Expert Commentary

Literature review of the epidemiology of influenza B disease in 15 countries in the Asia-Pacific region

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Influenza control strategies focus on the use of trivalent influenza vaccines containing two influenza A virus subtypes and one of the two circulating influenza type B lineages (Yamagata or Victoria). Mismatches between the vaccine B lineage and the circulating lineage have been regularly documented in many countries, including those in the Asia-Pacific region. We conducted a literature review with the aim of understanding the relative circulation of influenza B viruses in Asia-Pacific countries. PubMed and Western Pacific Region Index Medicus were searched for relevant articles on influenza type B published since 1990 in English language for 15 Asia-Pacific countries. Gray literature was also accessed. From 4834 articles identified, 121 full-text articles were analyzed. Influenza was reported as an important cause of morbidity in the Asia-Pacific region, affecting all age groups. In all 15 countries, influenza B was identified and associated with between 0% and 92% of laboratory-confirmed influenza cases in any one season/year. Influenza type B appeared to cause more illness in children aged between 1 and 10 years than in other age groups. Epidemiological data for the two circulating influenza type B lineages remain limited in several countries in the Asia-Pacific, although the co-circulation of both lineages was seen in countries where strain surveillance data were available. Mismatches between circulating B lineages and vaccine strains were observed in all countries with available data. The data suggest that a shift from trivalent to quadrivalent seasonal influenza vaccines could provide additional benefits by providing broader protection.

Keywords
Asia-Pacific, epidemiology, influenza B, literature review, seasonality, vaccine mismatch

WHAT THIS PAPER ADDS

• By bringing together data from across the region, we show that influenza contributes to the public health burden in Asia-Pacific countries, with a variable, but substantial proportion due to influenza B. Influenza vaccination policies are needed in Asia-Pacific countries, and the use of quadrivalent influenza vaccines could provide additional benefits.

1 | INTRODUCTION

Epidemic influenza causes global public health burden each season. The World Health Organization (WHO) estimates that influenza severely affects between three and five million individuals each year and causes between 250 000 and 0.5 million deaths.1 The influenza attack rate is highest in children, while complications including hospitalization and death occur most frequently in elderly individuals.1 Other
specific high-risk groups prioritized by WHO for vaccination include pregnant women, the highest priority group, followed by individuals with a compromised immune system and individuals with comorbidities such as pulmonary or cardiac disease.\(^2\)

Influenza type A and B viruses cause the vast majority of influenza disease in humans, and infection is preventable by vaccination. The relative proportion of influenza cases caused by type A and type B strains varies annually, reflecting antigenic drifts in the predominant strains and the host's level of immunity. In the last decade, influenza A viruses represented by three subtypes (A/H3N2, A/H1N1, and A/H1N1pdm09) have predominated during influenza seasons. Influenza B viruses are represented by two separate lineages (B/Victoria and B/Yamagata) that co-circulate. In the 1980s, the B/Yamagata/16/88 lineage and its variants spread worldwide, whereas B/Victoria/2/87 lineage viruses remained geographically restricted to Asia during the 1990s for reasons not wholly understood. In 2002, the B/Victoria lineage strains spread to the rest of the world.\(^2\) Influenza B has been isolated in up to 44% of laboratory samples in the United States from 2001 to 2002 through 2010-2011 seasons (excluding the 2009-2010 pandemic period), and in up to 60% of samples in Europe during the same period, with a seasonal average of 24% and 23% of samples, respectively.\(^7\)

Seasonal influenza vaccines are modified annually to include those antigenic variants that are likely to predominate in the following influenza season. Vaccine strain selection is performed by the WHO using data from the Global Influenza Surveillance and Response System, a network of over 140 institutions in 111 countries.\(^8\) The B/Yamagata and B/Victoria influenza strains are antigenically distinct, and vaccines using one lineage induce only low levels of cross-protection to the other lineage.\(^9,10\) Trivalent seasonal influenza vaccines only contain one influenza B lineage, and it is not always possible to predict which B lineage will predominate during the next influenza season.\(^11\) Mismatch between the vaccine lineage and circulating influenza B lineage has occurred regularly, which can have a significant impact on influenza vaccine efficacy.\(^6,12-14\) Since 2012, the WHO has recommended the inclusion of strains from both B lineages in quadrivalent seasonal influenza vaccines.\(^15\)

Co-circulation of both influenza type B lineages has also been documented throughout South-East Asia and Oceania.\(^5\) The use of influenza vaccine in many Asia-Pacific countries is limited, and the potential impact of quadrivalent influenza vaccines on illness and hospitalization rates in these countries is not known, but is also likely to be low.\(^16\) To obtain an epidemiological view of influenza type B in the Asia-Pacific region, we conducted a review of the available literature. We attempted to identify periods of influenza B lineage mismatch between vaccine and circulating strains in 15 countries within the Asia-Pacific region to better inform health authorities of the potential benefits of quadrivalent influenza vaccines for protection against seasonal influenza.

2 | METHODS

Fifteen countries were selected from within the Asia-Pacific region traversing all climatic zones (Figure 1). These included Northern
Full-text articles were reviewed to assess their relevance and methodological quality. Articles were excluded if the method sections were insufficiently described; if the content did not provide relevant information to the review objectives; if the article reported "pneumonia and influenza" as a combined outcome (unless pneumonia was described as a complication of influenza), outcomes from mathematical models; and if no quantitative data could be retrieved. Gray literature including WHO websites, local ministries of health, and WHO vaccine recommendations was also assessed for relevance. Extracted data included information on epidemiology and circulating strains. We did not collect clinical criteria or clinical case definitions of influenza, influenza-like illness (ILI), febrile illness, acute respiratory infection (ARI) disease, or severe acute respiratory illness (SARI) used in individual studies. Nor did we specify the methods for selecting cases for specimen collection or the influenza-testing method used for laboratory diagnosis. In our review, "laboratory-confirmed influenza" or a "positive sample" refers to a case of influenza confirmed by the method stated in the reporting paper.

An influenza B mismatch was defined as the circulating influenza B virus lineage strains differing from the B lineage representative strain included in the WHO-recommended influenza vaccine composition for that season. When <20% of the circulating influenza B strains differed from the WHO-recommended vaccine strain, we arbitrarily considered the degree of mismatch to be "low." A difference between 20% and 40% was considered as partial mismatch. We considered a significant mismatch as >40% and complete mismatch when ≥95% of the circulating influenza B lineage strains did not belong to the trivalent vaccine lineage.

The initial literature search in 2013 was conducted by Pallas Health Research and Consultancy B.V., the Netherlands. Quality control activities included review of the first 30% of titles and abstracts and of the first 10% of full-text articles in duplicate by two independent researchers from Pallas. Any disagreements were adjudicated by a third researcher. The search was updated in 2016 by BM, and the articles were selected by BM and JC.

Ethics approval was not required for this study. The majority of relevant publications concerned surveillance or other observational epidemiological studies for which no standard quality checklists are currently available.

3 | RESULTS

There were 121 English language articles included in the review (Figure 2), of which 120 articles provided information on influenza B strains as a proportion of all laboratory-confirmed influenza from data collected between 1990 and 2015 (Table 1). Most assessed specific, but diverse, populations of interest, such as patients...
| Country     | Influenza surveillance systems                                                                 | Doses distributed per 1000 population\(^a\) | Influenza vaccine coverage | Recommendation | National immunization program                                    | Recommending body                                                                 |
|------------|---------------------------------------------------------------------------------------------|---------------------------------------------|-----------------------------|----------------|-------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Australia  | State and Territory-based Influenza surveillance: General Practice Sentinel Surveillance, Influenza Complications Alert network, Emergency Department, Hospital Mortality, and Laboratory surveillance | 299.73 (2013)                               | 39% of adults ≥ 18 years, 73% of 65+ (2014) | All individuals from 6 months | Reimbursed for 65+, Aboriginal and Torres Strait Islander people, pregnant women, chronic disease | Australian Technical Advisory Group on Immunization                                |
| Cambodia   | National Influenza Center: ILI sentinel surveillance and hospital-based ALRI surveillance since 2006 | 2.21 (2013)                                 | 12% among ILI patients (May 2010-Dec 2012) | None           | No                                                                | Ministry of Health                                                                |
| China      | National Influenza Center: ILI sentinel and hospital-based surveillance since 2000            | 7.81 (2013)                                 | 9.0% (2011) overall, 7.4% in 60+ years, 9.4% chronic disease, 9.5% healthcare workers 26% in children 16 doses/1000 in Shanghai (Zhao 2015) Highest (108 doses/1000 population) in Beijing where vaccination is free or subsidized for some age groups | Healthcare workers, elderly 60+, pregnant women, children from 6 years | No national recommendation                                                      | National Health and Family Planning Commission                                    |
| Indonesia  | ILI sentinel surveillance, enhanced surveillance for seasonal, and avian influenza in East Jakarta | 1.81 (2011)                                 | No reports identified        | Prior to Hajj   | No                                                                | Indonesian Technical Advisory Group on Immunization, Indonesian Pediatrician Association, Adult Immunization Task Force, Medicine Specialist Association of Indonesia |
| Laos       | Laboratory-based surveillance from 2007, hospital-based surveillance (3-8 sites) of pneumonia from 2008, Department of Health | 15.21 (2013)                                | No reports identified        | Healthcare workers, elderly 50+, pregnant women, chronic disease, children | ?                                                                                 | Ministry of Health                                                                |
| Malaysia   | Sentinel surveillance for ILI (OPD) and SARI (hospital) Coordinated by the Surveillance Sector, Disease Control Division, Ministry of Health | 7.48 (2013)                                 | 7.2% of HCW in 2011          | Healthcare workers, chronic disease, elderly with ≥ 1 chronic disease, Haj pilgrims | No                                                                | Ministry of Health                                                                |
| Myanmar    | None                                                                                       | None recorded (2001)                        | No reports identified        | -              | No                                                                | -                                                                                |

