



## REVIEW ARTICLE

# Melioidosis in Asia: Hidden burden, epidemiological distribution, vaccine and therapeutic prospects, and public health priorities

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## ABSTRACT

Melioidosis is an under-recognized tropical infectious disease caused by *Burkholderia pseudomallei*, an environmental pathogen that persists mainly in soil and surface water across tropical and subtropical regions. In Asia, the burden of melioidosis remains poorly defined because many cases are underdiagnosed, underreported, or clinically misclassified as tuberculosis, pneumonia, sepsis, or other bacterial infections. This narrative review examines the epidemiological distribution, transmission pathways, risk factors, vaccine and therapeutic developments, public health challenges, and future control strategies for melioidosis in Asia. Current evidence shows that Southeast Asia remains a major endemic region, while South Asia accounts for a substantial share of the modelled global burden of melioidosis. Reports from East Asia and other ecologically suitable areas suggest potential geographic expansion, particularly in relation to rainfall, flooding, extreme weather events, and climate change. Major risk factors include diabetes mellitus, chronic kidney disease, chronic lung disease, agricultural exposure, low socioeconomic status, and limited access to timely diagnosis and treatment. Although clinical management still depends on prolonged antimicrobial therapy, several vaccine candidates, including live-attenuated, recombinant, glycoconjugate, vesicle-based, and nanoparticle-based platforms, have shown protective effects in preclinical models. However, no licensed vaccine is currently available. Strengthening laboratory capacity, clinician awareness, notifiable disease surveillance, environmental monitoring, and integration with non-communicable disease programs is essential to improve detection and reduce mortality. An integrated One Health framework that links human, animal, and environmental health may support more effective surveillance, prevention, and control of melioidosis across Asia.

**Keywords:** Melioidosis; *Burkholderia pseudomallei*; epidemiology; vaccine; public health.

## INTRODUCTION

*Burkholderia pseudomallei* (*B. pseudomallei*) is an environmental pathogen that attacks humans and many different types of animals, causing a disease called melioidosis. The genus *Burkholderia* has more than 80 species, but only *Burkholderia pseudomallei*, *Burkholderia mallei*, *Burkholderia cepacia*, and *Burkholderia gladioli* are generally recognized as pathogens in the human body. *Burkholderia* is found in the rhizosphere, soil, and water of tropical and subtropical regions, so melioidosis is endemic to parts of Southeast Asia, northern Australia, and the Indian subcontinent (Birnie *et al.*, 2019). In these regions, the prevalence of *B. pseudomallei* infection occurs highest during the rainy season because there is a translocation from underground reservoirs

through the mobilization of bacteria by water in the soil. In addition, melioidosis is also related to socioeconomic factors that generally occur in individuals with certain comorbidities such as diabetes mellitus, cardiovascular disease, chronic lung disease, and chronic kidney disease (Prinsloo *et al.*, 2023).

*B. pseudomallei* is an aerobic Gram-negative bacterium that does not ferment and has no spores. *B. pseudomallei* infection can be latent, chronic, or acute through wounds to the skin, respiratory system, digestive system, and can even increase the risk of exposure to certain environmental conditions (tropical storms or farm workers). Exposure to *B. pseudomallei* does not necessarily result in infection or clinically apparent melioidosis. When infection is established, outcomes may range from asymptomatic or subclinical infection to localized, acute, chronic, or disseminated melioidosis.

Disease expression is influenced by host susceptibility, route and intensity of exposure, and bacterial factors (Wiersinga *et al.*, 2018; Meumann *et al.*, 2024). Delayed clinical presentation after remote exposure has been reported, but prolonged latency appears to account for only a minority of clinically recognized cases. Melioidosis has a wide spectrum of manifestations, thus making it the great mimicker, because it has clinical variability, so it is difficult to recognize and can resemble other bacterial infections and diseases such as tuberculosis (Kingsley *et al.*, 2016; Wiersinga *et al.*, 2018).

Globally, melioidosis is recognized as a disease with a high mortality rate ranging from 20-61%, especially in some cases that develop into sepsis (Kingsley *et al.*, 2016; Zueter *et al.*, 2016; Corea *et al.*, 2018; Mukhopadhyay *et al.*, 2018; Chowdhury *et al.*, 2022; Mohapatra & Mishra, 2022b; Hussin *et al.*, 2023). In some cases, *B. pseudomallei* may persist intracellularly and within deep-seated infectious foci, contributing to chronic disease or relapse, particularly when eradication therapy is inadequate. Recurrent melioidosis may represent either relapse with the original infecting strain or reinfection with a new strain; therefore, recurrence should not be attributed uniformly to bacterial dormancy (Lewis & Torres, 2016; Wiersinga *et al.*, 2018; Meumann *et al.*, 2024). Patients with certain comorbidities can increase their risk of death when infected with melioidosis, which is why Melioidosis is one of the infectious diseases with significant clinical and public health impacts. Melioidosis is widely regarded as a neglected tropical infection, and increasing calls have been made for its formal recognition within the global neglected tropical disease agenda because of its substantial mortality, underdiagnosis, and disproportionate burden in resource-limited settings (Meumann *et al.*, 2024).

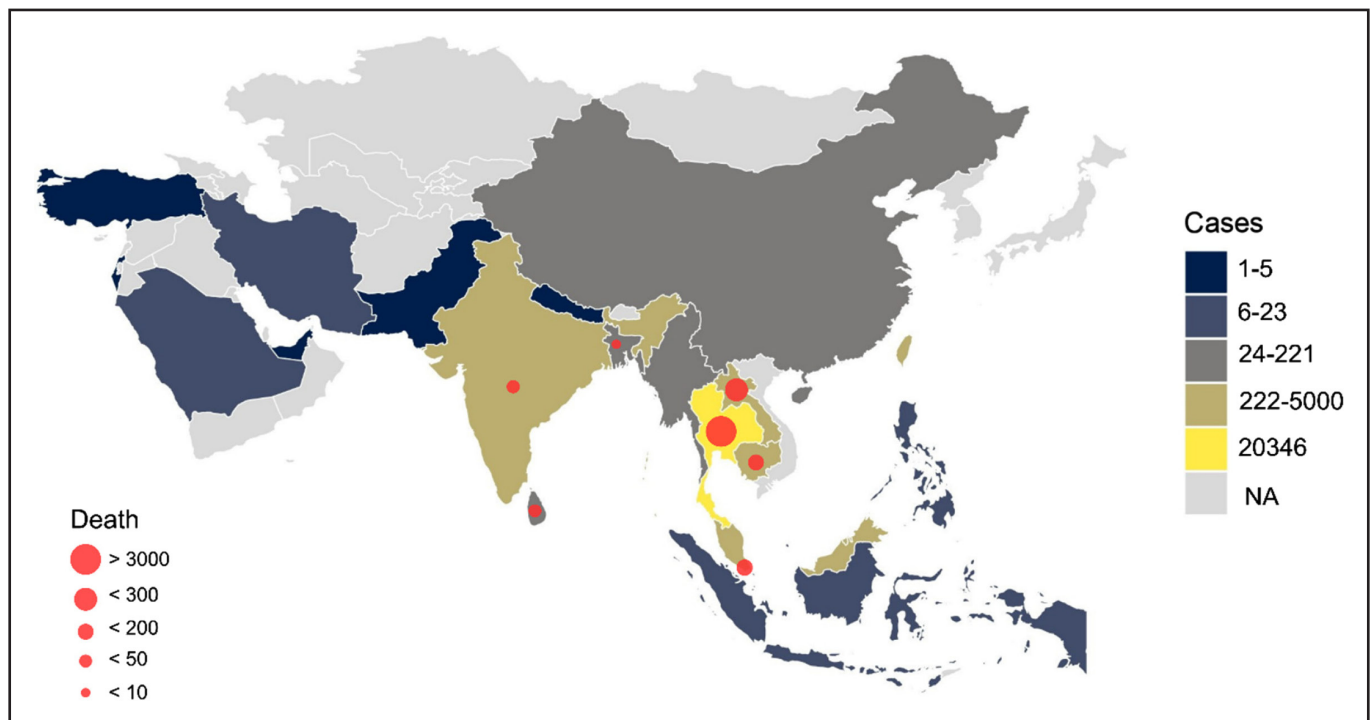
In recent years, the geographical distribution of melioidosis has expanded significantly, which is indicated by several reports from South Asia and has the potential to expand to East Asia in certain seasons (Selvam *et al.*, 2022). Even so, the available data cannot be used as a reference because it is still very limited. The limited data results in a hidden and expanding burden where many cases of

