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# Burden of Pertussis in Older Adults and Adults with Asthma/Chronic Obstructive Pulmonary Disease in Selected Asia-Pacific Locales: Targeted Literature Review


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# Disclosures

**JC** and **SS** are employed by and hold financial equities in GSK. **AL** and **JSE** were employees of Costello Medical at the time this study was conducted, which received fees from GSK for conducting this work; Costello Medical receives fees for its consulting services from a range of companies across the healthcare sector. **VB** was employed by and held financial equities in GSK at the time of this study.

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# Background

- Pertussis (whooping cough) is a bacterial respiratory disease characterised by flu-like symptoms, paroxysmal cough, and post-tussive vomiting.[1]
- While pertussis is most reported in childhood, it can occur at any age.[2]
- Compared with the general adult population, certain individuals are at elevated risk for pertussis, such as those ≥50 years of age (YOA) or with asthma or chronic obstructive pulmonary disease (COPD).[3–6]
- Despite evidence suggesting increased pertussis burden in high-risk individuals in Asia-Pacific (APAC), pertussis vaccination programmes targeting these individuals are generally lacking across the region.[7]

## Aim:

To conduct a **targeted literature review (TLR)** to understand the **epidemiology** and **burden of pertussis in selected APAC locales** (Australia, China, Hong Kong, Japan, New Zealand, Singapore, South Korea, and Taiwan).

1. Tozzi AE et al. CMAJ 2005;172(4):509-515; 2. Macina D et al. Infect Dis Ther 2021;10(3):1115-1140; 3. Bonanni P et al. Hum Vaccin Immunother 2023;19(1):2195786; 4. Jenkins VA et al. Hum Vaccin Immunother 2020;16(11):2609–2617; 5. Kandeil W et al. Expert Rev Vaccines 2019;18(5):439–455; 6. Aris E et al. COPD 2021;18(2):157–169; 7. Nam HL et al. Expert Rev Vaccines 2021;20(12):1603–1617. APAC: Asia-Pacific; COPD: chronic obstructive pulmonary disease; TLR: targeted literature review; YOA: years of age.

# Methods (1/4)

*Search strategy*

- The TLR was conducted in accordance with a pre-specified protocol and involved searching:

**Electronic databases**

**English**

- MEDLINE[a] (including MEDLINE In-Process, MEDLINE Daily and MEDLINE Epub Ahead of Print)
- Embase[a]

**non-English**

- **Chinese**: China National Knowledge Infrastructure, and Airiti Library
- **Japanese**: 医中誌[Ichushi] Web platform
- **Korean**: Research Information Sharing Service

**Grey literature**

- Congress proceedings from selected congresses[b]
- Government health department websites[c]

[a] MEDLINE and Embase were searched simultaneously via the Ovid SP platform. [b] Published in 2020–2022: European Congress of Clinical Microbiology & Infectious Diseases; IDWeek; European Respiratory Society; Asia Pacific Congress of Clinical Microbiology and Infection; International Congress on Infectious Diseases; Annual Scientific Meeting of the Thoracic Society of Australia and New Zealand and the Australia & New Zealand Society of Respiratory Science. [c] To identify national vaccination recommendations/guidelines for inclusion (if not identified via the database searches) from: Australia: Australian Government, Department of Health and Aged Care. China: National Health Commission of the People's Republic of China; Chinese Center for Disease Control and Prevention. Hong Kong: Department of Health, The Government of the Hong Kong Special Administrative Region; Centre for Health Protection. Japan: Ministry of Health, Labour and Welfare of Japan; National Institute of Infectious Diseases. New Zealand: Manatu Hauora Ministry of Health; Institute of Environmental Science and Research. Singapore: Ministry of Health Singapore. South Korea: Ministry of Health and Welfare; Korea Disease Control and Prevention Agency. Taiwan: Ministry of Health and Welfare; Taiwan Centers for Disease Control. TLR: targeted literature review.