(Continues)
| Country       | Influenza surveillance systems                                                                 | Doses distributed per 1000 population | Influenza vaccine coverage | Recommendation                                                                 | National immunization program                                                                 | Recommending body                                                                 | Recommending body                                                                 |
|--------------|-----------------------------------------------------------------------------------------------|---------------------------------------|---------------------------|--------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| New Zealand  | National Influenza surveillance: General Practice Sentinel Surveillance of ILI, Laboratory-based surveillance | 312.5 (2013)                          | 67.5% of 65+ (2014), 66% of healthcare workers (2015) | All individuals from 6 months                                                   | Reimbursed for Children 6 months < 5 with respiratory condition, 65+, pregnant women, chronic disease | Ministry of Health                                                               |                                                                                 |
| Philippines  | Sentinel surveillance for ILI (outpatient) and SARI (outpatient and hospital-based), laboratory-based surveillance, Department of Health | 35.28 (2013)                          | No reports identified     | Healthcare workers, chronic disease, elderly 60+, pregnant women, children (6 m - 18 years) | Reimbursed for elderly 60+ indigent population in 2014-15                                  | Department of Health, Input and advice from Philippine Society for Microbiology and Infectious Diseases, Pediatric Infectious Disease Society of the Philippines, Philippine Foundation for Vaccination |                                                                                 |
| PNG          | PNG National Influenza Centre, ILI surveillance in 2 hospitals                                  | 0 (2013)                              | No reports identified     | None                                                                            | No                                                                                           | Ministry of Health                                                               |                                                                                 |
| Singapore    | Outpatient (polyclinic and ED) attendance and admissions for ARI, influenza virus surveillance by National Influenza Centre | 78.48 (2013)                          | 30.6% among diabetics (2007) | Healthcare workers, chronic disease, elderly 65+, pregnant women, children (6 m - 5 years), Children 6-18 m on long-term aspirin, residents of nursing homes | No                                                                                           | Ministry of Health                                                               |                                                                                 |
| South Korea  | Korean Influenza Surveillance System (KISS): ILI surveillance at 630 sentinel clinics and 396 laboratories, Hospital-based Influenza Morbidity and Mortality (HIMM) and inpatient surveillance (ED surveillance) | 335.7 (2013)                          | 34.3% in the general population, 61.3% high-risk groups (2005), 82.4% of 65+ year-olds (2016) | Elderly 65+, pregnant women, chronic diseases, children 6 m-5 years, residents of nursing homes and long-term care facilities, healthcare workers, children 6 m-18 years on long-term aspirin, adults 50-64 years, household contacts and caregivers those at risk | Reimbursed for 65+, financially vulnerable, handicapped individuals, soldier, children 6-59 ms | Centers for Disease Control and Prevention                                        |                                                                                 |
| Taiwan       | Taiwan National Influenza Surveillance System (NISS): laboratory surveillance, sentinel ED and OPD ILI surveillance, case-based surveillance of influenza with complications and deaths | 312.5 (2013)                          | 40% <3 years of age, 80% in adults (2012) | All individuals from 6 months                                                   | Reimbursed for high-risk groups and 65+ years                                               | Centers for Disease Control and Prevention                                        |                                                                                 |
hospitalized for respiratory tract infections (RTI), patients in intensive care, and respiratory samples from in/outpatients with a broad range of underlying respiratory syndromes. In many studies, the age range of subjects/samples was not specified. Many studies included patients with diagnoses of low specificity for influenza such as "febrile illness," "ILI," and "acute lower respiratory tract infection" (ALRTI). There were 102 prospective studies (two studies included both prospective and retrospective components). Sample sizes in individual study groups ranged from 26 to more than 300,000.

3.1 Influenza surveillance and vaccine coverage in Asia-Pacific countries

With the exception of Myanmar, all of the countries studied use a sentinel site approach for influenza surveillance (Table 1). All countries with a surveillance program in place monitor ILI cases (ARI in Singapore and pneumonia in Laos instead of ILI) presenting to general practices or hospitals. In Myanmar, epidemiological studies funded by grant programs in Japan were conducted in two hospitals and general practice clinics in Yangon.

Six countries (Australia, New Zealand, South Korea, Taiwan, Thailand, and the Philippines) have/have had a publicly funded national seasonal influenza immunization program, and in all cases, this is/was limited to at-risk groups (Table 1).

China, Indonesia, Laos, the Philippines, Singapore, and Vietnam provide recommendations for immunization of risk groups (and Malaysia recommends vaccination of Hajj pilgrims) outside the national schedule. No policy for influenza vaccine use exists for Papua New Guinea, Cambodia, or Myanmar.

In countries with a policy to provide free vaccine for at-risk groups, vaccine uptake among these groups has been substantial: Approximately 73% of 65+-year-olds in Australia, 67.5% in New Zealand, 80% of adults in Taiwan, and 82.5% in 65+-year-olds in South Korea were reported to have received influenza vaccine (Table 1). In China, influenza vaccine coverage was reported as 26% in children and 7.4% in 60+-year-olds, but regional differences may exist due to subsidization of influenza vaccines in some regions.17,18 Approximately 300 doses of influenza vaccine were distributed per 1000 population in Australia and New Zealand, while fewer than 10 doses per 1000 population were distributed in Cambodia, China, Indonesia, Malaysia, and Papua New Guinea, suggesting that influenza vaccine use is negligible in these countries.19

3.2 Epidemiology of influenza type B in Asia-Pacific countries

3.2.1 Australia

Laboratory surveillance conducted by the WHO collaborating center and National Influenza Centers showed that during the period from 2005 to 2015, influenza B viruses predominated in two years: in 2005, 67% of circulating influenza viruses were type B, while 51% of the influenza B viruses mismatched the B strain contained in the seasonal...
influenza vaccine; in 2015, 62% of circulating influenza viruses were type B with a partial (36%) mismatch to the trivalent vaccine influenza B component (Table 3).20–22

We identified 18 articles that described influenza B in Australia reporting studies conducted from 1991 to 2015. Most of the articles reported data from laboratory-based influenza surveillance or clinic/hospital-based surveillance in various states/territories. Some of the studies were conducted in the same/overlapped seasons but in different groups of patients.

One study in 2002-2003 found that the proportion of influenza B was higher among influenza-positive specimens from state-wise influenza surveillance program of ILI patients at sentinel general practitioner (GP) clinics than among influenza-positive patients hospitalized with respiratory illness (11.5% vs 1.8%).23 Two studies conducted in 2006 reported higher influenza detection rate among outpatients with ILI comparing to hospitalized children with ILI, while the proportion of influenza B was higher among laboratory-confirmed influenza inpatients comparing to outpatients.24,25

Two studies with overlapping study period in 2007 found significantly higher influenza-positivity rate among ILI patients presenting to GP clinics than children with ARI presenting to hospital (46.9% vs 12.2%). The difference between the proportion of influenza B among the two groups of patients in these two studies was much smaller (12.7% vs 18.9%).26,27 Comparing to these two studies, another study encompassing the same study period reported a much lower influenza B proportion among hospitalized children with laboratory-confirmed influenza (2.5%).28

In 2012, GP clinic-based surveillance in Western Australia and Victoria reported similar influenza detection rate among ILI patients.29,30 The proportion of influenza B among influenza-positive samples obtained from ILI patients was significantly higher in Western Australia than in Victoria (43% vs 13.6%).

### 3.2.2 Cambodia

Since 2006, the National Influenza Centre in Cambodia carried out sentinel site-based ILI surveillance and hospital-based ALRI surveillance. Influenza viruses were detected from 5.8% to 18.7% of ILI patients between 2006 and 2011, and 1.4% to 3.6% of ALRI patients from 2007-2010. Proportion of influenza B among all influenza-positive samples ranged from 12.6% in 2009 to 64.8% in 2011. Influenza type A and B circulated year-round in Cambodia with peak activities during the rainy season between June and November.31-33

### 3.2.3 China

National surveillance of ILI has been carried out by the Chinese CDC in 95 sentinel hospitals in Northern provinces and 99 hospitals in southern provinces since 2000. From 2005-11, 64 306 laboratory-confirmed influenza cases were recorded by the ILI surveillance in the North. In Southern China, 122 215 laboratory-confirmed influenza cases were confirmed by the ILI surveillance during 2006-12. Around 30% of all positive samples were influenza B.34

Twenty-three articles reported on influenza B in China from 1995 until 2014 (Table 2). Most of the articles reported clinic/hospital-based ILI surveillance in one city/province and provided aggregated data over multiple seasons.

A study in Shenzhen in the southern province of Guangdong from 1995 to 2009 reported an annual influenza detection rate among ILI cases ranging from 0.2% in 1998 to 25% in 2009. The lowest proportion of influenza B among all influenza-positive samples was in 2008.35 Influenza B predominated in 4 of the 15 study years with the peak (79%) reported in 1997. Multiple influenza B outbreaks between 2004 and 2012 were reported in Guangdong province, including in 2010 following the peak of A/H1N1/pdm09.36 The 2010 influenza B peak was also reported in studies conducted in northern, central, and eastern part of China.37-40

A study conducted in central China assessed SARI hospitalizations by type of influenza and found that in 2010-11, A (H3N2) virus was associated with a higher SARI hospitalization rate (55/100 000) than both influenza B and A (H1N1)pdm09. In the following year, the incidence of SARI hospitalization was highest with influenza B (98/100 000).39

Between the 2009-14 seasons, on average, 45% of circulating B lineages in Shanghai differed antigenically from the vaccine strain. During the period from 2009 to 2012, B/Victoria lineage matching the seasonal influenza vaccines strain predominated over the B/Yamagata lineage. The proportion of B/Yamagata lineage exceeded 97% of all circulating influenza B viruses in late 2012 and resulted in complete vaccine B strain mismatch.41

### 3.2.4 Indonesia

We identified five articles with data relevant to Indonesia (Table 2). Three of these papers were based on ILI surveillance of multiple seasons, reporting a proportion of type B viruses between 25.4% and 36% among all influenza-positive samples during the overall study period.34,42,43 Two papers provided season-specific information on the proportion of influenza B among all ILI cases with laboratory-confirmed influenza in 2010-11 and 2011-12.44,45 One of them also provided data in SARI patients with laboratory-confirmed influenza in 2011-12. In that study, the influenza detection rate was higher among ILI than among SARI patients (34.5% vs 15.4%). In both patient groups, 47% of laboratory-confirmed influenza cases were influenza B.45

### 3.2.5 Laos

ILI virological surveillance started in Lao People’s Democratic Republic (PDR) in 2007. We identified four articles assessing influenza in Laos during the period from 2007 to 2011. One study based on ILI surveillance during the period 2008-10 reported influenza-positivity rate of 20.9%-23% in the three years. The proportion of influenza B among all influenza-positive samples dropped from 66.7% in 2008 to 2.7% in 2009 when A/H3N2 and A/H1N1pdm09 became predominant, then increased to 33.7% in 2010.46

