# Global burden of melioidosis in 2015: a systematic review and data synthesis

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## Summary

**Background** Melioidosis is an infectious disease caused by the environmental bacterium *Burkholderia pseudomallei*. It is often fatal, with a high prevalence in tropical areas. Clinical presentation can vary from abscess formation to pneumonia and sepsis. We assessed the global burden of melioidosis, expressed in disability-adjusted life-years (DALYs), for 2015.

**Methods** We did a systematic review of the peer-reviewed literature for human melioidosis cases between Jan 1, 1990, and Dec 31, 2015. Quantitative data for cases of melioidosis were extracted, including mortality, age, sex, infectious and post-infectious sequelae, antibiotic treatment, and symptom duration. These data were combined with established disability weights and expert panel discussions to construct an incidence-based disease model. The disease model was integrated with established global incidence and mortality estimates to calculate global melioidosis DALYs. The study is registered with PROSPERO, number CRD42018106372.

**Findings** 2888 articles were screened, of which 475 eligible studies containing quantitative data were retained. Pneumonia, intra-abdominal abscess, and sepsis were the most common outcomes, with pneumonia occurring in 3633 (35·7%, 95% uncertainty interval [UI] 34·8–36·6) of 10 175 patients, intra-abdominal abscess in 1619 (18·3%, 17·5–19·1) of 8830 patients, and sepsis in 1526 (18·0%, 17·2–18·8) of 8469 patients. We estimate that in 2015, the global burden of melioidosis was 4·6 million DALYs (UI 3·2–6·6) or 84·3 per 100 000 people (57·5–120·0). Years of life lost accounted for 98·9% (UI 97·7–99·5) of the total DALYs, and years lived with disability accounted for 1·1% (0·5–2·3).

**Interpretation** Melioidosis causes a larger disease burden than many other tropical diseases that are recognised as neglected, and so it should be reconsidered as a major neglected tropical disease.

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## Introduction

Melioidosis is caused by the environmental Gram-negative bacillus *Burkholderia pseudomallei*. The disease is characterised by sepsis, abscess formation, and a high case-fatality rate (10–50%) even when appropriately treated.[1–3] First recognised in 1911,[3] melioidosis primarily affects individuals with altered immune function and those in regular contact with soil and groundwater. The major endemic regions are southeast Asia and northern Australia, although melioidosis appears to be ubiquitous across the tropics.[4] Diagnosis can be difficult because of its diverse clinical manifestations and the inadequacy of conventional bacterial identification methods.[5] Additionally, many cases could be missed because of a paucity of diagnostic facilities.[6,7] A modelling study in 2016 that mapped documented human and animal cases, and the presence of environmental *B pseudomallei*, estimated the global incidence to be 165 000 (95% CI 68 000–412 000) human melioidosis cases per year worldwide, with 89 000 (36 000–227 000) deaths.[4] Most people with melioidosis live in low-income and middle-income countries. However, melioidosis is not included in the neglected tropical diseases (NTDs) listed by WHO.[3]

The disparity between the number of reported cases and the estimated number of actual cases is caused by under-recognition and under-reporting of melioidosis.[4] Symptomatic melioidosis infections are usually acute, but the broad range of clinical manifestations, from localised skin lesions to septic shock, hinders recognition.[8] Chronic melioidosis, defined as symptoms that last longer than 2 months, is present in approximately 11% of cases.[2] Unlike that of some NTDs,[9] the reported incidence of melioidosis is increasing, in part because of increasing awareness among physicians and researchers and the expansion of diagnostic services, although there could also be genuine increases in incidence.[10] Melioidosis often results in intensive care admission and it requires prolonged antibiotic therapy (up to 6 months),[3] which means that the disease has a high financial burden.

## Research in context

### Evidence before this study

We did a systematic review of MEDLINE, Embase, WHO Global Health Library, and the Melioidosis.info database for human melioidosis cases between Jan 1, 1990, and Dec 31, 2015, using a broad search strategy and combinations of search terms, *Burkholderia* spp, and disease names, without language restrictions. Our search returned 2888 results, 475 of which were included in our study. Previous studies have estimated incidence and mortality of melioidosis using regional cohorts. The only previous global estimates used 22 338 records of human and animal melioidosis, alongside the presence of environmental *Burkholderia pseudomallei,* to estimate the incidence (165 000 [95% CI 68 000–412 000]) and mortality (89 000 [36 000–227 000]) for the year 2015. However, no attempts have been made to calculate disability-adjusted life years (DALYs) of melioidosis.

### Added value of this study

To the best of our knowledge, this study is the first to provide global estimates of melioidosis in terms of years of life lost, years lived with disability, and DALYs, at national, regional, and global levels. As such, it is the most comprehensive assessment of the burden of melioidosis to date. We found that symptomatic melioidosis infections result in about 4·6 million DALYs annually. The burden of melioidosis is similar to or greater than some of the officially recognised neglected tropical diseases (NTDs), such as intestinal nematode infection (4·6 million DALYs) and dengue (2·9 million DALYs).

### Implications of all the available evidence

These data will inform public health policy by recognising melioidosis as an NTD, determining which countries carry a high burden, and placing melioidosis on the radar for these countries. Countries with a high burden can address the issue by strengthening surveillance systems, preventive measures, and availability of minimal diagnostic facilities and antibiotic options. Additionally, the contribution of risk factors and other factors of health utilisation should allow more targeted population interventions, and should lead to the official recognition of melioidosis as a major NTD.

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The disability-adjusted life-year (DALY) can be used to summarise morbidity, disability, and mortality into a single metric. DALY data provide additional information to incidence or prevalence and mortality data, allowing for comparison of disease burden across populations and diseases.[11] DALYs of some NTDs have been estimated previously, which has shown the relative importance of these diseases compared with other causes of ill health,[9] but an estimate of DALYs has not been done for melioidosis to date.

The aim of our study was to quantify the global burden of melioidosis in terms of DALYs. We combined the modelled estimates of the global incidence and mortality of melioidosis[4] with a systematic review of the published literature on its clinical impact, to calculate the global DALYs for melioidosis for 2015 by age, sex, and country. In addition, we examined the relationship between melioidosis burden and Socio-Demographic Index (SDI),[12] a composite indicator based on income, education, and fertility. Furthermore, we analysed the relationship between melioidosis burden and Healthcare Access and Quality (HAQ) Index,[13] a score developed for the Global Burden of Disease (GBD) studies, and which can be used as a robust method for tracking universal health access. By further evaluating the proportion of patients who present with known risk factors (ie, diabetes, chronic liver disease or alcohol abuse, chronic renal failure, and chronic lung disease), we provide important information for melioidosis control policies.

## Methods

### Search strategy and selection criteria

We did a systematic review by searching MEDLINE, Embase, WHO Global Health Library, and the Melioidosis.info database for reports of human melioidosis published between Jan 1, 1990, and Dec 31, 2015, with no language restrictions. A broad search strategy and combinations of search terms, *Burkholderia* spp, and disease names were used to capture a range of outcomes associated with melioidosis (appendix pp 3–4). We included studies of culture-confirmed cases of melioidosis in human beings (for a full list of inclusion and exclusion criteria, see appendix p 5). Two independent reviewers (JS and HSV) screened titles and abstracts for relevance, and any disagreement about eligibility between reviewers was resolved by discussion, or if no agreement could be reached, by a third author (EBi). EBi, HSV, and JS did the search of published works, and quantitative data extraction was divided between the three reviewers. EBi and HSV cross-checked a random subset of the included studies (approximately 30%), in which we found a discrepancy of less than 2% (appendix pp 7–8). Because of the scarcity of data on post-infectious sequelae in the initial systematic review, an expert opinion-guided supplementary search for a limited number of post-infectious or septic sequelae (ie, post-neurological infection or abscess) was done (appendix pp 3–4). We did the review according to guidance from the Cochrane handbook of interventions and reported the systematic review according to PRISMA and GATHER[14] guidelines where applicable (appendix pp 9–12).