# Methods (2/4)

*Study selection*

- Eligible articles on the clinical and epidemiological outcomes,[a] and healthcare resource use (HCRU)[b] related to pertussis were identified based on the pre-specified inclusion and exclusion criteria:
  - ✓ Adults ≥50 YOA and/or adults ≥18 YOA with asthma or COPD who were infected, previously infected, or at risk of pertussis
  - ✓ Published between January 2011–December 2022
  - ✓ Publications and/or abstracts in English, Korean, Japanese, or Chinese only
  - ✓ Interventional studies, observational studies, economic evaluations, guidelines and recommendations
  - ✗ Editorials, notes or comments, narrative reviews, books, case reports, case studies

**Title or abstract review**

Each abstract was reviewed against the eligibility criteria by a single reviewer.[c]

**Full-text review**

Full-text articles that were considered as relevant after the title/abstract review stage were sourced. Each full-text article was then reviewed against the eligibility criteria by a single reviewer.[d]

[a] Articles were eligible if they reported the incidence, prevalence, and/or seroprevalence of pertussis; case-fatality and/or mortality rate of pertussis; risk factors for pertussis; clinical manifestations of pertussis; complications related to pertussis; and/or Tdap vaccination recommendations for the populations of interest. [b] Articles were eligible if they reported the direct cost or resource use associated with pertussis (e.g., hospitalisations, emergency department visits), and/or the indirect cost or resource use associated with pertussis (e.g. work absenteeism, presenteeism, productivity loss). [c] A second reviewer was available to discuss and address any areas of uncertainty. Where the applicability of the inclusion criteria was unclear, the article was included at this stage to ensure that all potentially relevant studies were captured. [d] A second reviewer was available to discuss and address any areas of uncertainty. In cases where the article did not provide sufficient information for certainty that the inclusion criteria were met, the article was excluded to ensure that only relevant articles were included in the TLR. COPD: chronic obstructive pulmonary disease; HCRU: healthcare resource use; Tdap: Tetanus, reduced diphtheria and acellular pertussis; TLR: targeted literature review; YOA: years of age.

# Methods (3/4)

*Data extraction*

- Data were extracted into a pre-specified extraction grid, in Microsoft Excel, by a single individual for each included study.
- The following key information was extracted:
  - **Characteristics of the included studies**: study design, study objective, data cuts, population, inclusion/exclusion criteria, and geographic regions the study was conducted in
  - **Characteristics of the included population**: age, sex, race/ethnicity, smoking status, and existing comorbidities (asthma, COPD, and others)
  - **Epidemiological outcomes**: incidence, prevalence, and seroprevalence of pertussis
  - **Clinical outcomes**: case fatality, mortality, clinical symptoms, risk factors for pertussis, complications related to pertussis, and Tdap vaccination recommendations for the population of interest
  - **HCRU outcomes**: direct and indirect cost and resource use*
  - **Quality-of-life (QoL) outcomes**: QoL and utilities*

*Data on HCRU and QoL outcomes are not included in this presentation. COPD: chronic obstructive pulmonary disease; HCRU: healthcare resource use; KAP: knowledge, attitudes, and practices; QoL: quality of life; Tdap: Tetanus, reduced diphtheria and acellular pertussis.