Two studies assessing influenza among patients hospitalized with ALRI showed that the influenza-positivity rate (12.7%) and influenza B
### TABLE 2  Articles reporting the proportion of influenza B among all laboratory-confirmed influenza

| Author            | Design                        | Study years          | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|-------------------|-------------------------------|----------------------|-------------------------------------------------------------------------------------|-----------------------------|-------------------------------------------------------------------|----------------------------------------------------------------------------|
| **Australia**     |                               |                      |                                                                                     |                             |                                                                   |                                                                            |
| Roche (2002)^17   | Passive-laboratory-based surveillance | 1991-2000          | Laboratory reports (nationwide network)                                             | 340 730                     | 16 805 (4.9, 4.6-87.2 annually)                                   | 3614 (21.5, 12.8-95.4 annually)                                           |
| Teichtahl (1997)^18 | Case-control study            | Aug 1993-July 1994  | Hospitalized adults with asthma exacerbation                                        | 79                          | 20 (25.2)                                                        | 2 (10.0)                                                                  |
| Moore (2009)^39   | Retrospective descriptive     | May 1997-Dec 2005   | Specimens from children <18 years (1 hospital)                                       | 32 741 specimens           | 1951 (6.0)                                                       | 304 (15.6)                                                               |
| Kelly (2000)^100  | Prospective laboratory-supported surveillance | 1998-1999         | Patients with ILI (17-26 general practitioners)                                     | 152                         | 65 (42.8)                                                        | 3 (4.6)                                                                  |
| Cai (2015)^34     | Prospective national surveillance of patients with ILI | 2001-2012           | Laboratory-confirmed influenza                                                       | 179 137                     | 179 137(100)                                                     | 28 700 (16.0)                                                           |
| Druce (2005)^23   | Prospective hospital-based surveillance | May-Sept 2002 & 2003 | Hospitalized patients with respiratory illness Specimens collected from state-wide influenza surveillance program | 3095                        | Only data by age                                                  | 1159                                                                      |
| Fielding (2007)^25 | Prospective surveillance      | May-Oct 2006        | Patients with ILI (74 general practitioners)                                         | 384                         | 126 (32.8)                                                       | 15 (11.9)                                                                |
| Iskander (2009)^24 | Prospective hospital-based surveillance | June-Oct 2006      | Hospitalized children <5 years with ILI (1 hospital)                                | 273                         | 31 (11.4)                                                        | 9 (29.0)                                                                 |
| Lambert (2008)^26 | Prospective hospital-based surveillance | July 2006-Aug 2007 | Children with ARI presenting to hospital (1 hospital)                                | 303 specimens (295 patients) | 37 (12.2)                                                        | 7 (18.9)                                                                 |
| Lester-Smith (2009)^28 | Retrospective descriptive     | Jan-Dec 2007        | Hospitalized children with influenza (1 hospital)                                    | 122                         | 122 (100)                                                        | 3 (2.5)                                                                  |
| Miller (2008)^27  | Prospective surveillance      | Apr-Sept 2007       | Patients with ILI (21 sentinel general practices)                                   | 403                         | 189 (46.9)                                                       | 24 (12.7)                                                                |
|                    |                               |                      | Notified laboratory-confirmed influenza                                              |                             | 1343                                                             | 186 (13.8)                                                               |
| Grant (2011)^21   | Prospective and retrospective surveillance | 2010               | Patients with ILI (32 general practices) Notifications of laboratory-confirmed influenza to Health Department | 478                         | 170 (35.6)                                                       | 4 (2.4)                                                                  |
| Macesic (2013)^122 | Prospective hospital-based surveillance | April-Nov 2010 & 2011 | Community-acquired influenza (8-15 hospitals)                                       | 572                         | 572 (100)                                                        | 58 (10.1)                                                                |

(Continues)
| Author               | Design                      | Study years   | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|----------------------|-----------------------------|---------------|-------------------------------------------------------------------------------------|-----------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------|
| Levy (2014)<sup>29</sup> | Prospective surveillance    | 2010-2012     | Patients with ILI (31-57 general practices)                                         | 448 (2010) 351 (2011) 1361 (2012) | 146 (32.6) 84 (29.9) (2011) 603 (44.3) (2012)                        | 56 (38.4) (2010) 18 (20.7) (2011) 259 (43) (2012)                        |
| Fielding (2013)<sup>30</sup> | Prospective surveillance    | 2012          | Patients with ILI (41 general practices)                                           | 709                         | 280 (39.5)                                                          | 38 (13.6)                                                          |
|                      |                             |               | Notified laboratory-confirmed influenza                                             | 5058                        | 5058 (100)                                                          | 745 (14.7)                                                          |
|                      |                             |               | Influenza complications network                                                   | 389                         | 389 (100)                                                           | 50 (12.8)                                                           |
| Sullivan (2014)<sup>123</sup> | Prospective surveillance    | 2012          | Patients with ILI (110 General practices nationally)                                | 1414                        | 593 (41.9)                                                          | 106 (17.9)                                                          |
| Jennings (2015)<sup>124</sup> | Prospective surveillance    | 15 Jun-12 Jul 2015 | Laboratory-confirmed influenza (13 laboratories in New South Wales)                | 1234                        | 1234 (100)                                                          | 821 (66.5)                                                          |
|                      |                             | 1 Apr-18 Jul  | Laboratory-confirmed influenza presenting to Emergency Departments (4 hospitals)   | 88                         | 88 (100)                                                            | 41 (46.6)                                                           |
| WHO<sup>55</sup>    | Prospective national surveillance | Jan-Sept 2015 | Laboratory-confirmed influenza                                                     | Not given                   | -                                                                  | (61%)                                                             |
|                      |                             |               | Laboratory-confirmed influenza from general practices                              | 2565                        | (30.9%)                                                             | (64%)                                                             |
|                      |                             |               | Hospitalized laboratory-confirmed influenza                                        | -                           | -                                                                  | (52%)                                                             |

**Cambodia**

| Author               | Design                      | Study years   | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|----------------------|-----------------------------|---------------|-------------------------------------------------------------------------------------|-----------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------|
| Buecher (2010)<sup>31</sup> | Prospective hospital-based surveillance | Feb-May 2005-2007 | Patients with ILI during dry season (5 hospitals)                                   | 234                        | 4 (1.7)                                                             | 2 (50)                                                              |
| Mardy (2009)<sup>32</sup> | Prospective hospital- and clinic-based surveillance | 2006-2008 | Patients with ILI (5 outpatient departments) and ALRTI (2 hospitals) (2007-08) | 3148 (ILI) 1868 (ALRI)      | 334 (10.7) (5.8-15.3 annually) 64 (3.4) (1.4-3.6 annually) | ILI & ALRTI 148 (43.8) (34-57.7 annually) |
| Kasper (2012)<sup>125</sup> | Prospective hospital-based surveillance | Dec 2006-Dec 2009 | Acutely ill patients with fever (9 hospitals in South-central Cambodia)              | 9968                        | 1983 (19.9)                                                          | 631 (31.8)                                                          |

(Continues)
| Author              | Design                        | Study years | Patient population                                      | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|---------------------|-------------------------------|-------------|--------------------------------------------------------|----------------------------|---------------------------------------------------------------------|------------------------------------------------------------------|
| Saha (2014)        | Prospective clinic-based surveillance | 2006-2011  | Patients with ILI at sentinel centers                  | 10 105                     | 1574 (15.6) (7.6–18.8 annually)                                      | (22.9–65.6) (annually)                                             |
| Horm (2014)        | Prospective hospital-based surveillance | 2009-2011  | Patients with ILI (11 sites nationally) and ALRTI (2 hospitals) | 7376 (ILI) 2248 (ALRI)     | 1262 (16.9) (14.5–18.7 annually)                                      | 59 (2.6) (1.5–3 annually)                                          |
| Timmermans (2016)  | Prospective surveillance      | May 2010-Dec 2012 | Patients with ILI (4 sites in Western Cambodia) | 586                        | 168 (29.7)                                                            | 76 (45.2)                                                       |
| China              |                               |             |                                                        |                            |                                                                     |                                                                  |
| Cheng (2013)       | Prospective hospital- and clinic-based surveillance (Shenzhen) | 1995-2009  | Patients with URTI until 2003 (8 sites), ILI after 2003 (22–31 sites) | 25 377                     | 2678 (10.6) (0.2–25 annually)                                         | 757 (28.3) (2–79 annually)                                        |
| Tang (2008)        | Prospective hospital-based descriptive (Gangzhou) | Jan-2001-Dec 2006 | Hospitalized children <14 years with ALRI | 34 885                     | 760 (2.2)                                                             | 72 (9.5)                                                        |
| Lin (2013)         | Prospective hospital and laboratory-based surveillance (Guangdong) | Jan 2004-Dec 2012 | Patients with ILI (14 hospitals) | 107 115                     | 17 454 (16.3)                                                         | 4978 (28.5)                                                     |
| Timmermans (2016)  | Prospective surveillance      | May 2010-Dec 2012 | Patients with ILI (4 sites in Western Cambodia) | 586                        | 168 (29.7)                                                            | 76 (45.2)                                                       |
| Cai (2015)         | Prospective national ILI surveillance | 2006-2012  | Laboratory-confirmed influenza (South) | 122 215                     | 122 215 (100)                                                        | 35 910 (29.4)                                                   |
| Yang (2009)        | Prospective outpatient surveillance (Beijing) | May 2006-Jan 2010 | Patients ≥ 14 years with ARI (1 hospital) | 7776                        | 1854 (23.8)                                                           | 405 (21.8)                                                     |
| Ji (2010)          | Retrospective hospital-based descriptive (Suzhou) | Jan 2007-Dec 2008 | Hospitalized children <5 years respiratory infection (1 hospital) | 7789                        | 120 (1.5)                                                             | 25 (20.8)                                                      |
| Guo (2012)         | Prospective outpatient surveillance (Zhuhai City) | 2008             | Patients with ILI (28 hospitals) | 1485                        | 135 (9.1)                                                             | (23.7)                                                          |
| Peng (2012)        | Prospective hospital-based surveillance (Wuhan) | Jul 2008-Jun 2010 | Children ≤ 14 years with ILI (1 hospital) | 1472                        | 455 (30.9)                                                            | 100 (22.0)                                                     |
| Author       | Design                                | Study years | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|--------------|---------------------------------------|-------------|-------------------------------------------------------------------------------------|-----------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Ge (2012)    | Prospective outpatient surveillance (Shanghai) | Jun 2009-May 2011 | Children with ILI (1 hospital)                                                     | 2356                        | 608 (25.8)                                                         | 142 (23.4)                                                                    |
| Lu (2013)    | Prospective descriptive (Jinan)        | Aug 2009-Sept 2010 | Patients ≥ 14 years with ARI (1 hospital)                                          | 596                         | 124 (20.8)                                                        | 75 (60.5)                                                                     |
| Wei (2013)   | Prospective hospital-based surveillance | Apr 2009-Mar 2011 | Patients with ILI                                                                  | 6143                        | 1645 (26.8)                                                       | 348 (21.2)                                                                    |
| Zhu (2013)   | Laboratory-based descriptive (Hubei & Zhejiang) | 2009-2010 | Patients with respiratory infection (inpatients and outpatients)                   | 341                         | 54 (15.8)                                                         | 18 (33.3)                                                                     |
| Zhao (2015)  | Prospective outpatient surveillance (Shanghai) | 2009-2014 | Patients with ILI                                                                  | 71 354                      | 19 974 (28.0)                                                     | 6688 (33.5)                                                                   |
| Li (2013)    | Prospective outpatient surveillance (Zhuhai City) | Jan-Dec 2010 | Patients with ILI (1 hospital)                                                      | 924                         | 187 (20.2)                                                        | 96 (51.3)                                                                     |
| Yu (2013)    | Prospective hospital-based surveillance (Jingzhou City) | 2010-2012 | Hospitalized patients with SARI (4 hospitals)                                     | 16 208                      | 2057 (12.7)                                                       | 998 (48.5)                                                                    |
| Huo (2012)   | Prospective outpatient surveillance (Nanjing) | Nov 2010-Oct 2011 | Patients with ILI (2 hospitals, 1 laboratory)                                     | 486                         | 178 (36.3)                                                        | 37 (20.8)                                                                     |
| Chen (2014)  | Prospective hospital-based surveillance (Changsha) | 2010-2012 | Patients with ILI (2 hospitals)                                                    | 2955                        | 278 (9.4)                                                         | 83 (29.9)                                                                     |
| Wang (2014)  | Retrospective modeling study (Gangzhou)  | Jan 2010-Dec 2012 | Patients with ILI                                                                    | 8258                        | 1081 (13.1)                                                       | 360 (33.3)                                                                    |
| Yu (2012)    | Prospective hospital-based descriptive (Beijing) | May 2010-Apr 2011 | Patients ≥ 14 years in ED with ARI (1 hospital)                                    | 416                         | 70 (16.8)                                                         | 3 (4.3)                                                                       |
| Fu (2015)    | Prospective clinic-based surveillance (Shanghai) | Jan 2011-Dec 2013 | Patients with ILI (2 hospitals)                                                     | 1970                        | 392 (19.9)                                                        | 162 (41.3)                                                                    |
| Ju (2014)    | Prospective hospital descriptive (Huizhou) | Jul 2011-Jul 2013 | Hospitalized patients with ILI (1 hospital)                                        | 1046                        | 209 (20.0)                                                        | 74 (35.4)                                                                     |
| Wang (2016)  | Prospective hospital-based surveillance (Suzhou) | Apr 2011-Mar 2014 | Children <5 years with ILI presenting to outpatient or ED                           | 3662                        | 619 (16.9)                                                        | 349 (56.4)                                                                    |
| Indonesia    | Laboratory-based surveillance          | Aug 1999-Jan 2003 | Children >4 and adults with ILI at 6 sentinel centers                              | 1372                        | 130 (9.5)                                                         | 33 (25.4)                                                                     |