Melioidosis are not reported and diagnosed, so there is a possibility of geographical expansion of Melioidosis to new areas. This indicates that Melioidosis is not only a regional health problem, but also a global threat that is a serious challenge in the epidemiology of infectious diseases because it still receives less attention.

Through this complexity, this review article aims to explore the epidemiological distribution of melioidosis, especially its increasing burden on geographical distribution in the Asian continent. Current treatment strategies for melioidosis are still limited to antibiotic therapy, requiring a specific understanding of the immune response and bacterial persistence during *B. pseudomallei* infection. Understanding these mechanisms is expected to contribute to immunological targets for future vaccine development and alternative therapies to improve bacterial clearance and reduce mortality in melioidosis patients. Factors related to melioidosis are expected to be used to inform the public and those at risk of being affected regarding prevention and management. Therefore, a broader and more integrated review combining epidemiological perspectives and the One Health approach is needed to better understand the hidden and expanding burden of melioidosis in Asia.

### Epidemiological Distribution of Melioidosis in Asia

Geographically, the distribution of melioidosis in Asia is concentrated primarily in tropical regions. Based on data compiled from the global melioidosis database (<https://melioidosis.info>), reported cases and estimated deaths of melioidosis in Asia from 1910 to 2024 show an uneven distribution across the continent, with the highest concentration observed in Southeast Asia and a substantial burden also identified in South Asia (Figure 1). This database-based mapping provides an overview of the geographic distribution of melioidosis and helps illustrate the hidden and expanding burden of the disease in Asia. Therefore, Figure 1 is presented as an initial reference before discussing country-specific epidemiological studies that further explain the distribution pattern, endemicity, and regional burden of melioidosis.



**Figure 1.** Geographic distribution of melioidosis cases and deaths in Asia (1910–2024). The map illustrates the distribution of reported melioidosis cases and estimated deaths across Asia, with color gradients representing case numbers and circle size indicating mortality burden. Data were compiled from the global melioidosis database (<https://melioidosis.info>) covering the period 1910–2024.

In line with the distribution shown in Figure 1, Southeast Asia is recognized as the main hyperendemic center of the disease (Limmathurotsakul *et al.*, 2016; Zhu *et al.*, 2020). In this region, Thailand, particularly northeastern Thailand, is one of the areas with the highest endemicity, accompanied by reports of high prevalence in Cambodia, as well as an increase in the identification of cases in Myanmar and Vietnam (Selvam *et al.*, 2022). Malaysia is also an important region in the regional distribution, while in Indonesia reported cases remain limited, although case findings in Makassar and suspected endemicity in Riau Province suggest that the disease's distribution is likely wider than what has been documented (Anggraini *et al.*, 2024). This pattern confirms that Southeast Asia remains the primary geographic epicenter of melioidosis in Asia.

South Asia is estimated to account for approximately 44% of the global melioidosis burden, highlighting the region as an important area for studying the disease despite potential underreporting in some countries (Limmathurotsakul *et al.*, 2016). In East Asia, melioidosis is mainly found in southern China, including Hainan, Guangdong, Guangxi, Fujian, and Taiwan, where *B. pseudomallei* has been reported since the 1970s (Zheng *et al.*, 2021). Phylogenetic studies show that most isolates from China are grouped with those from Southeast Asia and are closely related to isolates from Thailand, Malaysia, and Vietnam. This suggests a regional connection in the distribution of the pathogen across these areas (Zhu *et al.*, 2020; Zheng *et al.*, 2021).

Furthermore, the distribution of melioidosis across Asia is shaped by seasonal influences, especially within monsoon climates. Areas such as Hainan, which are characterized by heavy rainfall, cyclones, and tropical environmental conditions, are thought to increase exposure to *B. pseudomallei*, thereby affecting the timing and occurrence of cases (Zheng *et al.*, 2021). Consequently, the geographical distribution of melioidosis in Asia not only delineates the concentration of hyperendemic regions in Southeast Asia but also identifies South Asia as a region with a significant disease burden, and East Asia as a region ecologically, phylogenetically, and seasonally connected to the disease's epicenter in Southeast Asia. These ecological interactions and seasonal fluctuations ultimately form the basis for the significant variations in the incidence and mortality rates of melioidosis across different regions.

The estimated incidence and mortality burden of melioidosis varies substantially across countries and settings. These differences are influenced by disease endemicity, diagnostic capacity, quality of medical care, and the overall health status of the population. A global geospatial modelling study estimated that, in 2015, approximately 165,000 human melioidosis cases occurred worldwide (95% credible interval, 68,000-412,000), resulting in an estimated 89,000 deaths (36,000-227,000) (Limmathurotsakul *et al.*, 2016). However, the actual number of cases is probably higher than reported because of incorrect diagnoses and underreporting, especially in tropical areas (Zhu *et al.*, 2020; Zheng *et al.*, 2021; Selvam *et al.*, 2022). Case fatality rates also remain high, with global estimates ranging from 30–50%, generally reaching up to 40%, exceeding 70% when antimicrobial therapy is ineffective, and reaching 90% in patients with severe sepsis (Zheng *et al.*, 2021; Kain *et al.*, 2024). Northeastern Thailand remains one of the best-characterized endemic settings in Asia, with more than 2,000 culture-confirmed cases diagnosed annually in hospitals with microbiology facilities and a reported mortality rate of approximately 35% (Hinjoy *et al.*, 2018; Arushothy *et al.*, 2020; Selvam *et al.*, 2022; Kain *et al.*, 2024). Singapore reported 550 cases over a ten-year period, with an annual incidence of 0.6–2.4 per 100,000 between 2000 and 2015, and approximately one-fifth of cases resulted in death. In contrast, less than 1% of global deaths occur in high-income countries such as Singapore, Brunei Darussalam, and Australia, highlighting the significant impact of healthcare systems on patient outcomes (Limmathurotsakul *et al.*, 2016; Selvam *et al.*, 2022).

