



How does frailty impact the efficacy, reactogenicity, immunogenicity and safety of the adjuvanted recombinant zoster vaccine?

A secondary analysis of the ZOE-50 and ZOE-70 studies

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Disclosures

- **Dr. Andrew** reports grants from the GSK group of companies (GSK) during the study, as well as grants from GSK, the Canadian Frailty Network, the Canadian Institutes of Health Research, the Foundation for Influenza Epidemiology, and grants and personal fees from Sanofi and Pfizer outside the submitted work.

Dr. Levin reports grants and fees for Advisory Boards from GSK during the study and is serving as an Advisory Board member for GSK and Merck. **Mr. Matthews** is a freelance consultant for GSK. **Dr. Schmader** reports grants from GSK during the study. **Dr. McNeil** reports grants, personal fees and support for the conduct of clinical trials from GSK and Pfizer, personal fees and support for the conduct of clinical trials from Sanofi Pasteur, as well as personal fees from Merck outside the submitted work. **Dr. Kim, Mr. Dessart, Dr. Riley and Dr. Curran** are employees, and **Dr. Oostvogels and Dr. Schuind** former employees of GSK. **Dr. Kim, Dr. Oostvogels, Dr. Riley, Dr. Schuind and Dr. Curran** own GSK stock options or (restricted) shares. **Dr. Oostvogels** is an employee of CureVac AG and is inventor on a patent owned by GSK and relevant to RZV.

- Funding: GlaxoSmithKline Biologicals SA

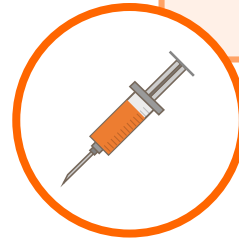
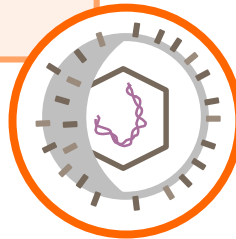
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Background: Importance of evaluating herpes zoster vaccine in frail older adults

Frail older adults are **more vulnerable to herpes zoster's** negative impact on health and quality of life¹

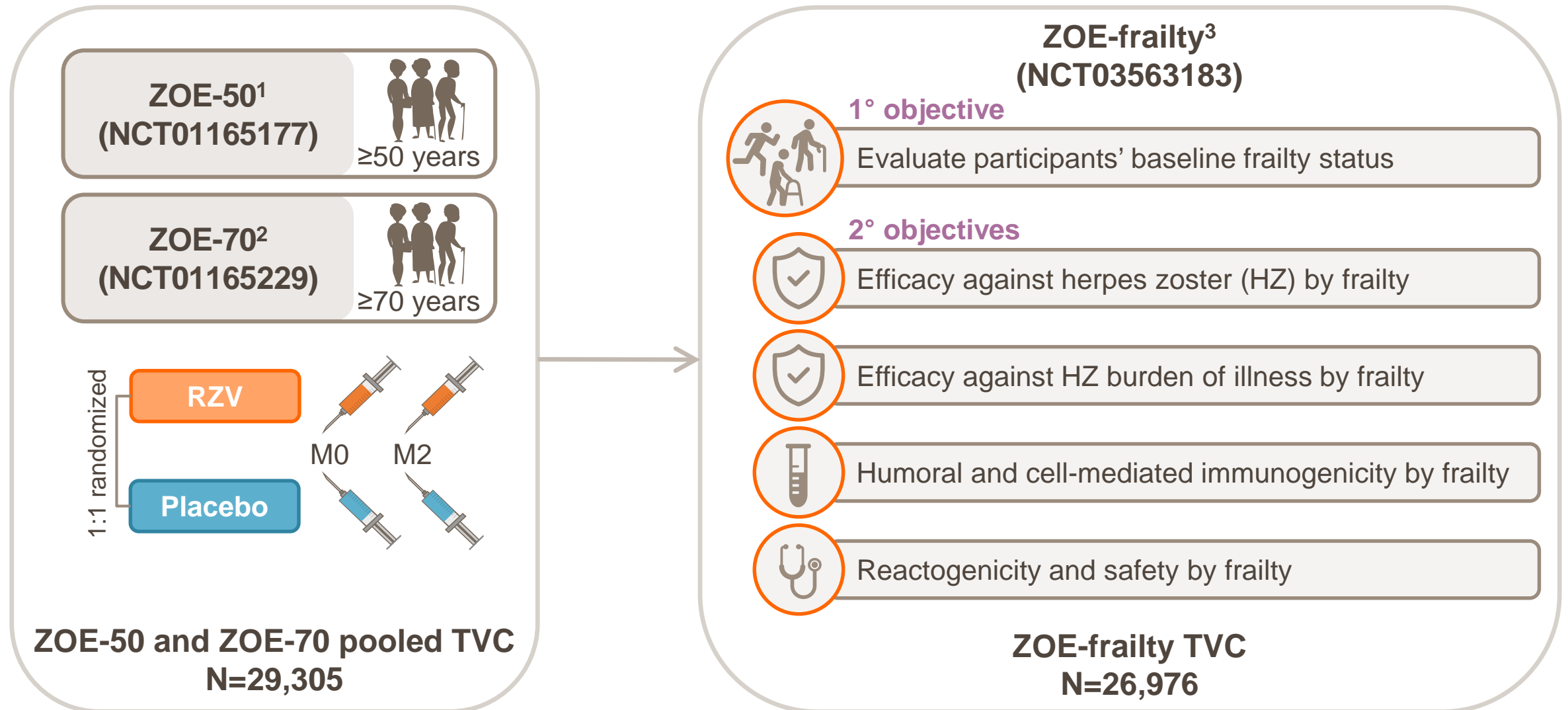
ZOE-50 and ZOE-70 randomized controlled trials showed **high efficacy of adjuvanted recombinant zoster vaccine (RZV)** in older adults^{2,3}