(Continues)
# Table 2 (Continued)

| Author          | Design                      | Study years          | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|-----------------|-----------------------------|----------------------|-------------------------------------------------------------------------------------|------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Kosasih (2013)  | Prospective health center and hospital-based Surveillance | Jan 2003-Dec 2007   | Inpatients and outpatients with ILI at 5 (2003) to 48 (2006-07) sentinel centers     | 21 030                       | 4236 (20.1)                                                         | 1487 (35.1)                                                                   |
| Caini (2015)    | Prospective national surveil lance of patients with ILI | 2003-2007            | Laboratory-confirmed influenza                                                       | 3653                         | 3653 (100)                                                         | 1314 (36.0)                                                                   |
| Saha (2014)     | Prospective clinic-based surveillance                          | 2010-2011            | Patients with ILI at sentinel centers                                               | 15 150 specimens             | 2511 (16.6)                                                        | (49.9 in 2010, 24.8 in 2011)                                                  |
| Storms (2015)   | Enhanced prospective surveillance in East Jakarta             | Oct 2011-Sept 2012   | Patients with ILI at 4 outpatient clinics                                          | 3278                         | 1131 (34.5)                                                        | 536 (47.4)                                                                   |
|                 |                             |                      | Patients with SARI at 6 hospitals                                                   | 1787                         | 276 (15.4)                                                         | 132 (47.8)                                                                   |
| Laos            |                             |                      |                                                                                        |                             |                                                                    |                                                                            |
| Vongphrachanh (2010) | Prospective hospital-based surveillance                        | Jan 2007-Dec 2008   | Patients with ILI presenting to hospital OPD/ED (3 hospitals)                       | 526                          | 155 (29.5)                                                         | 92 (59.3)                                                                    |
|                 |                             | Aug-Dec 2008         | Hospitalized ALRTI                                                                  | 79                           | 10 (12.7)                                                          | 4 (40.0)                                                                     |
| Khamphaphongphane (2013) | Laboratory-based surveillance                        | Jan 2008-Dec 2010   | Patients with ILI presenting to hospital OPD/ED (7 hospitals)                       | 2338 specimens              | 523 (22.4) (20.9-23 annually)                                     | 142 (27.7) (2.7-66.7 annually)                                                |
| Saha (2014)     | Prospective clinic-based surveillance                          | 2006-2011            | Patients with ILI at sentinel centers                                               | 5949                         | 1302 (21.9) (12.8-29.8 annually)                                  | (2.2-56.5 annually)                                                           |
| Sentilhes (2013) | Prospective hospital-based surveillance                        | Aug 2009-Oct 2010   | Patients hospitalized with ALRTI                                                    | 292 specimens               | 23 (7.9)                                                           | 5 (21.8)                                                                     |
| Malaysia        |                             |                      |                                                                                        |                             |                                                                    |                                                                            |
| Chan (1999)     | Retrospective descriptive                                      | Jan 1982-Dec 1997   | Children <24 months with LTRI                                                       | 5697                         | 77 (1.4)                                                           | 18 (23.4)                                                                    |
| Khor (2012)     | Retrospective hospital-based descriptive                      | 1982-2008            | Samples from hospitalized children ≤5 years (1 hospital)                            | 10 269                      | 297 (2.9)                                                          | 64 (21.9)                                                                    |
| Sam (2015)      | Laboratory-based surveillance                                 | 1995-2008            | Laboratory-confirmed influenza 1 month to 49 years                                  | 338                          | 338 (100)                                                          | 88 (26.0)                                                                    |
| Sam (2010)      | Retrospective descriptive                                    | 2002-2007            | Hospitalized children <15 years with laboratory-confirmed influenza                 | 132                          | 132 (100)                                                          | 35 (26.5)                                                                    |
| Saat (2010)     | Prospective laboratory-based surveillance                     | Jan 2005-Dec 2009   | Patients with ILI (nationwide)                                                      | 7117 specimens              | 993 (14.0) (10.2-31.6 annually)                                   | 305 (30.7) (18-51 annually)                                                   |
| Saha (2014)     | Prospective clinic-based surveillance                         | 2006-2011            | Patients with ILI at sentinel centers                                               | 10 323                      | 894 (8.7) (3.1-13.4 annually)                                     | (20.2-62.6, 2006-2010)                                                      |
| Author          | Design                        | Study years | Patient population                        | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|-----------------|-------------------------------|-------------|-------------------------------------------|-----------------------------|--------------------------------------------------------------------|------------------------------------------------------------------------|
| **Myanmar**     |                               |             |                                           |                             |                                                                    |                                                                        |
| Hasegawa (2006) | Prospective hospital- and     | Sept 2003-Dec 2004 | Patients with ILI (1 hospital, 2 general practitioners) | 616                         | 139 (22.6)                                                          | 6 (4.3)                                                                |
|                 | clinic-based surveillance     |             |                                           |                             |                                                                    |                                                                        |
| Hasegawa (2006) | Prospective hospital- and     | 2005        | Patients with ILI (1 hospital, 2 general practitioners) | 992                         | 268 (27.0)                                                          | 125 (46.6)                                                            |
|                 | clinic-based surveillance     |             |                                           |                             |                                                                    |                                                                        |
| Dapat (2009)    | Prospective hospital- and     | 2005-2007   | Patients with ILI (1 hospital, 1 clinic)   | 2618                        | 522 (19.9) (24 in 2005, 11.4 in 2006, 19 in 2007)                   | 267 (51.1) (42 in 2005, 0 in 2006, 67 in 2007)                          |
|                 | clinic-based surveillance     |             |                                           |                             |                                                                    |                                                                        |
| **New Zealand** |                               |             |                                           |                             |                                                                    |                                                                        |
| Huang (2008)    | Prospective national surveillance | 1997-2006  | All influenza diagnoses sentinel general practice, laboratory, hospital, and mortality surveillance | Average 718 annually       |                                                                    | (0-92 annually)                                                       |
|                 |                               |             |                                           |                             |                                                                    |                                                                        |
| Laing (2001)    | Prospective hospital-based    | Jul 1999-Jul 2000 | Hospitalized adults >18 with CAP | 474                         | 39 (8.2)                                                           | 8 (20.5)                                                              |
|                 | surveillance                   |             |                                           |                             |                                                                    |                                                                        |
| Caini (2015)    | Prospective national surveillance of patients with ILI | 2000-2012 | Laboratory-confirmed influenza | 17 629                      | 17 629 (100)                                                       | 2965 (16.8)                                                           |
| Jennings (2004) | Prospective hospital-based    | Jul-Nov 2001 | Children with ARI (1 hospital) | 75                          | 10 (13.3)                                                          | 7 (70.0)                                                              |
|                 | descriptive                    |             |                                           |                             |                                                                    |                                                                        |
| Huang (2007)    | Prospective national         | 2005        | Laboratory-confirmed influenza sentinel general practice, laboratory and hospital-based surveillance | 845                         | 845 (100)                                                          | 734 (86.9)                                                            |
|                 | surveillance                   |             |                                           |                             |                                                                    |                                                                        |
| Turner (2014)   | Prospective hospital- and     | Apr-Sept 2013 | Patients with ILI (18 sentinel general practices) and SARI (4 hospitals) | 1298 (ILI) 886 (SARI)      | 182 (21) 391 (30)                                                   | ILI&SARI 221 (39)                                                     |
|                 | clinic-based surveillance      |             |                                           |                             |                                                                    |                                                                        |
| WHO             | Sentinel ILI & SARI and       | Jan-Sept 2015 | Laboratory-confirmed influenza            | Not given                   | 5235 (100)                                                         | 680 (13%)                                                            |
|                 | laboratory surveillance        |             | Patients with ILI SARI patients           | 13891206                    | 614 (44.2%) 285 (23.6)                                             | 308 (50%) Not mentioned                                             |
| **Philippines** |                               |             |                                           |                             |                                                                    |                                                                        |
| Saha (2014)     | Prospective clinic-based      | 2006-2011   | Patients with ILI at sentinel centers     | 69 108                      | 12 607 (18.2) (6.9-33.1 annually)                                   | (Range 2.3-75.7)                                                     |
|                 | surveillance                   |             |                                           |                             |                                                                    |                                                                        |
| Suzuki (2012)   | Prospective descriptive       | May 2008-May 2009 | Hospitalized children 8 day-13 years with severe CAP (1 center) | 819                         | 29 (3.5)                                                           | 11 (37.9)                                                            |
| Author | Design | Study years | Patient population | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|--------|--------|-------------|--------------------|----------------------------|---------------------------------------------------------------|-----------------------------------------------|
| Tallo (2014) | Prospective clinic-based surveillance | Jan 2009-Dec 2011 | Patients with ILI and SARI at sentinel centers | 5915 (ILI) 2659 (SARI) | 1282 (21.7) (12.3-25.6 annually) 226 (8.5) (6-11.2 annually) | 397 (31.0) (6-61.2 annually) 72 (31.9) (11.4-49.4 annually) |
| Otomaru (2015) | Prospective clinic-based surveillance | Jan 2010-Mar 2013 | Patients with ILI at sentinel centers | 2031 | 225 (11.1) (3.2-16.0 annually) | 104 (46.2) (23.8-81.3 annually) |
| PNG | | | | | | |
| Kono (2014) | Prospective surveillance | 2010 | Patients with ILI (2 hospitals) | 300 | 88 (29.3) | 38 (43.2) |
| Singapore | | | | | | |
| Chew (1998) | Retrospective descriptive | Sept 1990-Sept 1994 | Patients tested for respiratory pathogens (2 hospitals) | 12 354 specimens | 426 (3.4) | 92 (21.6) |
| Chow (2006) | Retrospective surveillance | Jan 1996- Dec 2003 | Samples from outpatients or inpatients with ILI (National Influenza Centre) | 57 060 specimens | 3829 (6.7) | 333 (13.9) |
| Yang (2011) | Retrospective surveillance | 2004-2006 | Samples from outpatients or inpatients with ILI (Ministry of Health) | 29 329 specimens | 1291 (5.5) | 305 (23.6) (16.3-33.0 annually) |
| Seah (2010) | Prospective descriptive | Mar 2006-Apr 2007 | Military personnel with febrile respiratory illness (1 camp) | 1354 specimens | 489 (36.1) | 159 (32.5) |
| Virk (2014) | Prospective surveillance | May-Oct 2007 | Students and staff with ILI (National University of Singapore) | 266 | 56 (21.1) | 9 (16.1) |
| Tan (2015) | Prospective surveillance | 2007-2009 | Students and staff with ILI (National University of Singapore) | 500 | 164 (32.8) | 11 (6.7) |
| Saha (2014) | Prospective clinic-based surveillance | 2007-2011 | Patients with ILI at sentinel centers | 55 449 | 12 801 (23.1) | (2.7-79.1 2007-2011) |
| Cai (2015) | Prospective national surveillance of patients with ILI | 2007-2012 | Laboratory-confirmed influenza | 12 001 | 12 001 (100) | 2311 (19.3) |
| Yap (2012) | Prospective descriptive | May 2009-June 2010 | Military personnel with febrile respiratory illness (4 camps) | 2858 | 821 (28.7) | 269 (32.8) |
| Tan (2014) | Prospective surveillance | May 2009-Oct 2012 | Military personnel with febrile respiratory illness (5 camps) | 7733 | 972 (12.6) | 449 (46.2) |

