September 2026
Agency for Care Effectiveness (ACE), MOH

Evidence-to-Recommendation Framework for 2026 ACE Clinical Guideline on community-acquired pneumonia — assessment, diagnosis and antibiotic prescribing

Bhone Myint Kyaw, PhD, MBBS, Sonja CJH Chua, PhD, BSc (Pharm) (Hon), Yan Ting See, BSc (Life Sciences) (Hon), Expert Group for Community-Acquired Pneumonia ACG*, Valentina Ricci, MSc (Social Epidemiology), BSc (Physio), Phyllis AL Kim, MPH, MBChB

*List of members is acknowledged at the end of the article

Evidence to Practice Division, Agency for Care Effectiveness, Ministry of Health, Singapore

Abstract

This Evidence-to-Recommendation (EtR) framework underpins the ACE Clinical Guideline (ACG) for the management of non-severe bacterial community-acquired pneumonia (CAP) in adults, providing rationale and justifications for the guideline recommendations. Pneumonia remains a leading cause of morbidity and mortality in Singapore, accounting for 4.6% of hospitalisations and 23% of deaths in 2024. The ACG addresses management gaps that contribute to poor clinical outcomes, including diagnostic uncertainty, inappropriate prescribing and suboptimal treatment. The Grading of Recommendations Assessment, Development and Evaluation framework was followed to develop five evidence-based recommendations covering CAP assessment, diagnosis, and management with antibiotics. This EtR framework summarises the factors that have informed the direction and strength of the ACG recommendations, providing the rationale and decisions by the Expert Group to aid clinicians in understanding and applying the recommendations to their management of CAP. The ACG can be found at https://go.gov.sg/acg-cap

Introduction

The topic of community-acquired pneumonia (CAP) was proposed in the 2023 ACE Clinical Guideline (ACG) topic call to address the absence of national guidelines and the variations in CAP management across local care settings. Pneumonia remains a leading cause of morbidity and mortality in Singapore, accounting for 4.6% of all hospitalisations and 23.0% of deaths in 2024.[1, 2]

While penicillin-based antibiotics remain effective treatment options for most patients with CAP, there is increasing prevalence of drug-resistant *S. pneumoniae* internationally[3, 4] and in Singapore.[5, 6] Locally, macrolide-resistant *S. pneumoniae* isolates increased from 1998 to 2001, with these isolates commonly resistant to other antibiotics.[7, 8] Additionally, there is increased utilisation of antibiotics for respiratory infections post-COVID-19, with a concerning use of the WHO 'Watch' category antibiotics (fluoroquinolones, macrolides) from 2018-2023, with a compound annual growth rate of 2% for macrolide use.[9] Poor antimicrobial stewardship will ultimately lead to multidrug resistance, increasing healthcare burden, costs, and adverse patient events.

Interviews with domain experts (n=4) and primary care physicians (n=8) identified limited access to chest radiography, perceptions of patient convenience, and the fear of negative patient outcomes as key barriers to appropriate antimicrobial prescribing. Decision making for antibiotic prescribing is complex,[10] with diagnostic uncertainty being the main challenge.[11-13]

This ACG supports clinicians in their clinical assessment and diagnosis of bacterial CAP, and in making informed antibiotic treatment decisions for patients with non-severe CAP treated in the community setting.

Methods

This guideline was developed following the ACE methods and processes for ACG development.[14] A systematic search for international guidelines was conducted across databases including Guideline Central, GIN Library, ECRI Guidelines Trust, PubMed, Epistemonikos, and Trip Medical Databases, supplemented by manual retrieval from relevant specialty associations. Nine English-language guidelines published within the previous seven years were prioritised and assessed using the AGREE-II tool Domain 3 (Rigour of Development), applying a minimum 60% scaled domain score threshold. Overall, six high-quality guidelines were selected as main reference guidelines. Recent systematic reviews and meta-analyses were identified from PubMed and Google Scholar to complement guideline evidence.

A multidisciplinary expert group (EG) comprising five family medicine physicians, three infectious disease physicians, two emergency medicine physicians, one respiratory physician and two pharmacists was appointed to provide clinical expertise throughout guideline development.

Draft recommendations were formulated using the GRADE Evidence-to-Recommendation (EtR) framework, incorporating five key domains: balance of benefits and harms; certainty of evidence; values and preferences; resources and feasibility; and acceptability and other considerations. EG members individually rated recommendation appropriateness using the RAND/UCLA Appropriateness Method on a 1-9 scale, followed by structured discussions to achieve consensus.

