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New vaccines for the elderly: improving efficacy and safety

9:30 am

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Mater Health Services,
Brisbane

New vaccines for the elderly:
improving efficacy and safety

Paul Griffin

25th Annual Immunisation Forum

Friday 14th June 2024

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mater

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

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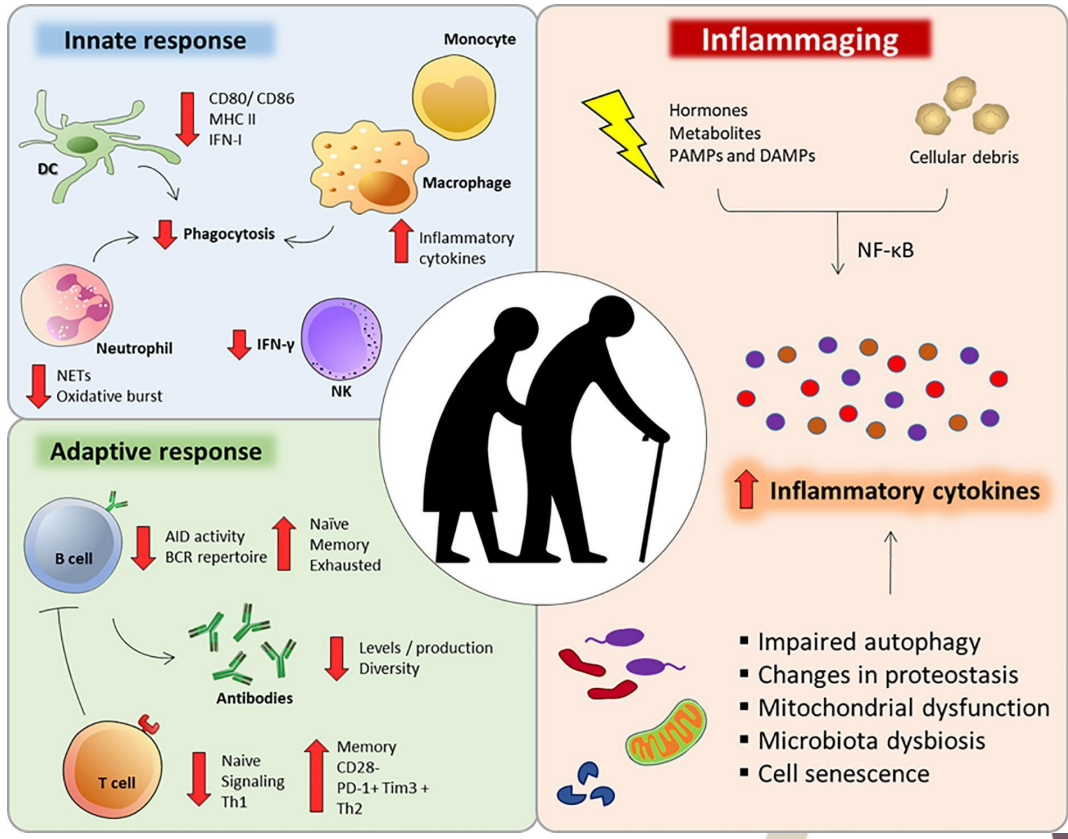
Disclosures

- Principal Investigator on numerous vaccine clinical trials
  - including the following SARS-CoV-2 vaccines;
    - UQ
    - Novavax (including approved vaccine and Omicron specific booster)
    - Serum Institute of India
    - Symvivo
    - Tetherex
    - Sanofi (mRNA and protein)
  - And many Influenza and RSV vaccine and antibody studies
    - Including with Moderna, Novavax, Vaxxas, Vir, Visterra
- Immunisation Coalition Director and Scientific Advisory Board Member
- Speaker Honoraria includes Seqirus, Novartis, Gilead, Sanofi and Janssen
- Medical Advisory Board Memberships including AstraZeneca, GSK, MSD, Seqirus and Pfizer
- Content of this presentation is mostly my own

Why are the elderly a particularly at-risk population

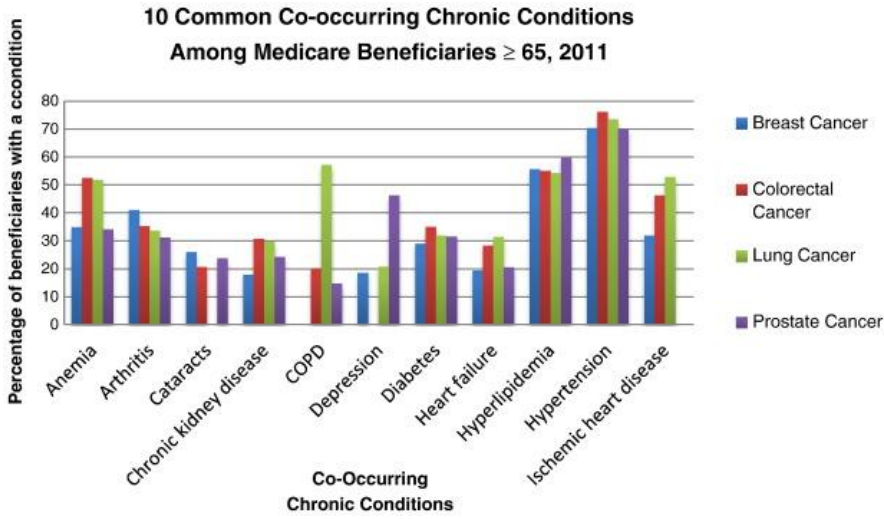
The Elderly

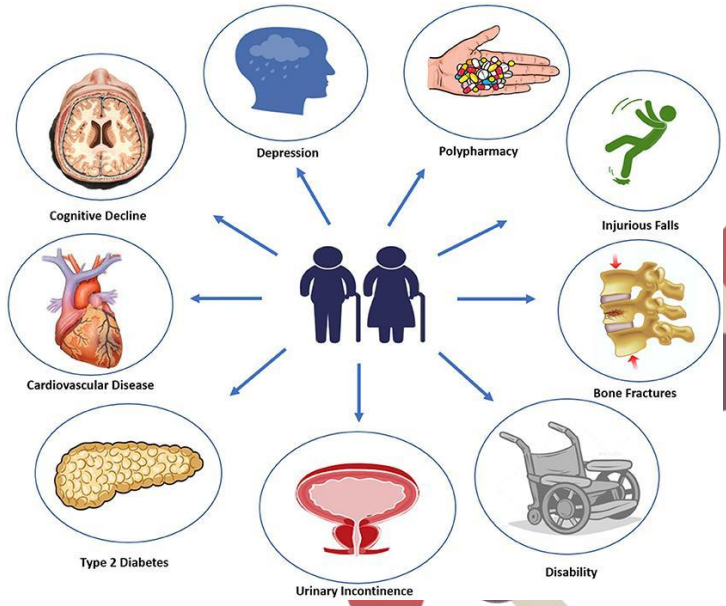
- Multiple factors contribute to requirement for specific vaccine recommendations for the elderly
  - Immune system: Immunosenescence
    - Deterioration of the immune system brought on by natural age advancement
    - Many contributing factors: inflammaging, thymic involution, naïve/memory cell ratio imbalance, dysregulated metabolism and epigenetic alterations
    - Impaired vaccine responses (and reduced protection via natural immunity)
    - Increased risk of disease and particularly severe outcomes
    - Also responsible for age related onset of other diseases and increased risk of neoplasms
    - Altered responses to infection, cytokine storm a factor in COVID-19
    - Vaccine strategies to address include, higher dose, adjuvants, more frequent boosters