(Continues)
### TABLE 2 (Continued)

| Author     | Design                          | Study years         | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|------------|---------------------------------|---------------------|-------------------------------------------------------------------------------------|-----------------------------|---------------------------------------------------------------------|--------------------------------------------------------------------------------|
| South Korea |                                                |                     |                                                                                     |                             |                                                                     |                                                                              |
| Yun (1995) | Prospective hospital-based descriptive    | Nov 1990-Apr 1994   | Children with ALRI + children visiting the OPD or with nosocomial ALRI              | 804 specimens (712 patients) | 42 (5.2)                                                            | 11 (26.2)                                                                    |
| Lee (2007) | Prospective clinical & laboratory-based surveillance | Sept 2000-Oct 2001 | Patients with ILI                                                                   | 2972                        | 144 (4.8)                                                           | 0 (0)                                                                       |
| Kim (2008) | Retrospective descriptive            | Mar 2004-Dec 2005   | Hospitalized children <15 years with LRTI with NPA                                  | 400                         | 76 (19)                                                             | 32 (42.1)                                                                   |
| Seo (2014) | Retrospective laboratory-based descriptive | Jan 2005-Dec 2008 | Children <19 years with ARI                                                            | 21 641 specimens            | 1116 (5.2)                                                          | 484 (43.4)                                                                   |
| Choi (2012) | Prospective descriptive            | Mar 2010-Feb 2011   | Adults ≥ 18 year in ICU with severe CAP or HCAP                                      | 198                         | 12 (6.1)                                                            | 1 (8.3)                                                                     |
| Noh (2013) | Prospective hospital-based surveillance | Sept 2011-Jun 2012 | Adults ≥ 18 years who visited an ED with ILI                                         | 1983                        | 846 (42.7)                                                          | 169 (20.0)                                                                   |
| Song (2013) | Prospective ED-based surveillance    | Oct 2011-Sept 2012  | Laboratory-confirmed influenza                                                        | 7213                        | 7213 (100)                                                          | 3217 (44.6)                                                                  |
| Wie (2013) | Prospective ED-based surveillance    | Oct 2011-May 2012   | Adults with ILI                                                                      | 2129                        | 850 (39.9)                                                          | 194 (22.8)                                                                   |
| Seo (2014) | Prospective ED-based surveillance    | Oct 2011-June 2012  | Patients with ILI at ED                                                              | 4490 tested                 | Not given                                                            | Max 58% of weekly samples                                                   |
| Choi (2015) | Retrospective case control           | Sept 2011-May 2012  | Patients visiting hospital with ILI                                                  | 7390 tested                 | 1130 (15.3)                                                         | 452 (40)                                                                    |
| Ahn (2015) | Retrospective laboratory-based descriptive | Jan 2012-Apr 2013 | Adults >16 tested for respiratory viruses                                            | 291 specimens (282 patients) | 47 (16.1)                                                            | 4 (8.5)                                                                     |
| Taiwan     |                                                |                     |                                                                                     |                             |                                                                     |                                                                              |
| Lin (2004) | Prospective hospital-based descriptive    | Aug 1995-July 1997  | Pediatric outpatients with URTI                                                        | 910                         | 112 (12.3)                                                          | 58 (51.8)                                                                   |
| Tsai (2001) | Prospective hospital and clinic-based Surveillance | Jan 1997-Dec 1999 | Children <12 years with RTI (inpatients and outpatients)                            | 6986                        | 565 (8.1)                                                            | 181 (32.0)                                                                   |
| Huang (2009) | Retrospective descriptive    | Jan 1997-May 2007   | Laboratory-confirmed influenza                                                        | 2651                        | 2651 (100)                                                          | 1168 (44.1)                                                                  |
| Hu (2004)  | Retrospective descriptive            | Jan 2000-Dec 2001   | Children with laboratory-confirmed influenza                                         | 197                         | 197 (100)                                                            | 124 (62.9)                                                                   |

(Continues)
| Author | Design | Study years | Patient population | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|--------|--------|-------------|-------------------|-----------------------------|---------------------------------------------------------------|------------------------------------------------------------------|
| Shih (2005) | Prospective laboratory surveillance | Oct 2000-Mar 2004 | Patients with suspected RTI (inpatients and outpatients) | 32 775 | 3244 (9.9) | 12.75 (39.3) |
| Chi (2008) | Retrospective hospital-based descriptive | Jan 2001-Dec 2006 | Children with LRTI (inpatients and outpatients) | 20 405 specimens | 745 (3.7) | 118 (15.8) |
| Jian (2008) | Prospective laboratory surveillance | 2003-2006 | Patients with suspected RTI (inpatients and outpatients) | 34 312 | 4007 (11.7) | 1336 (33.3) |
| Lin (2013) | Prospective laboratory and sentinel physician-based surveillance | 2003-2007 | Patients with URTI or LRTI symptoms | 12 190 | 1150 (9.4) | 651 (56.6) |
| Jian (2008) | Prospective laboratory surveillance | 2004-2005 | Laboratory-confirmed influenza | 1183 | 1183 (100) | 971 (82.1) |
| | | 2006-2007 | | 1534 | 1534 (100) | 1219 (79.5) |
| Wang (2009) | Retrospective and prospective descriptive | Nov 2006-Feb 2007 | Children <18 years with ILI (inpatients, ED, outpatients) | 198 specimens (196 children) | 101 (51.0) | 87 (86.1) |
| Chen (2012) | Prospective hospital-based descriptive | Jan 2009-March 2011 | Children <24 months hospitalized with bronchiolitis | 113 | 5 (4.4) | 0 (0) |
| Chuang (2012) | Prospective national surveillance | 2009-2010 | Samples from patients with ARTI | 14 788 specimens | 3970 (26.9) | 545 (13.7) |
| | | 2010-2011 | Samples from patients with ARTI | 11 813 specimens | 2767 (23.4) | 489 (17.7) |
| | | 2009-2010 | Patients with influenza hospitalized with | 1297 | 1297 (100) | 82 (6.3) |
| | | 2010-2011 | Pulmonary complications | 1751 | 1751 (100) | 50 (2.9) |
| Lo (2013) | Prospective national surveillance | Jun 2011-Jun 2012 | Outpatients with ILI | 14 943 | 3285 (22.0) | 2382 (72.5) |
| | | | Suspected influenza with complications | 2675 | 1704 (63.7) | 1034 (60.7) |