Conversely, more than 99% of melioidosis deaths occur in low- and middle-income countries (Limmathurotsakul *et al.*, 2016). In Indonesia, the true burden likely surpasses what is captured in standard reports. Annual estimates suggest more than 20,000 cases and more than 10,000 deaths, with an overall case-fatality rate of approximately 43% (Tauran *et al.*, 2018). This figure is consistent with the 41% rate documented in Riau Province in 2024, and it surpasses the 23% rate observed in China and the 33% rate in Malaysia (Anggraini *et al.*, 2024; Kusumawati *et al.*, 2025). Furthermore, Malaysia experiences a substantial mortality burden, with annual deaths exceeding 2,000, a number that surpasses fatalities from both dengue fever and tuberculosis. In Myanmar, *B. pseudomallei* is implicated in 1.1% of sepsis cases (Arushothy *et al.*, 2020; Kain *et al.*, 2024). By contrast, areas with stronger clinical recognition and management, such as the Northern Territory of Australia, demonstrate a mortality rate as low as 6%, while mortality remains at 17–18% among immunocompromised groups in Darwin. Moreover, in Northern Cambodia, the in-hospital mortality rate for children is 11.5% (Kain *et al.*, 2024; Norman *et al.*, 2024). These findings suggest that differences in mortality rates across countries reflect not only disease virulence but also disparities in early detection, access to therapeutic intervention, and availability of intensive care resources.

The distribution and occurrence of melioidosis are associated with a range of climatic and environmental factors. High rainfall is closely associated with increased incidence, as seen in Hainan, which showed a strong correlation between monthly rainfall and melioidosis cases, and in Darwin, where every additional 100 mm of rainfall increased incidence by 14%. Humidity, wind, and temperature are also important factors. For example, in Laos and Cambodia, more cases are seen when humidity and wind are high (Bulterys *et al.*, 2018). In Vietnam, the prevalence of *B. pseudomallei* increases during the summer (Vu *et al.*, 2025). Furthermore, typhoons, storms, and floods may increase human exposure by aerosolizing and spreading bacteria from contaminated soil and water, as shown in Taiwan and Australia (Merritt & Inglis, 2017; Ganeshalingam *et al.*, 2023; Chen *et al.*, 2025). Rainfall, flooding, humidity, and severe weather events have been associated with increased melioidosis incidence or environmental exposure in several endemic settings. Climate change may alter environmental conditions relevant to the persistence and geographic suitability of *B. pseudomallei*, but the magnitude and direction of future geographic expansion remain uncertain and require longitudinal environmental and clinical validation (Birnie *et al.*, 2022; Meumann *et al.*, 2024; Abrantes *et al.*, 2025; Li *et al.*, 2025).

### The Hidden Burden: Underdiagnosis and Underreporting

Melioidosis affects populations with low and middle socioeconomic backgrounds. This is the reason why most deaths from melioidosis occur in low-income countries. In countries in the South Asian region, there are two regions where melioidosis is categorized as an endemic disease, Bangladesh and Sri Lanka. Several publications from Bangladesh and Sri Lanka reported that there were more than 220 cases, while case studies in Pakistan showed that the presence of *B. pseudomallei* bacteria was obtained from soil samples in Lahore. The first case in Pakistan was reported in 1970 when a person developed diabetes with sternal sinuses and was investigated for four years, but was only diagnosed after being in London, England. Some cases of melioidosis in England and Wales were reported to be half of them from South Asia (Bangladesh, India, and Pakistan) before 1999.

From some of these cases, it was found that melioidosis has been very common in parts of South Asia for more than five decades, but it has been underdiagnosed, which means that melioidosis is not yet a notifiable disease in some countries. If melioidosis is not yet included in the notifiable disease, it is difficult to comprehensively describe the geographic distribution, thus causing a significant

gap between actual data and global estimates (Selvam *et al.*, 2022). Based on Gee *et al.* (2022), several cases of transmission of *B. pseudomallei* in the United States occurred through lavender and chamomile aromatherapy sprays imported from India. In addition to South Asia, melioidosis is also common in Southeast Asian countries such as Indonesia, Malaysia, Singapore, Thailand, Vietnam, and Myanmar.

The lack of diagnosis and reporting of melioidosis cases can occur through a variety of factors. In the case of the Indian region, the lack of awareness among doctors and microbiologists and the lack of laboratory support led to missed diagnosis, resulting in inappropriate drug management (Mukhopadhyay *et al.*, 2018). In addition, the reason melioidosis is a neglected disease is that the likelihood of spreading between humans is very small, however, the mortality rate that remains high in endemic areas can be significantly reduced through global control measures. Underdiagnosis and underreporting are shown in Table 1.

In most endemic areas of melioidosis, some doctors do not consider the disease in their diagnosis, so the future consequences can be potentially serious. A retrospective study at a district hospital in Perak, Malaysia, found that only 39.4% of culture-confirmed melioidosis patients initially received ceftazidime or a carbapenem as empirical therapy, illustrating the clinical consequences of low early suspicion for melioidosis (Nathan *et al.*, 2018; Tang *et al.*,

2019). Although several studies state that Indonesia is one of the endemic countries for melioidosis disease in Southeast Asia, the disease is rarely reported. One of the fatal cases occurred in 2015, where acute appendicitis became the initial clinical diagnosis in Melioidosis cases, then there were indications of pancreatitis and several other diseases that eventually led to sepsis accompanied by pneumonia (Tauran *et al.*, 2018). There was a delay in therapy due to the continuing deteriorating clinical condition, even though *B. pseudomallei* could be identified 2 weeks earlier before death. Misdiagnosis in some case reports in the Asian region is shown in Table 2. To find this out, of course, laboratory regulations are needed to confirm the correct diagnosis of melioidosis. However, geographical mapping of the distribution of *B. pseudomallei* is highly unlikely due to the lack of bacterial cultures of specimens in rural endemic areas where melioidosis is common, as well as challenges in isolating bacteria from environmental samples.

Medical laboratories are among the first facilities to support healthcare, but often laboratory facilities are underdeveloped or even not found in some low- and middle-income countries, especially remote and rural areas with high Melioidosis. However, in addition to inadequate laboratory facilities, many laboratory personnel or laboratory staff in charge are not familiar with *B. pseudomallei*, so many are misidentified as *Pseudomonas* species or only considered as a contaminant (Greer *et al.*, 2019). Although there are currently

