and to address them.

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