Recommendation 1a: Diagnose community-acquired pneumonia (CAP) based on clinical signs and symptoms.

Recommendation 1b: Order a chest X-ray if:

- **the diagnosis cannot be made based on clinical signs and symptoms alone, or**
- **other serious respiratory conditions are suspected.**

Strength of recommendation 1a: **Strong** Conditional

Strength of recommendation 1b: **Strong** Conditional

Summary: The ACG provides a strong recommendation for a clinical diagnostic approach to CAP, based on signs and symptoms. This allows appropriate empirical treatment to commence promptly to improve patient outcomes, without requiring a chest X-ray (CXR), despite the limited supporting evidence. This approach also aligns overall with international high-quality guidelines and considers patient values and preferences, plus resource and feasibility concerns. Whilst CXR is not mandatory for CAP diagnosis, it is indicated when clinical diagnosis remains uncertain and confirmation is required, or when underlying serious respiratory conditions (e.g. malignancy or tuberculosis) are suspected.[15] Strong recommendations are made based on favourable benefit/risk balance of CXR in these circumstances.

Balance of benefits and harms

The findings from the literature and international guidelines support diagnosing CAP using a combination of clinical signs and symptoms indicative of pneumonia, such as **cough**, **dyspnoea**, **pleural pain**, **fever**, **tachycardia**, **tachypnoea**, and **localised chest findings like crackles on auscultation**.[16, 17] Overall, reference guidelines emphasise using a constellation of signs and symptoms to diagnose CAP.[17-19]

A longitudinal cohort study (n=28,883) reported that some clinical signs are more likely to be associated with pneumonia, including **temperature** >37.8°C; **pulse** >100/min; **crackles on**

auscultation and **oxygen saturation <95%**;[20] most patients with pneumonia (86.1%) exhibited at least one of these four clinical signs and the positive predictive value of having at least one of these signs was 20.2% (95% CI 17.3–23.1).[20] However, **no single symptom reliably predicts CAP due to limited evidence, necessitating diagnosis based on multiple indicators.**[21]

Older patients may present with atypical symptoms (e.g. confusion, exacerbation of pre-existing conditions) which can obscure the diagnosis of pneumonia, potentially leading to adverse patient outcomes. While CXR is not mandatory, it can serve as an important tool in confirming the diagnosis, and CXR is warranted if the clinical diagnosis of CAP is uncertain.[22, 23]

Certainty of evidence	Values and preferences
Recommendation 1a: Evidence supporting clinical diagnosis is based on findings from observational studies with a high risk of bias, and the certainty of evidence on reported outcomes is assessed to be low. Recommendation 1b: The certainty of evidence for diagnostic accuracy of CXR was assessed to be very low due to imprecision of the reported findings (sensitivities of 32% to 93%, and specificities of 0% to 94%)[24, 25] plus the indirectness of the study population limiting the generalisability of the findings.	Recommendation 1a: No significant concerns or variability identified regarding patient preferences of outcomes. Recommendation 1b: No significant concerns were identified, despite possible variation in patient preferences for CXR.
Resources and feasibility	**Acceptability and other considerations**
Recommendation 1a: No resource concerns were identified as clinical diagnosis does not routinely require laboratory or imaging tests. Recommendation 1b: Immediate access to CXR may be limited in some primary care clinics, but follow-up imaging can be arranged for patients where required.	The clinical diagnosis of CAP based on signs and symptoms allows for timely treatment, although limitations exist in certain populations (e.g. older patients presenting with atypical symptoms). In such cases, CXR is recommended for diagnostic confirmation.

Expert Group deliberation of above factors

The EG agreed with a clinical diagnostic approach for CAP based on signs and symptoms, and requested for the ACG to include information about the different severities of CAP presentations. The EG also agreed that CXR should be conducted when there is diagnostic uncertainty using a clinical approach, or when other serious respiratory conditions are suspected.

Recommendation 2: Use the CRB-65 tool to help inform whether a patient with non-severe CAP should be treated in the community or hospital setting.

Strength of recommendation 1a: **Strong** Conditional

Summary: Appropriate treatment for patients with CAP is informed by the severity of the condition (based on the patient's history and clinical signs and symptoms), and the patient's risk of severe outcome from the condition (e.g. 30-day mortality).[26] Overall, the recommendation was assessed to be strong as the benefits of the CRB-65 substantially outweigh the limitations when used as intended—not rigidly, but to complement clinical judgement. The certainty of evidence on reported outcomes was assessed to be moderate, and there are no significant concerns regarding patients' values, preferences, or accessibility.

