$P < 0.001$, P-value for interaction $= 0.03$). Similar results have been noted in previous studies [5,6].

In conclusion, our findings show that HBV coinfection is associated with early mortality in HIV patients initiating ART, reinforcing the findings of previous studies [2,5,7]. The cause of this excess mortality is unclear; however, it does not appear to be secondary to clinically evident liver disease. We found HIV/HBV co-infection was associated with impaired immunological responses to ART despite adequate HIV virological suppression, suggesting a possible immune-mediated mechanism. Use of tenofovir-containing regimens significantly reduced mortality risk in HIV/HBV co-infected patients in our cohort. This highlights the need for robust HBV screening embedded in ART programmes to ensure effective treatment of individuals with HBV/HIV co-infection, particularly if tenofovir-based treatment regimens are not universally used in sub-Saharan African settings.

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Conflicts of interest

There are no conflicts of interest.

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What is the impact of a 20% funding cut in international HIV aid from the United States?

Funding for the response to the global HIV epidemic has been disproportionately higher than for other areas in health for decades, yielding outstanding health and economic results. Since the Global Fund was established in 2002, 27 million lives have been saved from HIV, tuberculosis and malaria [1]. Recently, the Copenhagen Consensus Center estimated that the return on investment for a $10 billion investment in global health was $200 billion, higher than any alternative investments [2]. However, all signals point to the decline in funding from international sources. The United States of America (US) has been a consistent leader among these international sources, in financing the global HIV response and in being largely responsible for substantial improvements in global health. HIV continues to be a priority for the US, with President Trump's commitment announced in January 2019 to stop HIV transmission in the US by 2030. However, predictions suggest a 20% cut in US bilateral HIV funding to high-burden, lower income countries for the 2019 fiscal year of $5.2 billion for fiscal year 2018. A 2018 Kaiser Family Foundation (KFF)/Joint United Nations Programme on HIV/AIDS (UNAIDS) report [3]

predicted that the declining trend in donor funding experienced over the last few years would continue in future. The expectation has always been that the emergency response would transition to one which is financed by local authorities, and the changing funding landscape indicates that now is the time to demonstrate this.

According to the KFF/UNAIDS report, the US contributes 82.5% of total international funding; therefore, a 20% cut of this 82.5% will represent a 17% cut in international funding. We aimed to estimate the potential impact of this cut in international funding. We estimated this impact using the Optima HIV global model [4], constituted of 44 individual national and subnational models representing 80% of the global HIV burden, which have been calibrated to local epidemics.

We modeled the epidemiological impact of three scenarios. In scenario (1), if there is a 17% funding cut to all internationally sourced targeted spending in 2019 (corresponding to the forecasted 20% reduction from the US), and this remains until 2030 without an increase in domestic funding, we estimate that there would potentially be a 35% increase in new HIV infections (550 000 in 2030) and 30% increase in HIV-related deaths (330 000 in 2030) compared with 2015 (Fig. 1). In scenario (2), we illustrate a situation where the entire international financing would decline linearly to 0% between 2019 and 2030, but domestic resources would continue to increase at historic rates, as informed by estimated 2000–2017 expenditure data [5]. It is projected that in 2030, there could be an additional 50% new HIV infections and 27% HIV-related deaths (800 000 and