**Table 1.** Reported Evidence and Diagnostic Visibility of Melioidosis in Asian Regions

| Asia Region    | Reported Evidence                        | Country                                           | Characteristics                                                                                             | Epidemiological                                                                                       | Reference                                                                                                |
|----------------|------------------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| Southeast Asia | Extensive to moderate                    | Thailand, Malaysia, Vietnam, Myanmar, Singapore   | Many clinical case reports and epidemiological studies; Thailand and Malaysia have annual incidence data    | High reported evidence; underreporting may still occur; relatively good reporting, but underreporting | Kingsley <i>et al.</i> , 2016; Limmathurotsakul <i>et al.</i> , 2016                                     |
|                | Moderate                                 | Brunei, Cambodia, Laos                            | Case reports are available, but the number of studies is limited; data based on local hospitals or research | Possible endemic, but underdiagnosed                                                                  | Kingsley <i>et al.</i> , 2016; Limmathurotsakul <i>et al.</i> , 2016; Turner <i>et al.</i> , 2016        |
|                | Limited                                  | Indonesia, Philippines                            | Few published case reports; available evidence is largely based on individual case reports                  | High underdiagnosis with more chances of original cases                                               | Kingsley <i>et al.</i> , 2016; Limmathurotsakul <i>et al.</i> , 2016; San Martin <i>et al.</i> , 2018    |
| South Asia     | Moderate and increasing                  | India (Odisha, Tamil Nadu), Sri Lanka, Bangladesh | In the last decade there has been an increase in publications; studies show fairly high exposure            | Increasing recognition and evidence of local transmission, although underreporting remains a concern  | Corea <i>et al.</i> , 2018; Limmathurotsakul <i>et al.</i> , 2016                                        |
|                | Limited to very limited                  | Nepal, Pakistan                                   | Case reports are very limited                                                                               | High underreporting with limited laboratory facilities                                                | Limmathurotsakul <i>et al.</i> , 2016; Mukhopadhyay <i>et al.</i> , 2018; Bhattarai <i>et al.</i> , 2024 |
| East Asia      | Moderate but geographically concentrated | South China, Taiwan, Hong Kong                    | Case reports in the form of imported cases                                                                  | Not an endemic area, but limited local potential                                                      | Lui <i>et al.</i> , 2018                                                                                 |
|                | Very limited                             | Korea, Japanese                                   | Case reports are mostly imported cases                                                                      | Not endemic territory                                                                                 | Limmathurotsakul <i>et al.</i> , 2016; Hadano, 2018; Lee <i>et al.</i> , 2023                            |
| West Asia      | Very limited                             | Saudi Arabia                                      | Case reports describe pneumonia, sepsis, or abscess; frequently associated with travel history              | Not endemic territory; sporadic and mostly imported, possible underdiagnosis                          | Alwarthan <i>et al.</i> , 2018; Alhatmi <i>et al.</i> , 2020; Almarhabi <i>et al.</i> , 2022             |

Note: Evidence categories reflect the density and diagnostic visibility of published evidence only. They are not standardized measures of incidence, prevalence, mortality, or endemicity and should not be used to rank the true disease burden between regions.

**Table 2.** Common Diagnostic Mimics and Reported Misdiagnosis Patterns of Melioidosis in Asia

| Region         | Reported Mimic         | Reported Evidence                                                                      | Remarks                             | Reference                                                                                                       |
|----------------|------------------------|----------------------------------------------------------------------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| Southeast Asia | Tuberculosis           | Chronic lung cases; exact proportion varies by study                                   | Tuberculosis-like signs             | Shrestha <i>et al.</i> , 2019; Mohapatra & Mishra, 2022a; Kannan <i>et al.</i> , 2025                           |
|                | Pneumonia              | Frequently reported as an initial clinical diagnosis; exact proportion varies by study | Often considered a regular CAP      | Tipre <i>et al.</i> , 2018; Nguyen <i>et al.</i> , 2022; Mohapatra & Mishra, 2022a; Kannan <i>et al.</i> , 2025 |
| South Asia     | Tuberculosis           | Very high                                                                              | The most common misdiagnoses        | Shrestha <i>et al.</i> , 2019; Mohapatra & Mishra, 2022a; Kannan <i>et al.</i> , 2025                           |
|                | Pneumonia              | Significant (no exact number)                                                          | Clinically difficult to distinguish | Tipre <i>et al.</i> , 2018; Nguyen <i>et al.</i> , 2022; Mohapatra & Mishra, 2022a; Kannan <i>et al.</i> , 2025 |
|                | Other bacterial sepsis | Non-specific                                                                           | Systemic presentation               | Shrestha <i>et al.</i> , 2019; Gangil <i>et al.</i> , 2025                                                      |
| East Asia      | Pneumonia              | Dominant                                                                               | More imported cases                 | Lee <i>et al.</i> , 2023                                                                                        |
|                | Tuberculosis           | Sporadic                                                                               | Non-dominant cases                  | Lee <i>et al.</i> , 2023                                                                                        |
| West Asia      | Tuberculosis           | Sporadic                                                                               | TB-like chronic presentation        | Alwarthan <i>et al.</i> , 2018                                                                                  |

modern automated systems for identifying *B. pseudomallei* through laser desorption ionization mass spectrometry, they can also be systematically incorrect in identifying *B. pseudomallei* if the database is not suitable. The standard in diagnostics can be the culture and isolation of *B. pseudomallei* from clinical specimens.

#### Transmission, Risk Factors, and Vulnerable Populations in Asia

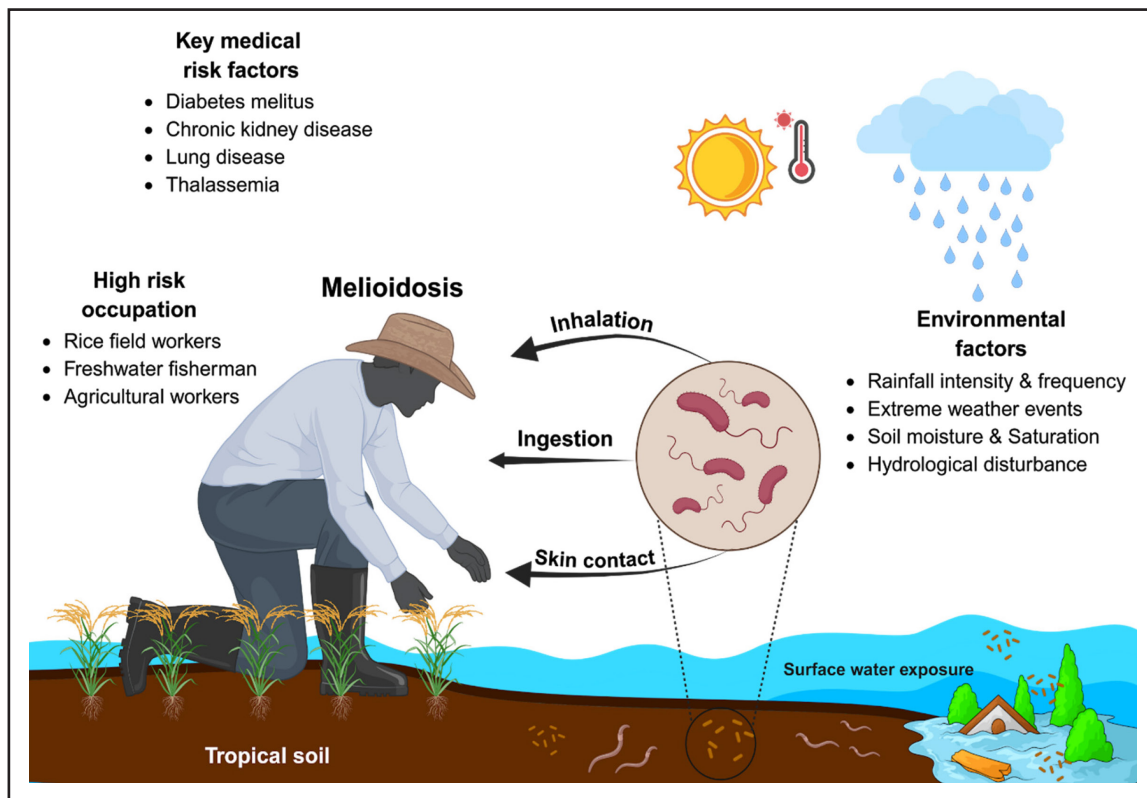
The bacterium *B. pseudomallei* thrives in moist soil and surface water, especially in Southeast and South Asia (Selvam *et al.*, 2022). People can get the disease through skin contact, inhaling aerosols, or drinking contaminated water (Chowdhury *et al.*, 2022). Mild cases are often not diagnosed. As a result, the actual impact of the disease is likely much greater than what is currently known (Hanson *et al.*, 2021). Among the various factors influencing susceptibility to infection through these transmission routes, diabetes mellitus stands out as the most significant risk factor. Studies show that about 45–50% of people with melioidosis have a history of diabetes (Chowdhury *et al.*, 2022; Selvam *et al.*, 2022). High blood sugar levels weaken the immune system, particularly neutrophils' ability to engulf and destroy pathogens. This increases the likelihood that *B. pseudomallei* will cause a widespread infection (Birnie *et al.*, 2022). Clinical studies from endemic settings indicate that diabetes may influence the clinical phenotype of melioidosis, with patients with diabetes showing a greater frequency of visceral abscesses and disseminated disease in some cohorts (Prideaux *et al.*, 2025). Some argue that preventing melioidosis requires more than just clinical management of diabetes. Environmental exposure must be controlled simultaneously.