Some treatments and vaccines are **less effective** in frail older adults⁴

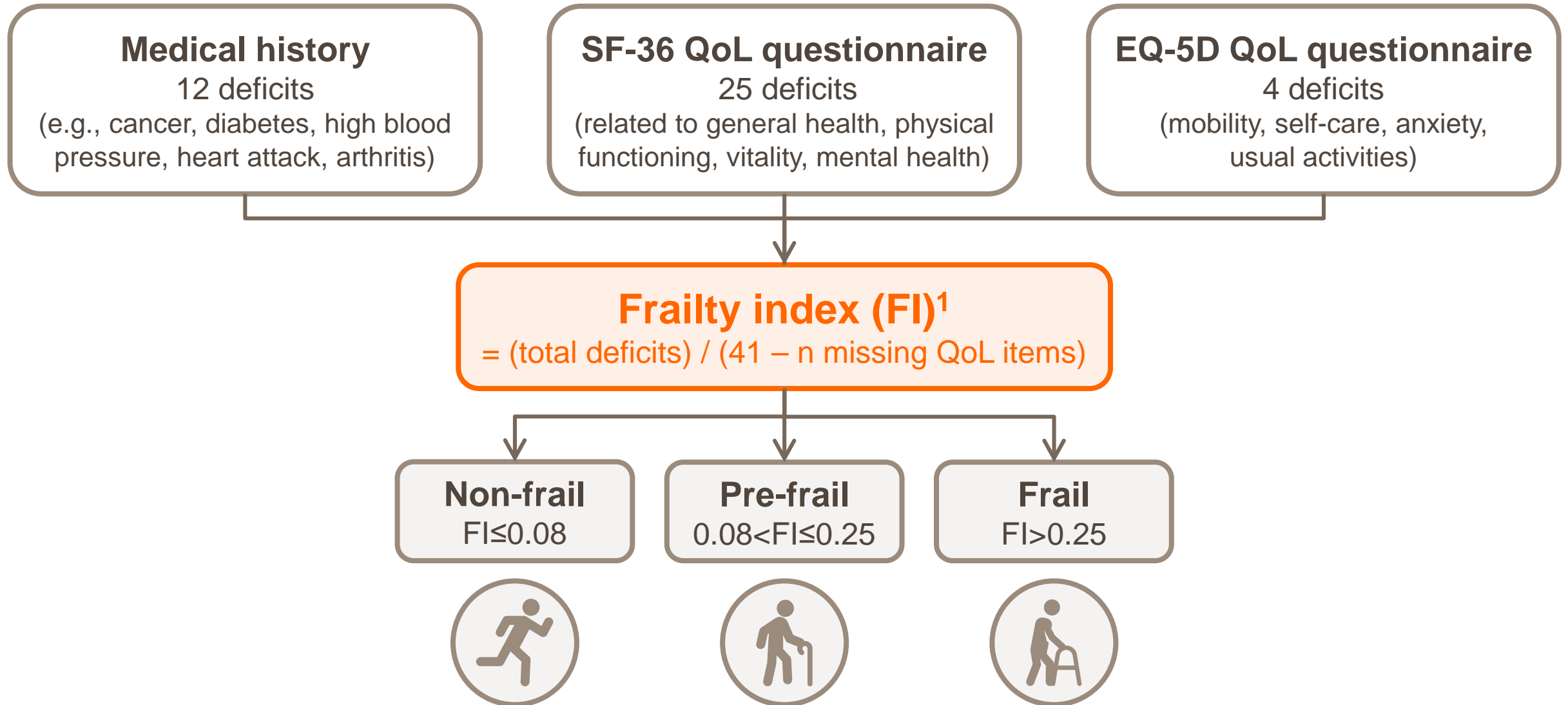
Our aim: Retrospective evaluation of frailty in ZOE-50/70 participants based on collected health status data and patient reported outcomes