The Elderly

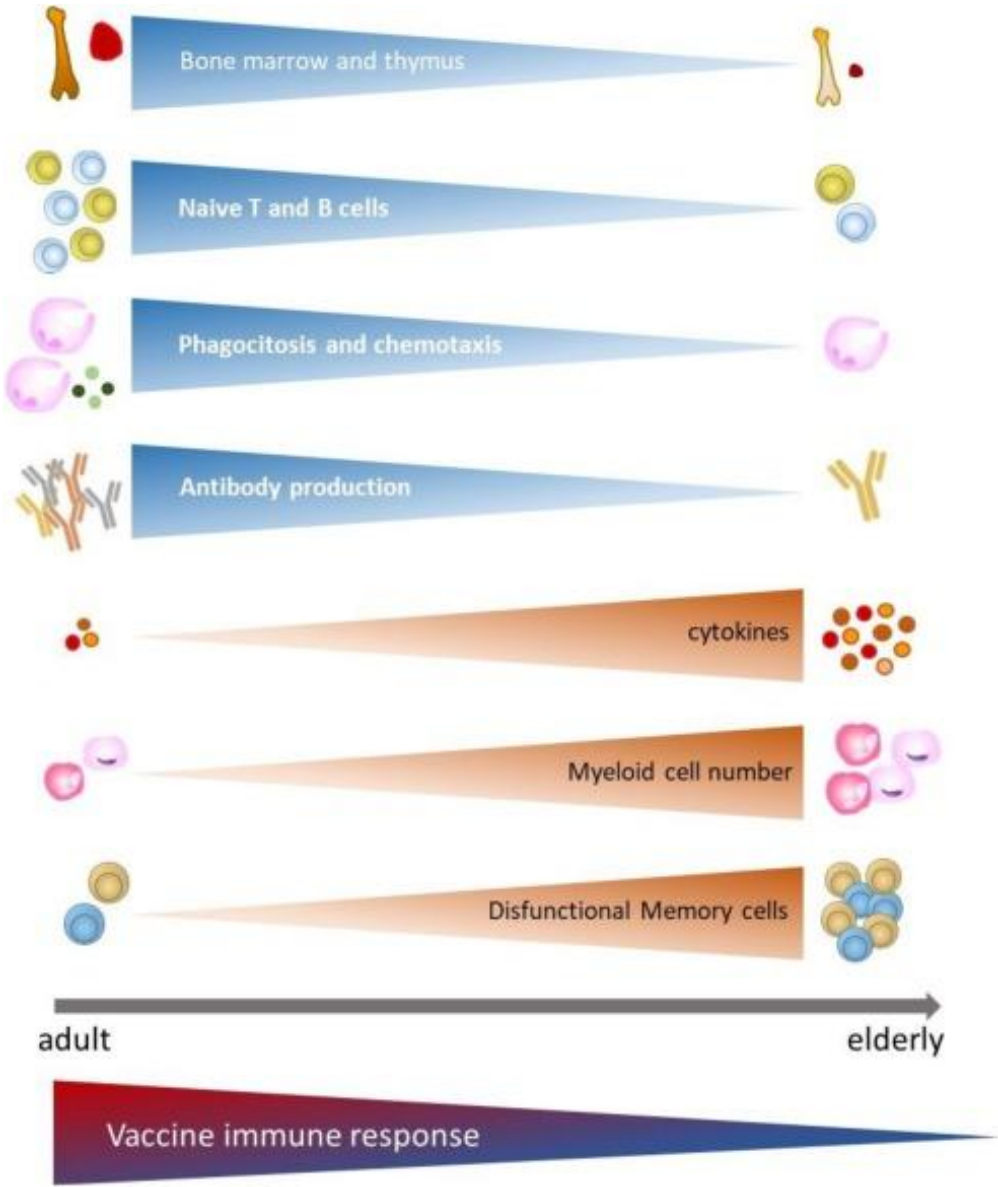
- Risk profile
  - In addition to Immunosenescence, risk profile also changes
    - Accumulation of comorbidities
      - 4 in 5 Australians aged 65 and over have at least one chronic condition
      - Exogenous immunosuppression to address neoplastic and inflammatory conditions
    - Residential care facilities
      - 499 current active outbreaks of COVID-19
    - Frailty, often then exacerbated by infection
    - Cognitive decline
    - Malnutrition
- Examples include
  - Compared to 18-39, over 75 years 9 times more likely to die from COVID-19
  - US over 150000 older adults hospitalised due to RSV and up to 10 000 deaths
  - 70 to 85 percent of seasonal flu deaths aged 65 or older





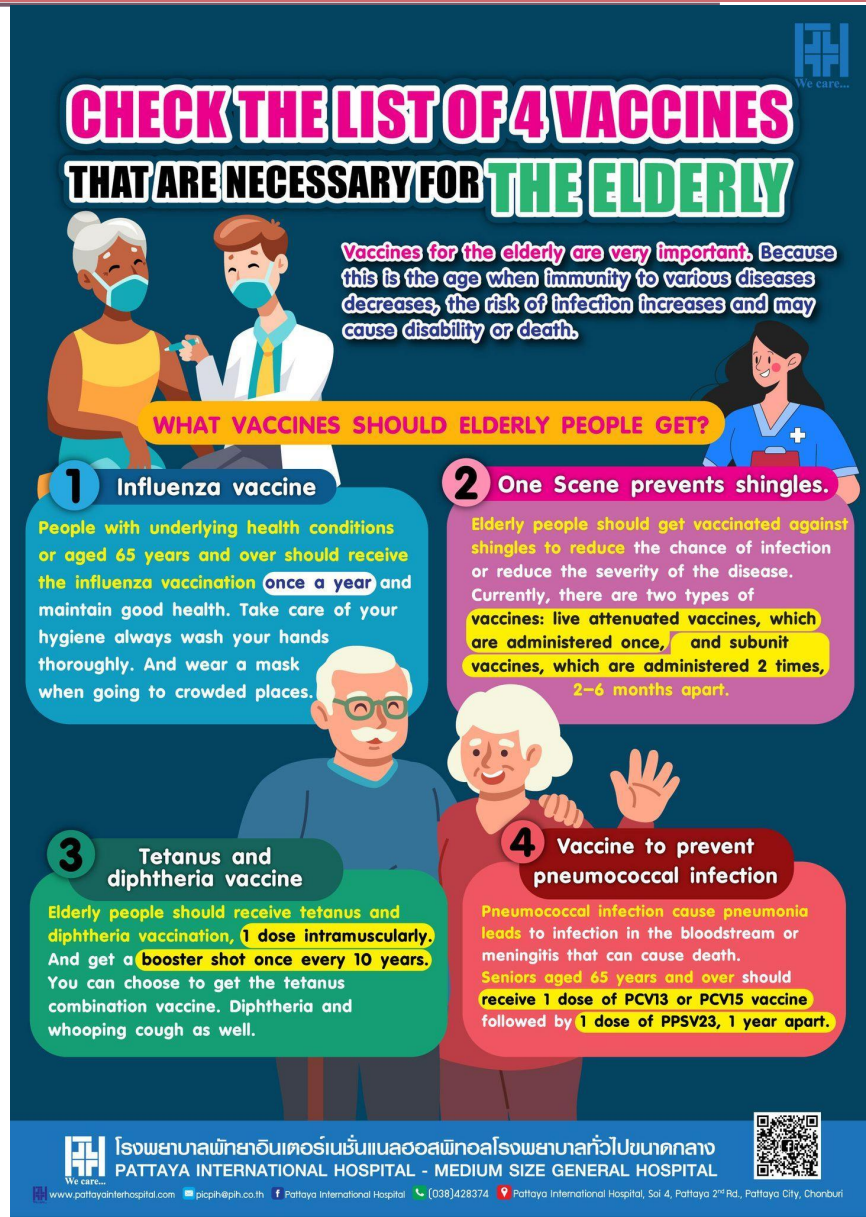
Vaccines For Older Adults

- Influenza
  - Recommended for all from 6 months annually
  - Funded on the NIP for high risk including over 65's
  - Augmented or enhanced vaccines for over 60's
- RSV
  - 2 approved options for 60 and over
  - Not yet funded
  - Recommendations by ATAGI
    - 75 and over, ATSI 60 to 74, 60 to 74 with additional risk
- Covid
  - Same vaccines but more frequent booster if highest



Vaccines For Older Adults

- Pneumococcal disease
  - Single dose recommended and funded for adults aged 70 and over (Aboriginal and Torres Strait Islander adults aged 50 years and over)
- Shingles
  - Registered and recommended 50 and over
  - Free on NIP for over 65's or younger with risk
    - ATSI from 50
    - immunocompromised from 18 years
- Tetanus
  - Booster if over 50 and not received in preceding 10 years
- Pertussis



RSV

RSV Morbidity and Mortality in Adults

- Healthy adults <50 years of age
  - Infected repeatedly throughout their lives
  - Typically have symptoms restricted to the upper respiratory tract, mostly mild
  - One study of 256 military trainees with respiratory symptoms
    - RSV identified in 11%[1]

- Adults ≥50 years of age and adults with underlying conditions
  - Morbidity
    - An important and under recognized cause of LRTI
    - Annual incidence 5.5%[2]
    - Detected in 11% of outpatients ≥ 60 years of age with acute respiratory illness[3]
    - Annual hospitalization rate 15 per 10 000 residents[4]
  - Mortality
    - Systematic review: mortality rate among adults hospitalized with RSV was 6 to 8 percent[5]
    - Among hematopoietic cell transplant recipients, mortality rates of 70 to 100 percent have been

1. O'Shea, M. K., et al. (2005). "Symptomatic respiratory syncytial virus infection in previously healthy young adults living in a crowded military environment." Clin Infect Dis 41(3): 311-317.
2. Falsey, A. R., et al. (2005). "Respiratory syncytial virus infection in elderly and high-risk adults." N Engl J Med 352(17): 1749-1759.
3. Belongia, E. A., et al. (2018). "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 5(12): ofy316.
4. Widmer, K., et al. (2012). "Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus and influenza virus in older adults." J Infect Dis 206(1): 56-62.
5. Colosia, A. D., et al. (2017). "The epidemiology of medically attended respiratory syncytial virus in older adults in the United States: A systematic review." PLoS One 12(8): e0182321.
6. Hertz, M. I., et al. (1989). "Respiratory syncytial virus-induced acute lung injury in adult patients with bone marrow transplants: a clinical approach and review of the literature." Medicine (Baltimore) 68(5): 269-281.