Exposure to soil and surface water increases vulnerability. Rice field workers, freshwater fishermen, and agricultural workers face high infection risk (Chowdhury *et al.*, 2022; Selvam *et al.*, 2022). Occupational exposure to soil and surface water, particularly among rice farmers, is a well-established risk factor for melioidosis in Thailand (Suputtamongkol *et al.*, 1999). Holistic prevention strategies are essential. Evidence suggests that using personal protective equipment, community education, and environmental management lowers disease. These non-medical interventions, while critical, are often neglected in endemic regions. Seasonal rainfall and natural disasters further amplify risks. Specifically, heavy rainfall pushes *B. pseudomallei* upwards in soil and water (Zheng *et al.*, 2023; Norman *et al.*, 2024). A significant correlation ( $r \approx 0.74$ ) exists

between monthly rainfall and melioidosis in Hainan, China (Chen *et al.*, 2025). Flooding increases bacterial contact and widens the disease range, promoting aerosol transmission. Recent discussions highlight weather-based prediction systems as innovative but not yet widely used tools for prevention and resource allocation (Norman *et al.*, 2024). Therefore, the transmission of melioidosis in endemic regions reflects the combined influence of environmental reservoirs, occupational exposure, climatic variation, and host susceptibility, as summarized in Figure 2.

Other coexisting health conditions also significantly affect vulnerability to melioidosis. Chronic kidney disease, lung disease, thalassemia, and immunodeficiency disorders greatly increase the risk of infection and related complications (Birnie *et al.*, 2022; Selvam *et al.*, 2022; Norman *et al.*, 2024). As a result, patients with these conditions are more likely to experience severe clinical outcomes, including organ failure (Prideaux *et al.*, 2025). Recent research also shows that comorbidity identification and management should not be limited to hospital-based care, but should also involve community-level strategies, especially in endemic areas where exposure risk remains high (Chowdhury *et al.*, 2022). This approach is important because vulnerable populations often face overlapping risks, including medical susceptibility, repeated environmental exposure, and limited access to timely diagnosis and treatment.

Socioeconomic factors further widen the risk gap between vulnerable and general populations. Communities with low educational levels, limited healthcare access, and low socioeconomic status are more frequently exposed to melioidosis and have higher mortality rates (Mukhopadhyay *et al.*, 2018; Hanson *et al.*, 2021). To address these issues, prevention strategies should directly target social determinants of health, including sanitation improvement, workplace safety, access to protective equipment, and broader healthcare access. Community education, environmental management, and personal protective equipment are important non-medical interventions, but they are often neglected in endemic regions. Recent studies also highlight the importance of combining targeted social interventions with clinical prevention methods to reduce both incidence and mortality. Interventions that focus on communities and the environment are more effective than approaches that rely on a single clinical strategy alone (Mohapatra & Mishra, 2022b).



**Figure 2.** Transmission pathways and risk factors of melioidosis in Asia. The figure illustrates the environmental transmission of *B. pseudomallei* from tropical soil and surface water through percutaneous inoculation and inhalation, particularly during rainfall and extreme weather events. Agricultural workers are at increased risk due to frequent exposure, while climatic factors further enhance transmission and susceptibility in endemic regions. (Created with BioRender).

The reviewed evidence suggests that melioidosis in Asia is driven by complex interactions among biological, environmental, seasonal, medical, occupational, and socioeconomic determinants. Multidimensional prevention strategies are therefore needed to reduce disease burden in endemic regions. These strategies should include comprehensive diabetes management, routine identification of comorbidities, environmental protection, use of personal protective equipment among high-risk workers, community education, and weather-based seasonal forecasting. A combined approach may improve prevention, support earlier public health response, and help reduce the health gap between vulnerable and general populations in endemic regions.

#### Vaccines and Therapeutics

The development of effective vaccines and therapeutic strategies for melioidosis remains a major priority because *Burkholderia pseudomallei* causes severe disease, is difficult to diagnose early, and requires prolonged antimicrobial treatment (Wiersinga et al., 2018; Meumann et al., 2024). Its close genetic and antigenic relationship with *Burkholderia mallei*, the causative agent of glanders, also supports the development of cross-protective countermeasures against both pathogens (Sengyee et al., 2025). Although no licensed vaccine is currently available, several candidates have shown promising protection in preclinical animal models. To provide a focused overview, Table 3 summarizes selected vaccine candidates that demonstrated notable protective effects in animal challenge studies. The table includes representative platforms such as live-attenuated vaccines, recombinant vector-based vaccines, glycoconjugate and recombinant subunit vaccines, membrane vesicle-based formulations, and nanoparticle-based antigen delivery systems. These examples are intended to highlight major vaccine approaches, animal models, challenge strains, protection levels, and references rather than provide an exhaustive list of all melioidosis vaccine studies.

Based on Table 3, live-attenuated vaccine candidates have generated strong protective signals in several preclinical melioidosis models. Their broad antigenic exposure may induce multiple immune responses. Several candidates, including *B. mallei* batA KO mutant, *B. pseudomallei* 668 mutant derivatives, and *B. pseudomallei*  $\Delta$ tonB  $\Delta$ hcp1/PBK001, showed substantial acute or chronic protection in mouse models. However, their strong immunogenicity must be balanced against safety concerns, particularly the possibility of persistence, reversion to virulence, or infection in immunocompromised hosts (Bergstrom et al., 2024; Meumann et al., 2024). Therefore, safer platforms have also been developed, including recombinant vector-based vaccines such as rLVS  $\Delta$ capB formulations expressing selected *B. pseudomallei* antigens, which showed encouraging survival outcomes and long-term protection in animal models.