Aim: Retrospective evaluation of frailty in ZOE-50/70 participants



TVC, total vaccinated cohort; **M**, month. **1.** Lal et al. N Engl J Med 2015;372:2087–96; **2.** Cunningham et al. N Engl J Med 2016;375:1019–32; **3.** Curran et al. J Am Geriatr Soc; in press.

Methods: Determination of frailty index and categories



Methods: Measures



Vaccine efficacy: $VE = \frac{\text{herpes zoster incidence in RZV group}}{\text{herpes zoster incidence in placebo group}} \times 100$



Humoral immunogenicity: anti-glycoprotein E (gE) ELISA



Cell-mediated immunogenicity: flow cytometry → frequencies of CD4+ T cells expressing ≥2 activation markers (IFN-γ, IL-2, TNF-α, CD40 ligand) after ex vivo stimulation with gE



Reactogenicity: solicited AEs in random subset (7 days after each dose)



Safety: unsolicited AEs (30 days after each dose), unsolicited AEs with medically attended visit (8 months post-dose 1), SAEs (14 months post-dose 1), deaths and pIMDs (entire study)

Results: Demographics and frailty were balanced between RZV and placebo groups and frailty increased with age

Demographics

Mean age, years

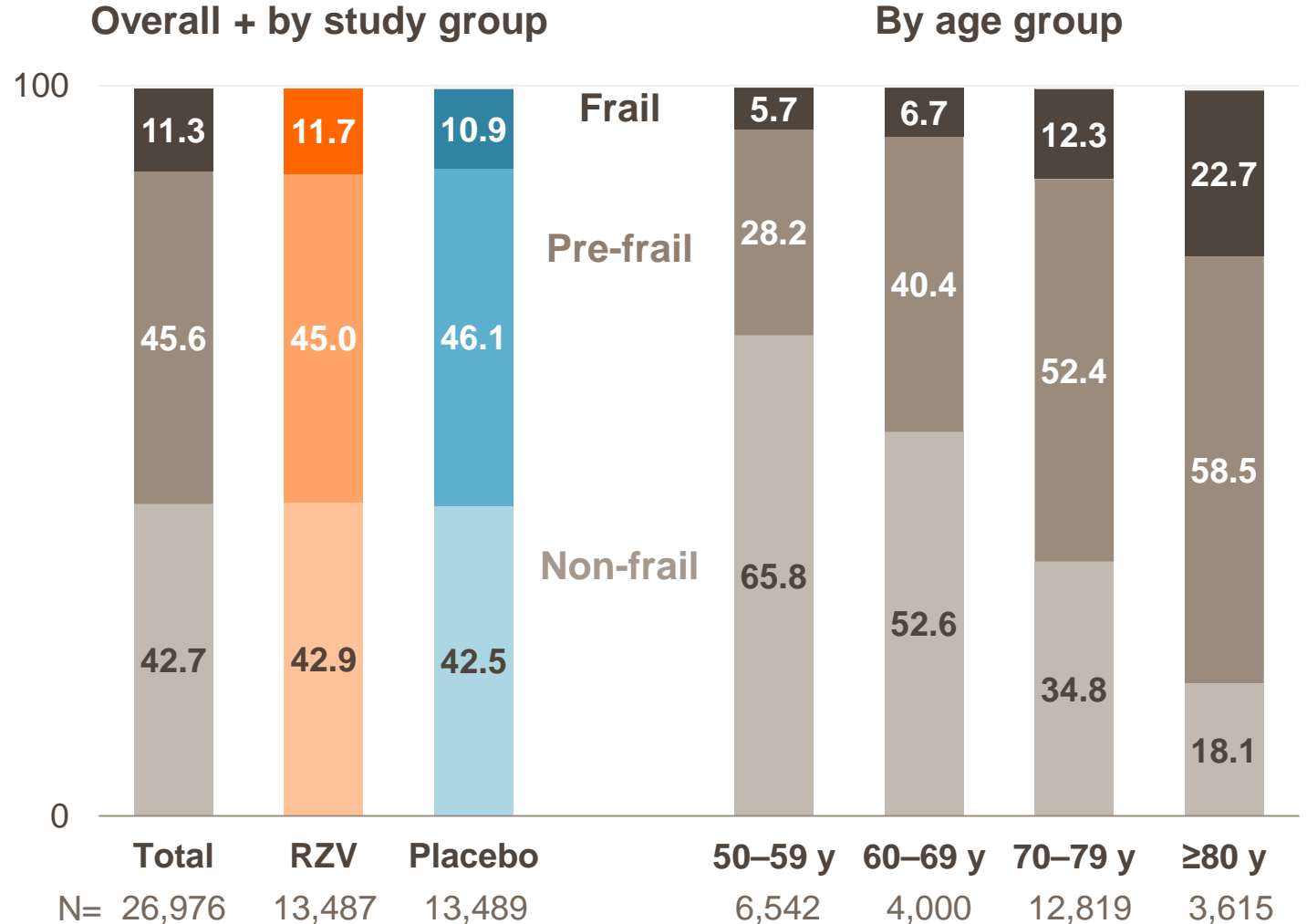


% Female

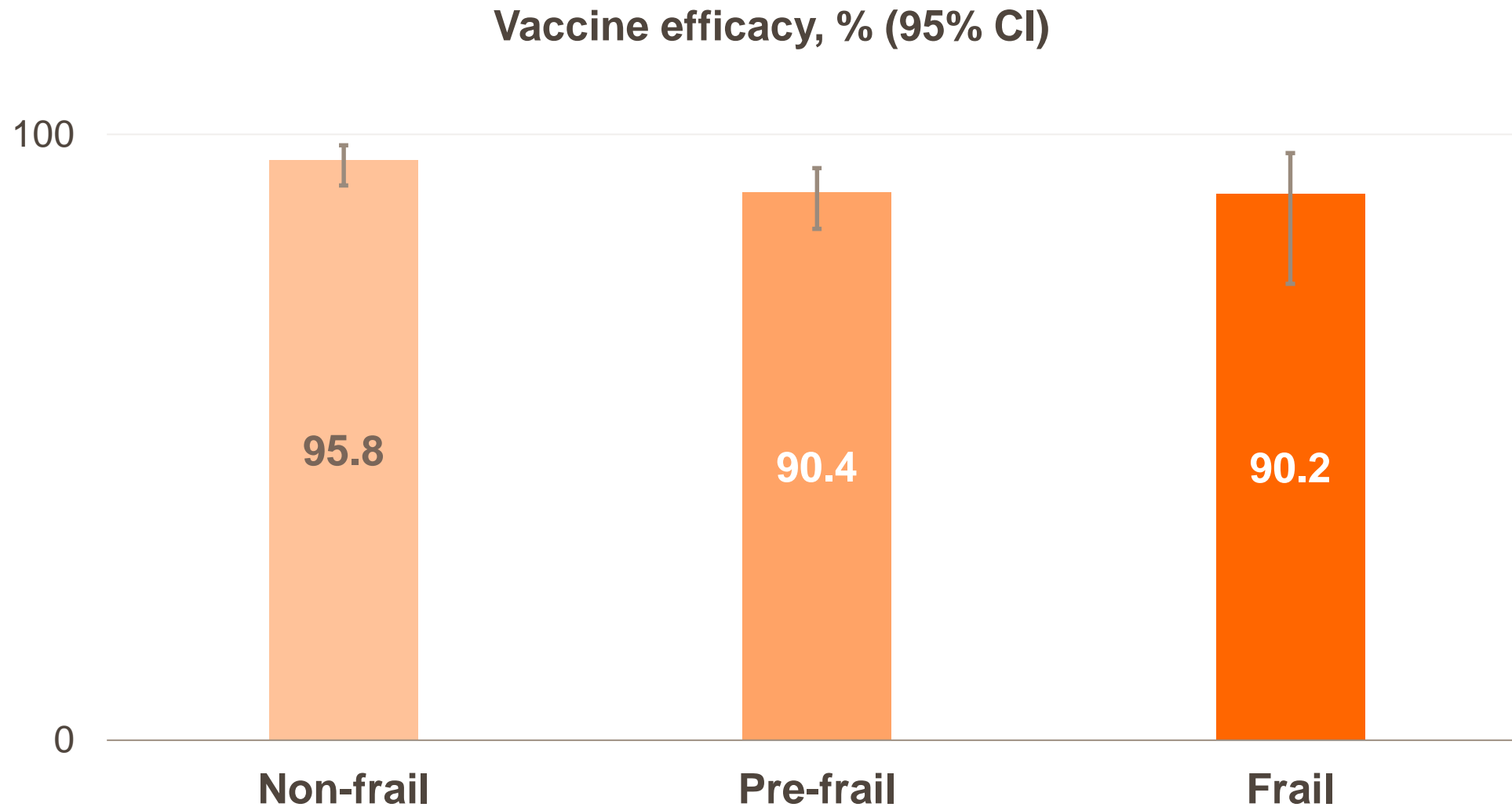


Total vaccinated cohort.