History of RSV Vaccines

- Shortly after isolation, NIH initiated a program to develop a vaccine using same approach applied successfully to polio and influenza
  - Formalin-inactivated
- Clinical trials in 1965-66 produced unexpected results
  - No protection against RSV in vaccinees
  - RSV infection caused more severe disease in vaccinees
    - 16-fold increase in hospitalisations
      - 2 fatalities amongst the youngest patients (no prior

This is to confirm our telephone contact over the weekend in which we stated that we felt that no further inactivated alum precipitated respiratory syncytial virus vaccine should be administered to infants until certain findings could be evaluated. We reached this conclusion in our laboratory on Thursday, December 29, 1966 on the basis of data which I will recount below.

- Key lessons learnt to facilitate development of an RSV vaccine

F protein

1980s

Scientists identified the RSV fusion “F” protein, a surface protein that helps the virus infect human cells.

1990s

NIAID researchers found mice exposed to the RSV F protein produced a more protective immune response compared to mice exposed to other surface proteins.

2000s

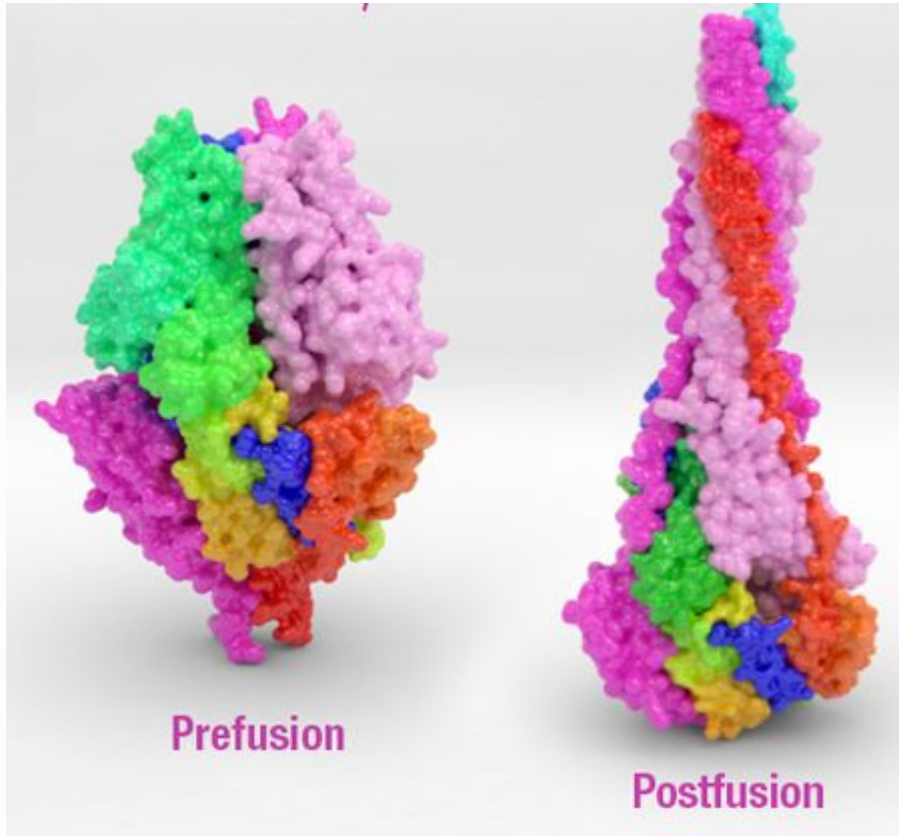
Two forms of the RSV F protein were identified, later determined to be the prefusion and postfusion states.

2010s

NIAID scientists locked the RSV F protein in its prefusion state, which was a more protective vaccine candidate. **Read more below.**

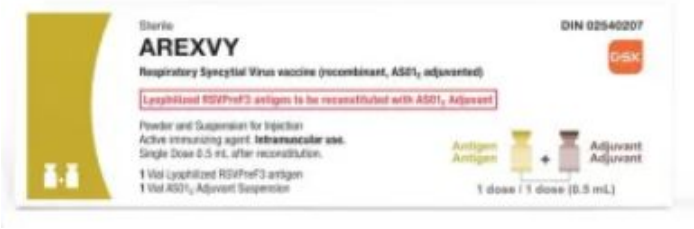
2020s

Vaccine candidates using the locked RSV prefusion F protein began Phase 3 clinical trials.



Approved RSV Vaccines

- Both single dose
  - GSK: Arexvy®
    - Recombinant subunit prefusion RSV F glycoprotein antigen (RSVPreF3) proprietary AS01E adjuvant
    - Approved May 3, 2023, by the FDA for individuals **60 years and older**
      - Also approved by the EU June 7, 2023
      - TGA approved Jan 8 / Entered onto ARTG 14 Jan 2024
        - indicated for individuals 60 years and older for prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV).
          - The use of this vaccine should be in accordance with official recommendations



  - Pfizer: Abrysvo®
    - Bivalent (RSV A and B) recombinant RSV prefusion F (RSVpreF) (no adjuvant)
    - Approved by the FDA
      - May 31, 2023, also for individuals aged **60 years and older**.
      - August 21, 2023, for the Prevention of Respiratory Syncytial Virus (RSV) in Infants Through Active Immunization of Pregnant Individuals **32-36 Weeks of Gestational Age**

Evidence

- GSK: Arexvy
  - Adjuvanted recombinant (prefusion F)
  - Large Phase 3 Clinical Trial
    - 60 years of age or older
    - 25000 participants (randomised 1:1)
  - Highly Efficacious
    - RSV associated LRTD 82.6%
    - Severe RSV-associated LRTD 94.1%
  - Safe
    - Some AE's but most mild to mod and resolved in the 4-day solicited period
      - Pain and fatigue most common

1. Papi, A., et al. (2023). "Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults." N Engl J Med 388(7): 595-608.

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

Papi A et al. DOI: 10.1056/NEJMoa2209604

CLINICAL PROBLEM

Older adults with respiratory syncytial virus (RSV) infection are at risk of lower respiratory tract disease, potentially leading to exacerbation of underlying conditions, hospitalization, and death. There are no licensed RSV vaccines or prophylactic interventions for older adults.

CLINICAL TRIAL

Design: An ongoing phase 3, international, randomized, placebo-controlled trial assessed the efficacy and safety of an $AS01_E$-adjuvanted respiratory syncytial virus (RSV) prefusion F protein–based candidate vaccine (RSVPreF3 OA) among adults ≥60 years of age.

Intervention: 25,040 participants in 17 countries were assigned to receive a single dose of the RSVPreF3 OA vaccine or placebo before the RSV season. The primary objective was to show vaccine efficacy against RSV-related lower respiratory tract disease during one RSV season.

RESULTS

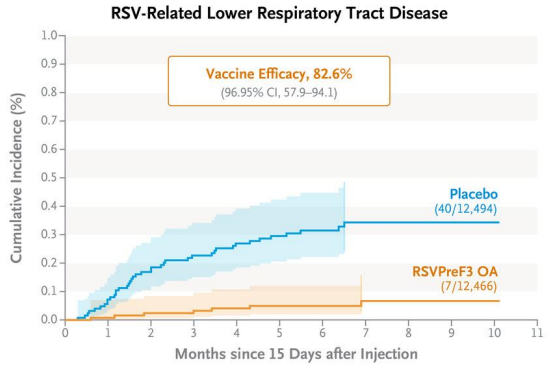
Efficacy: During a median follow-up of 6.7 months, among 24,960 participants with evaluable data, vaccine efficacy against RSV-confirmed lower respiratory tract disease was >80%.

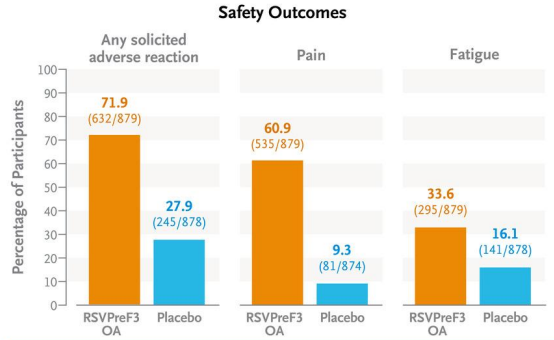
Safety: Solicited adverse events occurred more often with the vaccine than with placebo; most were mild to moderate in severity and resolved within the 4-day solicitation period. Pain was the most common solicited injection-site reaction with the vaccine, and fatigue was the most common solicited systemic reaction.