Balance of benefits and harms

The CRB-65 [**C**onfusion, **R**espiratory rate ≥30/min, **B**lood pressure (systolic <90 mmHg or diastolic ≤60 mmHg), age ≥**65** years] is useful for identifying patients' mortality risk.[27-29] A recent systematic review (SR) and meta-analysis (MA) of the CRB-65 (29 studies) found the CRB-65 can be used by clinicians to estimate 30-day mortality risk, and can serve as a useful tool in conjunction with clinical judgement.[27] Patients in the low-risk group with a score of 0 have a very low mortality risk (0.5% compared to a typical mortality rate of 4% for CAP) and can, in most cases, safely be treated as outpatients.[27]

The CRB-65 is preferred for its simplicity and good overall performance.[27, 28, 30] Nonetheless, it may oversimplify complex clinical presentations and lead to inappropriate disposition decisions when important contextual factors such as social circumstances, functional status, or specific comorbidities are inadequately considered. Overall, the benefits of CRB-65 substantially outweigh the limitations when used as intended, that is, as a tool to complement clinical judgement.

Certainty of evidence

The CRB-65 has been extensively validated through multiple studies, with a recent SR and MA (29 studies) providing favourable results relating to its performance.[27] The certainty of evidence supporting CRB-65 use in primary care is assessed to be moderate.

Values and preferences

Most patients with non-severe CAP may value home-based care when clinically appropriate. Patients generally appreciate transparent risk communication, and the CRB-65 facilitates this by offering concrete, understandable criteria that clinicians can explain, helping patients comprehend why specific care recommendations are made and thereby reducing anxiety about treatment decisions.

Resources and feasibility

Compared to other tools which require laboratory testing, the CRB-65 is more feasible and easily implemented in the primary care setting as it requires no additional equipment or test and can be completed during routine consultation without workflow disruption or additional staff time.

Acceptability and other considerations

The CRB-65 is assessed to be associated with high patient acceptability as it involves only non-invasive clinical assessments that patients routinely expect during medical consultations. The use of the CRB-65 tool may align well with patient preferences for shared decision-making, where individual circumstances, social support, and personal preferences for home care or institutional medical settings can be considered alongside clinical factors.

Expert Group deliberation of above factors

The EG agreed to mention the CRB-65 in the recommendation as the main assessment tool to help determine the best site of care for patients with non-severe CAP, whilst clarifying that its use is not mandatory nor stand-alone. The EG emphasised the importance of clinical judgement in making objective decisions with the aid of CRB-65.

Recommendation 3: Do not routinely conduct microbiological testing for patients who are deemed suitable for treatment in the community setting.

Strength of recommendation 3: **Strong** Conditional

Summary: Microbiological testing for patients with CAP in community settings is frequently associated with low diagnostic yields and delayed results from conventional cultures that do not influence initial treatment decisions. Additionally, limited availability of testing equipment and on-site laboratory facilities, along with insufficient evidence regarding the cost-effectiveness of routine testing, further limit implementation.[31] While newer tests like point-of-care tests (e.g. urine antigen tests) show promise, further evidence is required before they can be recommended for routine use.[32] Overall, routine testing of blood and sputum culture as well as urine antigen tests and tests for atypical infections are not recommended for patients with non-severe CAP who are deemed suitable for treatment in the community setting.

Balance of benefits and harms

Routine microbiological testing including blood and sputum cultures, Gram stain and culture of respiratory secretions, pneumococcal and legionella urine antigen tests, and tests for atypical infections are not routinely recommended for the management of CAP in primary care settings.[18, 33, 34] While urine antigen testing for *Legionella* and *Streptococcus pneumoniae* can be valuable in severe cases or during outbreaks, it is not recommended for routine use.[18, 33, 34]

Blood culture: Blood cultures are routinely recommended in severe CAP or cases with risk factors for multidrug-resistant organisms like *Staphylococcus aureus* or *Pseudomonas aeruginosa*, but not typically for non-severe CAP due to a low diagnostic yield and limited impact on initial antibiotic treatment selection.[35, 36]

Gram stain and culture testing (sputum and respiratory secretion): There is limited evidence supporting these tests in initial treatment decision for patients with non-severe CAP. International guidelines agree that these tests are not necessary for management of non-severe CAP in the community setting.[18, 33, 37-39]

Urine antigen tests for *Streptococcus pneumoniae* (pneumococcus) and *Legionella pneumophila*: Literature findings, including randomised trials, have reported no clear benefits for these tests.[33, 40-42]

Certainty of evidence

The certainty of evidence for diagnostic accuracy of tests for CAP varies by test, with some point-of-care tests such as urine antigen tests showing more promise but requiring further robust evidence synthesis.[31,43,44] High-quality evidence is needed to provide clarity on test performance, as many studies lack rigor or focus on specific subsets of patients.