**Thailand**

| Author | Design | Study years | Patient population | Number tested for influenza | Number (n) (proportion, %) of N with suspected influenza (2 hospitals) | Number (n) (proportion, %) of N with ILI (University) | Number (n) (proportion, %) of N with complications |
|--------|--------|-------------|-------------------|-----------------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| Suzuki (1997) | Prospective surveillance | Each August 1991-1994 | Patients with suspected influenza | 186 specimens | 32 (17.2) | 11 (34.4) |
| Sirivichayakul (2000) | Prospective descriptive | June 1998-May 1999 | Nursing students with ILI (University) | 106 | 35 (33.0) | 2 (5.7) |
| Thawatsupha (2000) | Prospective hospital-based surveillance | Jan-Dec 2001 | Outpatients with ARI (6 hospitals) | 711 specimens | 338 (54.6) | 102 (30.2) |

(Continues)
| Author                  | Design                          | Study years     | Patient population                                                                 | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|-------------------------|---------------------------------|-----------------|--------------------------------------------------------------------------------------|----------------------------|---------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Olsen (2010)            | Prospective hospital-based surveillance | Sept. 2003-Dec 2005 | Hospitalized patients with acute LRTI (all hospitals in 2 provinces)                | 3910                      | 586 (15.0)                                                          | 150 (25.6)                                                                  |
| Suntarattiwong (2007)   | Prospective descriptive hospital-based study | July 2004-July 2005 | Hospitalized children 0-5 years with LRTI (1 hospital)                               | 456                       | 39 (8.6)                                                            | 5 (12.8)                                                                    |
| Chittaganpitch (2011)   | Prospective surveillance        | 2004-2010       | Patients with ILI at 11 sentinel centers, Sep-Dec 2010 Inpatients with SARI at 3 hospitals | 19 121                     | 3896 (20.4) (15-25 annually)*                                       | 1284 (33.0 range 13-43)*                                                  |
| Simmerman (2009)        | Prospective hospital-based surveillance | Jan 2005-Dec 2008 | Hospitalized patients with pneumonia (all hospitals in 2 provinces)                 | 13 119                     | 1391 (10.6) (4.1-16.0 annually)                                     | 444 (31.9) (range 13.6-44.9 per year)                                       |
| Hara (2011)             | Hospital-based descriptive      | 2006-2008       | Hospitalized patients with CAP (hospital and HIV center)                              | 119                       | 7 (5.9)                                                             | 1 (14.3)                                                                    |
| Saha (2014)             | Prospective clinic-based surveillance | 2007-2011      | Patients with ILI at sentinel centers                                                | 17 421                     | 3802 (21.8) (18.4-25.5 annually)                                    | (12.9-42.9)                                                                |
| Baggett (2012)          | Prospective active, population-based Surveillance | Jan 2009-Dec 2010 | Hospitalized patients with acute LRTI (all hospitals in 2 provinces)                | 7207                      | 902 (12.5)                                                          | 120 (13.3)                                                                  |
| Prachayangprecha (2013) | Prospective hospital-based surveillance | Jun 2009-Jul 2012 | Patients with ILI attending hospitals in Bangkok                                        | 6050                      | 2969 (49.0)                                                         | 3% of tested samples                                                        |
| Dawood (2014)           | Prospective hospital-based surveillance | July-Dec 2010, 2011 | Hospitalized patients with ARI (all hospitals in 2 provinces)                          | 1545                      | 279 (18.1)                                                          | 32 (11.5)                                                                  |
| Tewawong (2015)         | Laboratory-based surveillance   | Jan 2010-Feb 2014 | Samples from patients with ILI (3 provinces)                                          | 14 418 specimens          | 3050 (21.2)                                                         | 471 (15.4)                                                                  |
| Vietnam                 | Prospective laboratory-based surveillance |                                  |                                                                                        |                            |                                                                     |                                                                              |
| Nguyen (2007)           |                                  | 2001-2003       | Outpatients with ILI (12 centers)                                                    | 4708                      | 119 (2.5)                                                           | 59 (49.6) (range 0-77)                                                     |
| Do (2011)               | Prospective hospital-based descriptive | Nov 2004-Jan 2008 | Hospitalized children <15 years with ARI (1 center)                                  | 309                       | 51 (16.5)                                                           | 24 (47.1)                                                                  |
| Nguyen (2009)           | Prospective hospital and clinic-based surveillance | Jan 2006-Dec 2007 | Outpatients with ILI (15 clinics)                                                     | 11 082                    | 2112 (19.1)                                                         | 585 (27.7)                                                                  |
| Nguyen (2013)           | Prospective surveillance        | Jan 2006-Dec 2010 | Outpatients with ILI (7-15 centers)                                                   | 29 804                    | 6616 (21.9) (18-26 annually)                                       | 2163 (33.2) (23.3-51.6 annually)                                           |

*Continued*
### TABLE 2 (Continued)

| Author        | Design                                      | Study years | Patient population                        | Number tested for influenza | Number (n) (proportion, %) of N with laboratory-confirmed influenza | Number (n) (proportion, %) of type B among all laboratory-confirmed influenza |
|---------------|---------------------------------------------|-------------|-------------------------------------------|----------------------------|------------------------------------------------------------------|------------------------------------------------------------------------|
| Saha (2014)44 | Prospective clinic-based surveillance        | 2006-2011   | Patients with ILI at sentinel centers     | 29 499                     | 5241 (17.8)                                                       | (Range 0-41.3.8)                                                      |
| Caini (2015)34| Prospective national surveillance of patients with ILI | 2006-2013   | Laboratory-confirmed influenza             | 8647                       | 8647 (100)                                                        | 3011 (34.8)                                                          |
| Takahasi (2013)75 | Prospective descriptive                     | Sept 2009-Aug 2010 | Hospitalized patients ≥ 15 years with LRTI (1 center) | 323                        | 45 (13.9)                                                        | 13 (28.9)                                                            |
| WHO Western Pacific region | Regional ILI and laboratory surveillance | 2006 | Data from national influenza centers (patients with ILI) | 65 103 | 7425 (11.4) | 3032 (40.8) |
| 2007          | 92 939                                      | 11 143 (12.0) | 3846 (34.5) |
| 2008          | 94 274                                      | 11 025 (11.7) | 3599 (32.6) |
| 2009          | 366 164                                     | 115 554 (31.6) | 4886 (4.2) |
| 2010          | 307 584                                     | 51 573 (16.8) | 25 565 (49.6) |

ALRTI, acute (lower) respiratory tract infection; CAP, community-acquired pneumonia; ED, emergency department; GP, general practice; HCAP, healthcare-associated pneumonia; HIV, human immunodeficiency virus; ICU, intensive care unit; ILI, influenza-like illness; LRTI, lower respiratory tract infections; NPA, nasopharyngeal aspirate; OPD, outpatient department; PNG, Papua New Guinea; P&I, pneumonia and influenza; RTI, respiratory tract infection; SARI, severe acute respiratory illness.

*Percentage from 2004 data not taken as only 11 subjects included in the 2004 surveillance.
proportion among ALRI cases (40%) with laboratory-confirmed influenza in 2008 were higher comparing to the findings in 2009-10 (7.9% and 21.8%, respectively).47,48

3.2.6 | Malaysia

Six articles were identified for Malaysia reporting studies conducted between 1982 and 2011, of which four reported aggregated data across multiple seasons.

From 2005-2009, national ILI surveillance detected influenza in 10.2% (2008) to 31.6% (2006) of ILI cases.49 In this period, the proportion of influenza B was lowest in 2008 (18%) and highest in 2005 (51%). Peak season of influenza fell between May and August.

Complete influenza B strain mismatch with Southern Hemisphere vaccine B strain was observed in 2005 and 2009 and significant mismatch in 2007 (Table 5).

Laboratory-based surveillance of ILI patients presenting to sentinel centers showed that the percentage of samples tested positive for influenza ranged between 3.1 and 13.4% in 2006-11.44,49 The percentage of B strains among the influenza-positive samples was 30.7% on average from 2005 to 2009, and 20.2% to 62.6% annually between 2006 and 2010.

3.2.7 | Myanmar

Three articles reported the results of sentinel site-based surveillance study in Myanmar between 2003 and 2007.50–52 The proportion of influenza-positive samples obtained from patients with ILI ranged from 11.4% in 2006 to 24%-27.0% in 2005. Few influenza B cases were detected in 2003-04 and 2006. The proportion of influenza-positive samples that were type B ranged from 42%-46.6% in 2005 with a majority of influenza B isolates belonging to the Victoria lineage. In 2007, 67% of influenza viruses were influenza B and all belonged to the B/Victoria lineage.50–52

3.2.8 | New Zealand

Seven articles describing influenza in New Zealand between 1990 and 2015 were identified. National influenza surveillance data showed that during 1997-2008, on average 718 cases of laboratory-confirmed influenza were detected every year.53 Influenza surveillance in 2005 recorded the highest influenza B activity since 1990 with co-circulation of influenza strains from B/Victoria and B/Yamagata lineages, which resulted in significant B strain mismatch with the recommended vaccine composition.54 In 2015, 44.2% of patients with ILI and 23.6% SARI patients tested positive for influenza.55 The proportion of influenza B among all influenza-positive samples was 13%, but half of them mismatched the B strain contained in the influenza vaccines for that season (Table 3).

3.2.9 | Papua New Guinea

In the one study identified as providing information on influenza in Papua New Guinea, 29.3% of samples from patients with ILI received by the Papua New Guinea National Influenza Centre in 2010 had laboratory-confirmed influenza, of which 43.2% were influenza type B.56

3.2.10 | Philippines

Four articles provided information on influenza type B in the Philippines. Three articles reported clinic-based surveillance of patients with ILI in different regions during an overlapping period from 2006 to 2013. The largest study in 2006-11 collected 69 108 specimens, and the influenza virus detection rate varied between 6.9% (in 2008) and 33.1% (2009).54,57–59 Influenza B was the predominant type circulating in 2008 (75.7%) as well as in 2010 (50.1%).