LIMITATIONS AND REMAINING QUESTIONS

- A small number of frail participants and participants ≥80 years of age were included; longer follow-up is needed to determine efficacy in these subgroups.
- The trial had limited ability to detect rare side effects.
- Public health measures to limit Covid-19 transmission reduced the spread of RSV and altered the RSV season.
- Additional RSV seasons need to be studied to better understand vaccine efficacy.

Links: Full Article | NEJM Quick Take | Perspective





CONCLUSIONS

A single dose of an $AS01_E$-adjuvanted RSV prefusion F protein–based candidate vaccine (RSVPreF3 OA) given before the RSV season showed high efficacy against RSV-related lower respiratory tract disease and had an acceptable safety profile in adults ≥60 years of age.

Evidence ≥ 60 y.o.a.

- Pfizer: Abrysvo
  - Bivalent
    - RSV A and B 60 mcg each
  - Large Phase 3 Clinical Trial
    - 60 years of age or older
    - 34 284 randomised 1:1
  - Safe
    - Local reactions higher in vaccine group (12% versus 7%)
    - Systemic events similar
  - Highly efficacious
    - Lower respiratory tract illness (≥ 2 symptoms) 66.7%
    - Lower respiratory tract illness (≥ 3 symptoms) 85.7%

The NEW ENGLAND JOURNAL of MEDICINE

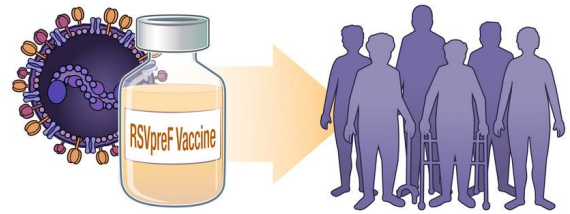
RESEARCH SUMMARY

Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

Walsh EE et al. DOI: 10.1056/NEJMoa2213836

CLINICAL PROBLEM

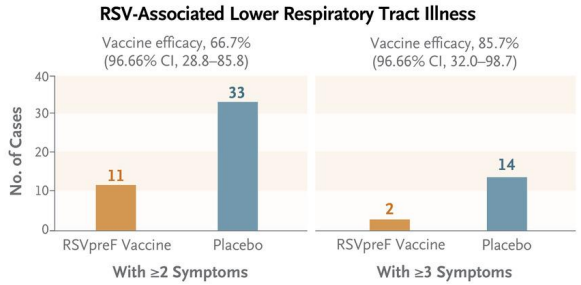
Respiratory syncytial virus (RSV) infection causes substantial illness in older adults, yet no RSV vaccine is currently approved by the Food and Drug Administration. Previously, an RSV challenge study showed that the investigational bivalent RSV prefusion F protein–based (RSVpreF) vaccine (containing stabilized prefusion F glycoproteins from the two major cocirculating antigenic subgroups, RSV A and RSV B) had high efficacy against symptomatic RSV infection in healthy adults who were 18 to 50 years of age, but its efficacy in older adults is unknown.



CLINICAL TRIAL

Design: An ongoing, phase 3, multinational, double-blind, randomized, placebo-controlled trial evaluated the efficacy and safety of RSVpreF vaccine in adults ≥60 years of age during a single RSV season.

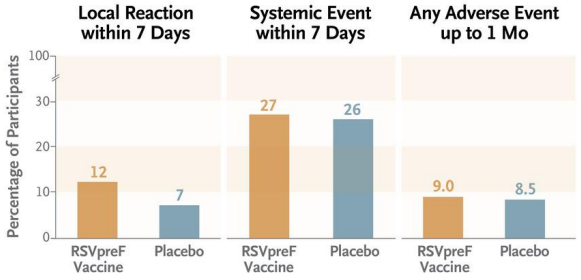
Intervention: 34,284 participants received one intramuscular 120-μg dose of RSVpreF vaccine (containing 60 μg each of RSV A and RSV B antigens) or placebo. The two primary end points were vaccine efficacy against RSV-associated lower respiratory tract illness with either ≥2 signs or symptoms or ≥3 signs or symptoms in the first RSV season (starting on day 15 after the injection).



RESULTS

Efficacy: The RSVpreF vaccine was effective in preventing RSV-associated lower respiratory tract illness with ≥2 or ≥3 signs or symptoms.

Safety: Local reactions were more common with RSVpreF vaccine than with placebo within 7 days after injection; incidences of systemic events were similar in the two groups. Incidences of adverse events through 1 month after injection were also similar in the two groups.



LIMITATIONS AND REMAINING QUESTIONS

- Immunocompromised persons were excluded from the trial.
- Given the sample size, additional safety data are needed.
- The current prespecified interim analysis was limited to one RSV season; future analyses may assess whether vaccine efficacy persists beyond one season.

Links: Full Article | NEJM Quick Take | Editorial

CONCLUSIONS

In adults ≥60 years of age, one dose of RSVpreF vaccine prevented RSV-associated symptomatic lower respiratory tract illness, with no apparent safety concerns, during a single RSV season.

1. Walsh, E. E., et al. (2023). "Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults." N Engl J Med 388(16): 1465-1477.

RSV vaccine approved by TGA

AREXVY will soon be available for patients aged 60 and over, sparking hope it will ease the pressure on Australia's overflowing hospitals.

Last year, 127,944 cases of RSV were reported in Australia.

Many older Australians will soon be better protected against the highly infectious respiratory syncytial virus (RSV), thanks to a new vaccine about to hit the market.

This week, the Therapeutic Goods Administration (TGA) approved AREXVY for those aged 60 and over, in a decision described as a 'turning point' for public health.

- Arexvy
  - Approved by the TGA in Australia 8th January 2024

RSV vaccine approved by TGA

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'Very relieved:' First RSV vaccine administered in Australia

Story by Mikala Theocharous • 1d • 2 min read

29th February 2024

Health Topics mentioned in this article

+122 Q&A : Common Cold | +95 Q&A : Flu | +48 Q&A : Cardiomyopathy

The first Respiratory Syncytial Virus (RSV) vaccine has been administered in Australia, following the jab's recent approval by the country's medical watchdog.

Keith Forrest, 60, was the first person in the country to receive the shot in the clinic.

Forrest is awaiting a heart transplant and did not hesitate to get the vaccine to help combat the potentially deadly symptoms of RSV.

READ MORE: Man shot inside office in Sydney's CBD, another arrested

Forrest's heart became damaged after he caught the flu in 2008 and he developed cardiomyopathy from the virus.
© Nine

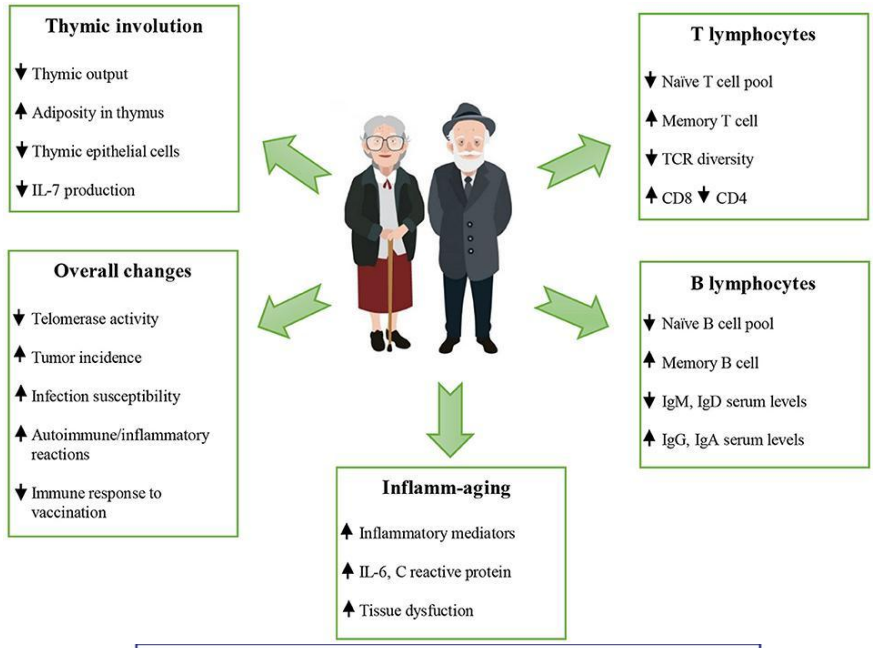
Challenges of RSV vaccination

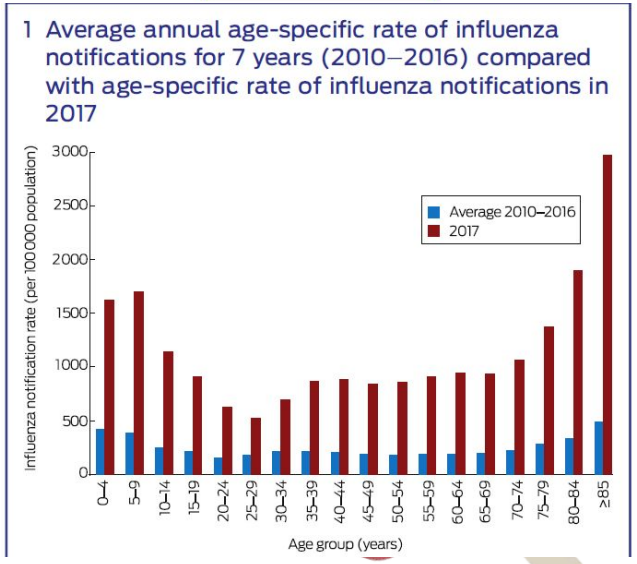
- Uptake
  - Fatigue, misinformation, lack of trust of public health
  - Underappreciation of significance of RSV
  - Confusion of role of maternal vaccination given availability of Nirsevimab
  - Adverse events
    - Some discussion of rare cases of Guillain-Barre syndrome
- Timing challenging
  - Different seasonality in different regions
  - Overlap with Influenza vaccine campaign
- Specific target groups
  - Vaccines for the elderly increasingly complicated (Pneumococcal, Shingrix, increased frequency of COVID-19, enhanced vaccines for Flu).
    - Underappreciation of the significance of RSV
  - While approved for 60 and over, recommended for 75 and over or younger with specific risks

