Bridging the gap in the prevention of respiratory syncytial virus infection among older adults in Hong Kong

Ivan FN Hung[1,2] *, MD (HK), FRCP (Lond), **Ada WC Lin**[3], FHKAM (Medicine), FHKCCM, **Jane CK Chan**[4], MD, PDipID, **Tony NH Chan**[5], FHKAM (Medicine), FRCP (Edin), **Philip Eng**[6,7], MMed, FRCP (Lond), **Angus HY Lo**[8], FHKAM (Medicine), FRCP (Edin), **Martin CS Wong**[9,10], MD, MPH, **William KK Wong**[5], FHKAM (Medicine), FRCP (Edin)

[1] *Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China*
[2] *Gleneagles Hospital Hong Kong, Hong Kong SAR, China*
[3] *HKSH Medical Group, Hong Kong SAR, China*
[4] *Hong Kong Chinese Medical Association, Hong Kong SAR, China*
[5] *The Hong Kong Geriatrics Society, Hong Kong SAR, China*
[6] *Mount Elizabeth Hospital, Singapore*
[7] *National University of Singapore, Singapore*
[8] *Premier Medical Centre, Hong Kong SAR, China*
[9] *The Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China*
[10] *Editor-in-Chief,* Hong Kong Medical Journal

* Corresponding author: ivanhung@hku.hk

This article was published on 29 May 2024 at www.hkmj.org.

Hong Kong Med J 2024;30:196–9
https://doi.org/10.12809/hkmj245156

Respiratory syncytial virus (RSV) is an important pathogen that causes acute respiratory tract illness and exacerbations of chronic cardiopulmonary disease among adults.[1-3] Although most RSV infections in adults are mild, advanced age, chronic cardiopulmonary disease, and immunocompromising conditions can predispose individuals to higher risks of morbidity and mortality.[1,3,4] Respiratory syncytial virus will become an increasingly important threat to countries/regions with an ageing population, such as Hong Kong. In 2046, older persons are projected to constitute 36% of Hong Kong's total population,[5] underscoring the need to better understand the RSV disease burden to protect this vulnerable population.

Respiratory syncytial virus disease burden in older adults is substantial but often underestimated

Respiratory syncytial virus is a major cause of morbidity and mortality in older adults. In 2019, adults aged >70 years had the highest worldwide mortality rate of 34.5 per 100 000 individuals.[5] Recent studies have shown that, in older adults, RSV causes more severe infections than influenza.[6,7] Older patients hospitalised for RSV have longer hospital stays, higher risks of pneumonia and bacterial superinfection, a higher risk of intensive care unit admission, a greater likelihood of repeat hospitalisation, and higher in-hospital and 1-year mortality rates than older patients hospitalised for influenza.[6,7]

Respiratory syncytial virus infection imposes a substantial economic burden on older adults. In the United States, the national direct cost of RSV-related hospitalisations among adults aged ≥60 years was estimated to be US$1.5 to 4.0 billion in 2005.[8] Furthermore, severe RSV can cause functional decline and insidious deterioration of respiratory health, along with high mortality, in frail older adults.[9-12] Exacerbations of congestive heart failure and other chronic conditions can substantially contribute to disease burden among older adults.[3,13]

Changes in respiratory syncytial virus seasonality can hinder reduction of its disease burden

Respiratory syncytial virus circulation is seasonal, typically peaking between April and November in Hong Kong.[14] An understanding of RSV seasonality can facilitate effective public health planning and resource allocation. However, disruptions in RSV seasonality could lead to off-season outbreaks that affect health system performance.[14] For example, the implementation of infection control measures during the coronavirus disease 2019 pandemic and their subsequent relaxation has led to an atypical surge in RSV activity across many countries in the post–coronavirus disease 2019 era,[15-17] highlighting the need for year-long disease surveillance.

Existing challenges that lead to the underestimation of respiratory syncytial virus burden in older adults

Respiratory syncytial virus infection is challenging to diagnose because of its non-specific clinical

symptoms.[14,18] Although rapid antigen diagnostic tests and nucleic acid amplification tests are important tools for RSV detection, their diagnostic accuracy in adults is generally poor due to the lower viral load in such patients, especially when upper respiratory tract specimens are used for testing.[9,18,19] Therefore, clinicians must be aware of the limitations of current assays while supporting the development of more sensitive assays for adults.

Additionally, the testing rate among adult patients remains suboptimal,[14] resulting in underdiagnosis of RSV infection. The absence of disease surveillance protocols and lack of systemic data collection mechanisms lead to further underestimation of the RSV disease burden in Hong Kong.[14] Currently, RSV is not one of the statutory notifiable infectious diseases according to the Centre for Health Protection.[14] A surveillance system that allows clinicians to submit data regarding positive RSV cases would be helpful in terms of monitoring its incidence and disease burden.