For the **Meliodosis.info database** see http://www.melioidosis.info/info.aspx?pageID=107

See **Online** for appendix

### Data synthesis

We synthesised global epidemiological data on melioidosis to quantify disease burden using the DALY metric, which comprises time lost due to morbidity (years lived with disability [YLD]) and time lost due to mortality (years of life lost [YLL]). 1 DALY is equivalent to 1 year of healthy life

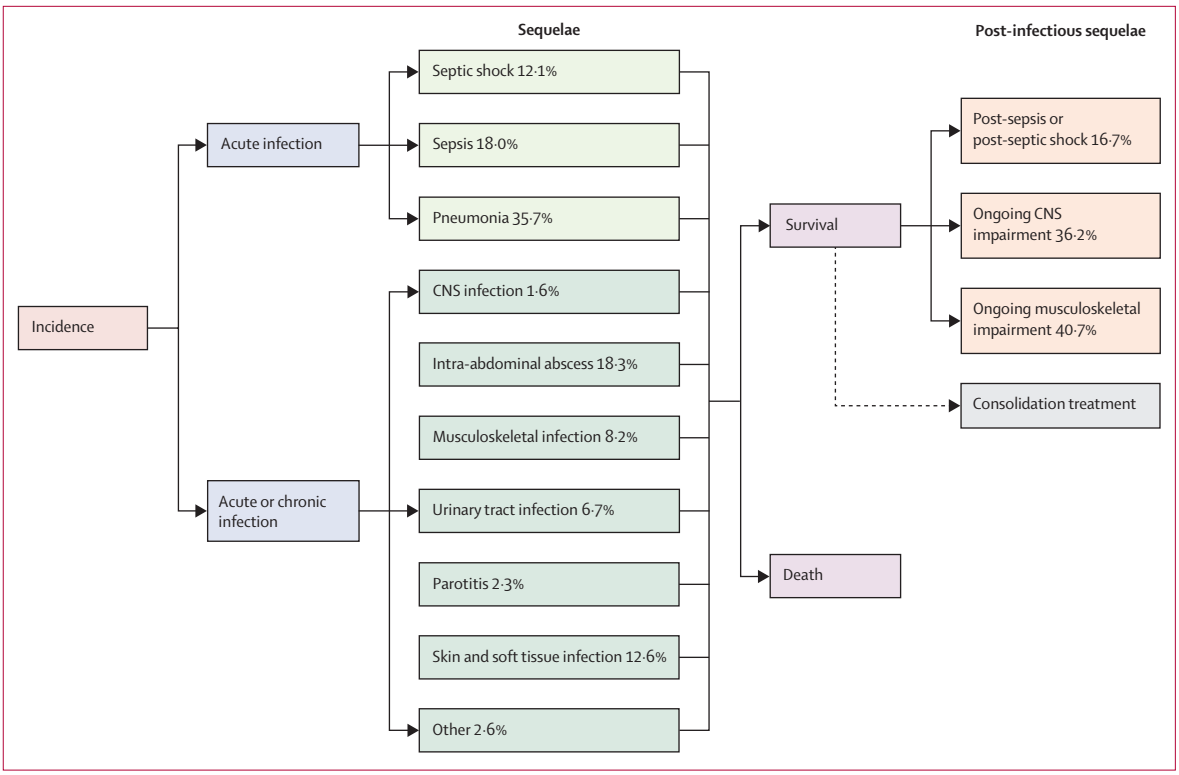


***Figure 1:*** **Simplified disease model used to estimate the global burden of melioidosis**
The prevalence (%) of each sequela among patients with melioidosis is shown. All surviving patients were considered to receive oral antibiotic treatment. Sequelae data on post-acute melioidosis consequences were also extracted from additional literature searches for sepsis and septic shock,[15] ongoing neurological impairment,[16] and ongoing musculoskeletal problems.[17,18]

lost.[11] An incidence-based model of melioidosis disease states (sequelae) and post-infectious sequelae was developed to quantitatively assess the melioidosis disease burden (figure 1).[19]

Disability weights reflect the severity of disease, ranging from 0 (perfect health) to 1 (equivalent to death). For this study, the disability weights for health outcomes from the GBD study were adopted if possible;[20] otherwise, a new disability weight for "intensive care admission" was used from a European study of 30 660 responses.[21] If exact matches were not available, proxy disease outcomes were identified on the basis of the closest matching description and expert agreement (table 1). A flowchart of the analytical model for DALY calculation and the development of a melioidosis database is included in the appendix (p 13).

For the **UN World Population Prospects 2017** see https://population.un.org/wpp

Based on the published literature, clinical expertise, and consensus among the expert panel, we identified ten disease states (or sequelae) of melioidosis (table 1): septic shock, sepsis, pneumonia, CNS infection, intra-abdominal abscess, musculoskeletal infection, urinary tract infection, parotitis (including lymphadenitis), skin and soft tissue infection, and other sequelae (mainly pericarditis and mycotic aneurysms). Although we modelled individual outcomes and sequelae, overlap was allowed; thus, multifocal or disseminated cases of infection were implicitly included. Oral antibiotic treatment was considered as an additional health state in non-fatal cases. Post-infectious sequelae data for melioidosis were extracted from additional literature searches for sepsis and septic shock,[15] ongoing neurological impairment,[16] and ongoing musculoskeletal problems,[17,18] which were validated against expert opinion. These models of sequelae and post-infectious sequelae allowed quantification of the global burden of melioidosis in DALYs. Because of the scarcity of quality epidemiological data on melioidosis, and to reduce duplication of effort, we extracted mortality and incidence estimates from a 2016 modelling study[4] and estimated DALYs on the basis of the 2015 estimates of the UN World Population Prospects 2017 revision.

In addition, we established the age and sex distribution of melioidosis cases by WHO region on the basis of the data from our systematic review. We used the same age and sex distribution for all countries within each region. The case definition of melioidosis was isolation of *B pseudomallei* from any site, ensuring that all types of culture-positive melioidosis were captured, including localised and disseminated forms. All included cases represented symptomatic infection. Relapses or recrudescences of infection were counted as separate cases.