Influenza

Vaccines-augmented vaccines for the elderly

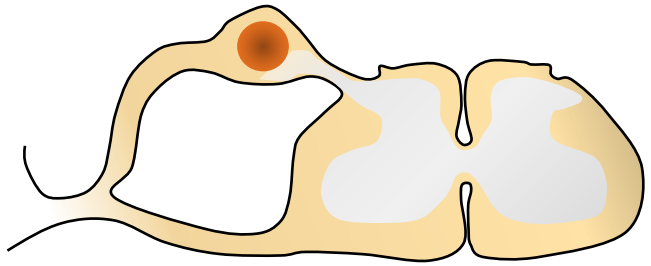
- Elderly are at increased risk of influenza, increased risk of complications and also known to respond less well to vaccination due to immunosenescence
- Recently enhanced vaccines have become available to address
  - Fluad Quad (65)
    - Adjuvanted, MF59
  - Fluzone (60)
    - High dose, 4 times the amount of adjuvant
- Studies suggest a relative improvement in effectiveness of approximately 20 to 25%





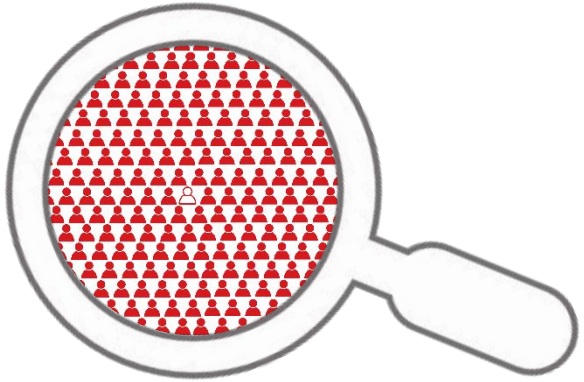
Shingles

WHO IS AT RISK OF SHINGLES?



Viral reactivation leads to shingles

After control of primary varicella infection, VZV becomes **latent** in the sensory ganglia[1]



up to

99.5%

of adults aged 50 years and older have already been exposed to VZV which puts them at risk of developing shingles[2,3,4*]

about

1 in 3

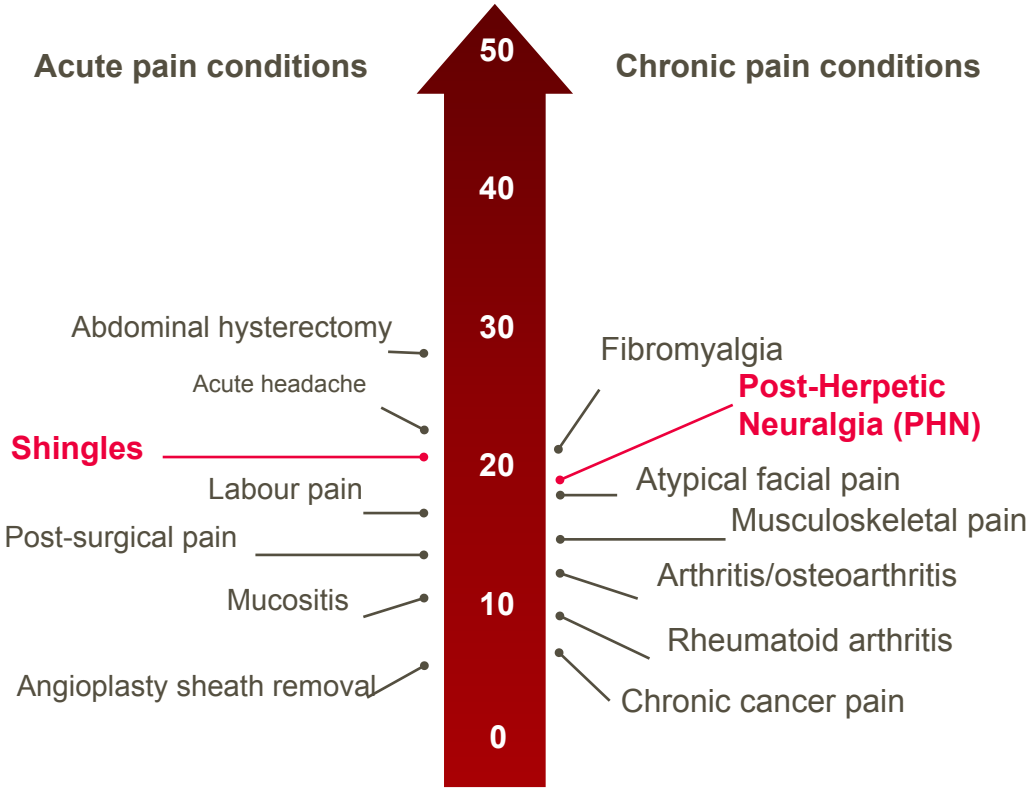
people will develop shingles in their lifetime[2,3,4*]

The image of VZV latent in dorsal root ganglion is adapted from Zerboni L, et al. 2014.[5]
SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox).
VZV, varicella zoster virus.

*Includes US data. May not be representative of the Australian population.

1. Centers for Disease Control and Prevention. MMWR. 2008 June;57(RR-5):1-30 2. Centers for Disease Control and Prevention. About Shinges (Herpes Zoster) Available at: https://www.cdc.gov/shingles/about/index.html (accessed June 2024) 3. Centers for Disease Control and Prevention. Shingles Facts and Stats. Available at: https://www.cdc.gov/shingles/dataresearch (accessed June 2024 4. National Centre for Immunisation Research and Surveillance (NCIRS). Zoster (shingles) vaccines (Shingrix® [RZV] and Zostavax® [ZVL]) – frequently asked questions. Available at: https://ncirs.org.au/zoster-shingles/zoster-shingles-vaccines-shingrixr-rzv-and-zostavaxr-zvl-frequently-asked-questions (accessed June 2024). 5. Zerboni L, et al. Nat Rev Microbiol. 2014 Mar;12(3):197-210.

Shingles can cause a burning, stabbing, deep aching pain[1]

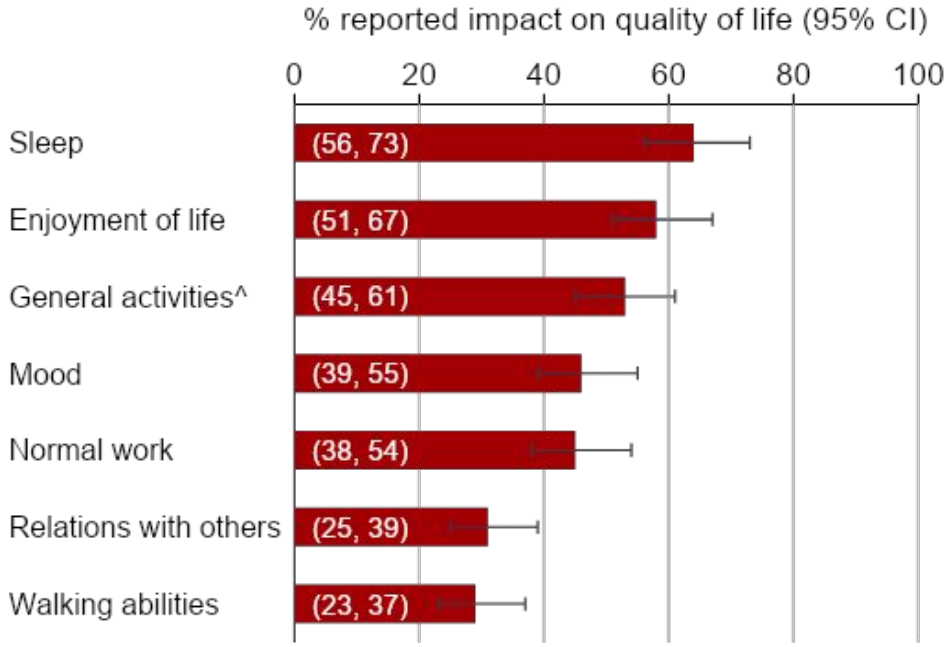


Comparison of total pain rating index scores using the short-form McGill Pain Questionnaire for acute and chronic pain conditions[2*]

Figure modified from Katz J et al.[2] with permission from Elsevier

Pain is a personal, subjective experience influenced by many variables and is difficult to compare across different pain types and studies and between people.