# Methods (4/4)

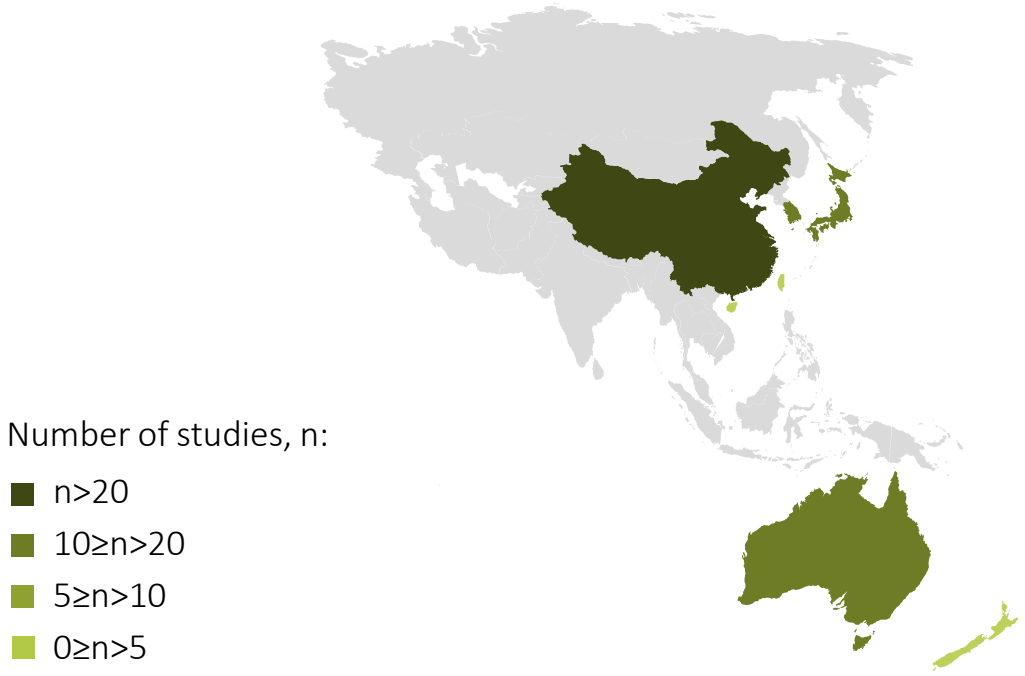
*Quality assessment*

- The quality of all included studies were assessed as follows:
  - Quantitative & qualitative studies: Alberta Heritage Foundation for Medical Research (AHFMR) checklist[1]
  - Practice guidelines: Appraisal of Guidelines for Research & Evaluation Instrument (AGREE II)[2]

1. Kmet LM et al. Standard quality assessment criteria for evaluating primary research papers from a variety of fields. 2004; 2. AGREE Trust. AGREE II Tool. Available from: https://www.agreetrust.org/resource-centre/agree-ii/. AGREE II: Appraisal of Guidelines for Research & Evaluation Instrument; AHFMR: Alberta Heritage Foundation for Medical Research.

# Results (1/5)

- A total of **5,085 records** were identified, of which 103 (**79 unique studies**) were relevant and included:



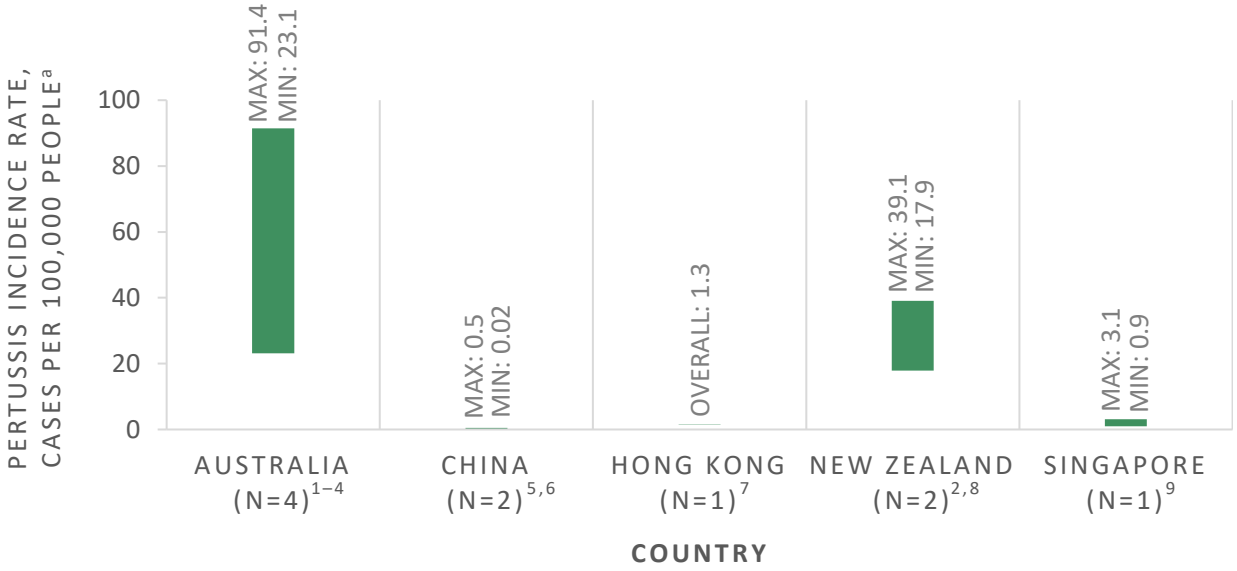

- China (33 studies)
- Australia (15 studies)*
- Japan (11 studies)
- South Korea (10 studies)*
- New Zealand (4 studies)*
- Hong Kong (2 studies)*
- Singapore (2 studies)*
- Taiwan (2 studies)*

