health databases and cancer registries. However, viable screening tests for HPV-associated oropharyngeal cancer do not yet exist.[10] High-resolution anoscopy is the gold standard for diagnosing anal precancer, but high-resolution anoscopy is not widely available, which could hamper comprehensive screening of high-risk groups beyond HIV-positive individuals.[7] HPV vaccination has already led to significant changes in cervical high-risk HPV infection and precancer rates in younger women.[11,12] The decrease of cervical (and anal) HPV16/18 infection and precancer could make targeted secondary anal cancer prevention feasible despite insufficient resources, especially if high-resolution anoscopy could be preceded by anal high-risk HPV testing. Hopefully, the findings presented by Lin and colleagues[9] will encourage the initiation of prospective trials evaluating screening programmes for all women with an elevated risk for anal cancer.

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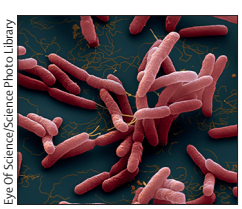
Reducing the melioidosis burden: public health, chronic disease prevention, or improved case management?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Melioidosis, which often presents as an acute, fulminant illness and has a case fatality rate of 10–50%, is caused by *Burkholderia pseudomallei*. In *The Lancet Infectious Diseases*, Emma Birnie and colleagues[1] describe the global burden of melioidosis in terms of disability-adjusted life-years (DALYs) for the first time. The analysis is based on a modelled estimate of the global incidence and mortality of melioidosis,[2] with additional data from a systematic review of the clinical impact of melioidosis. This is an important and well executed study. With these findings, we can compare the burden of melioidosis across regions of the world, and to some extent, compare the global burden of melioidosis with that of other infectious diseases.

Two findings of the study warrant special mention. First, 99% of the DALY burden of melioidosis was attributed to deaths from melioidosis (years of life lost [YLL]). Second, a high DALY burden for melioidosis was estimated in countries with few or no reported melioidosis cases. This finding was driven by a predictive modelling study of the global distribution of melioidosis,[2] in which Limmathurotsakul and colleagues estimated 165 000 melioidosis cases and 89 000 deaths worldwide in 2015. Of note, Limmathurotsakul and colleagues suggested that melioidosis was "severely under-reported in 45 countries in which it is known to be endemic" and "probably endemic in a further 34 countries that have

never reported the disease". Their models were informed by geolocated records of melioidosis cases, detections of *B pseudomallei*, and environmental suitability for *B pseudomallei*. These modelled incidence rates outside the regions traditionally associated with melioidosis clearly require further verification.

Birnie and colleagues[1] argue that melioidosis should be reconsidered for inclusion in WHO's portfolio of neglected tropical diseases (NTDs). They argue that investment in research and development for melioidosis lags behind other neglected and emerging or re-emerging tropical diseases with similar or smaller global disease burdens. However, their comparisons did not include all the diseases in the WHO list of NTDs;[3] Buruli ulcer, dracunculiasis (Guinea worm), mycetoma, scabies, snakebite, and yaws were missing. Classification as an NTD implies an available and effective public health approach exists to minimise disease burden. WHO recommends five strategies for NTD prevention—namely, preventive chemotherapy, intensified case detection and case management, control of vectors and intermediate hosts, veterinary public health, and provision of safe water, sanitation, and hygiene.[4] Of these, intensified case detection and case management could reduce the case fatality rate of melioidosis to less than 15%, as reported in Australia.[5] The other strategies would be unlikely to effectively reduce the burden of melioidosis, because infection usually results from exposure to *B pseudomallei* through broken skin or inhalation, and less commonly via ingestion of *B pseudomallei*-contaminated water.

Birnie and colleagues estimated that 46% of patients with melioidosis have diabetes, which highlights the interaction between the global diabetes epidemic and melioidosis in under-resourced tropical populations.[6] Perhaps an integrated approach to prevention and control of type 2 diabetes would more effectively reduce the global burden of melioidosis than any of the five strategies for NTD prevention advocated by WHO. Other public health approaches, such as community education and reducing environmental exposure, might be effective against several diseases, such as melioidosis and leptospirosis.