MORE THAN JUST A RASH, CAN BE DEBILITATING TO DAILY LIFE[3]



Impact of shingles on activities of daily living from 261 newly diagnosed Canadian patients: rated by interference of pain ≥5 (out of 10).

^General activities include cooking, going to the bathroom, putting on clothes, climbing stairs.[3]

This figure has been independently created by GSK from original data first published in *CMAJ*[3]

1. Johnson RW, et al. BMC Med. 2010 Jun;8:37. 2. Katz J, et al. Surg Clin North Am. 1999;79(2):231-252. 3. Drolet M, et al. CMAJ. 2010 Nov 9;182(16):1731-6.

Shingles can have serious and long-lasting complications[1,2]

Post-Herpetic Neuralgia (PHN)

Most commonly defined as neuropathic pain which persists for longer than 3 months after the onset of the rash. Definitions can vary.[2]

Herpes Zoster Ophthalmicus (HZO)

Can affect up to 25% of patients with shingles[1]

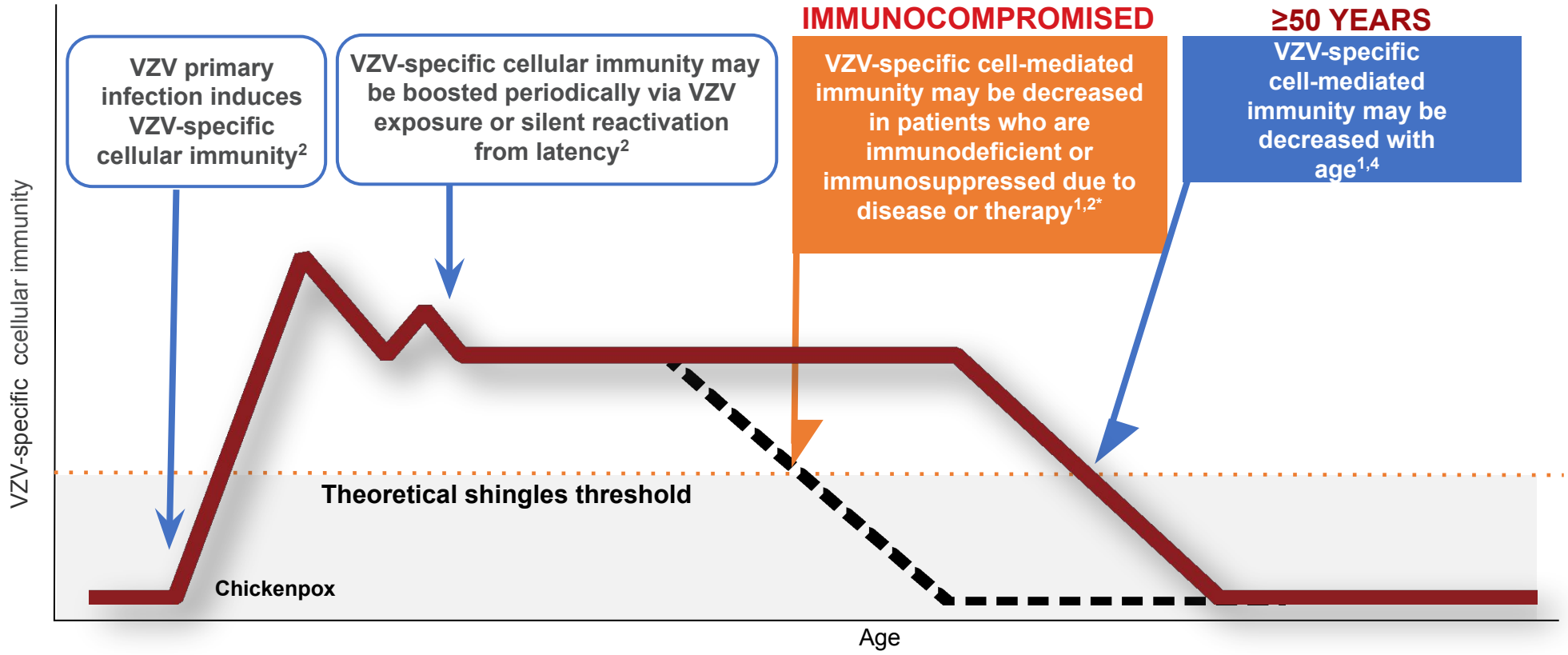
May lead to vision loss in rare cases[1]

Other complications

- Disseminated disease[2]
- Hearing loss[1]
- Scarring[2]
- Neurological complications[2]
- Cardiovascular and cerebrovascular events[3]

1. Centers for Disease Control and Prevention. MMWR. 2008 June;57(RR-5):1-30. 2. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook. Australian Government Department of Health and Aged Care, Canberra, 2022, immunisationhandbook.health.gov.au (Accessed April 2023). 3. Erskine, N; PLoS One; 2017; 12:1-18. 4. McKay SL, et al. Clin Infect Dis. 2019 Nov;ciz1090. 5. Kennedy PGE, et al. Viruses. 2018;10(11):609.

SHINGRIX TARGETS THE DECLINE IN VZV-SPECIFIC CELLULAR IMMUNITY[1-4]



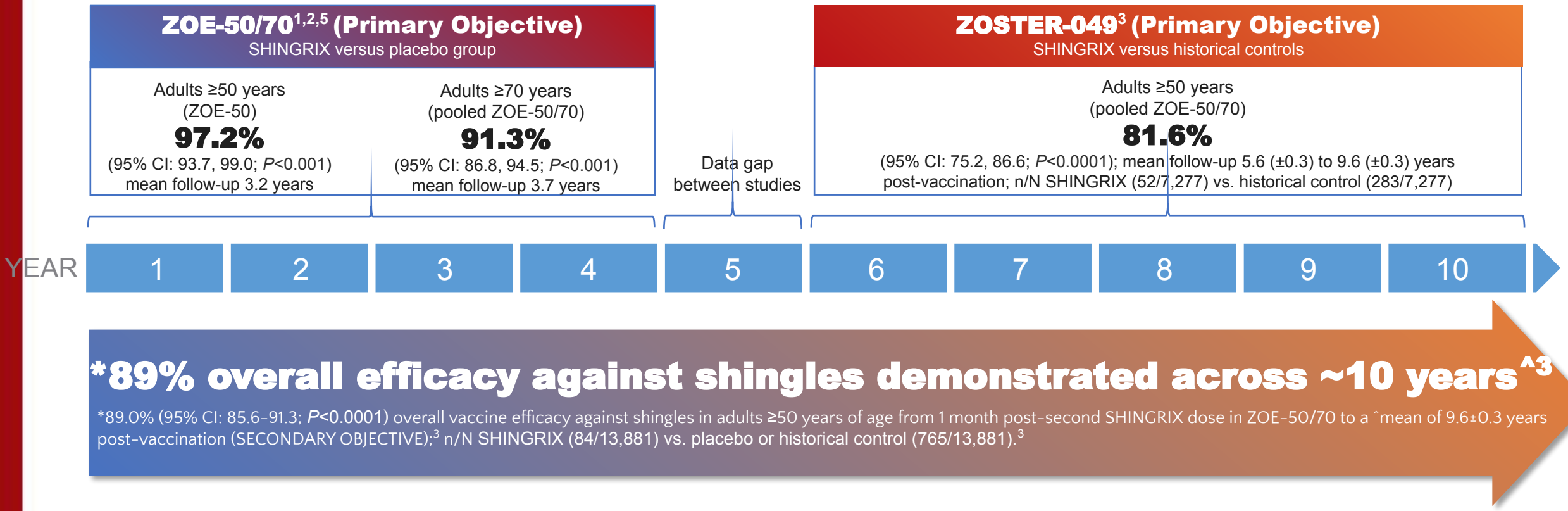
Cellular immunity decline below the theoretical shingles threshold is associated with an increased risk of shingles.

This illustration has been independently created by GSK from information first published in the New England Journal of Medicine.

*Immunodeficiency caused by medical conditions or immunosuppressive medications may also increase the risk of shingles.[2,4] VZV,varicella zoster virus.

1. Centers for Disease Control and Prevention. MMWR. 2008 June;57(RR-5):1-30; 2. Kimberlin DW, et al. N Engl J Med. 2007 Mar;356(13):1338-43; 3. Dworkin RH, et al. Clin Infect Dis. 2007 Jan;44(suppl 1):S1-26; 4. Levin MJ, Smith JG, Kaufhold RM, et al. JID. 2003;188:1336-1344.

