therapy era), coupled with a poorly sensitive test (Ziehl–Neelsen microscopy). Indeed, in individuals who are smear-negative, Xpert MTB/RIF has a negative predictive value of 93% (vs 87% for all patients with suspected tuberculosis given a smear, with sensitivity of 40% and prevalence of 20%), leaving some doubt as to the true rule-out value for a single test. In this context, prescription of clinician behaviour within diagnostic randomised controlled trials can be ethically problematic. However, as countries increasingly achieve widespread antiretroviral coverage leading to true decreases in tuberculosis prevalence, burdens on health systems related to overdiagnosis of tuberculosis could increase.

Patients with history of previous tuberculosis treatment account for about 12% of global tuberculosis cases (nearly 700 000 people in 2012) and are notified twice before, and, of those with suspected tuberculosis medicines at least (42%) had been initiated on anti-HIV-infected, and 68 of 86 (79%) had abnormalities consistent with previous infection, including bronchiectasis and atelectasis resulting from scarring or fibrosis. In high-HIV burden settings with low diagnostic capacity, retreatment of tuberculosis in the modern era represents a common pathway for individuals with chronic lung disease who remain symptomatic after repeated interactions with the public health system. In this group, empiric treatment exposes patients to drug toxicities and increased health-care costs without benefit, imposing unnecessary and potentially substantial costs on national tuberculosis programmes. Continued movement towards universal antiretroviral coverage and widespread access to sensitive diagnostic tests might ultimately regain the confidence of clinicians working in resource-constrained settings that when a test result is negative tuberculosis treatment can safely be withheld.

We declare no competing interests.

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models of innovation must be explored.

Мédecins Sans Frontières, in consultation with other stakeholders, has developed the “3P Project” (Push, Pull, Pool), an incentive framework for tuberculosis drug regimen development. The 3P Project aims to deliver affordable, effective new regimens for tuberculosis more efficiently, through an open, collaborative approach to drug development, and through novel approaches to finance and coordination of research and development, including push funding (ie, through grants), pull funding (ie, through milestone prizes), and pooling of intellectual property to ensure open collaborative research and fair licensing for high-quality low-cost production of the final products.

We agree with Zumla and colleagues that the specialty cannot be complacent, and that to speed up regimen development and re-engage the private sector in tuberculosis research and development novel approaches are necessary.

We declare no competing interests.

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HIV infection and Buruli ulcer in Africa

In a recent Personal View on Buruli ulcer, Daniel O’Brien and colleagues highlighted the urgent need for research on HIV-Buruli ulcer co-infection. Whether HIV infection is a risk factor for Buruli ulcer is unknown, because the few studies published show contrasting results. In Ghana, HIV was not associated with Buruli ulcer (six of 116 Buruli ulcer cases with HIV versus one of 116 controls, p=0·89), whereas a significant association was found in Benin (11 of 426 versus two of 613, p=0·003). This discrepancy could result from HIV being differentially associated with subgroups of Buruli ulcer, such as severe Buruli ulcer. Sporadic case reports described patients with HIV with both severe and non-severe evolution, for example. However, as emphasised by O’Brien and colleagues, no published epidemiological data exist on the association between HIV and severity of Buruli ulcer.

We did a large cohort study in a highly endemic region of Benin, and addressed the question of the effect of HIV on the severity of Buruli ulcer. Clinical and laboratory data were prospectively obtained from all consecutive patients with Buruli ulcer seen between 2005 and 2011 at the Centre de Dépistage et de Traitement de l’Ulcére de Buruli (CDTUB) in Pobe, Benin. Clinical Buruli ulcer cases were confirmed by PCR and tested for HIV infection with two serological tests. As suggested in our study, severe Buruli ulcer was defined as presenting with oedematous, bone, large (≥15 cm in diameter), or multifocal lesions. The effect of HIV on Buruli ulcer severity was tested by logistic regression, as implemented in the glm function of the R software. Access to the data registry was approved by the institutional review board of the CDTUB and the national Buruli ulcer control authorities.

1511 Buruli ulcer cases were included, of whom 78% (n=1177) were PCR-confirmed. HIV testing was positive in 34 of all 1511 patients (2·3%) and in 25 of 500 patients (5·0%) aged 15–49 years. This proportion is significantly higher than is the 1·1% estimate reported for this age group in Benin in 2012 (p=0·0001). More than 70% (n=24) of patients with HIV developed severe Buruli ulcer, compared with 50% (n=723) of HIV-negative patients (odds ratio [OR] 2·77, 95% CI 1·32–6·33; p=0·006). A focus on PCR-confirmed Buruli ulcer cases further validated this finding (OR 2·59, 1·06–7·27; p=0·037). The effect of HIV on Buruli ulcer severity was driven mainly by an increased frequency of large or oedematous lesions in patients with HIV and Buruli ulcer. The effect of HIV on Buruli ulcer severity was driven mainly by an increased frequency of large or oedematous lesions in patients with HIV and Buruli ulcer (OR for large lesions in patients with Buruli ulcer with and without HIV 2·32, 95% CI 1·16–4·76, p=0·0174; OR for oedematous lesions 1·93, 0·94–3·86, p=0·0740; OR for bone lesions 0·96, 0·15–3·24, p=0·95; and OR for multifocal lesions 1·55, 0·25–5·29, p=0·58). Adjustment for age and sex did not modify the results.

Although HIV-Buruli ulcer co-infection is a rare clinical event, our data support O’Brien and colleagues’ hypothesis of a significant effect of HIV infection on Buruli ulcer severity. We also report evidence suggestive of a higher incidence of HIV infection in patients with Buruli ulcer compared with the general population, although the absence of local controls in our design calls for further confirmation. This evidence offers insights of profound significance with regards to Buruli ulcer physiopathology, and opens new avenues for the development of novel preventive and therapeutic strategies.