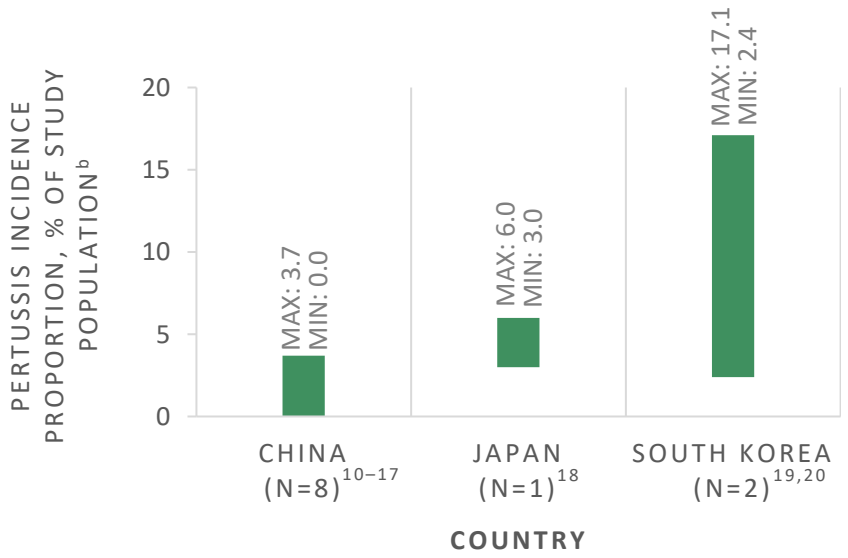
*There were two studies that reported outcomes on multiple regions, of which one reported data for Australia and New Zealand, and the other reported data for Australia, Hong Kong, New Zealand, Singapore, South Korea, and Taiwan.

# Results (2/5)

*Pertussis incidence varied widely in adults ≥50 YOA*

- Limited studies (n=31) reported pertussis incidence in this group: Australia (n=10), China (n=12), Hong Kong (n=1), Japan (n=2), New Zealand (n=3), Singapore (n=2), South Korea (n=4), and Taiwan (n=1).




- Additionally, across locales, there was no consistent trend in incidence rates either with age or over time.

The included studies were varied in their case definitions of pertussis. [a] Studies reporting incidence rates in terms of the number of cases per 100,000 people. [b] Studies reporting incidence rates in terms of percentage incidence of the study population. 1. Pearce R et al. Respirology 2022;27(SUPPL 1):68; 2. Peer V et al. PLoS One 2020;15(4):e0231570; 3. Pillsbury A et al. Commun Dis Intell Q Rep 2014;38(3):E179–E194; 4. Saul N et al. Western Pac Surveill Response J 2017;8(2):5–11; 5. 张军 et al. 微生物学免疫学进展 2021;49(02):68–72; 6. 刘淑霞 et al. 预防医学论坛 2021;27(09):663–665; 7. Centre for Health Protection, Hong Kong. Consensus Recommendations on Pertussis Vaccination for Pregnant Women in Hong Kong; 8. Wall R et al. N Z Med J 2011;124(1332):52–61; 9. Ministry of Health, Singapore. Communicable Diseases Surveillance in Singapore 2018. Available at: https://www.moh.gov.sg/docs/librariesprovider5/default-document-library/communicable-diseases-surveillance-in-singapore-2018.pdf; 10. 迪力娜尔·阿布都拉. 疾病预防控制通报 2011;26(05):79–80+90; 11. 赵继民 et al. 中国公共卫生管理 2019;35(06):789–792; 12. Zheng ZY et al. Chinese Journal of Disease Control and Prevention 2022;26(6):624–630; 13. 沙小兰 et al. 现代预防医学 2020;47(03):395–400+428; 14. 青承昀. 预防医学情报杂志 2019;35(07):671–676; 15. 李瑶 et al. 当代医学 2021;27(15):171–173; 16. 季路 et al. 上海预防医学 2022;34(08):774–779; 17. 刘倩 et al. 河南预防医学杂志 2020;31(08):577–579; 18. Ministry of Health, Labour and Welfare, Japan. 2018年第1週から第16週(*)に感染症発生動向調査(NESID)に報告された百日咳症例のまとめ. Available at: https://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000207162.pdf; 19. Park S et al. J Korean Med Sci 2014;29(9):1232-1239; 20. Lee SY et al. J Korean Med Sci. 2015;30(7):988–990. Max: maximum; Min: minimum; YOA: years of age.