SHINGRIX DEMONSTRATED HIGH EFFICACY* SUSTAINED ACROSS ~10 YEARS^.[1-5] EFFICACY CONTINUES TO BE MONITORED[3]



The image has been independently created by GSK from the original data first published in Lal et al.[1], Cunningham et al.[2], and Strezova A, et al.[3]

Interim open-label long-term efficacy assessed in participants ≥50 years of age during the pivotal trials (N=13,881) and the long-term follow-up (LTFU) study (N=7,277). In the absence of an unvaccinated placebo group for the LTFU study (mean 5.6±0.3 years to 9.6±0.3 years post-vaccination) historical control estimates were used.

SHINGRIX versus placebo recipients from the ZOE-50/70 trials, adjusted for age and region.[1,2,5]

No data are available for year 5 because that period corresponds to the gap between ZOE-50/70 and the ZOSTER-049 follow-up study.[1-4]

SHINGRIX versus matched historical controls from the placebo group in the ZOE-50/70 studies, adjusted for region.[3]

Data collection for year 10 was incomplete at the data lock point.

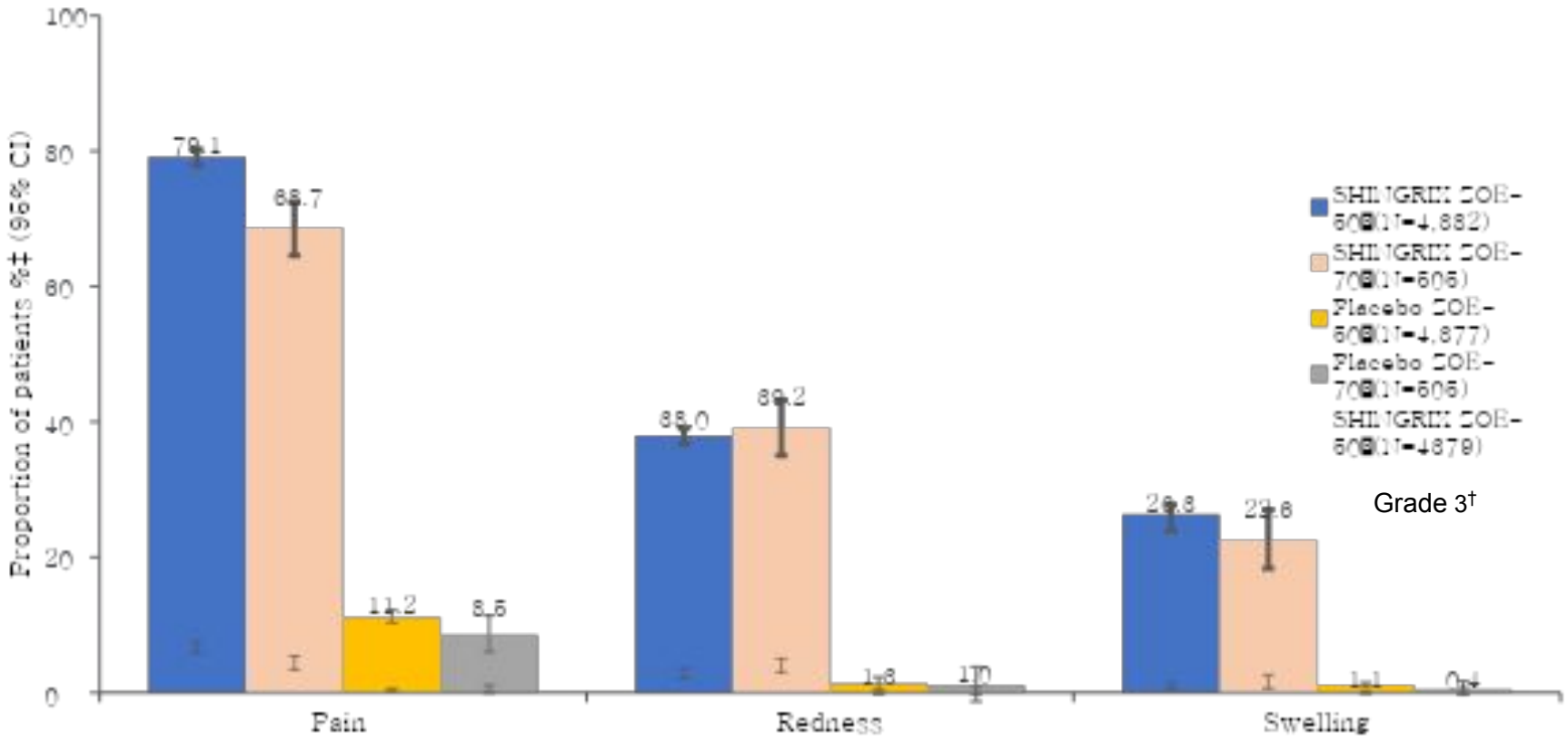
Efficacy evaluated in the modified total vaccinated cohort, which included participants who received both doses of study vaccine in ZOE-50/70 and did not develop a confirmed case of shingles within 1 month of dose 2.

CI, confidence interval; N, number of individuals included in each group; n, number of individuals having at least one confirmed shingles episode.

1. Lal H, et al. N Engl J Med 2015;372:2087–96. 2. Cunningham AL, et al. N Engl J Med 2016;75:1019–32. 3. Strezova A. et al. Open Forum Infec Dis 2022; ofac485, https://doi.org/10.1093/ofid/ofac485. 4. Boutry C, et al. Clin Infect Dis. 2022;74(8):1459-1467. 5. SHINGRIX Approved Product Information

solicited <u>local</u> adverse reactions reported up to 7 days post-vaccination[1–5*]

In immunocompetent adults 50 years and above from the ZOE pivotal trials.



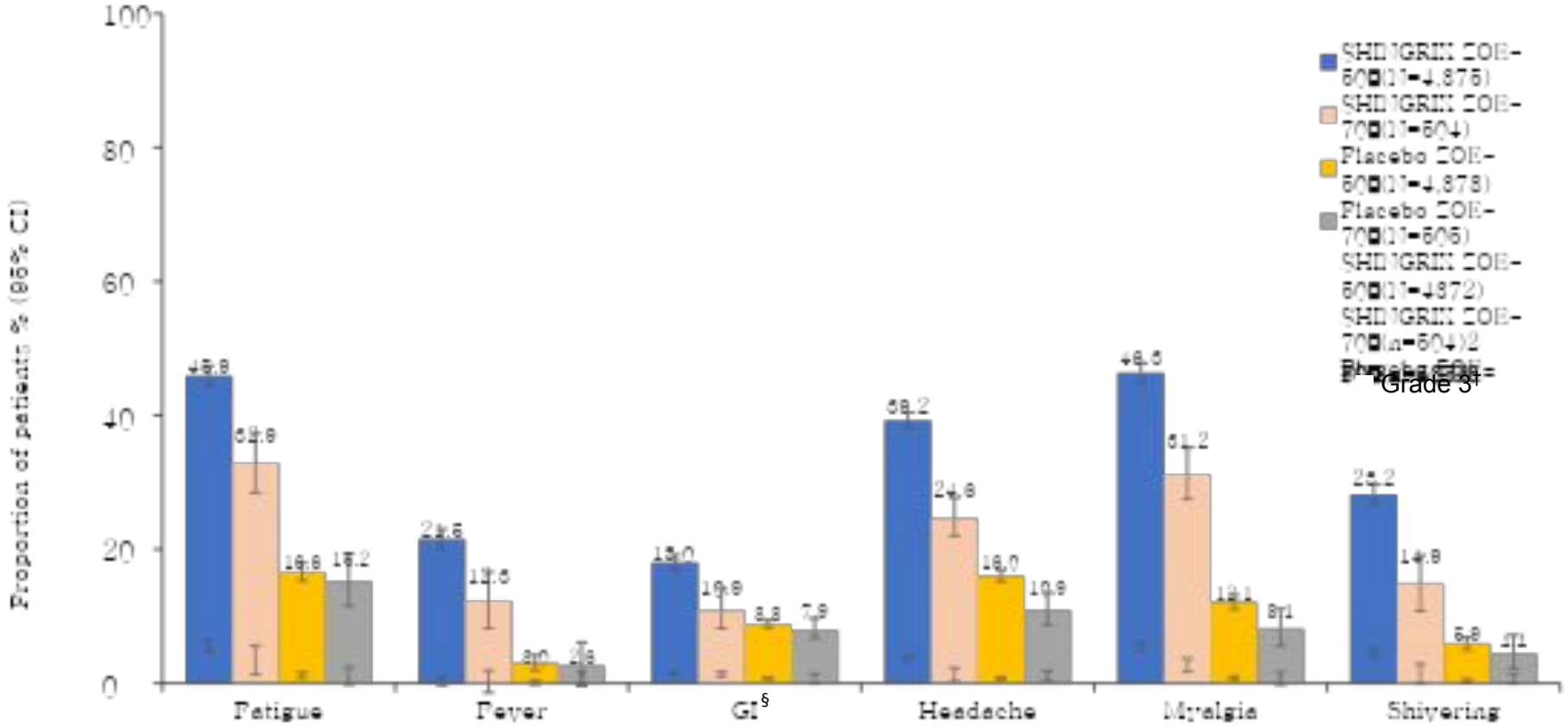
The median duration of solicited local reactions in the SHINGRIX group, including grade 3 reactions, was 3 days or less[5]

*Subgroup of age stratified subjects recorded injection-site reactions and systemic reactions on diary cards for 7 days after each injection; †Grade 3, redness and swelling at the injection site were scored as grade 3 for those more than 100 mm. All other symptoms were scored as 3 for preventing normal activity; ‡Percentage of subjects reporting the symptom at least once when the intensity is maximum. Data for any grade reactions from reference 1 and 2, Grade 3 reaction from reference 3 and 4.