| | Proxy disease outcome | Description | Disability weight (95% CI) |
|---|---|---|---|
| Septic shock* | Intensive care unit admission | Used as a surrogate for septic shock | 0·655 (0·579–0·727) |
| Sepsis* | Infectious disease: acute episode (severe) | Has high fever and pain, and feels very weak, which causes great difficulty with daily activities | 0·133 (0·088–0·190) |
| Pneumonia* | Infectious disease: acute episode (severe) is equivalent to lower respiratory infections (severe) | Has high fever and pain, and feels very weak, which causes great difficulty with daily activities | 0·133 (0·088–0·190) |
| CNS infection (brain or spinal) | Motor plus cognitive impairment (severe) | Cannot move around without help, and cannot lift or hold objects, get dressed, or sit upright; has very low intelligence, speaks few words, and needs constant supervision and help with all daily activities | 0·542 (0·374–0·702) |
| Intra-abdominal abscess (eg, liver, spleen, pancreas) | Abdominal or pelvic problems (moderate) | Has pain in the belly and feels nauseous; has difficulties with daily activities | 0·114 (0·078–0·159) |
| Musculoskeletal infection (osteomyelitis or septic arthritis) | Osteoarthritis (severe) | Severe pain in the leg, which makes the person limp and causes a lot of difficulty walking, standing, lifting and carrying heavy things, getting up and down, and sleeping | 0·165 (0·112–0·232) |
| Urinary tract infection (eg, prostatitis) | Epididymo-orchitis | Has swelling and tenderness in the testicles and pain during urination | 0·128 (0·086–0·180) |
| Parotitis (plus lymphadenitis) | Infectious disease: acute episode (moderate) | Has a fever and aches, and feels weak, which causes some difficulty with daily activities | 0·051 (0·032–0·074) |
| Skin and soft tissue infection | Mild cellulitis | Has a slight, visible physical deformity that is sometimes sore or itchy; others notice the deformity, which causes some worry and discomfort; has a low fever and mild discomfort, but no difficulty with daily activities | 0·027 (0·015–0·042) |
| Other (mainly pericarditis and mycotic aneurysms) | Infectious disease: acute episode (severe) | Has high fever and pain, and feels very weak, which causes great difficulty with daily activities | 0·133 (0·088–0·190) |
| Oral treatment | Generic uncomplicated disease: worry and daily medication | Has a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities | 0·049 (0·031–0·072) |
| Post-sepsis and septic shock sequelae | Infectious disease: post-acute effects (fatigue, emotional lability, and insomnia) | Is always tired and easily upset; the person feels pain all over the body and is depressed | 0·217 (0·179–0·251) |
| Ongoing neurological impairment | Infectious disease: post-acute effects (fatigue, emotional lability, and insomnia) | Is always tired and easily upset; the person feels pain all over the body and is depressed | 0·217 (0·179–0·251) |
| Ongoing musculoskeletal problems | Osteoarthritis (severe) | Severe pain in the leg, which makes the person limp and causes a lot of difficulty walking, standing, lifting and carrying heavy things, getting up and down, and sleeping | 0·165 (0·112–0·232) |

Proxy disease outcomes with established disability weights were selected from the GBD 2015 update,[18] with the exception of septic shock, for which intensive care unit admission was used as a surrogate.[19] We considered all pneumonia cases to be severe, because a priori evidence shows that primary pneumonia caused by *Burkholderia pseudomallei* is acute in most patients (>90%) and often rapidly progresses to sepsis and death.[20] GBD=Global Burden of Disease. *Only acute cases were included.

***Table 1:*** **Disability weights by melioidosis disease state for the calculation of disability-adjusted life-years**

YLDs were calculated for the main melioidosis symptoms (eg, sepsis and pneumonia), as well as for antibiotic treatment (table 1), and lifelong post-infectious sequelae among surviving patients. Our systematic review provided data on the durations of health states and on the probabilities of developing the considered symptoms. All surviving patients were assumed to receive antibiotic treatment. The probabilities of developing post-infectious sequelae among surviving cases were derived from the literature.[15–18] Disability weights were derived from the GBD study.[20] YLLs, YLDs, and post-infectious sequelae were calculated using the WHO standard life expectancy table,[23] and the GBD standard life expectancy table[12] was used in a scenario analysis. The case data from our systematic review were used to derive an age and sex distribution of incident cases and deaths by WHO region (appendix p 18). DALYs were calculated by country, and subsequently aggregated at the regional and global levels. Based on our case data, we also calculated the proportion of patients who presented with known melioidosis risk factors (ie, diabetes, chronic liver disease or alcohol abuse, chronic renal failure, and chronic lung disease).

Parameter uncertainty was quantified and propagated with 10 000 Monte Carlo simulations (appendix p 18). The resulting uncertainty distributions were summarised by the mean and 95% uncertainty interval (UI), defined as the distribution's 2·5th and 97·5th percentile. In subsequent analyses, we used linear regressions to analyse the associations between the country-specific log-transformed melioidosis DALYs and the countries' SDI scores[12] and HAQ indices[13] for 2015 (appendix p 15). With Spearman's rank correlation analysis, we also quantified the association between global DALYs for melioidosis and other NTDs, and their respective levels of funding

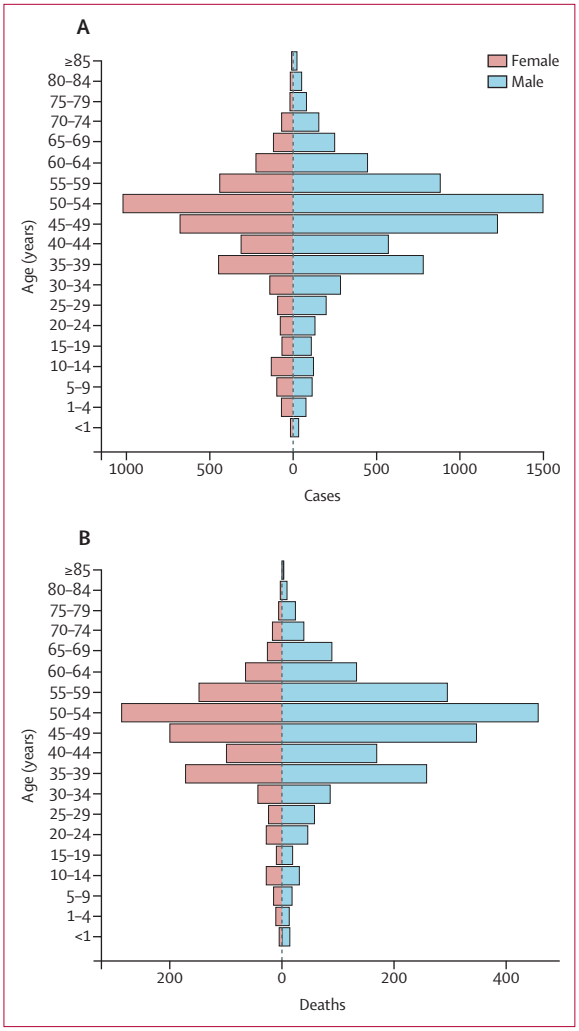


***Figure 2:*** **Age and sex distribution of melioidosis incident cases (A) and deaths (B)**

For the **WHO Global Observatory on Health Research and Development** see http://www.who.int/research-observatory

according to the WHO Global Observatory on Health Research and Development.[24] All analyses were done in R 3.5.1. The study is registered with PROSPERO, number CRD42018106372.

### Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the final report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Results

Our systematic review identified 2888 studies, of which 475 were included in the quantitative analyses (appendix p 6). In total, data for 11767 cases from five of six WHO regions were available (appendix p 14). The age and sex distribution of incidence was similar to that of mortality (figure 2), and also to DALY age and sex distribution. Regional differences in the median age of incidence were observed; the median age was 37 years in the American region, compared with 50 years in the South-East Asian region, 48 years in the Western Pacific region, 49 years in the African region, and 60 years in the Eastern Mediterranean region (appendix pp 19–21). For those younger than 14 years, the age and sex distributions of melioidosis incidence were similar in all regions, whereas for those aged 14 years and older, the ratio of male to female melioidosis incidence and mortality was 1·8 to 1 (figure 2).