Surveillance in Baguio city in the North and in the Eastern Visayas region during 2010-11 showed that regional circulation of influenza viruses and predominant types varied in the same season. Influenza detection rate among ILI patients and the proportion of influenza B among all influenza-positive samples in Baguio city (25.6% and 61.2%, respectively) were higher than in Eastern Visayas region (16% and 54%) in 2010 but lower in 2011 (12.3% and 22% in Baguio city; 14.6% and 37% in Eastern Visayas region, respectively).60,61 Surveillance in Baguio city also assessed influenza among SARI patients. In all three study years, influenza detection rates were lower among SARI patients than patients with ILI, while the proportion of influenza B was higher among SARI patients with laboratory-confirmed influenza than ILI patients with laboratory-confirmed influenza in 2009 and 2011.60

3.2.11 | Singapore

In Singapore, the National Influenza Centre carries out influenza virus surveillance using samples from public hospitals and sentinel clinics.62 Ten articles reporting data in Singapore from 1990 until 2012 were identified (Table 2). Four articles report the results of the national surveillance of samples from inpatients and outpatients presenting to sentinel centers with ILI between 1996 and 2012. The percentage of all samples with laboratory-confirmed influenza ranged from 2.5% in 2007 to 50.4% in 2010.36,44,62,63 The proportion of influenza-positive samples that were influenza B was lowest in 2009 (2.7%) and highest in 2007 (79.1%).

Several studies reported influenza detection rates and proportions of influenza B viruses in various seasons among specific groups. Among students and staff at the National University of Singapore presenting with ILI, 21.1% had laboratory-confirmed influenza in 2007 and 32.8% in 2007-09. Although the study conducted in 2007-09 detected a higher influenza-positivity rate, the proportion of influenza B was lower comparing to the study in 2007 (6.7% vs 16.1%) as influenza A/H1N1pd09 became the predominant type in the second half of the 2007-09 study.64,65

Three studies evaluated influenza in military personnel with febrile respiratory illness in 2006-07, 2009-10, and 2009-12.66-68 Influenza detection rate was 36.1% and 28.7% in the two earlier seasons, both with the proportion of influenza B at 33%. Season-specific influenza
positivity and the proportion of influenza B after 2010 were not reported.

3.2.12 | South Korea

Eleven articles reported the distribution of influenza A and B viruses in South Korea between 1990 and 2013 (Table 2). Six studies were conducted in hospital emergency or outpatient departments, one included hospitalized children, one included adults in the intensive care unit (ICU), and three studies reported laboratory surveillance. Between 2007 and 2015, the Korean Influenza Surveillance System reported three influenza seasons with around 50% or higher proportion of influenza B; all three seasons had B lineage mismatch of >20% (Table 3). The highest percentage of influenza B positive samples was reported in a retrospective laboratory-based study in which 43.4% of children and 55.8% of adults with laboratory-confirmed influenza had type B.69 The study period encompassed the 2007-08 influenza season, in which 64.1% of circulating influenza viruses were type B strains with a complete vaccine mismatch (Table 3).

3.2.13 | Taiwan

Thirteen studies conducted between 1995 and 2012 were identified for Taiwan (Table 2). Five articles reported data in children, and no studies specifically reported on influenza B in adults. All studies conducted before 2009 detected influenza B from the study population, but information on B lineages was not reported. The proportion of influenza-positive samples that were type B varied across seasons, age groups, and diagnoses. One study conducted in 2009-11 with low level of B strain mismatch found that in both seasons, the proportion of influenza B among all laboratory-confirmed influenza cases was lower among patients hospitalized with pulmonary complications of influenza (2.9%-6.3%) comparing to patients with acute respiratory tract infection (ARTI, 13.7%-17.7%).70 In the following season (2011-12) when influenza B was predominant and the circulating B strain significantly mismatched the vaccine strain, one study reported a significantly higher proportion of influenza B in both ILI patients with laboratory-confirmed influenza (72.5%) and patients of suspected influenza with complications (60.7%), suggesting that the high proportion of influenza B together with the significant B strain mismatch (86%) resulted in heavy morbidity in that season.71

National Influenza Surveillance by the Taiwan CDC showed that since 2009, in all but one season, the proportion of influenza B viruses was >20% among all influenza viruses detected, including in 2009 during the A/H1N1pdm09 pandemic. Significant influenza B mismatches were observed in three seasons, especially in 2011-12 when 76% of the circulating influenza viruses were type B (Table 3).

3.2.14 | Thailand

Influenza sentinel surveillance throughout Thailand during 2005-10 found that 15-25% of samples from ILI patients tested positive for influenza. The highest proportion of influenza B among all laboratory-confirmed influenza patients was 40% in 2007, while the lowest was 13% in 2009.72

Thirteen relevant articles were identified for Thailand that reported for seasons between 1998 and 2014. One large laboratory-based surveillance study detected influenza viruses in 18.4%-25.5% of samples collected from patients with ILI between 2007 and 2011.44,73 The percentages of influenza-positive samples that were influenza B ranged from 12.9% in 2009 to 42.9% in 2008.73

Seven articles included hospitalized patients with RTIs, pneumonia, or SARI from 2003 to 2011. The percentage of clinical specimens with laboratory-confirmed influenza varied from 4.1% among patients hospitalized with pneumonia in 2006 to 21.1% among hospitalized SARI patients in 2010. Among hospitalized patients, the highest proportion (45%) of laboratory-confirmed influenza cases that were influenza B was seen in 2008, when circulation of influenza B predominated but with significant mismatch with the influenza B strain included in the Southern Hemisphere vaccine.74

3.2.15 | Vietnam

National influenza surveillance using sentinel sites across Vietnam reported influenza detection rates among ILI patients between 18% and 26% during 2006-10. In this period, the lowest proportion of influenza B among all laboratory-confirmed influenza cases was in 2007 and 2009 at 23%. The proportion of influenza B was highest (51.6%) in 2010 following the A/H1N1pdm09 pandemic.44,57-59

There were seven published articles reporting relevant data from Vietnam. Five articles reported influenza or ILI surveillance during various periods from 2001 to 2013. Two studies assessed influenza among patients hospitalized with respiratory infections. Influenza was detected in 13.9% of patients aged 15 years or older during September 2009-August 2010, and 28.9% of all influenza viruses detected belonged to the B type.75

3.2.16 | Distribution of influenza B by age group

There were 22 articles that provided information on influenza B in different age groups (Table 4). The grouping of ages differed between studies which hinders easy comparisons.

In studies reporting age-stratified data, the proportions of influenza caused by influenza type B were higher among children aged between 1 and 10 years than in older age groups.23,30,46,50,51,56,58,59,76-85 In 17 studies using comparable age strata, between 10.9% and 90% of all influenza B cases were detected in children aged <10 years (Table 4). Considering 18 studies with a cutoff at <20 years of age, in all but one study, more than 50% (and up to 100%) of all influenza type B cases occurred in age strata that included children and adolescents until 20 years of age. With some exceptions, in most studies (19/21), few influenza B cases (≤13.1%) were reported in adults aged 65+ years. Within the limitations of data, the age distribution of influenza B followed similar trends in each country.
TABLE 3 Circulating and vaccine influenza type B lineages in northern and Southern Hemisphere temperate/subtropical countries

| Year   | Vaccine lineage | Circulating lineage (%) | Degree of mismatch | Circulating lineage (%) | Degree of mismatch | Circulating lineage (%) | Degree of mismatch |
|--------|----------------|-------------------------|--------------------|-------------------------|--------------------|-------------------------|--------------------|
|        |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |   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Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |               | Victoria | Yamagata |   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One study from Victoria, Australia, estimated the rate of notified laboratory-confirmed influenza cases (reported in 2012 to the Victorian Department of Health) to be 154/100,000 persons in those aged 0–4 years, 137/100,000 in those aged ≥65 years, and 61–90/100,000 for other age groups. The proportion of notified cases that were influenza B was highest in those aged 5-15 years (30.3%) and 15-29 years (20.5%), followed by those aged 30-49 years (14.2%), 50-64 years (10.7%), <5 years (8.7%), and ≥65 years (8.6%).

### 3.3 Circulating influenza B strains

The available data indicate that both Yamagata and Victoria influenza type B lineages have circulated in Asia-Pacific countries during the last decade. The ratio of Yamagata to Victoria strains varied from year to year, and sometimes differed between countries in the northern and Southern Hemispheres within the same season (Table 3). Furthermore, the predominant lineage was not always the same in countries within the same region. For example, in 2012, an influenza type B Victoria strain predominated in Australia, whereas a Yamagata strain predominated in New Zealand (Table 3). In 2007, a Yamagata strain predominated in Malaysia, whereas a Victoria strain predominated in Indonesia (Table 5).

In Northern Hemisphere and tropical countries, mismatches with the Northern Hemisphere vaccine occurred in 2004-05 in Thailand; 2005-06 in Malaysia, Indonesia, Myanmar, and Thailand; 2006-07 in Thailand; 2007-08 in South Korea and Indonesia; 2008-09 in China; 2011-12 in Taiwan; 2012-13 in Thailand; 2012-13 and 2013-14 in South Korea and China; and 2013-14 and 2014-15 in Taiwan.

In Southern Hemisphere and tropical countries, mismatches with the Southern Hemisphere trivalent influenza vaccine occurred in 2005 in Australia, New Zealand, Malaysia, Indonesia, Thailand, and Myanmar; 2006 in Thailand; 2007 in Australia; New Zealand