Values and preferences

There is a lack of evidence pertaining to patient outcomes preferences and values associated with routine testing. Some patients may request test(s) to reduce the risk of complications and transmission, whilst others may value symptom resolution and early recovery and favours routine testing despite limited evidence. Overall, no significant variability in values and preferences is expected.

Resources and feasibility

Routine microbiological testing in CAP may be associated with significant resource and feasibility challenges in primary care settings. Many primary care clinics may lack on-site microbiology laboratories, requiring sample transport to centralised facilities, whilst the 24-72-hour turnaround time for culture results often exceeds the clinical decision-making window for

Acceptability and other considerations

The acceptability of routine microbiological testing in CAP is limited by patient discomfort and anxiety with sample collection. Healthcare providers may show reduced enthusiasm due to low diagnostic yields, delayed results that rarely influence initial treatment decisions, and workflow disruptions.[45]

immediate antibiotic therapy. Direct laboratory and transport costs, alongside indirect costs from staff time and follow-up consultations, further reduce the feasibility of routine testing in the primary care.	

Expert Group deliberation of above factors

The EG agreed with the recommendation to avoid the routine use of microbiological tests for managing patients with non-severe CAP in community settings. The word 'routine' was intentionally included in the recommendation as the EG acknowledged the importance of clinical judgement when deciding the best care for each individual patient. The EG stated that it would be helpful to list the various microbiological tests in the supporting text, along with a brief reason why these tests were typically not required.

Recommendation 4: Prescribe empirical antibiotic therapy for patients with non-severe CAP:
4a: Use amoxicillin for patients at low risk of complications.

4b. Use amoxicillin + clavulanic acid for patients at higher risk of complications.

4c: Use doxycycline, azithromycin or clarithromycin as an alternative antibiotic for patients with penicillin or beta-lactam allergy.

Strength of recommendation 4a: **Strong** Conditional

Strength of recommendation 4b: **Strong** Conditional

Strength of recommendation 4c: **Strong** Conditional

Summary: *Streptococcus pneumoniae* is the primary bacterial cause of CAP in Singapore, with *Haemophilus influenzae* and *Staphylococcus aureus* also common.[46-48] Favourable benefit/risk balance supports strong recommendations on initiating empirical antibiotic treatment for patients with CAP – in alignment with published literature. No significant concerns were identified regarding patient values and preferences, though some variability in patient acceptability is expected depending on the antibiotic's dosing and frequency. Recommended antibiotics were identified based on assessment of international literature and available (albeit limited) local antimicrobial susceptibility data, sense-checked against the WHO AWaRe classification.

Balance of benefits and harms

Comparison of different antibiotic regimens in patients with non-severe CAP in outpatient settings showed similar clinical outcomes across antibiotic types.[49] The findings from an SR comparing cephalosporins against amoxicillin + clavulanic acid showed similar clinical success rates.[49] Two Cochrane SRs similarly found insufficient evidence to recommend one antibiotic over another for outpatient CAP treatment.[50, 51] Regarding antibiotic duration, SRs and MAs consistently indicated that shorter courses (≤5 days) are as effective as longer courses of antibiotics (>5 days).[52-56]

Empirical antibiotic selection should also consider patient-specific factors. In pregnant patients, antibiotic selection should be based on proven safety, using only antibiotics which are safe during pregnancy.[33, 34, 57] Similarly, older patients with CAP may require additional risk-benefit assessments given age-related differences in pharmacokinetics, adverse effects, and outcomes.[58-61]

There is limited evidence relating to coverage of atypical infections, particularly for outpatient settings. A large MA (28 trials n=5,939) found no difference in 30-day mortality, total adverse events,

and treatment discontinuation with empirical atypical coverage in hospitalised CAP patients,[62] though some studies reported reduced mortality,[63] and improved clinical stability.[64]

In a) patients with more severe symptoms who remain suitable for community management, b) patients who fail to improve after 48 hours of initial antibiotic treatment, or c) patients at risk of complications (e.g. patients with underlying comorbidities), an antibiotic with broader spectrum or combination therapy with two antibiotics may be appropriate.