Figure independently created by GSK from the original data reported in Lal et al[1] and Cunningham et al.[2]
CI, confidence interval; N, number of participants with available results.
1. Lal H, et al. N Engl J Med 2015;372:2087–96. 2. Cunningham AL, et al. N Engl J Med 2016;75:1019–32. 3. Study 110390: GSK Clinical Study Report 2016.Available at: https://www.gsk-studyregister.com/study/3283 (Accessed April 2023) 4. Study 113077; GSK Clinical Study Report 2016. Available at: https://www.gsk-studyregister.com/en/trial-details/?id=113077 (Accessed April 2023). 5. Lopez-Fauqued, M et al. Vaccine 2019;37:2482-2493.

solicited SYSTEMIC adverse reactions reported up to 7 days post-vaccination[1–5*]

In immunocompetent adults 50 years and above from the ZOE pivotal trials.



The median duration of solicited systemic reactions in the SHINGRIX group, including grade 3 reactions, was 2 days or less[5]

*Subgroup of age stratified subjects recorded injection-site reactions and systemic reactions on diary cards for 7 days after each injection; †Grade 3: temperature >39°C (preferred route: oral); all other symptoms were scored as 3 for preventing normal activity; ‡Fever (≥37.5°C/≥99.5°F); §GI symptoms included nausea, vomiting, diarrhea, and/or abdominal pain. Data for any grade reactions from reference 1 and 2, Grade 3 reaction from reference 3 and 4.

CI, confidence interval; N, number of participants with available results. GI, gastrointestinal; N, number of subjects with at least 1 documented dose; %, percentage of subjects reporting the symptom at least once when the intensity is maximum.
1. Lal H, et al. N Engl J Med 2015;372:2087–96. 2. Cunningham AL, et al. N Engl J Med 2016;75:1019–32. 3. Study 110390: GSK Clinical Study Report 2016.Available at: https://www.gsk-studyregister.com/study/3283 (Accessed April 2023). 4. Study 113077; GSK Clinical Study Report 2016. Available at: https://www.gsk-studyregister.com/en/trial-details/?id=113077 (Accessed April 2023). 5. Lopez-Fauqued, M et al. Vaccine 2019;37:2482-2493.

ATAGI & NCIRS CLINICAL ADVICE ON SHINGLES VACCINES[1,2]

ATAGI and NCIRS recommendation	
All immunocompetent people aged ≥50 years and people aged ≥18 years who are immunocompromised, or shortly expected to be immunocompromised, are recommended to receive vaccination to prevent HZ and its complications, unless contraindicated.[1,2]	The optimal age to receive vaccination depends on the patient's age and immune status, the duration of protection of the chosen vaccine, and the individual's desire to protect themselves from the disease.

For full recommendations, please refer to the ATAGI Australian Immunisation Handbook (AIH)[1] and the NCIRS "Zoster vaccines (Shingrix® [RZV] and Zostavax® [ZVL]) – FAQs" website"[2]. These materials should be read in conjunction with the Product Information.

ATAGI, Australian Technical Advisory Group for Immunisation; HZ, herpes zoster; NCIRS, National Centre for Immunisation Research and Surveillance.

1. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health and Aged Care, Canberra, 2022. Available at: immunisationhandbook.health.gov.au (Accessed November 2023). 2. National Centre for Immunisation Research and Surveillance (NCIRS). Zoster vaccines (Shingrix® [RZV] and Zostavax® [ZVL]) – FAQs. Available at: https://ncirs.org.au/zoster/zoster-vaccines-shingrixr-rzv-and-zostavaxr-zvl-faqs (accessed November 2023).

SHINGRIX:
AVAILABLE ON THE NATIONAL IMMUNISATION PROGRAM[1]

Help to protect your adult patients against shingles:

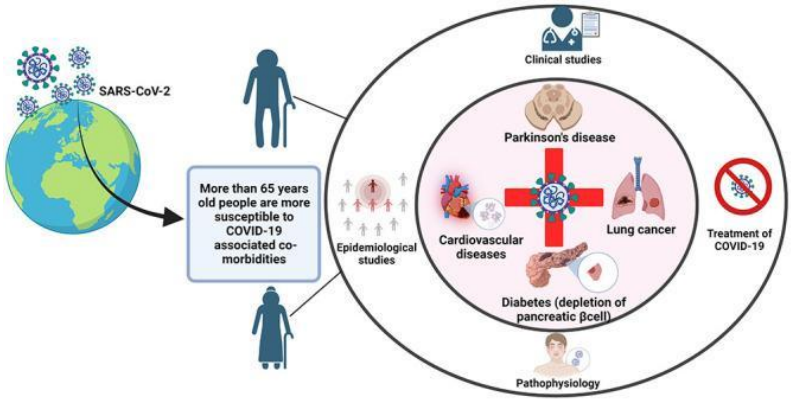
≥18 years old	≥50 years old	≥65 years old	≥18 years old	50 – 64 years old
Immunocompromised with conditions at 'high risk' of shingles: **These conditions include:** • **haematopoietic stem cell transplant,** • **solid organ transplant, haematological malignancy** • **advanced or untreated HIV.**	**First Nations people**	**Individuals**	**At increased risk of shingles** All other conditions excluding NIP 'high risk' conditions	**Individuals**
SHINGRIX NIP	**SHINGRIX NIP**	**SHINGRIX NIP**	**SHINGRIX private script**	**SHINGRIX private script**

1.Department of Health. NIP Shingles Vaccination Advice for vaccination providers
https://www.health.gov.au/resources/publications/national-immunisation-program-shingles-program-advice-for-vaccination-providers?language=en (accessed November 2023)

COVID-19

Risk Factors for Severe Disease

- Understanding of risk has evolved, however risk factors identified early in pandemic have changed little (relevant for intervention)
  - Advanced age
    - Reduced immune responses, Immunosenescence
    - Association with comorbidities and frailty
    - Underlying pro-inflammatory state
  - Male Sex
    - Genetic and hormonal factors
    - Lifestyle factors
    - Higher ACE2 levels on the endothelium
  - Comorbidities
    - Direct and via reduced vaccine response and greater risk of transmission
      - Diabetes
      - Cardiovascular
      - Obesity
      - Residential aged care resident



Zhang, R., et al. (2022). "Risk factors and protective factors for alcohol-related liver disease: A systematic review and meta-analysis." Alcohol Clin Exp Res 46(12): 2128-2136.
Chatterjee, S., et al. (2023). "Association of COVID-19 with Comorbidities: An Update." ACS Pharmacol Transl Sci 6(3): 334-354.

ATAGI

- 2024 Advice
- Risk based approach
- Not all risks considered
  - Healthcare worker or other high-risk profession
  - Travel
  - Pregnancy

75 years and older

- Recommended every 6 months.

65-74 years

- Recommended at least every 12 months, but can receive every six months. Talk to your healthcare provider about the risks and benefits..

18-64 years

- **With severe immunocompromise:** Recommended at least every 12 months, but can receive every six months. Talk to your healthcare provider about the risks and benefits.
- **Without severe immunocompromise:** Can receive every 12 months.

5-17 years

- **With severe immunocompromise:** Can receive every 12 months.
- **Without severe immunocompromise**: Not recommended.

Under 5 years

- Not recommended.

COVID-19 vaccine advice and recommendations for 2024 | Australian Government Department of Health and Aged Care

Conclusion

Conclusions

- The elderly are a particularly challenging group when it comes to preventing infection
  - Higher risk, outcomes worse, so a higher priority
  - More challenging to achieve desired effect
  - Many confounders
- Many strategies available to try to overcome
  - Adjuvants
  - Higher doses
  - More frequent boosters
- Perhaps the two biggest recent advances
  - RSV vaccines
  - Shingrix
    - Relatively high levels of efficacy and reasonable safety profiles

END

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