Because of the high DALY burden attributed to melioidosis by Birnie and colleagues,[1] melioidosis warrants inclusion as a stand-alone condition in future global burden of disease estimates. This would enable direct comparison with other conditions in a disease-agnostic manner and would allow appropriate allocation of resources for melioidosis research and prevention. However, different methods could result in substantially different estimates of the DALY burden of melioidosis. The YLL of a fatal melioidosis case with comorbid diabetes would be attributed to melioidosis by Birnie and colleagues, whereas the YLL would be attributed to the underlying diabetes by the Global Burden of Disease study.[7] Because 99% of the DALY burden of melioidosis was due to YLLs, and diabetes prevalence was 46% among melioidosis cases, taking the approach of the Global Burden of Disease study could halve the estimated DALY burden of melioidosis. Sepsis and antimicrobial resistance also complicate the disease burden estimate, because these conditions can be ascribed their own burden or be incorporated into that of melioidosis.[8] A middle ground would be to attribute weight (and allocate YLL) to multiple causes of death, thus including YLL for both melioidosis and diabetes when these conditions are both present.[9]

The impressive effort by Birnie and colleagues to estimate the global DALY burden of melioidosis should be commended. The next step will be to verify the large numbers of predicted but unrecognised cases in areas where endemic melioidosis has not yet been documented. Importantly, this verification will inform clinical treatment guidelines for sepsis in these areas.

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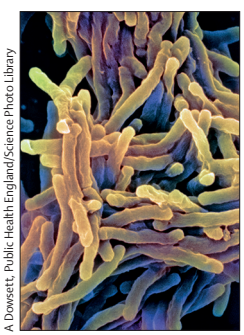
The burden of latent multidrug-resistant tuberculosis



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In the past 10 years, there has been renewed interest in the early phases of the natural history of tuberculosis.[1] Estimates suggest that around 25% of the world's population could have latent tuberculosis infection,[2] 5–10% of whom will develop active disease during their lifetime[3] (10% annually among people with HIV).[4] Failure to implement effective tuberculosis control measures to manage latent infection threatens elimination goals.

Groups at high risk of active tuberculosis are the focus of programmatic management of latent tuberculosis infection.[5] Once active disease is ruled out, tuberculosis preventive therapy can be offered. However, such therapy is thought to be ineffective against multidrug-resistant (MDR) strains (ie, those resistant to isoniazid and rifampicin), and is thus rarely used to treat contacts of people with MDR tuberculosis.

In *The Lancet Infectious Diseases*, Gwenan Knight and colleagues[6] investigated the global burden of latent tuberculosis to provide the first estimates of the prevalence of latent MDR tuberculosis infection. They used surveillance and survey data, estimated annual risks of infection, and informative priors for patterns of increase to develop and validate a novel cohort method to calculate this burden. Knight and colleagues estimated that around 19 million people could be latently infected with MDR tuberculosis (10% of whom were infected in 2013 and 2014—ie, the most recent 2 years included in the model), representing around 1·2% of the total burden of latent infection. Children younger than 15 years, who progress to active disease more quickly than adults and therefore are a sentinel event suggesting recent local transmission, had more than double the risk of latent MDR tuberculosis infection that adults had. These data show that transmission of MDR strains of tuberculosis is worryingly high and probably increasing, and should be urgently addressed. Knight and colleagues also estimated that, even if all tuberculosis transmission was halted, reactivation of latent infections would mean that the future burden of MDR disease would still be substantial.[6] Their work thus clearly emphasises the need for interventions to limit both transmission and reactivation of latent MDR tuberculosis infection.

Knight and colleagues' findings have important implications at the individual and population level and for policy. Given that the prevalence of latent MDR tuberculosis infection will continue to rise if MDR tuberculosis transmission rates persist, an increasing proportion of people—and children especially—with latent infections[7] might not benefit from recommended tuberculosis preventive therapy regimens, and thus will be at increased risk of developing active MDR tuberculosis.[8] At the population level, as the prevalence of latent tuberculosis infection decreases, the partial protective effect against reinfection or reactivation that latent infection with drug-susceptible tuberculosis provides[9] against MDR strains will also diminish, thus increasing the risk of latent infection with MDR strains. In the meantime, Knight and colleagues' study emphasises the need to strengthen epidemiological surveillance of MDR tuberculosis and programmatic management of active and latent infections to reduce transmission of MDR tuberculosis (and thus the number of people with latent MDR tuberculosis). Only 25% of people with active MDR tuberculosis are detected (compared with 64% of people with all types of tuberculosis in 2017).[10] Early identification of cases, prompt initation of highly effective treatment, and close treatment follow-up will help to shorten the infectious period, and MDR tuberculosis preventive therapies will clear infections or prevent disease progression.

Further research priorities for diagnosis and treatment of latent MDR tuberculosis have been identified by Knight and colleagues. First, there is an urgent need to accelerate research into preventive therapy regimens