4589 (88·4%) of 5194 identified melioidosis cases (for which acute or chronic status was known) were acute and 605 (11·6%) of 5194 cases were chronic. The most common outcomes were pneumonia (occurring in 3633 [35·7%] of 10175 [UI 34·8–36·6]), intra-abdominal abscess (1619 [18·3%] of 8830 [17·5–19·1]), and sepsis (1526 [18·0%] of 8469 [17·2–18·8]). 1240 (12·6%) of 9833 patients (UI 12·0–13·3) presented with skin and soft tissue infection, 3633 (12·1%) of 10175 (11·4–12·8) with septic shock, 805 (8·2%) of 9833 (7·7–8·7) with musculoskeletal infection, 654 (6·7%) of 9833 (6·2–7·2) with urinary tract infection, 256 (2·6%) of 9832 (2·3–2·9) with other infections, such as pericarditis and mycotic aneurysms, 225 (2·3%) of 9833 (2·0–2·6) with parotitis, and 158 (1·6%) of 9827 (1·4–1·9) with CNS infections (denominators differ because the information of the disease states was not available for all cases; appendix pp 22–23). Chronic post-sepsis or post-septic shock sequelae, most commonly general malaise or weakness, cognitive impairment, and readmission, were predicted to occur in 16·7% (UI 0·5–52·1) of patients with sepsis or septic shock.[15] Ongoing neurological impairment (functional and cognitive impairment) was predicted to occur in 36·2% (UI 24·5–48·9) of patients with CNS infection,[16] and ongoing musculoskeletal impairment (arthritic symptoms and mobility problems) was predicted to occur in 40·7% (UI 34·1–47·4) of patients with musculoskeletal infection (appendix pp 22–23).[17,18] Of the outcomes measured, septic shock had the shortest duration of symptoms before admission (mean 8·2 days [SD 8·4]) and the shortest duration of hospitalisation (14·5 days [15·8]). Pneumonia had a mean duration of symptoms prior to admission of 10·9 days (SD 10·6) and of hospitalisation of 21·4 days (17·3). Musculoskeletal infection and intra-abdominal abscess had the longest durations of symptoms prior to admission (mean 63·3 days [SD 168·8] for musculoskeletal infection and 67·4 days [206·4] for intra-abdominal abscess), and the longest durations of hospitalisation (mean 33·9 days [56·2] for musculoskeletal infection and 32·9 days [60·2] for intra-abdominal abscess). The mean duration of consolidation therapy was 129·5 days (SD 48·0).

Overall, by integrating the predicted incidence and mortality data with our disease model,[4] we estimated that melioidosis was responsible for 4635636 DALYS

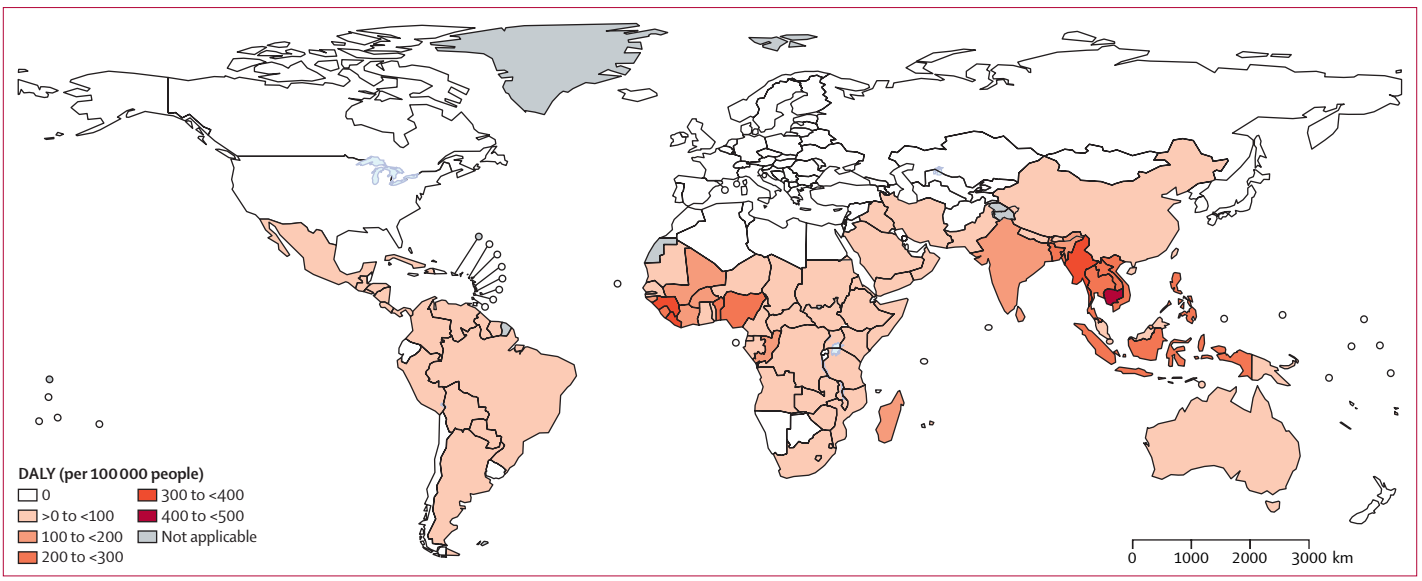


*Figure 3:* **Estimated DALYs per 100 000 people for melioidosis by country in 2015**
DALY=disability-adjusted life-year.

(UI 3 164 157–6 602 075) in 2015, corresponding to 84·3 DALYs (57·5–120·0) per 100 000 population (YLL 458 094 [UI 3 114 498–6 550 593]; YLD 50 542 [22 778–97 825]). YLLs accounted for 98·9% (UI 97·8–99·5) of the total DALYs. The highest total burden was in India, where melioidosis resulted in 1 596 733 DALYs (UI 503 727–3 320 277), whereas Cambodia had the most DALYs per 100 000 population (414·6 [111·9–919·4]; appendix pp 25–27). In 2015, India, Indonesia, Bangladesh, Nigeria, and Vietnam combined accounted for 70·5% (UI 57·7–80·9) of the global melioidosis burden (3 307 178 DALYs [1 892 971–5 251 783]; appendix pp 25–27). Of the WHO regions, the South-East Asian region had the highest burden of DALYs (158·1 per 100 000 population [UI 88·3–256·0]), followed by the African region (84·1 [43·4–152·5]) and the West Pacific region (45·6 [27·7–69·5]; figure 3, table 2).

YLDs accounted for 1·1% (UI 0·5–2·3) of the total melioidosis DALYs. Post-infectious sequelae contributed most to the YLDs (86·8% [UI 70·2–95·2]), followed by symptoms (9·9% [3·0–25·5]) and oral antibiotic treatment (3·4% [1·0–8·0]). Among patients with melioidosis, 46·1% (UI 45·2–47·0) also had underlying diabetes or newly diagnosed hyperglycaemia, 9·3% (8·8–9·8) had chronic kidney disease, 7·4% (6·9–7·9) had chronic liver disease or alcohol abuse, and 3·4% (3·0–3·7) had chronic lung disease (appendix pp 24). Diabetes alone accounted for 2 137 433 DALYs (UI 1 459 182–3 046 177).

Total DALYs per country showed a negative association with both SDI and HAQ Index (appendix p 28). Some countries had discrepancies between access to health care and DALYs, such as Thailand and Singapore (appendix pp 28–31). Additionally, despite having high SDI scores, the Philippines, Indonesia, and Thailand have a high burden of melioidosis (appendix pp 28–31). For example, Thailand, despite having good access to health care (70·8 HAQ Index) and good socio-demographic development (0·705 SDI), still shows a high melioidosis DALY burden (212·6 per 100 000 people; UI 72·4–430·1). The scenario analysis using GBD life expectancy tables found a burden of 4 093 110 (UI 2 790 743–5 826 117) DALYs, which was 11·7% lower than the result using the WHO life expectancy table (appendix pp 25–27).

Spearman's rank correlation analysis showed no clear association between the DALY burden and the amount of global investment (p=0·892), which should prompt re-evaluation of how resources are allocated for NTDs (appendix pp 32–33).

## Discussion

This systematic review and data synthesis is the first study to provide estimates of the global burden of melioidosis in terms of DALYs. We estimated that in 2015 the global burden of melioidosis was 4·6 million DALYs (UI 3·2–6·6 million), corresponding to 84·3 DALYs (57·5–120·0) per 100 000 population. YLLs accounted for 98·9% (UI 97·7–99·5) of the total DALYs.