### TABLE 4 Age distribution of confirmed influenza B cases (as a percentage of all influenza B)

| Country    | Data source                      | No. of influenza B cases | Age distribution (%) | <5 | 5-9 | 10-19 | 20-49 | 50-64 | ≥65 |
|------------|----------------------------------|--------------------------|----------------------|----|----|-------|-------|-------|-----|
| Australia  | Surveillance (Notified influenza cases) | 745                      | 6.4                  | 45 (5-14) | 46 (15-49) | 10 | 13 |
|            | GP surveillance                   | 38                       | 5                    | 24 (5-14) | 63 (15-49) | 5 | 3  |
|            | Surveillance (Complications alert network) | 50                       | 10                   | 8 (5-14) | 44 (15-49) | 8 | 30 |
|            | Clinical samples                  | 55                       | 0                    | 10.9  | 0   | 34.5  | 34.5  | 20.0  |
|            | Surveillance                      | 133                      | 4.5                  | 10.5  | 35.3 | 24.8  | 23.3  | 6.0   |
| China      | Clinical patients                 | 83                       | 14.5                 | 34.9 (5-14) | 25.3 (15-24) | 22.9 (25-59) | 2.4 (≥60) |
|            | Clinical patients                 | 162                      | 5.6                  | 34.0 (5-14) | 14.2 (15-24) | 43.2 (25-59) | 3.1 (≥60) |
|            | Clinical patients                 | 96                       | 29.2                 | 68.8 (5-14) | 0 (15-24) | 2.1 (25-59) | 0 (≥60) |
|            | Clinical patients                 | 74                       | 21.6                 | 43.2 (5-14) | 18.9 (15-24) | 16.2 (25-59) | 0 (≥60) |
|            | Clinical patients                 | 404                      | -                    | - (5-14) | 29.5 (15-24) | 65.5 (25-59) | 5.0 (≥60) |
|            | Clinical patients                 | 75                       | -                    | - (5-14) | 50.7 (15-24) | 49.3 (25-59) | 0 (≥60) |
|            | Clinical patients                 | 6688                     | 9.7                  | 23.5 (6-17) | 61.4 (18-64) | 5.5  |      |
| Indonesia  | Surveillance                      | 1487                     | 15.0                 | 33.8 (5-12) | 8.5 (13-17) | 38.0 (18-49) | 3.6 | 1.1 |
| Laos       | Surveillance                      | 142                      | 25.4                 | 34.8 (5-17) | 39.8 (18-64) | 0   |      |
| Malaysia   | Clinical patients                 | 338                      | 73.8                 | 16.4  | 8.2  | 1.6   | -    | -    |
| Myanmar    | Clinical patients                 | 125                      | 43.2                 | 32.6  | 13.8 | 2.2 (20-59) | 0 (≥60) |
| PNG        | Surveillance                      | 38                       | 76                   | 24 (≥5) |      |      |      |      |
| Singapore  | Clinical samples                 | 92                       | 45.3                 | 10.5  | 8.2  | 36.0 (≥20) |      |      |
| South Korea| Surveillance                     | 3217                     | 48.7                 | 18.4  | 5.0  | 7.7   | 6.5  | 13.1 |
| Thailand   | Surveillance                      | 120                      | 25.8                 | 43.8 (5-17) | 12.5 (18-49) | 15.6 | 12.5 |
| Vietnam    | Surveillance                      | 585                      | 22                   | 41.5 (5-14) | 17.4 (25-64) | 1.7  |      |

N. number; PNG, Papua New Guinea; GP, general practice; ILI, influenza-like illness; LRTI, lower respiratory tract infection. Shading indicates values covering the combined shaded age groups.
Table 5: Circulating and vaccine influenza type B lineages in tropical countries

| Year   | Vaccine lineage | % type B (Malaysia (clinical samples)) | Circulating lineage (%) | % type B (Indonesia (surveillance)) | Circulating lineage (%) | % type B (Laos (surveillance)) |
|--------|----------------|----------------------------------------|-------------------------|------------------------------------|-------------------------|---------------------------------|
| 2005   | Yamagata       | 51                                     | 99                      | 1                                 | Predominant             | -                               |
| 2006   | Victoria       | 43                                     | 94                      | 6                                 | Predominant             | -                               |
| 2007   | Victoria       | 30                                     | 27                      | 73                                | Predominant             | -                               |
| 2008   | Yamagata       | 18                                     | 0                       | 100                               | 66.7                    | -                               |
| 2009   | Yamagata       | 22                                     | 97                      | 3                                 | 2.7                     | 100                             |
| 2010   | Victoria       | -                                      | -                       | -                                 | 33.7                    | 98.4                            |

| Year | Thailand (surveillance clinical samples) | Cambodia (surveillance) | Myanmar (clinical samples) |
|------|------------------------------------------|-------------------------|---------------------------|
| 2004 | Yamagata                                 | 16                      | 32                        | 68                          | -                        | -                               |
| 2005 | Yamagata                                 | 32                      | 41                        | 59                          | -                        | 42                              | 85                             |
| 2006 | Victoria                                 | 29                      | 55                        | 45                          | 0                        | 0                               | -                              |
| 2007 | Victoria                                 | 34                      | 62                        | 38                          | 57.7                     | All                             | 67                             | 100                           |
| 2008 | Yamagata                                 | 40                      | 40                        | 60                          | 34                       | None                            | -                              | -                             |
| 2009 | Yamagata                                 | 12                      | 100                       | 0                            | 12.6                     | All                             | -                              | -                             |
| 2010 | Victoria                                 | 35                      | 100                       | 0                            | 23.1                     | All                             | -                              | -                             |
| 2011 | Victoria                                 | -                       | 90                        | 10                           | 64.8                     | All                             | -                              | -                             |
| 2012 | Yamagata                                 | -                       | 0                         | 100                          | -                        | -                               | -                              | -                             |
| 2013 | Yamagata                                 | -                       | 0                         | 100                          | -                        | -                               | -                              | -                             |
| 2014 | Yamagata                                 | -                       | 0                         | 100                          | -                        | -                               | -                              | -                             |

*2011-2014 limited to 35 isolates over the 5-year period.

and Malaysia; 2008 in Australia and New Zealand; 2009 in Australia, Malaysia, Laos, Thailand, and Cambodia; 2012 in New Zealand and Thailand; and 2015 in Australia and New Zealand.

In countries that provided seasonal numerical estimates of lineage distribution, the majority of mismatched seasons in each country were significant or complete mismatches (Tables 3 and 5). In mismatched years without precise estimates of the distribution of type B lineages, the available descriptions suggest that all of the mismatches were likely to be significant or complete.

4 | DISCUSSION

The evidence we reviewed from the published literature indicates that influenza is an important cause of morbidity in the Asia-Pacific region and affects all age groups. Influenza type B was identified in all 15 of the countries studied, and the proportion of influenza B isolated in clinical specimens from different settings varied markedly from season to season, ranging between 0% and as high as 92%. This variability is consistent with the unpredictable seasonal influenza burden that
results from co-circulation of several types/lineages, the degree of antigenic drift, combined with the hosts’ immune status, which together ensure the continuing ability of the virus to cause illness.9

Significant or complete mismatches between the circulating and trivalent vaccine type B strain were observed on numerous occasions in countries with available data. Our study was not designed to quantify the possible public health implications in seasons where vaccine mismatch existed. Influenza vaccine efficacy is reduced when there is a mismatch between vaccine and circulating strains, suggesting that a mismatch season is likely to be associated with a higher clinical disease burden.14,86 87

Influenza B causes similar morbidity as influenza A.87 In mismatch seasons, hospitalization due to influenza type B can exceed that due to influenza A in all age groups.71 The available data suggest that consistent with observations in other regions,7,9 in the Asia-Pacific region, influenza B occurs more frequently in children aged between 1 and 10 years than in other age groups and causes more severe disease in this age group than influenza A.88

Evidence suggests differences in the age distribution of patients infected with the B/Yamagata or B/Victoria lineages, with the latter appearing to be more frequently identified in younger age groups.89-93 Although the lineage seems to have generally no impact on the clinical outcome of the infection, recent data from Hong Kong suggested that B/Victoria viruses may be associated with more influenza B hospitalization in children compared with B/Yamagata viruses.94 Both the B/Yamagata and B/Victoria lineages have been included in recommendations by WHO since September 2012 for the Southern Hemisphere vaccines for 2013 and thereafter for both hemispheres, but extensive use of quadrivalent vaccines ceased until 2015 or later, and then, it was mostly used in developed countries such as USA, Japan, Australia, and some European countries. As younger children have a globally higher probability of being infected with the influenza B viruses, this group is most likely to benefit more from a quadrivalent vaccine containing both lineages due to the frequent mismatch and co-circulation of both influenza B lineages.

The articles included in this review varied with respect to their design, population characteristics (eg, age range, mild vs severe cases), the illness definition selected for study (specific vs non-specific diagnoses), the laboratory methods used to detect influenza, and the methods of case surveillance (population-based, laboratory-based, hospital or emergency department-based, sentinel general practice). Therefore, the results of individual studies cannot be easily compared and are unlikely to be broadly representative. In some articles, data were not stratified per year, and only an average proportion of influenza type B over the study period could be obtained. In many studies, proportions of influenza B among any laboratory-confirmed influenza cases were only available within a specified population. Most information was retrieved for China, Australia, South Korea, and Taiwan, but four articles or fewer were identified for Laos, Myanmar, the Philippines, and Papua New Guinea.

This review has identified important knowledge gaps within the region. In several countries, the epidemiology of influenza and influenza type B is not well described, little is known about the age groups most affected by influenza type B and the relative contribution of the two type B lineages to the disease burden. Epidemiological data for the two circulating influenza B lineages in the Asia-Pacific region are extremely limited. Co-circulation of Yamagata and Victoria lineages occurred in most countries where strain surveillance data were available, with considerable fluctuation from year to year. A variable, but substantial influenza B burden, as well as variable mismatch between circulating lineages and vaccine lineages was observed in all countries with available data regardless of geographical location, suggesting that a shift from trivalent to quadrivalent seasonal influenza vaccines that include both influenza B lineages would be beneficial in many seasons. Establishing or enhancing existing influenza surveillance networks in individual countries across the Asia-Pacific region is needed to contribute to an improved understanding of the burden of influenza. Education of the medical profession and public, vaccine implementation strategies including the development of specific national recommendations in countries where they are lacking, and improved access to influenza vaccines, are needed to improve influenza vaccine uptake and reduce the influenza disease burden in Asia-Pacific countries.

Few countries in the Asia-Pacific region have policies, recommendations, or funding methods in place supporting influenza immunization, and those that do limit publicly funded re-imbursement to at-risk groups. Our review provides evidence of a substantial influenza burden in the Asia-Pacific. The data suggest that countries in the Asia-Pacific stand to benefit from development of immunization policy targeting influenza prevention. Additionally, quadrivalent influenza vaccines that reduce the likelihood of vaccine mismatch among influenza type B strains are likely to provide improved protection against influenza type B infection.

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CONFLICT OF INTEREST

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CONTRIBUTORSHIP

LJ, QSH, and WJK participated in the design of the review. LJ also participated in assembling and analysis of data and provided Asia-Pacific regional knowledge for the interpretation of the published material collected. QSH, IB, P-IL, and WJK participated in assembling and interpreting the data. MS, P-IL, and WJK participated in the analysis and interpretation of data. PB and BAM participated in collecting, assembling, analysis, and interpretation of data. BAM also participated in the design of the review. JC participated in the design of the review, collecting the data, the supervision of the analysis, and the interpretation of data. All authors were involved in the development of this manuscript, had full access to the data, and gave final approval before submission.

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GlaxoSmithKline Biologicals SA was the funding source and was involved in design and conduct of the study; management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript and decision to submit the manuscript for publication. Pallas was involved in the design of the study and conducted the literature review. GlaxoSmithKline Biologicals SA funded all costs associated with the development and the publishing of the present manuscript. The corresponding author had full access to the data and was responsible for submission of the publication. The Melbourne WHO Collaborating Centre for Reference and Research on Influenza is supported by the Australian Government Department of Health.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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