Frailty status, %

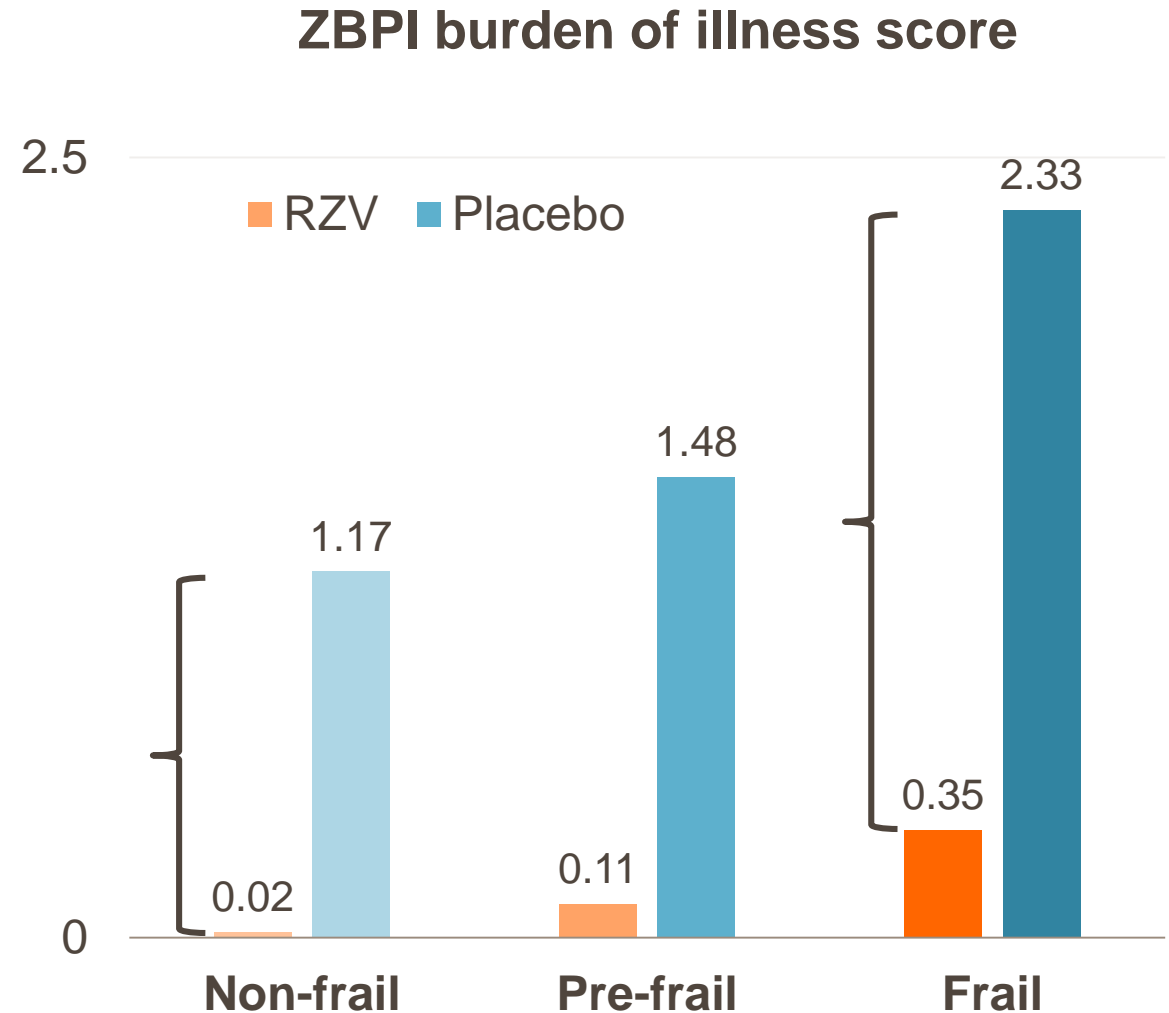