Certainty of evidence	Values and preferences
The certainty of evidence for antibiotic selection in non-severe CAP is low to moderate. While multiple SRs provide consistent findings that different antibiotic classes achieve similar clinical outcomes, the indirectness of the findings limits their generalisability and reduces confidence in specific recommendations.	No significant issues are observed regarding patient values and preferences in antibiotic selection in CAP. Patients generally value antibiotics that resolve symptoms quickly with minimal adverse effects.
Resources and feasibility	**Acceptability and other considerations**
Most antibiotics for CAP are available in most primary care settings and there is no observed issue regarding resource and feasibility.	Patient acceptability varies for different antibiotic options, with amoxicillin + clavulanic acid historically associated with gastrointestinal adverse effects which might reduce patient acceptability and treatment adherence. Alternative antibiotics should be considered for affected patients. In general, patients prefer and adhere better to antibiotics requiring less frequent dosing.

Expert Group deliberation of above factors

The EG agreed to recommend amoxicillin as the preferred first-line for non-severe CAP in patients with low risk of complications. This aligns with antimicrobial stewardship principles, and the dosing of amoxicillin 1 g three times daily provides a higher daily amoxicillin dose against *S. pneumoniae* compared to standard amoxicillin + clavulanic acid dosing.

For patients with a higher risk of complications, the EG recommended amoxicillin + clavulanic acid (+/- a macrolide). For patients with penicillin or beta-lactam allergy, the EG agreed to recommend doxycycline, azithromycin, or clarithromycin. Levofloxacin was positioned as a ‘reserved’ option from an antimicrobial stewardship perspective.

Recommendation 5a: Ask patients and carers to monitor their symptoms and seek immediate medical attention if their condition does not improve or worsens.

Recommendation 5b: Schedule a follow-up consultation for patients with non-severe CAP if required, prioritising those at high risk of complications.

Strength of recommendation 5a: **Strong** Conditional

Strength of recommendation 5b: **Strong** Conditional

Summary: The recommendations emphasise the importance of self-monitoring, care escalation, and follow up for CAP patients on antibiotic treatment, particularly for those at higher risk of complications, despite limited supporting evidence. The need for these measures depends on treatment response and individual patient circumstances. These measures serve as a crucial safety net, enabling immediate and appropriate intervention whilst preventing progression to severe cases that require more intensive and costly interventions. The potential benefits outweigh harms, especially for patients with a higher risk of complications, though there may be variations in patients' values, acceptability and preferences.

Balance of benefits and harms

Patient empowerment improves treatment adherence and patient participation in management.[65] Self-monitoring and care escalation (where required) enable early detection of treatment failure, reducing time to appropriate treatment and minimising unnecessary hospitalisation. Systematic follow-up similarly enables early detection of treatment failure, allowing timely antibiotic modification, care escalation, or investigation for complications whilst providing opportunities to monitor recovery and address patient concerns. Despite limited evidence, the benefits outweigh harms when follow-up is applied judiciously to patients with concerning symptoms or risk factors rather than as universal routine practice.

Certainty of evidence

The certainty of evidence for self-monitoring and systematic follow-up protocols for patients with CAP is low to very low. Most evidence supporting follow-up practices comes from clinical experience, expert opinion, and extrapolation from hospital-based studies rather than dedicated RCTs comparing different follow-up approaches or frequencies.

Values and preferences

Patients' values and preferences may vary, with some patients preferring minimal healthcare contact once feeling better and therefore viewing routine follow-up as an unnecessary burden, whilst others value proactive monitoring. Overall, there are no significant concerns.

Resources and feasibility

For self-monitoring by patients and carers, there are no concerns about resource utilisation and feasibility. Follow up for patients with CAP may present resource challenges, including additional staff and patient time. It may be associated with resource overutilisation. Prioritising follow up of patients at higher risk of complications addresses clinical needs and acknowledges the need to rationalise available resources.

Acceptability and other considerations

Patient acceptability may vary, with some finding self-monitoring and follow-up empowering and reassuring, whilst others view them as unnecessary once they feel better, potentially leading to delayed treatments or missed appointments.

Expert Group deliberation of above factors

The EG agreed with the position of the two recommendations: the first helps patients and carers to monitor treatment response and recognise signs of clinical deterioration warranting follow-up or urgent medical attention, whilst the second targets high-risk patients identified at diagnosis for prioritised follow-up. The EG noted that deterioration timelines vary significantly between patients, with some (e.g. older patients) potentially deteriorating in less than a day.