However, the protection levels reported in Table 3 should not be directly compared across vaccine platforms because the studies used different animal models, challenge strains, challenge routes, challenge doses, and observation periods. For example, the  $\Delta$ tonB  $\Delta$ hcp1/PBK001 live-attenuated candidate achieved 100% survival following aerosol challenge in C57BL/6 mice, whereas several recombinant vector candidates were evaluated using intranasal challenge in BALB/c mice. Similarly, nanoparticle-based candidates showed different survival outcomes depending on challenge dose, with some formulations providing higher protection against low-dose than high-dose challenge. These differences highlight that reported survival percentages are context-dependent and should be interpreted as evidence of protection under specific experimental conditions rather than as directly comparable measures of vaccine efficacy.

Defined antigen-based, vesicle-based, and nanoparticle-based approaches also show strong potential as safer vaccine strategies. In Table 3, CPS-CRM197-based formulations, recombinant subunit BpOmpW with SAS adjuvant, *B. pseudomallei* Bp82 outer

**Table 3.** Comparative Summary of Representative Preclinical Melioidosis Vaccine Platforms, Experimental Models, and Protective Outcomes

| Vaccine Platform and Representative Candidates                                                                                       | Experimental Model and Challenge Model                                                                                                                                                | Protection                                                                                                                                                                                                                      | Reference                                                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Live-attenuated:<br><i>B. mallei</i> batA KO;<br><i>B. pseudomallei</i> 668 mutants;<br><i>B. pseudomallei</i> ΔtonB<br>Δhcp1/PBK001 | BALB/c and C57BL/6 mice;<br>challenges included <i>B. mallei</i><br>ATCC 23344 and <i>B. pseudomallei</i><br>1026b or K96243. Aerosol<br>challenge was used for<br>ΔtonB Δhcp1/PBK001 | Approximately 50-100% survival<br>depending on candidate, challenge<br>strain, and assessment period.<br>Selected candidates produced<br>sterile spleens, reduced organ<br>bacterial burden, or partial<br>sterilizing immunity | Zimmerman <i>et al.</i> , 2017;<br>Amemiya <i>et al.</i> , 2019;<br>Khakhum <i>et al.</i> , 2019 |
| Recombinant vector-based:<br>rLVS ΔcapB formulations<br>expressing Hcp6-Hcp1,<br>Hcp6-Hcp2, Hcp6-Hcp1-Hcp2,<br>or Hcp6-Hcp1-LolC     | BALB/c mice challenged with<br><i>B. pseudomallei</i> 1026b; intranasal<br>challenge, with intradermal<br>or intranasal immunization<br>evaluated in selected formulations            | Approximately 75–100% survival in<br>selected experimental conditions;<br>some formulations provided<br>long-term protection and<br>50–63% sterilizing immunity                                                                 | Tullius <i>et al.</i> , 2024                                                                     |
| Defined antigen-based:<br>CPS-CRM197, CPS-CRM197/Hcp1,<br>CPS-CRM197/TssM, and recombinant<br>BpOmpW with SAS adjuvant               | C57BL/6 or BALB/c mice<br>challenged with<br><i>B. pseudomallei</i> K96243<br>or strain 576                                                                                           | Approximately 67–100% survival<br>for CPS-based formulations;<br>CPS-CRM197/Hcp1 produced<br>70% sterilizing immunity.<br>BpOmpW produced 75% survival<br>in the evaluated models                                               | Casey <i>et al.</i> , 2016;<br>Burtneck <i>et al.</i> , 2018                                     |
| Membrane vesicle-based:<br><i>B. pseudomallei</i> Bp82 OMVs<br>and hcp1MV with or without<br>Freund's adjuvant                       | C57BL/6 and BALB/c mice and<br>rhesus macaques; challenges<br>included <i>B. mallei</i> China 7 or<br><i>B. pseudomallei</i> BPC006                                                   | Approximately 60–100% survival<br>depending on model. Selected<br>studies reported reduced pathology<br>or no detectable bacteria in target<br>organs at early post-infection<br>assessment                                     | Baker <i>et al.</i> , 2017;<br>Zhu <i>et al.</i> , 2022                                          |
| Nanoparticle-based:<br>AuNP-Flg-LPS, AuNP-Combo-LPS,<br>AuNP-OmpW-LPS, AuNP-OpcP-LPS,<br>AuNP-HA-LPS, and<br>AuNP-Combo2-LPS         | C57BL/6 mice challenged with<br><i>B. pseudomallei</i> K96243 or<br><i>B. mallei</i> 23344; low- and<br>high-dose challenges were<br>used in selected studies                         | Approximately 50–100% survival<br>depending on antigen combination<br>and challenge dose; selected<br>formulations reduced lung<br>colonization or bacterial burden<br>in the lungs and liver                                   | Muruato <i>et al.</i> , 2017;<br>Tapia <i>et al.</i> , 2020                                      |

Note: All vaccine candidates summarized in this table remain at the preclinical stage, and reported survival or protection rates from animal challenge studies should not be interpreted as evidence of clinical efficacy in humans.

membrane vesicles, hcp1MV, and AuNP-LPS antigen combinations demonstrated varying levels of protection in BALB/c mice, C57BL/6 mice, and rhesus macaques. These findings suggest that antigen selection, adjuvant formulation, and delivery system design strongly influence vaccine efficacy. In particular, vesicle-based and nanoparticle-based formulations may improve antigen presentation and immune stimulation while avoiding some limitations associated with live-attenuated vaccines.

A central challenge in melioidosis vaccine development is the identification of reliable immune correlates of protection. Because *B. pseudomallei* is a facultative intracellular pathogen and also expresses important surface polysaccharides, protection likely requires both humoral and cellular immunity (Wiersinga *et al.*, 2018; Meumann *et al.*, 2024). Antibodies against conserved polysaccharide antigens such as CPS and OPS/LPS may support opsonophagocytosis, complement activation, and bacterial clearance. At the same time, T cell-mediated responses are needed to control intracellular infection and reduce bacterial persistence in deep tissues (Bergstrom *et al.*, 2024; Sengyee *et al.*, 2025). The candidates summarized in Table 3 support this concept because the most promising formulations generally combine broad antigen exposure, defined antigen targeting, or enhanced delivery systems that can strengthen immune recognition.

Despite these preclinical advances, vaccine development remains incomplete, and clinical management still depends on prolonged antimicrobial therapy. Current treatment generally involves an intensive phase with intravenous ceftazidime or meropenem for 10 to 14 days, followed by an eradication phase using oral co-trimoxazole for 3 to 6 months (Wiersinga *et al.*, 2018;

Meumann *et al.*, 2024; Sengyee *et al.*, 2025). This long treatment course is needed because *B. pseudomallei* can persist intracellularly, form deep-seated abscesses, and relapse when eradication therapy is inadequate (Meumann *et al.*, 2024; Oliveira *et al.*, 2024). Clinical management also remains difficult because of delayed diagnosis, severe sepsis, limited access to microbiological confirmation, and poor adherence during the eradication phase (Wiersinga *et al.*, 2018; Meumann *et al.*, 2024). These limitations show why vaccine development remains important, especially for populations in endemic areas and individuals with high-risk conditions.