A safe and effective vaccine is needed to reduce respiratory syncytial virus disease burden

The current approach to managing RSV infection in adults focuses on supportive care.[3] Whereas immunoprophylaxis with monoclonal antibodies is recommended for infants and young children, there are no clinical data supporting these treatments for high-risk adults.[3] In the absence of guideline-directed management, some clinicians do not recommend RSV testing for adults with suspected acute lower respiratory tract infection (ALRTI). Considering the high RSV disease burden and lack of RSV-specific treatment, a safe and effective vaccine is urgently needed to prevent RSV-related severe illness among high-risk adults.

The quest for an effective RSV vaccine began in the 1960s and encountered multiple obstacles. The discovery of the RSV fusion (F) glycoprotein in its pre-F conformation has renewed interest in vaccine development. The RSV pre-F protein (RSVpreF) has emerged as an attractive candidate vaccine target because of its conserved neutralising epitope.[20,21]

The multinational phase III RENOIR trial (RSV Vaccine Efficacy Study in Older Adults Immunized against RSV Disease) showed that the bivalent RSVpreF vaccine had respective efficacy rates of 84.4% and 81.0% for preventing ALRTI and medically attended RSV-associated acute respiratory tract illness over two RSV seasons among immunocompetent adults aged ≥60 years.[22] Importantly, the RSVpreF vaccine also demonstrated a favourable safety profile. A recent study showed that concomitant administration of RSVpreF and seasonal inactivated influenza vaccine elicited robust RSV serum-neutralising responses and appeared to have a favourable safety profile among adults aged 50 to 85 years,[23] thereby supporting annual concomitant immunisation with seasonal inactivated influenza vaccine.

Based on the RENOIR trial, the United States Food and Drug Administration approved bivalent RSVpreF vaccine for use in adults aged ≥60 years.[24] Subsequently (in June 2023), the United States Centers for Disease Control and Prevention's Advisory Committee on Immunisation Practices voted to recommend that adults aged ≥60 years receive a single dose of RSV vaccine through a shared clinical decision-making process.[24]

Driving the successful implementation of respiratory syncytial virus vaccination in older adults

It is important to conduct a public awareness campaign that educates the general public about the risks of RSV infections among high-risk individuals, especially older adults. This campaign should address vaccine hesitancy by highlighting the safety and efficacy of vaccines against severe RSV while dispelling misconceptions about the safety of the vaccine.

Additionally, it is imperative to establish a continuous medical education programme focused on respiratory care for primary care physicians and other specialists who manage high-risk patients. This programme should cover the role of diagnostic testing in patients with suspected ALRTI to guide disease management (despite the absence of effective treatment) and vaccination against severe RSV in high-risk populations. Ideally, the programme should emphasise the public health benefits of RSV vaccination beyond reducing disease severity. Moreover, the programme should discuss strategies to encourage vaccination uptake among older adults with cognitive impairment and/or their family members.

Additional research to improve confidence in respiratory syncytial virus vaccination

Local epidemiological studies could help to define RSV prevalence in general and high-risk populations, quantify the RSV disease burden, and identify its impacts on public health and healthcare services. These data could also aid in defining target populations that would experience the greatest benefit from RSV vaccination. Furthermore, a local cost-effectiveness analysis based on local epidemiological data could help demonstrate the value of RSV vaccination in target populations.

Research concerning the durability of protection conferred by an RSV vaccine in high-risk adults could guide appropriate dosing intervals and vaccination schedules. Additional efficacy and safety data concerning the co-administration of an RSV vaccine with other respiratory virus vaccines could support simplified immunisation schedules for adults.

Post-marketing studies could provide additional information regarding the real-world effectiveness and safety of an RSV vaccine in target populations, especially individuals with multimorbidity and immunocompromised conditions. Future real-world studies could also include assessments of vaccine effectiveness in reducing other clinical outcomes, such as the rates of RSV infection, hospitalisation, intensive care unit admission, ventilator use, and mortality.

Author contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

IFN Hung is an advisory board member for Pfizer, GlaxoSmithKline, AstraZeneca, MSD, and Moderna. P Eng served as an advisory board member for Pfizer, GlaxoSmithKline, AstraZeneca, and Boehringer Ingelheim. MCS Wong is an honorary medical advisor for GenieBiome Ltd, BGI Health (HK) Company Limited, and Sunrise; an advisory committee member for Pfizer; an external expert for GlaxoSmithKline; and a member of the advisory board for AstraZeneca; he has also been paid consultancy fees for providing research advice. Other authors declare no conflicts of interest.

Funding/support

Funding for this study was provided by Pfizer Hong Kong. Editorial and medical writing support was provided by Weber Shandwick Health HK, funded by Pfizer Hong Kong. The funders had no role in study design, data collection/analysis/interpretation or manuscript preparation.