The worldwide estimates in this study include geographical areas, such as south Asia, South America, and Africa, where the burden of melioidosis has previously been underappreciated and where it might have been misattributed to other febrile illnesses, such as malaria and tuberculosis.[6,7] The global burden of melioidosis, as expressed in DALYs, is greater than that of leptospirosis (2·90 million), dengue (2·86 million), schistosomiasis (2·63 million), lymphatic filariasis (1·24 million), and leishmaniasis (1·06 million;

| | YLLs (95% UI) | YLLs per 100 000 (95% UI) | YLDs (95% UI) | YLDs per 100 000 (95% UI) | DALYs (95% UI) | DALYs per 100 000 (95% UI) |
|---|---|---|---|---|---|---|
| African region | 769 448 (394 742–1 399 395) | 83·5 (42·8–151·8) | 5817 (2240–12 735) | 0·63 (0·24–1·38) | 775 266 (400 236–1 405 485) | 84·1 (43·4–152·5) |
| Angola | 984 (61–3199) | 3·5 (0·2–11·5) | 8·8 (0·6–30·9) | 0·03 (0·00–0·11) | 993 (68–3206) | 3·6 (0·2–11·5) |
| Benin | 29 154 (6264–69 760) | 275·7 (59·2–659·6) | 240·5 (44·3–671·2) | 2·27 (0·42–6·35) | 29 395 (6510–69 975) | 277·9 (61·6–661·6) |
| Burkina Faso | 20 685 (2802–56 695) | 114·2 (15·5–313·1) | 165·1 (20·3–508·6) | 0·91 (0·11–2·81) | 20 850 (2948–56 834) | 115·1 (16·3–313·8) |
| Cameroon | 17 362 (2608–46 249) | 76·0 (11·4–202·5) | 140·5 (19·8–419·7) | 0·62 (0·09–1·84) | 17 503 (2738–46 378) | 76·6 (12·0–203·1) |
| Central African Republic | 4479 (792–11 460) | 98·5 (17·4–252·1) | 33·0 (5·2–94·7) | 0·73 (0·12–2·08) | 4512 (825–11 489) | 99·2 (18·1–252·7) |
| Chad | 13 457 (1460–38 811) | 96·1 (10·4–277·0) | 103·4 (10·4–331·3) | 0·74 (0·07–2·36) | 13 561 (1567–38 928) | 96·8 (11·2–277·9) |
| Congo | 8295 (1854–19 696) | 166·1 (37·1–394·3) | 67·5 (13·2–186·1) | 1·35 (0·26–3·73) | 8363 (1921–19 769) | 167·4 (38·5–395·7) |
| Côte d'Ivoire | 36 423 (7354–89 402) | 157·6 (31·8–386·9) | 263·7 (44·3–755·8) | 1·14 (0·19–3·27) | 36 686 (7599–89 665) | 158·8 (32·9–388·0) |
| DR Congo | 7214 (769–20 814) | 9·5 (1·0–27·3) | 61·0 (6·2–196·5) | 0·08 (0·01–0·26) | 7275 (830–20 871) | 9·5 (1·1–27·4) |
| Equatorial Guinea | 194 (39–477) | 16·5 (3·3–40·6) | 1·4 (0·3–4·0) | 0·12 (0·02–0·34) | 196 (41–478) | 16·6 (3·4–40·7) |
| Eritrea | 845 (59–2675) | 17·4 (1·2–55·2) | 8·5 (0·7–28·5) | 0·17 (0·01–0·59) | 854 (68–2683) | 17·6 (1·4–55·3) |
| Ethiopia | 8399 (874–24 387) | 8·4 (0·9–24·4) | 75·9 (8·0–242·2) | 0·08 (0·01–0·24) | 8475 (950–24 473) | 8·5 (1·0–24·5) |
| Gabon | 1410 (323–3323) | 73·1 (16·7–172·2) | 11·9 (2·2–33·4) | 0·62 (0·11–1·73) | 1422 (335–3335) | 73·7 (17·4–172·8) |
| The Gambia | 255 (6–940) | 12·9 (0·3–47·5) | 2·8 (0·2–10·3) | 0·14 (0·01–0·52) | 257 (9–942) | 13·0 (0·5–47·6) |
| Ghana | 13 096 (1335–38 275) | 47·5 (4·8–138·8) | 107·3 (9·7–352·1) | 0·39 (0·04–1·28) | 13 203 (1443–38 382) | 47·9 (5·2–139·2) |
| Guinea | 42 961 (8864–104 561) | 355·3 (73·3–864·7) | 333·1 (60·7–928·4) | 2·75 (0·50–7·68) | 43 294 (9190–104 890) | 358·0 (76·0–867·5) |
| Guinea-Bissau | 3315 (375–9442) | 187·2 (21·2–533·3) | 26·1 (2·8–82·2) | 1·47 (0·16–4·64) | 3341 (402–9472) | 188·7 (22·7–535·0) |
| Kenya | 3187 (413–8852) | 6·7 (0·9–18·7) | 28·9 (3·5–89·9) | 0·06 (0·01–0·19) | 3216 (442–8879) | 6·8 (0·9–18·8) |
| Liberia | 14 131 (2751–35 137) | 314·1 (61·1–780·9) | 110·7 (18·6–316·5) | 2·46 (0·41–7·03) | 14 242 (2868–35 269) | 316·5 (63·7–783·8) |
| Madagascar | 27 359 (5851–65 662) | 112·9 (24·1–270·9) | 235·5 (43·4–657·0) | 0·97 (0·18–2·71) | 27 594 (6107–65 878) | 113·9 (25·2–271·8) |