# Results (3/5)

*Pertussis incidence varied widely in adults ≥50 YOA*

- Across studies, the following factors varied and may therefore account for the observed differences in pertussis incidence:

**Geographic location** (e.g., different locales, or different cities/regions within a locale)
Studies in Australia reported a general trend of lower incidence rates in older ages, but Japan and Singapore reported the opposite. Studies in South Korea and China saw mixed trends.

**Population characteristics** (e.g., general population versus a specific patient population)

**Time or time period of study/data**

**Age group** (e.g., ≥50 YOA versus ≥60 YOA)

**Diagnostic practice,[a] methods, and criteria**

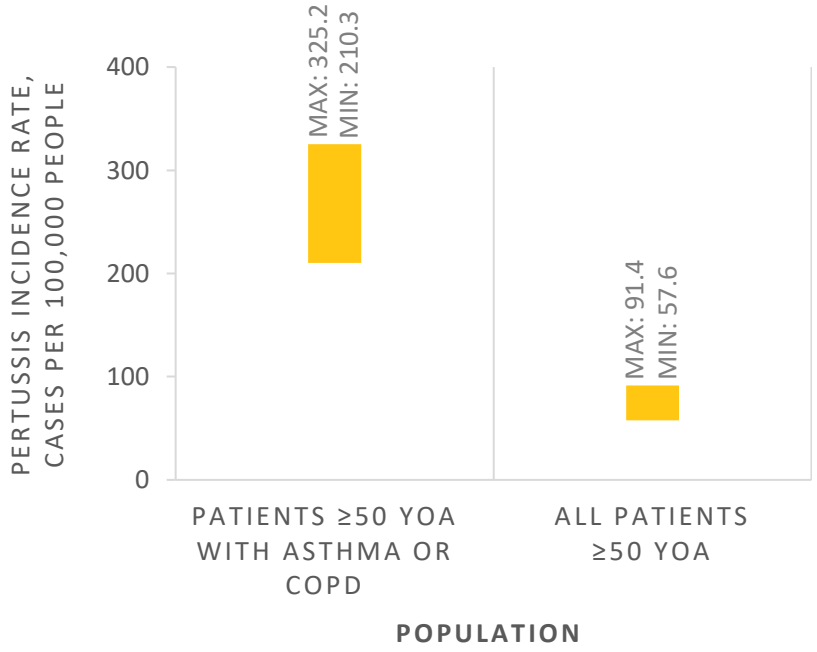
[a] Refers to how often (e.g., routinely or rarely) physicians perform diagnostic testing for pertussis in clinical practice. YOA: years of age.

# Results (4/5)

*Higher pertussis incidence rates were reported in patients ≥50 YOA with asthma or COPD*

- Studies reporting pertussis incidence rates in these patient groups were limited:

**Australia (n=1)[1, a]**



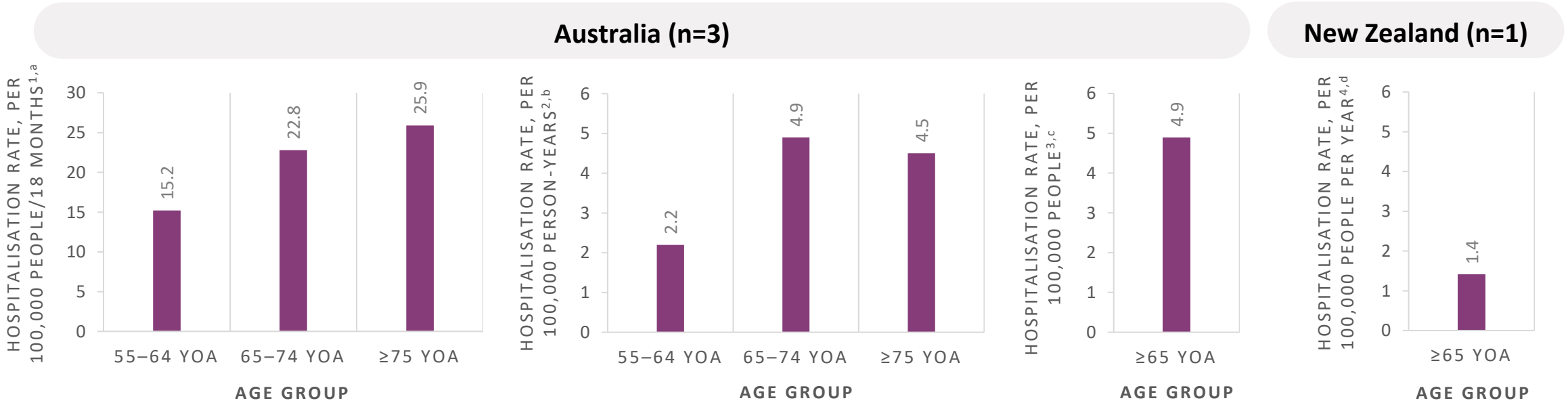

**South Korea (n=1)[2, b]**


[a] Study reported data from 2015–2019.[1] [b] Study reported data from 2009–2018.[2] 1. Pearce R et al. Respirology 2022;27(SUPPL 1):68; 2. Kim H et al. ERS 2021;58(SUPPL 65). COPD: chronic obstructive pulmonary disease; Max: maximum; Min: minimum; YOA: years of age.

# Results (5/5)

*Studies on pertussis-related hospitalisation rates and deaths in adults ≥50 YOA were limited*

- Only studies from Australia and New Zealand reported pertussis-related hospitalisation rates, which generally increased with age:




- Separately, one Japanese study reported 0.0–1.0 pertussis death/year between 2006–2017.[5]

[a] Study reported data from 2008–2009.[1] [b] Study reported data from 2006–2012; based on participants who had a linked hospitalisation record in the APDC database where either the primary or a secondary diagnosis was coded with ICD-10-AM code A37 (whooping cough), or where the primary hospital diagnosis was coded with ICD-10-AM J-codes (respiratory disease) or code R05 (cough) and the admission occurred within a week prior and up to 6 weeks subsequent to the linked pertussis diagnosis date.[2] [c] Study reported data from 2006–2010; based on data from the Australian Institute of Health and Welfare National Hospital Morbidity Database, where all hospital admissions between 1 January 2006–31 December 2010 were included based on ICD-10-AM code A37 (whooping cough) or a subcode listed as the principal or other diagnosis.[3] [d] Study reported data from 2000–2009.[4] 1. Clarke MF et al. Epidemiol Infect 2013;141(3):463–471; 2. Karki S et al. Vaccine 2015;33(42):564–5653; 3. Pillsbury A et al. Commun Dis Intell Q Rep 2014 Sep 30;38(3):E179–94; 4. Wall R et al. N Z Med J 2011;124(1332):52–61; 5. Ministry of Health, Labour and Welfare, Japan. 2019. 沈降精製百日せきジフテリア破傷風混合ワクチン(DTaP). Available at: https://www.mhlw.go.jp/content/10906000/000565709.pdf. APDC: Admitted Patient Data Collection; DTaP: Diphtheria, Tetanus, acellular Pertussis; ICD-10-AM: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification; YOA: years of age.

# Strengths of the TLR

- **Well-defined inclusion criteria** were applied.
- **Comprehensive literature search** of both English and non-English electronic databases, as well as **manual searches** of conference proceedings and government websites of relevant regions.
  - Allowed studies published in various languages to be captured, minimising the risk of language bias.
- **Quality assessment** of the included studies were conducted.

TLR: targeted literature review.

# Limitations of the TLR

- Strict inclusion criteria on the target age group (i.e., ≥50 YOA) resulted in the exclusion of studies that reported data in adults within a wider age range e.g., 40–60 YOA.
- Limited to studies published from 2011 onwards, which may have hence excluded earlier studies reporting relevant data.
  - Nevertheless, this approach was taken to collect data that are most reflective of the current clinical, economic, and epidemiological landscape.
  - Therefore, the risk of missing relevant data was considered low.
- Employed a single-reviewer approach, as opposed to a dual-reviewer approach utilised in systematic reviews, thereby introducing a small chance that relevant data were missed.
  - However, stringent eligibility criteria were applied throughout, with a second reviewer available to advise on any cases of uncertainty.

TLR: targeted literature review; YOA: years of age.

# Conclusions

Data on the burden of pertussis were **limited** across APAC and are **likely underestimated** due to low awareness, atypical or non-specific symptom presentation, and underutilisation of molecular diagnostics.

Pertussis incidence rates **varied widely** and where reported, were observably **heightened in patients with asthma or COPD**. Data on pertussis mortality were notably limited.

**Greater pertussis awareness** is needed among patients and healthcare professionals.

Further studies may **improve understanding** and **inform strategies** for regional pertussis prevention and control, particularly in individuals at increased risk for the disease.

APAC: Asia-Pacific; COPD: chronic obstructive pulmonary disease.

# Thank you

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