References

1. Belongia EA, King JP, Kieke BA, et al. Clinical features, severity, and incidence of RSV illness during 12 consecutive seasons in a community cohort of adults ≥60 years old. Open Forum Infect Dis 2018;5:ofy316.
2. Nam HH, Ison MG. Respiratory syncytial virus infection in adults. BMJ 2019;366:l5021.
3. Villanueva DH, Arcega V, Rao M. Review of respiratory syncytial virus infection among older adults and transplant recipients. Ther Adv Infect Dis 2022;9:20499361221091413.
4. Branche AR, Saiman L, Walsh EE, et al. Incidence of respiratory syncytial virus infection among hospitalised adults, 2017-2020. Clin Infect Dis 2022;74:1004-11.
5. Du Y, Yan R, Wu X, et al. Global burden and trends of respiratory syncytial virus infection across different age groups from 1990 to 2019: a systematic analysis of the Global Burden of Disease 2019 study. Int J Infect Dis 2023;135:70-6.
6. Ambrosch A, Luber D, Klawonn F, Kabesch M. Focusing on severe infections with the respiratory syncytial virus (RSV) in adults: risk factors, symptomatology and clinical course compared to influenza A/B and the original SARS-CoV-2 strain. J Clin Virol 2023;161:105399.
7. Ackerson B, Tseng HF, Sy LS, et al. Severe morbidity and mortality associated with respiratory syncytial virus versus influenza infection in hospitalised older adults. Clin Infect Dis 2019;69:197-203.
8. Grace M, Colosia A, Wolowacz S, Panozzo C, Ghaswalla P. Economic burden of respiratory syncytial virus infection in adults: a systematic literature review. J Med Econ 2023;26:742-59.
9. Coultas JA, Smyth R, Openshaw PJ. Respiratory syncytial virus (RSV): a scourge from infancy to old age. Thorax 2019;74:986-93.
10. Branche AR, Saiman L, Walsh EE, et al. Change in functional status associated with respiratory syncytial virus infection in hospitalized older adults. Influenza Other Respir Viruses 2022;16:1151-60.
11. Juhn YJ, Wi CI, Takahashi PY, et al. Incidence of respiratory syncytial virus infection in older adults before and during the COVID-19 pandemic. JAMA Netw Open 2023;6:e2250634.
12. Begley KM, Monto AS, Lamerato LE, et al. Prevalence and clinical outcomes of respiratory syncytial virus vs influenza in adults hospitalised with acute respiratory illness from a prospective multicentre study. Clin Infect Dis 2023;76:1980-8.
13. Kujawski SA, Whitaker M, Ritchey MD, et al. Rates of respiratory syncytial virus (RSV)-associated hospitalization among adults with congestive heart failure—United States, 2015-2017. PLoS One 2022;17:e0264890.
14. Chan WS, Yau SK, To MY, et al. The seasonality of respiratory viruses in a Hong Kong Hospital, 2014–2023. Viruses 2023;15:1820.
15. Eden JS, Sikazwe C, Xie R, et al. Off-season RSV epidemics in Australia after easing of COVID-19 restrictions. Nat Commun 2022;13:2884.
16. Bardsley M, Morbey RA, Hughes HE, et al. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. Lancet Infect Dis 2023;23:56-66.
17. Zheng Z, Warren JL, Artin I, Pitzer VE, Weinberger DM. Relative timing of respiratory syncytial virus epidemics in summer 2021 across the United States was similar to a typical winter season. Influenza Other Respir Viruses 2022;16:617-20.
18. Talbot HK, Falsey AR. The diagnosis of viral respiratory disease in older adults. Clin Infect Dis 2010;50:747-51.
19. Chartrand C, Tremblay N, Renaud C, Papenburg J. Diagnostic accuracy of rapid antigen detection tests for respiratory syncytial virus infection: systematic review and meta-analysis. J Clin Microbiol 2015;53:3738-49.
20. Mazur NI, Higgins D, Nunes MC, et al. The respiratory syncytial virus vaccine landscape: lessons from the graveyard and promising candidates. Lancet Infect Dis 2018;18:e295-311.
21. Melero JA, Mas V, McLellan JS. Structural, antigenic and immunogenic features of respiratory syncytial virus glycoproteins relevant for vaccine development. Vaccine

2017;35:461-8.
22. Walsh EE, Pérez Marc G, Zareba AM, et al. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. N Engl J Med 2023;388:1465-77.
23. Falsey AR, Walsh EE, Scott DA, et al. Phase 1/2 randomised study of the immunogenicity, safety, and tolerability of a respiratory syncytial virus prefusion F vaccine in adults with concomitant inactivated influenza vaccine. J Infect Dis 2022;225:2056-66.
24. Melgar M, Britton A, Roper LE, et al. Use of respiratory syncytial virus vaccines in older adults: recommendations of the Advisory Committee on Immunisation Practices–United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793-801.