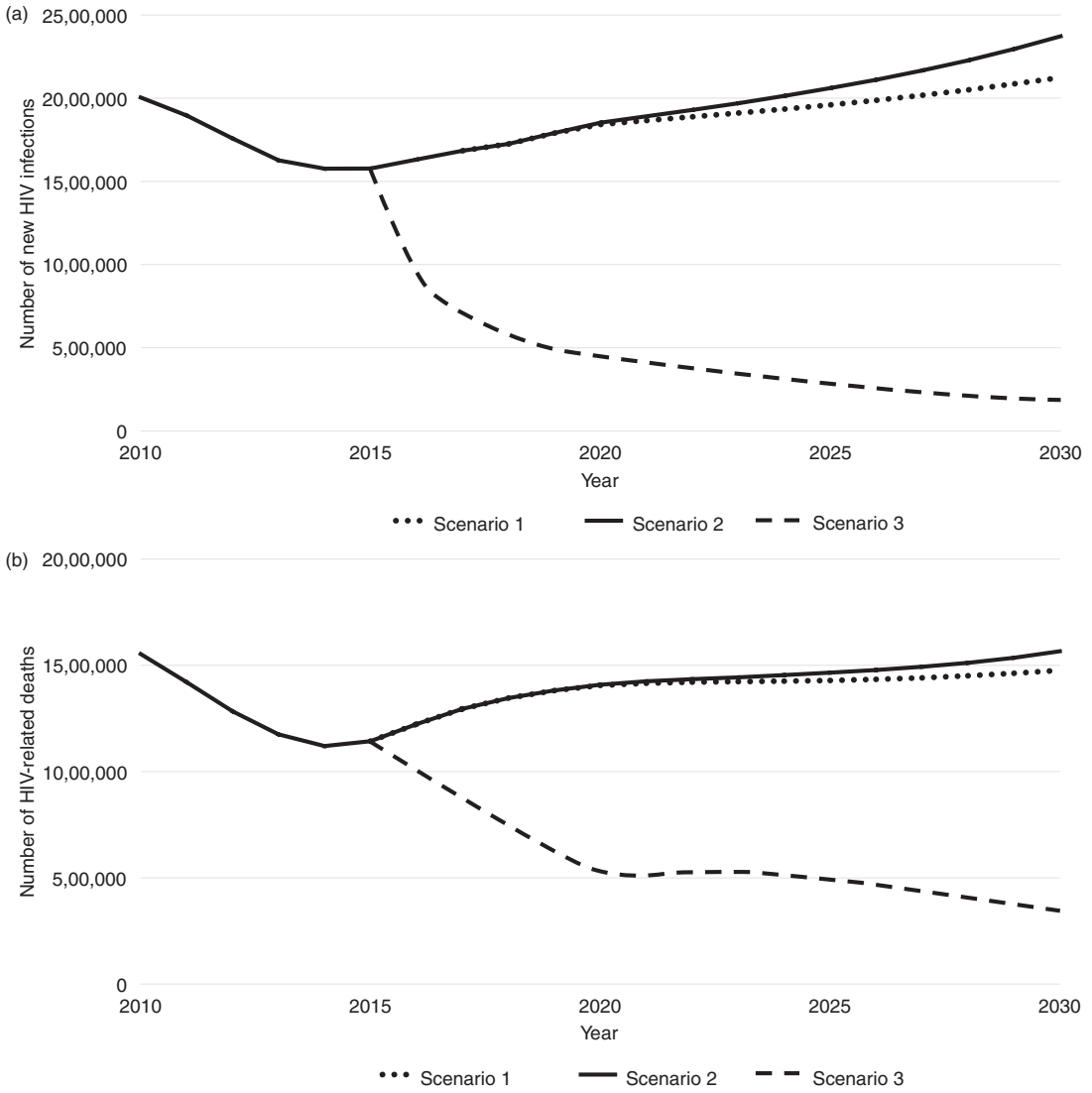

Fig. 1. Projected trajectory of (a) new HIV infections and (b) HIV-related deaths according to three scenarios. (1) a 17% cut in international funding maintained to 2030; (2) incremental decrease to exit of international funding by 2030 with continued increases in domestic financing; (3) following Fast-Track 90-90-90 strategy towards ending AIDS.

400 000 more, respectively, than in 2015) under these conditions. Scenario (3) depicts the Fast-Track 90–90-90 investment strategy towards ending AIDS [6], and as illustrated in Fig. 1 will require very strong commitment by local authorities with support from the global community. For these scenarios, we assumed that available funding prioritization would be retained for treatment programs (accounting for 76% of targeted spending, including antiretroviral therapy, prevention of mother-to-child transmission, and opiate substitution therapy), and the remaining funding would be prioritized towards the most cost-effective programs for reducing new infections and deaths in each context.

Although this analysis is a modeled projection with inherent limitations [4], it emphasizes the disconcerting impact of reduced aid, which will negatively affect marginalized populations. Unsurprisingly, sub-Saharan Africa, the region with the highest HIV burden and most dependent on international funding, would be the most affected region by decreased donor funding. New infections would increase disproportionally on a per capita basis among women aged 15–49 years and key populations, including female sex workers and their clients.

Although there is a strong nationalist case for globalism and international donor support for HIV to continue, now is also the time for high HIV-burden countries to assume more financial responsibility for their epidemic responses. Though some countries have been successful in funding their own HIV response – South Africa, for example, financed 77% of its HIV budget in 2016 [7] – it may be very difficult for most countries to similarly prioritize HIV financing to the same extent with domestic funds [8,9]. UNAIDS has warned of the critical nature of the current global $5 billion shortfall from the $26 billion estimated to be required for an effective HIV response by 2020 [10]. Regardless of how this gap is filled, investing more now will not only save lives, but also future resource needs.

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Are we using the correct methods to measure efficacy in HIV trials?

The results of a randomized double-blind study comparing tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF), each coformulated with elvitegravir, cobicistat, and emtricitabine (E/C/F), for initial HIV-1 treatment at week 144 have been published recently [1]. This study found that E/C/F/TAF is superior to E/C/F/TDF in virologic efficacy, with 84.2% vs. 80.0% patients having HIV-1 RNA less than 50 copies/ml (difference 4.2%; 95% confidence interval: 0.6–7.8%). We were extremely surprised by these results, given the pronounced similarity between TAF and TDF (recall that TAF is a prodrug of TDF) and that at weeks 48, 96, and 144 virologic failure was practically the same in both groups.

The current study comprised two controlled double-blind phase 3 trials [2] and followed the Food and Drug Administration (FDA) recommendations to measure efficacy, which was defined as the percentage of participants with HIV-1 RNA less than 50 copies/ml at different time frames. This percentage was analysed using the FDA-snapshot algorithm, which expresses a