Recent preclinical studies suggest that future control strategies may need to combine vaccination with post-exposure antibiotic therapy. In this approach, vaccination primes protective immunity, while antibiotics suppress early bacterial growth and reduce systemic spread (Sengyee *et al.*, 2025). Vaccine candidates based on defined antigens and improved delivery platforms may therefore support integrated prevention and treatment strategies when combined with appropriate antimicrobial therapy. However, these strategies remain preclinical and require further validation in models that reflect high-risk human populations, including diabetic and immunocompromised hosts (Wiersinga *et al.*, 2018; Meumann *et al.*, 2024). Overall, the most feasible future direction is an integrated vaccine-therapeutic approach that can reduce mortality, prevent relapse, and support melioidosis control in endemic and high-risk settings (Meumann *et al.*, 2024; Sengyee *et al.*, 2025).

#### Public Health Challenges

Melioidosis remains a significantly under-recognised bacterial infection in Asia, despite its severity, high mortality, and expanding

geographic distribution (Mukhopadhyay *et al.*, 2018). The public health burden of the disease is driven not only by its clinical complexity, but also by persistent challenges in clinical recognition, laboratory diagnosis, surveillance, treatment adherence, and policy prioritisation. These challenges limit timely case detection, obscure accurate estimation of disease burden, and weaken coordinated public health responses. As a result, melioidosis continues to be underestimated in many endemic and potentially endemic settings, particularly in resource-limited areas where diagnostic and surveillance systems remain insufficient (Mohapatra & Mishra, 2022a; Selvam *et al.*, 2022).

Clinical recognition and laboratory diagnosis represent major barriers to effective control. Melioidosis presents with non-specific and variable clinical features that may resemble tuberculosis, pneumonia, sepsis, or other common infections. This clinical similarity reduces early suspicion and may lead to delayed or inappropriate treatment, thereby increasing the risk of severe disease and mortality (Dance & Limmathurotsakul, 2018). The problem is further compounded by limited microbiological resources, particularly in rural and resource-constrained areas, where culture facilities may be unavailable and *B. pseudomallei* may be misidentified or overlooked. These diagnostic limitations perpetuate underdiagnosis and obscure the true epidemiological burden of melioidosis.

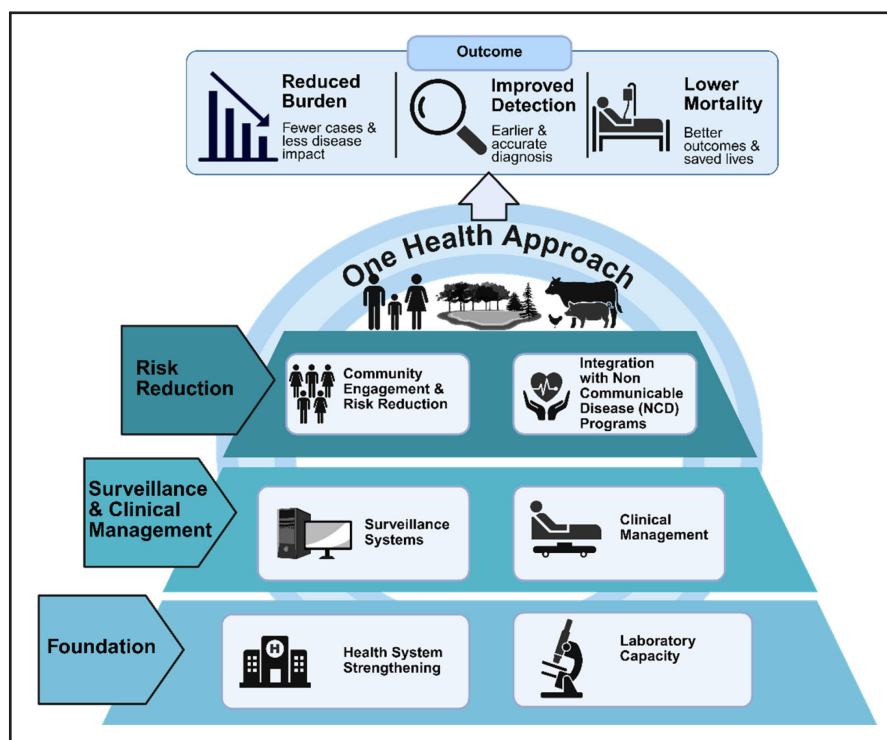
Surveillance and reporting systems also remain major public health weaknesses. In many Asian countries, melioidosis is not consistently included as a notifiable disease, and reporting systems are often fragmented across health facilities, laboratories, and public health authorities. This situation contributes to substantial underreporting and weak policy prioritisation. At the same time, the burden of disease is amplified by the high prevalence of diabetes, occupational exposure to soil and surface water, and environmental conditions that favour the persistence and transmission of *B. pseudomallei* (Selvam *et al.*, 2022). Seasonal rainfall, flooding, and contaminated soil and water reservoirs further complicate

prevention because transmission risk changes across time and geographic areas (Birnie *et al.*, 2022).

Complex treatment regimens, inadequate follow-up, and limited policy attention further constrain melioidosis control. Treatment requires prolonged antimicrobial therapy, and poor adherence may increase the risk of relapse, recurrence, and additional financial burden, especially in resource-limited settings. These challenges are intensified by insufficient awareness among healthcare providers and communities, as well as the continued marginalisation of melioidosis within national and regional public health agendas (Chowdhury *et al.*, 2022; Dance & Limmathurotsakul, 2018). Therefore, public health responses to melioidosis must address not only clinical management, but also diagnostic capacity, surveillance strengthening, community awareness, environmental risk reduction, treatment adherence, and sustained policy commitment. These interconnected challenges provide the basis for developing integrated strategies to address the expanding burden of melioidosis in Asia.

### Strategies to Address the Expanding Burden

The persistent underrecognition and expanding geographic distribution of melioidosis in Asia necessitate a coordinated and multidimensional response (Limmathurotsakul *et al.*, 2016). The complexity of the disease driven by diagnostic limitations, weak surveillance systems, environmental exposure, and policy neglect cannot be addressed through isolated interventions. Instead, an integrated strategy is required, combining health system strengthening, surveillance reform, clinical improvement, and cross-sectoral collaboration (Yopa *et al.*, 2023). Within this framework, the One Health approach provides a unifying perspective that links human, environmental, and animal health. The integrated framework shown in Figure 3 provides a conceptual overview of how these strategies can be organized into foundational, surveillance and clinical, and risk-reduction levels to achieve improved detection, reduced burden, and lower mortality.



**Figure 3.** Integrated strategy framework for melioidosis control in Asia. The figure illustrates a multi-layered strategy comprising foundational health system strengthening and laboratory capacity, integrated surveillance and clinical management, and risk reduction through community engagement and integration with NCD programs. A One Health approach underpins all levels, linking human, environmental, and animal health to address transmission dynamics and improve control. Collectively, these coordinated interventions aim to achieve reduced disease burden, improved detection, and lower mortality. (Created with BioRender).