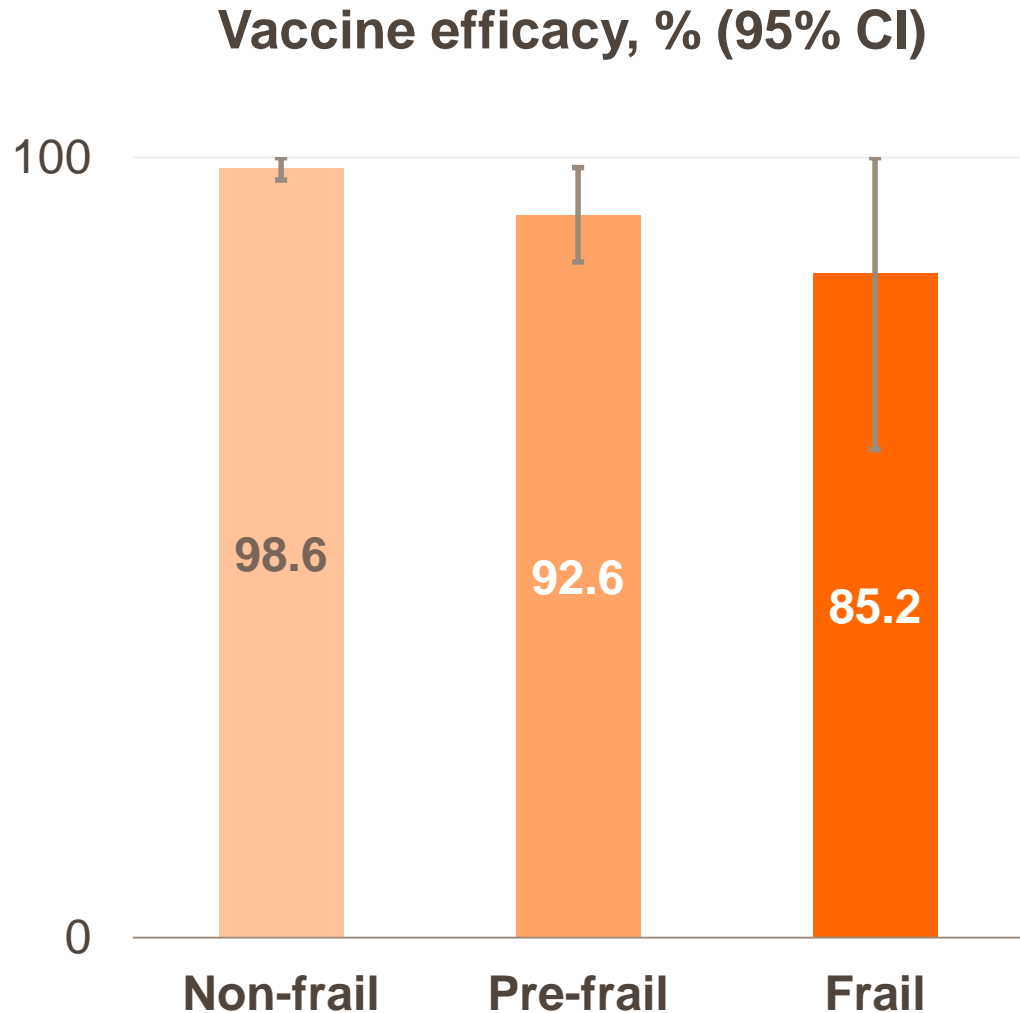