| Malawi | 6894 (1242–17 539) | 39·2 (7·1–99·8) | 57·1 (9·4–163·3) | 0·33 (0·05–0·93) | 6951 (1303–17 587) | 39·6 (7·4–100·1) |
| Mali | 19 197 (2763–51 629) | 109·9 (15·8–295·6) | 150·8 (19·6–458·9) | 0·86 (0·11–2·63) | 19 348 (2913–51 768) | 110·8 (16·7–296·4) |
| Mauritania | 958 (74–2977) | 22·9 (1·8–71·2) | 8·0 (0·6–27·7) | 0·19 (0·01–0·66) | 966 (82–2987) | 23·1 (2·0–71·4) |
| Mauritius | 101 (9–302) | 8·0 (0·7–24·0) | 2·4 (0·2–8·0) | 0·19 (0·02–0·63) | 103 (11–304) | 8·2 (0·9–24·2) |
| Mozambique | 7613 (966–21 195) | 27·2 (3·4–75·7) | 62·4 (7·7–192·1) | 0·22 (0·03–0·69) | 7675 (1026–21 253) | 27·4 (3·7–75·9) |
| Niger | 12 146 (1034–36 906) | 61·0 (5·2–185·5) | 103·4 (8·5–349·0) | 0·52 (0·04–1·75) | 12 249 (1130–37 026) | 61·6 (5·7–186·1) |
| Nigeria | 426 571 (89 803–1 031 369) | 235·4 (49·6–569·2) | 3070·0 (550·8–8589·8) | 1·69 (0·30–4·74) | 429 641 (92 865–1 034 804) | 237·1 (51·3–571·1) |
| Senegal | 2097 (118–6906) | 14·0 (0·8–46·1) | 18·4 (1·1–65·1) | 0·12 (0·01–0·43) | 2115 (135–6929) | 14·1 (0·9–46·3) |
| Sierra Leone | 19 140 (3758–47 287) | 264·5 (51·9–653·4) | 132·4 (23·2–374·5) | 1·83 (0·32–5·18) | 19 272 (3884–47 455) | 266·3 (53·7–655·7) |
| South Africa | 856 (64–2678) | 1·5 (0·1–4·8) | 8·2 (0·7–27·1) | 0·01 (0·00–0·05) | 864 (72–2686) | 1·6 (0·1–4·9) |
| South Sudan | 1189 (120–3492) | 10·0 (1·0–29·4) | 10·9 (1·2–34·7) | 0·09 (0·01–0·29) | 1200 (131–3504) | 10·1 (1·1–29·5) |
| Tanzania | 9561 (1272–26 347) | 17·7 (2·4–48·9) | 85·6 (10·5–264·3) | 0·16 (0·02–0·49) | 9647 (1354–26 437) | 17·9 (2·5–49·1) |
| Togo | 5030 (748–13 431) | 67·8 (10·1–181·1) | 39·4 (5·1–119·3) | 0·53 (0·07–1·61) | 5070 (783–13 474) | 68·4 (10·6–181·7) |
| Uganda | 1026 (37–3620) | 2·6 (0·1–9·0) | 9·7 (0·5–36·1) | 0·02 (0·00–0·09) | 1036 (47–3629) | 2·6 (0·1–9·0) |
| Zambia | 3635 (424–10 318) | 22·6 (2·6–64·1) | 30·7 (3·6–95·8) | 0·19 (0·02–0·60) | 3666 (454–10 350) | 22·8 (2·8–64·3) |
| Zimbabwe | 230 (15–733) | 1·5 (0·1–4·6) | 2·2 (0·2–7·4) | 0·01 (0·00–0·05) | 232 (18–735) | 1·5 (0·1–4·7) |
| Region of the Americas | 68 431 (36 003–118 711) | 11·9 (6·3–20·7) | 1291 (460–2892) | 0·23 (0·08–0·50) | 69 722 (37 135–120 070) | 12·2 (6·5–20·9) |
| Argentina | 565 (37–1801) | 1·3 (0·1–4·1) | 11·3 (0·7–40·5) | 0·03 (0·00–0·09) | 577 (47–1815) | 1·3 (0·1–4·2) |
| Bolivia | 573 (49–1735) | 5·3 (0·5–16·2) | 5·8 (0·5–19·5) | 0·05 (0·00–0·18) | 579 (55–1741) | 5·4 (0·5–16·2) |
| Brazil | 26 116 (3852–69 412) | 12·7 (1·9–33·7) | 516·5 (63·9–1598·3) | 0·25 (0·03–0·78) | 26 632 (4304–70 044) | 12·9 (2·1–34·0) |
| Colombia | 4808 (725–12 722) | 10·0 (1·5–26·4) | 88·0 (11·6–267·2) | 0·18 (0·02–0·55) | 4896 (806–12 817) | 10·2 (1·7–26·6) |
| Costa Rica | 391 (71–988) | 8·1 (1·5–20·5) | 10·8 (1·6–32·0) | 0·23 (0·03–0·67) | 402 (81–1000) | 8·4 (1·7–20·8) |
| Cuba | 426 (21–1428) | 3·7 (0·2–12·5) | 16·8 (0·8–62·1) | 0·15 (0·01–0·54) | 442 (34–1444) | 3·9 (0·3–12·6) |
| El Salvador | 3206 (769–7411) | 50·8 (12·2–117·4) | 59·0 (11·6–160·4) | 0·93 (0·18–2·54) | 3265 (827–7 470) | 51·7 (13·1–118·3) |
| Guatemala | 2454 (443–6205) | 15·1 (2·7–38·2) | 30·7 (4·7–89·8) | 0·19 (0·03–0·55) | 2485 (474–6234) | 15·3 (2·9–38·4) |
| Guyana | 449 (86–1118) | 58·4 (11·2–145·5) | 4·7 (0·7–13·8) | 0·61 (0·09–1·80) | 453 (90–1122) | 59·0 (11·7–146·0) |
| Haiti | 1129 (89–3472) | 10·5 (0·8–32·4) | 8·9 (0·8–29·3) | 0·08 (0·01–0·27) | 1138 (98–3481) | 10·6 (0·9–32·5) |
| Honduras | 2894 (400–7833) | 32·3 (4·5–87·4) | 45·1 (6·2–135·5) | 0·50 (0·07–1·51) | 2939 (443–7879) | 32·8 (4·9–87·9) |