Strengthening diagnostic capacity represents a foundational step in addressing the expanding burden of melioidosis, particularly at district and provincial healthcare levels. Although microbiological culture remains the cornerstone of diagnosis, it should be supported by improved laboratory training, standardized identification protocols, quality assurance, referral systems, and the introduction of rapid diagnostic tools where feasible (Miller *et al.*, 2018). These measures are essential to reduce misidentification of *B. pseudomallei* and improve early case detection. At the same time, clinician awareness must be strengthened so that melioidosis is considered in the differential diagnosis of common infectious syndromes, including pneumonia, sepsis, abscesses, and tuberculosis-like presentations. Beyond diagnosis, robust and integrated surveillance systems are also needed to generate more accurate burden estimates. Incorporating melioidosis into national notifiable disease frameworks, strengthening reporting mechanisms, and improving data integration across laboratories, hospitals, and public health authorities can enhance epidemiological understanding and support more effective resource allocation and policy decision-making. Sentinel surveillance in high-risk settings, such as agricultural and flood-prone areas, may also provide early detection of emerging hotspots (Hantrakun *et al.*, 2019; Mariappan *et al.*, 2022).

In addition to diagnostic and surveillance strengthening, control strategies must address population vulnerability, clinical management, and policy commitment. The strong association of melioidosis with diabetes and occupational exposure highlights the need to integrate prevention with non-communicable disease programs and community-based interventions (Chowdhury *et al.*, 2018; Suntornsut *et al.*, 2021). Screening and management of diabetes, targeted health education, promotion of protective behaviors, and use of personal protective equipment among high-risk workers may reduce susceptibility and exposure in endemic communities, particularly in rural and resource-limited settings where contact with soil and surface water is common (Suntornsut *et al.*, 2021). Sustainable control also requires access to effective antimicrobial therapy and strengthened follow-up systems to reduce mortality and prevent relapse (Oliveira *et al.*, 2024). At the policy level, greater recognition of melioidosis within national health agendas is needed to secure funding, strengthen long-term surveillance, and sustain public health commitment (Fuady *et al.*, 2024). The integration of these strategies within a One Health framework can enable coordinated action across clinical, environmental, veterinary, and public health sectors, ultimately transforming melioidosis from a neglected disease into a more effectively managed public health priority (Mariappan *et al.*, 2022).

#### Future Direction

Although there is increasing acknowledgement of melioidosis as a significant yet underappreciated infectious disease in Asia, substantial knowledge deficiencies persist, hindering effective control measures. Future endeavours must transcend reactive clinical management, advancing towards proactive, interdisciplinary, and innovation-driven strategies. A major goal is to improve epidemiological and clinical research, particularly through population-based studies, enhanced surveillance systems, and standardized reporting mechanisms to generate more accurate estimates of incidence, mortality, and disease burden across Asia (Fairchild *et al.*, 2018; Shen *et al.*, 2025). Particular attention should be directed toward countries where melioidosis remains underdiagnosed and underreported, including Indonesia, Myanmar, Laos, Cambodia, and several South Asian nations. A better understanding of disease spectrum, susceptibility patterns, and long-term outcomes, especially among populations increasingly affected by metabolic disorders such as diabetes mellitus, is essential for improving risk stratification and developing targeted prevention strategies (Sugandh *et al.*, 2023).

Recent developments in genomics and molecular epidemiology present transformative opportunities for advancing our understanding of *B. pseudomallei* (Bianconi *et al.*, 2023). Whole-

genome sequencing can support outbreak investigation, characterize the geographic population structure of *B. pseudomallei*, and help distinguish relapse or persistent infection from reinfection through comparison of paired clinical isolates (Seng *et al.*, 2023). Integrating genomic information with epidemiological, environmental, and clinical data may enable more accurate mapping of high-risk areas and improve public health decision-making (Scarpa & Casu, 2024). Furthermore, genomic characterization of virulence determinants and antimicrobial resistance mechanisms may facilitate the development of improved diagnostic tools, targeted therapeutics, and precision surveillance approaches.

The development of effective vaccines and environmental surveillance systems remains another critical research priority (Curlin *et al.*, 2011). Although no licensed vaccine is currently available, advances in immunology, vaccinology, and emerging platforms such as mRNA technology offer promising directions for future development, particularly for high-risk populations (Saxena *et al.*, 2025). Future vaccine research should focus on identifying robust correlates of protection, optimizing antigen selection, and advancing promising preclinical candidates into human clinical trials. Additional studies are also required to evaluate vaccine efficacy and therapeutic outcomes in vulnerable populations, including individuals with diabetes mellitus, chronic kidney disease, and immunocompromised conditions. Concurrently, enhanced environmental mapping of *B. pseudomallei* through standardized sampling strategies and geospatial modeling could improve the identification of environmental reservoirs and support predictive risk assessments. Ultimately, rainfall patterns, flooding, and extreme weather events significantly influence human exposure pathways and the subsequent dissemination of the disease (McMichael, 2015).

Lastly, to turn these advances into real improvements in public health, we need to improve implementation science, health systems research, and collaboration between regions. To make diagnostics, treatment adherence, and integration with current health programs better, especially those that deal with non-communicable diseases, we need strategies that can be used in different situations and on a larger scale (Hategeka *et al.*, 2022). Because environmental risks cross borders and there are problems that affect the whole region, Asia will need to work together in a coordinated way, sharing data, working together on research networks, and making joint policy decisions (Shrestha *et al.*, 2022; Adrot *et al.*, 2025). Ultimately, integrating surveillance, environmental monitoring, vaccine development, clinical management, and policy interventions within a One Health framework offers the most sustainable pathway to mitigate the burden of melioidosis, transforming it from a neglected disease into a recognized and effectively controlled public health priority across Asia.

#### CONCLUSION

Melioidosis in Asia is simultaneously an epidemiological, diagnostic, and health-system challenge. The most important evidence gaps are not simply a shortage of case reports, but the absence of population-based incidence studies, denominator-based surveillance, standardized laboratory confirmation, longitudinal environmental sampling, and comparable treatment-outcome data from high-risk populations. Near-term priorities should therefore include: (1) establishing notifiable or sentinel surveillance in high-risk settings; (2) strengthening culture identification, reference-laboratory confirmation, and external quality assurance; (3) generating comparable incidence, mortality, and case-fatality estimates with explicit denominators and uncertainty; (4) monitoring antimicrobial susceptibility, adherence, relapse, reinfection, and treatment-related adverse events; and (5) evaluating vaccine candidates in models that better reflect diabetes, chronic kidney disease, and immunocompromise. Regionally harmonized One Health surveillance linking human cases, environmental reservoirs, animal infections, genomic data, and climate indicators would

provide a stronger basis for targeted prevention and resource allocation. Progress should be judged by earlier diagnosis, lower mortality and recurrence, and more accurate measurement of disease burden, rather than by publication volume alone.

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## Conflicts of Interest

The authors declare no conflict of interest.

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## AI Disclosure

The authors declare that artificial intelligence (AI)-based tools were used to improve the grammar, clarity, and readability of the manuscript. No AI-based tools were used to generate images, figures, or scientific data. The authors have reviewed and verified all content and take full responsibility for the accuracy and integrity of the manuscript.

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