Implementation

Systematic implementation of evidence-based recommendations encourages timely and accurate diagnosis, and prompt treatment initiation, while reducing inappropriate antibiotic use. Such efforts reduce growing antimicrobial resistance, improve patient outcomes and lower associated healthcare utilisation and costs.

To drive sustained behaviour change, implementation activities must target capacity, opportunity and motivation barriers. Suggested activities include:

- **Integration into clinical pathways:** Embed recommendations within organisational protocols and clinical pathways, ensuring alignment with current workflows and resource considerations.
- **Education and training:** Enhance clinician's confidence and knowledge in CAP diagnosis and management through expert-led discussions and the integration of guideline recommendations into training programmes. Topics should include CAP clinical presentations; use of the CRB-65 to guide right-siting; appropriate empirical antibiotic selection and dosing for different patient groups; clear self-monitoring guidance for all patients, and prioritised follow-up care for patients at higher risk of complications.
- **Antimicrobial stewardship units (ASUs):** Consider establishing ASUs within Primary Care Networks to promote responsible antibiotic use or extending existing ASUs within public healthcare institutions to PCN clinics to form a support network for GPs in cases of uncertainty, provide access to educational sessions and support antibiotic utilisation monitoring.
- **Digital support tools:** Integrate recommendations into clinical decision support systems for point-of-care management (e.g. creating customised medication order sets with prespecified antibiotics and dosing for different patient groups) to guide appropriate use.
- **Monitoring and feedback:** GPs in particular are encouraged to participate in the GP-Antimicrobial Utilisation Surveillance Initiative (GP-AMU) to contribute antimicrobial utilisation data and receive data-driven feedback benchmarking their antibiotic prescribing against sector averages. Explore establishing prospective microbiological data collection methods to monitor evolving local resistance patterns and inform adjustments to antibiotic appropriateness over time.
- **Patient empowerment:** Explore patient materials and programs to increase patient literacy on antimicrobial stewardship principles, including importance of treatment adherence, warning signs and symptoms to monitor during antibiotic treatment, and when to seek further medical attention, particularly for those not scheduled for follow-up.

Conclusion

This EtR framework summarises the evidence base, rationale and expert deliberations that underpin the ACG recommendations for managing non-severe bacterial CAP.

The recommendations apply across all care settings, but are particularly relevant to primary care. Aligned with Singapore's National Strategic Action Plan on Antimicrobial Resistance and endorsed by the Communicable Diseases Agency Singapore, the guideline aims to provide guidance for primary care practitioners to optimise the management of non-severe CAP through accurate assessment and diagnosis, reducing the need for unnecessary diagnostic tests and ensuring prompt and appropriate empirical antibiotic therapy and dosing.

Collectively, the adoption of these recommendations and strategies reinforces national efforts to combat growing antimicrobial resistance and advance antimicrobial stewardship while improving clinical outcomes for patients with non-severe CAP.

Acknowledgement

*The Expert Group for the ACE Clinical Guideline on Community-Acquire Pneumonia: Prof John Arputhan Abisheganaden, Respiratory & Critical Care Medicine (Tan Tock Seng Hospital); Dr Joanne Khor, Family Medicine (National University Polyclinics); Dr Chan Si Min, Infectious Disease Medicine, Paediatrics (National University Hospital); Adj A/Prof Kuan Win Sen, Emergency Medicine (National University Hospital); Dr Lee Tau Hong, Infectious Disease Medicine (Mount Elizabeth Medical Centre); Dr Derek Li Shi'an, Family Medicine (Raffles Medical Group, Serangoon Central); Ms Cheryl Lim Li Ling, Pharmacy (Sengkang General Hospital); Dr Ranjeev Kumar Nanta Kumar, Emergency Medicine (Khoo Teck Puat Hospital); Dr I Gusti Ngurah Prawira Suartha Oka, Family Medicine (SingHealth Polyclinics); Dr Keith Tan, Family Medicine (Yishun Polyclinic, National Healthcare Group Polyclinics); Ms Tan Sock Hoon, Pharmacy (Tan Tock Seng Hospital); Prof Tan Thuan Tong, Infectious Disease Medicine (Singapore General Hospital); Dr Teo Cheng Rong, Family Medicine (Healthway Medical Clinic, Limbang Shopping Centre).

We also gratefully acknowledge Dr Michelle Koo for her contribution in editorial review in the development of this article.

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