(Table 2 continues on next page)

| | YLLs (95% UI) | YLLs per 100 000 (95% UI) | YLDs (95% UI) | YLDs per 100 000 (95% UI) | DALYs (95% UI) | DALYs per 100 000 (95% UI) |
|---|---|---|---|---|---|---|
| (Continued from previous page) | | | | | | |
| Mexico | 16 128 (2 711–41 615) | 12·8 (2·2–33·1) | 327·5 (45·3–987·2) | 0·26 (0·04–0·78) | 16 456 (3012–41 937) | 13·1 (2·4–33·3) |
| Nicaragua | 2205 (379–5651) | 36·3 (6·2–92·9) | 33·2 (4·8–98·3) | 0·55 (0·08–1·62) | 2238 (411–5690) | 36·8 (6·8–93·6) |
| Panama | 1995 (465–4657) | 50·3 (11·7–117·3) | 37·9 (7·3–103·9) | 0·95 (0·18–2·62) | 2033 (500–4694) | 51·2 (12·6–118·3) |
| Paraguay | 455 (12–1670) | 6·9 (0·2–25·2) | 8·6 (0·4–32·3) | 0·13 (0·01–0·49) | 464 (19–1679) | 7·0 (0·3–25·3) |
| Peru | 1227 (155–3389) | 3·9 (0·5–10·8) | 22·1 (2·7–68·8) | 0·07 (0·01–0·22) | 1249 (175–3411) | 4·0 (0·6–10·9) |
| Suriname | 439 (94–1052) | 79·4 (16·9–190·2) | 6·6 (1·1–18·5) | 1·18 (0·20–3·35) | 446 (100–1059) | 80·6 (18·1–191·4) |
| Venezuela | 2970 (533–7511) | 9·5 (1·7–24·1) | 57·6 (8·6–170·0) | 0·19 (0·03–0·55) | 3028 (590–7569) | 9·7 (1·9–24·3) |
| Eastern Mediterranean region | 18 448 (6357–42 250) | 4·4 (1·5–10·1) | 101 (31–252) | 0·02 (0·01–0·06) | 18 549 (6460–42 347) | 4·4 (1·5–10·1) |
| Iran | 279 (10–981) | 0·4 (0·0–1·2) | 3·0 (0·1–11·3) | 0·00 (0·00–0·01) | 282 (12–983) | 0·4 (0·0–1·2) |
| Iraq | 562 (9–2200) | 1·6 (0·0–6·1) | 3·4 (0·1–14·5) | 0·01 (0·00–0·04) | 566 (12–2204) | 1·6 (0·0–6·1) |
| Oman | 84 (20–194) | 2·0 (0·5–4·6) | 1·1 (0·2–3·2) | 0·03 (0·00–0·08) | 85 (21–195) | 2·0 (0·5–4·7) |
| Pakistan | 11 193 (848–34 627) | 5·9 (0·4–18·3) | 56·7 (4·3–189·9) | 0·03 (0·00–0·10) | 11 250 (900–34 705) | 5·9 (0·5–18·3) |
| Saudi Arabia | 675 (65–1992) | 2·1 (0·2–6·3) | 10·0 (0·9–32·7) | 0·03 (0·00–0·10) | 685 (73–2002) | 2·2 (0·2–6·3) |
| Somalia | 1776 (166–5271) | 12·8 (1·2–37·9) | 7·8 (0·7–25·1) | 0·06 (0·01–0·18) | 1783 (174–5280) | 12·8 (1·3–38·0) |
| Sudan | 1555 (95–5014) | 4·0 (0·2–13·0) | 7·9 (0·5–27·2) | 0·02 (0·00–0·07) | 1563 (102–5023) | 4·0 (0·3–13·0) |
| Yemen | 2324 (398–5934) | 8·6 (1·5–22·0) | 10·7 (1·6–31·0) | 0·04 (0·01–0·12) | 2334 (408–5945) | 8·7 (1·5–22·1) |
| South-East Asian region | 2 974 407 (1 649 716–4 835 486) | 156·5 (86·8–254·4) | 30 640 (12 500–62 865) | 1·61 (0·66–3·31) | 3 005 047 (1 678 472–4 866 872) | 158·1 (88·3–256·0) |
| Bangladesh | 471 829 (162 015–944 388) | 292·7 (100·5–585·8) | 4974·0 (1366·2–11 993·1) | 3·09 (0·85–7·44) | 476 803 (166 451–949 640) | 295·8 (103·3–589·1) |
| Bhutan | 433 (87–1052) | 55·0 (11·1–133·6) | 3·8 (0·6–11·3) | 0·49 (0·07–1·44) | 437 (91–1055) | 55·4 (11·6–134·0) |
| India | 1 583 214 (490 572–3 306 747) | 120·9 (37·5–252·6) | 13 518·2 (3390·5–33 835·7) | 1·03 (0·26–2·58) | 1 596 733 (503 727–3 320 277) | 122·0 (38·5–253·6) |
| Indonesia | 532 334 (132 919–1 210 328) | 206·2 (51·5–468·8) | 6146·9 (1297·3–16 219·8) | 2·38 (0·50–6·28) | 538 480 (138 880–1 216 825) | 208·6 (53·8–471·3) |
| Myanmar | 187 137 (52 103–407 584) | 357·1 (99·4–777·8) | 1595·8 (372·1–4085·8) | 3·05 (0·71–7·80) | 188 733 (53 729–409 251) | 360·2 (102·5–781·0) |
| Nepal | 25 799 (6147–59 555) | 90·0 (21·5–207·8) | 258·7 (54·0–689·6) | 0·90 (0·19–2·41) | 26 057 (6394–59 808) | 90·9 (22·3–208·7) |
| Sri Lanka | 30 677 (8849–65 909) | 148·1 (42·7–318·2) | 834·2 (196·1–2158·5) | 4·03 (0·95–10·42) | 31 511 (9655–66 771) | 152·1 (46·6–322·3) |
| Thailand | 142 641 (46 506–291 800) | 207·8 (67·7–425·0) | 3305·2 (847·9–8 261·3) | 4·81 (1·23–12·03) | 145 946 (49 726–295 285) | 212·6 (72·4–430·1) |
| Timor-Leste | 343 (40–964) | 27·7 (3·2–77·7) | 2·8 (0·3–8·7) | 0·22 (0·02–0·70) | 346 (43–967) | 27·9 (3·5–77·9) |
| West Pacific region | 754 360 (454 818–1 157 728) | 44·8 (27·0–68·8) | 12 693 (5185–26 073) | 0·75 (0·31–1·55) | 767 053 (466 874–1 170 486) | 45·6 (27·7–69·5) |
| Australia | 1963 (450–4584) | 8·2 (1·9–19·3) | 99·4 (18·6–275·6) | 0·42 (0·08–1·16) | 2062 (536–4697) | 8·7 (2·3–19·7) |
| Brunei | 481 (159–981) | 115·2 (38·0–234·8) | 14·9 (3·5–38·4) | 3·57 (0·84–9·20) | 496 (173–995) | 118·8 (41·5–238·4) |
| Cambodia | 63 674 (16 627–142 051) | 410·3 (107·1–915·4) | 654·4 (141·0–1 723·3) | 4·22 (0·91–11·11) | 64 328 (17 359–142 676) | 414·6 (111·9–919·4) |
| China | 136 733 (47 558–272 254) | 9·8 (3·4–19·5) | 3225·6 (879·8–7 859·5) | 0·23 (0·06–0·56) | 139 958 (50 709–275 425) | 10·0 (3·6–19·7) |
| Fiji | 103 (13–283) | 11·5 (1·5–31·7) | 1·6 (0·2–5·1) | 0·18 (0·02–0·57) | 105 (15–285) | 11·7 (1·7–31·9) |
| Laos | 14 058 (3998–30 345) | 211·0 (60·0–455·4) | 111·8 (25·4–291·2) | 1·68 (0·38–4·37) | 14 170 (4110–30 455) | 212·6 (61·7–457·0) |
| Malaysia | 28 564 (7665–63 033) | 93·0 (24·9–205·2) | 912·3 (195·0–2 430·6) | 2·97 (0·63–7·91) | 29 476 (8435–64 088) | 95·9 (27·5–208·6) |
| Papua New Guinea | 4311 (997–10 032) | 54·4 (12·6–126·7) | 33·4 (6·7–89·2) | 0·42 (0·08–1·13) | 4344 (1031–10 064) | 54·9 (13·0–127·1) |
| Philippines | 240 606 (95 218–453 084) | 236·5 (93·6–445·4) | 2975·7 (933·9–6893·3) | 2·93 (0·92–6·78) | 243 582 (98 035–456 063) | 239·5 (96·4–448·4) |
| Singapore | 2808 (284–8173) | 50·7 (5·1–147·6) | 201·7 (22·5–632·9) | 3·64 (0·41–11·43) | 3010 (456–8379) | 54·4 (8·2–151·4) |
| Vietnam | 261 059 (65 691–591 358) | 279·0 (70·2–632·0) | 4 462·2 (940·4–11 849·0) | 4·77 (1·00–12·66) | 265 521 (70 102–596 432) | 283·8 (74·9–637·4) |
| Global | 4 585 094 (3 114 498–6 550 593) | 83·4 (56·6–119·1) | 50 542 (22 778–97 825) | 0·92 (0·41–1·78) | 4 635 636 (3 164 157–6 602 075) | 84·3 (57·5–120·0) |

UI=uncertainty interval. YLL=years of life lost. YLD=years lived with disability. DALY=disability-adjusted life-years.

*Table 2:* **Melioidosis global DALY distribution with breakdown per country in 2015**

appendix pp 32–33). Despite the burden per million DALYs of melioidosis being greater than that estimated for some of the officially recognised neglected and re-emerging tropical diseases by WHO, global investment for melioidosis is low (appendix pp 32–33).

Our scenario analysis, which represents differences between the WHO and GBD life expectancy tables alone, showed that DALY estimates were 11·7% higher with the WHO life expectancy table than with the GBD life expectancy table (appendix pp 25–27).

An incidence-based approach as opposed to a prevalence-based approach was preferred by the authors because it has been shown to provide a more reliable metric for infectious diseases.[19,25]

The results of our systematic review showed that incidence, mortality, and DALYs from melioidosis were approximately twice as high for men as for women, a similar finding to that in tuberculosis.[26] As with tuberculosis, several explanations have been given for the sex difference in melioidosis risk, such as differential occupational exposures, differential access to health care, differential exposure to risk factors, and genetic variation.[3,26] This interplay of risk factors and age–sex distribution of melioidosis cases, deaths, and DALYs has strategic implications for melioidosis control programmes by enabling high-risk groups to be targeted.

The gold standard for diagnosis of melioidosis is culture; therefore, we limited our case definition to only culture-confirmed melioidosis to reduce bias, and excluded cases confirmed by serological tests, which have low sensitivity and specificity.[3] However, the estimated sensitivity of culture of melioidosis is only 60·2%.[3] Future studies using more robust serological tests than those currently available could provide better estimates of the burden of melioidosis that could be incorporated into DALY calculations.

In 2015, the top four risk factors for melioidosis globally (diabetes or newly diagnosed hyperglycaemia, chronic renal disease, chronic liver disease or alcohol abuse, and chronic lung disease) were present in 46·1%, 9·3%, 7·4%, and 3·4% of melioidosis cases, respectively (appendix p 24). Thus, efforts to prevent these risk factors or provide a cost-effective vaccine targeted at at-risk groups such as rice farmers with diabetes, could have a substantial effect on the burden of melioidosis. While many countries go through demographic and epidemiological transitions, low-income and middle-income countries are particularly likely to be affected by the double burden of melioidosis and diabetes.[27] Global YLLs for diabetes increased by 45·3% between 1990 and 2015, rising from rank 27 to rank 15 in the GBD listing of top YLLs.[28] Diabetes is associated with a 12 times higher relative risk of acquiring melioidosis in endemic regions[3,10] and with the global diabetes pandemic, there is potential for the melioidosis burden to increase greatly, particularly in low-income and middle-income countries. In our analysis, HIV occurred in less than 1% of melioidosis cases, and did not appear to be associated with acquiring melioidosis, which is consistent with evidence from previous smaller cohorts.[3,29]

Our study has several limitations. Reliable incidence and mortality data for calculating the global burden of melioidosis were scarce. Therefore, the global case numbers of incidence and deaths were based on modelling of a comprehensive database of 22 338 geographically located records of human and animal melioidosis, alongside the presence of environmental *B pseudomallei*.[7] Because of the imperfections in data sources, we believe our method of integrating existing information and knowledge through a systematic literature review and data synthesis provides a more robust assessment of melioidosis epidemiology than has been done previously. We did not include all possible sequelae in our outcome tree designed to calculate DALYs because of paucity of data, particularly for the rarest sequelae. Specific disability weights were not available for most of the disease outcomes (eg, septic shock, sepsis, CNS infection, intra-abdominal abscess, musculoskeletal infection, urinary tract infection, parotitis, skin and soft tissue infection, and post-infectious sequelae) and proxy disease states were decided on the basis of the best matching descriptions and expert opinion. Further studies generating disability weights should include these missing disease outcomes. In particular, the absence of a disability weight for sepsis,[30] a critical illness that is associated with considerable disability, is a problem when calculating disease burdens. We believe that it is insufficient to use the severe acute infectious disease disability weight[30] for sepsis, given the mounting evidence of prolonged disability and involvement of organ dysfunction in sepsis (as stated in the definition in the Sepsis-3 guidelines).[31]

Few data were available for the outcomes of post-melioidosis sequelae, such as those following sepsis or septic shock, CNS infection, and musculoskeletal infection. Therefore, such outcomes were extracted through a review of additional published literature guided by an expert panel.[15-18] These post-infectious sequelae were modelled on the remaining life expectancy of survivors, but a shortened life expectancy was not accounted for. Although YLDs did not appear to contribute substantially to overall DALYs in melioidosis, we only accounted for a small number of post-infectious sequelae. Given that 86·8% (UI 70·2–95·2) of YLDs were caused by the post-infectious sequelae component, further studies on long-term disease outcomes are warranted. Because we used expert panel facilitation, the proportions of post-infection sequelae should be interpreted carefully.

We were unable to include any regional differences in disease presentation and sequelae, which could be linked to virulence,[3] because of scarcity of data. Additionally, because of the paucity of detailed data, we were unable to differentiate the transition between disease states, and therefore we assumed this to be similar across health-care systems globally. As yet, reactivation of latent melioidosis does not seem to play a major role in the total burden of melioidosis; however, data on this subject are scarce and we are unable to determine the exact rate of reactivation.

Furthermore, we did not account for trends of increasing or decreasing melioidosis incidence that could have occurred within and between countries, because of the small amount of data available. We found that extracting data from regional or national databases was not representative, as exemplified by data validation in

Thailand (appendix pp 4).[32] In addition, the nature of our study and modelling work only allowed us to generate estimates up to 2015. Extrapolation of estimates beyond this time point was considered, but it would have led to further widening of UIs. Accurate population estimates are also only available up to 2015, and we wanted to avoid the ambiguity of modelling estimates of estimates. To be consistent with using incidence and mortality rates for 2015, we only included data up to 2015 in our systematic review.[4] Despite these limitations, we believe the systematic methodology we have used has yielded more robust estimates than would otherwise have been obtained using limited source data of countrywide health statistics or vital registration forms.

Access to health care and sociodemographic development are associated with the burden of melioidosis in DALYs. In countries with an SDI score of less than 0·25, communicable causes account for 30–45% of total disability, with NTDs as a prominent contributor.[33] Of note, the majority of melioidosis-endemic countries have an SDI score of more than 0·25 (appendix pp 28–31). The association between SDI and HAQ Index and disease burden in DALYs can be used to identify outliers that have a discrepant relationship; these countries can be targeted for improvement, and can provide insights into which public interventions contribute towards narrowing the melioidosis burden. With this information, efforts that target factors other than those reflected in SDI scores (which include a reduction in income inequality, improved fertility, or increased years of education) could be made to improve life expectancy and reduce disease burden (all-age YLDs), emphasising the role of policy interventions beyond traditional health service delivery. For example, as SDI score increases, the proportion of the workforce that is in agriculture would be expected to decrease as countries transition to having fewer agriculutre-based jobs, which could reduce the burden of melioidosis because agricultural workers are at increased risk of the disease. Of note, SDI scores are still incomplete, because important features of societal function are missing (including political stability, gender equity, urbanisation, technology penetration, and infrastructure).[34] Because melioidosis is caused by a saprophytic organism, climate change will also affect geographical spread and incidence of the disease. Knowledge gaps in epidemiological parameters for melioidosis should be addressed. For instance, DALYs should be characterised according to seasonal changes, given the close relationship between melioidosis incidence and monsoons and severe weather events, which could guide future interventions.

Incidence data for melioidosis could vary depending on the surveillance system of the country (including whether it considers melioidosis a problem or not) and on the definition of cases by isolation of bacteria or detection by PCR or immunoassay.[30] Strengthening of melioidosis notification and vital registration systems is needed to improve the quality of data.[26] Until such systems are fully developed and integrated at national levels, variation in estimates is unavoidable. We hope that this analysis will highlight the burden of the disease to endemic countries, and the need to improve surveillance of melioidosis to adapt control measures. A key priority should be worldwide collaboration to improve and develop basic microbiological diagnostic facilities, and expand their capacity, to provide the foundations for gathering surveillance data.[35] The expansion of such facilities would have wider implications for other diseases and pathogens, including better clinical management of patients.

Global collaborations on NTDs, led by WHO, have resulted in the scale-up of control and elimination programmes, and enhanced access to medicines.[36] We propose that similar global efforts should be implemented for melioidosis because our estimates provide a clear rationale for considering melioidosis as a major NTD. Melioidosis also meets the criteria proposed by WHO for classifying a condition as an NTD: first, the disease disproportionally affects populations living in poverty, causing important morbidity and mortality; second, it primarily affects populations living in tropical and subtropical regions; third, it is amenable to broad control, elimination, or eradication strategies; and fourth, it is relatively neglected by research funding allocation.[37] Recognition of melioidosis as an NTD could increase international attention and much-needed funding for surveillance, research, and treatment of the disease. Because of the saprophytic nature of melioidosis and the fact that it can also affect a wide range of animal species, a One Health approach is warranted.

#### Contributors

EBi, HSV, BD, JAH, and WJW conceived the protocol. RS did the literature search. EBi, HSV, and JS collected the data. The expert panel consisted of DABD, DL, BD, JAH, and WJW. EBi and HSV synthesised the data. EBi, HSV, and BD did the statistical analyses and prepared all tables and figures. BD, JH, and WJW supervised the whole process. EBi, HSV, BD, JAH, and WJW prepared the first draft. All other authors gave critical feedback, provided guidance on methods, and reviewed the report.

#### Declaration of interests

We declare no competing interests.

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