Results: Vaccine efficacy against herpes zoster was >90% across frailty categories

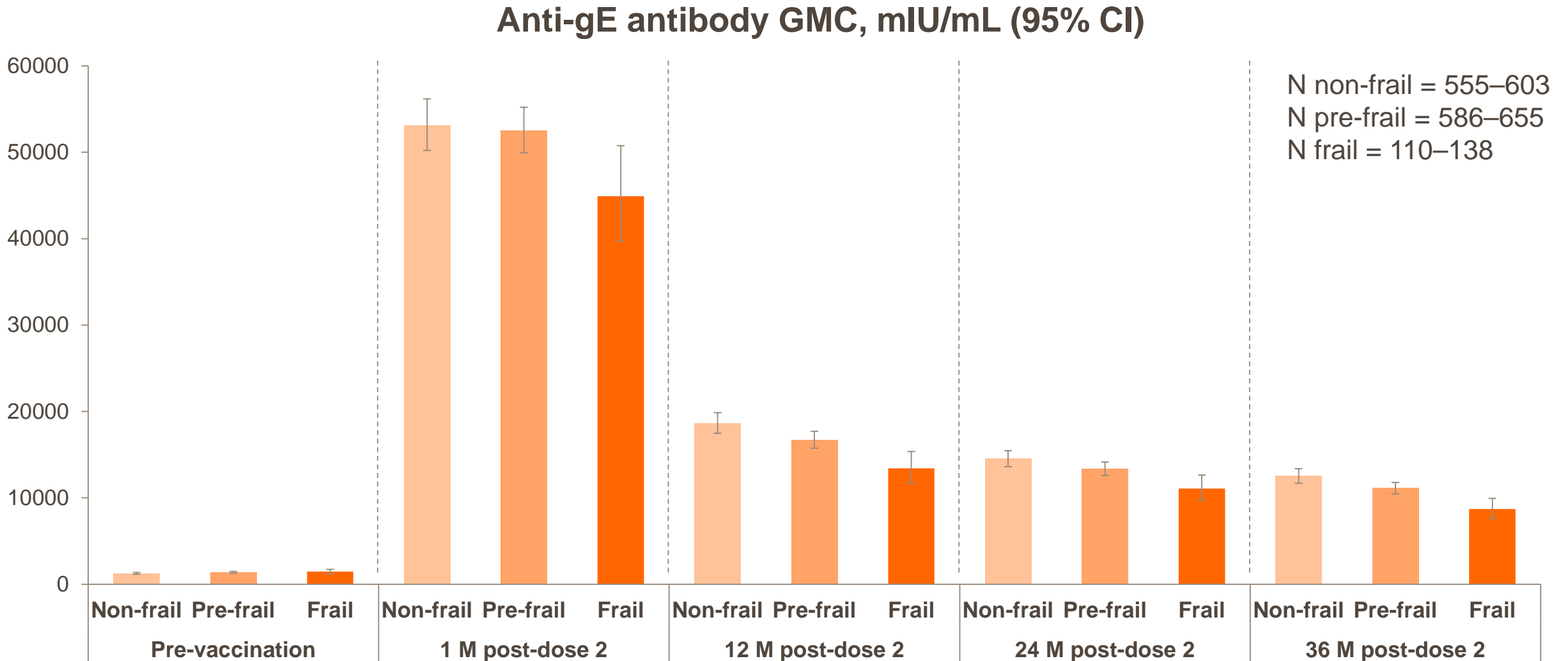


First or only episode of herpes zoster during entire study period, modified total vaccinated cohort. **CI**, confidence interval.

Results: Vaccine efficacy against zoster burden of illness decreased with frailty, but absolute reduction in burden of illness was largest in frail participants

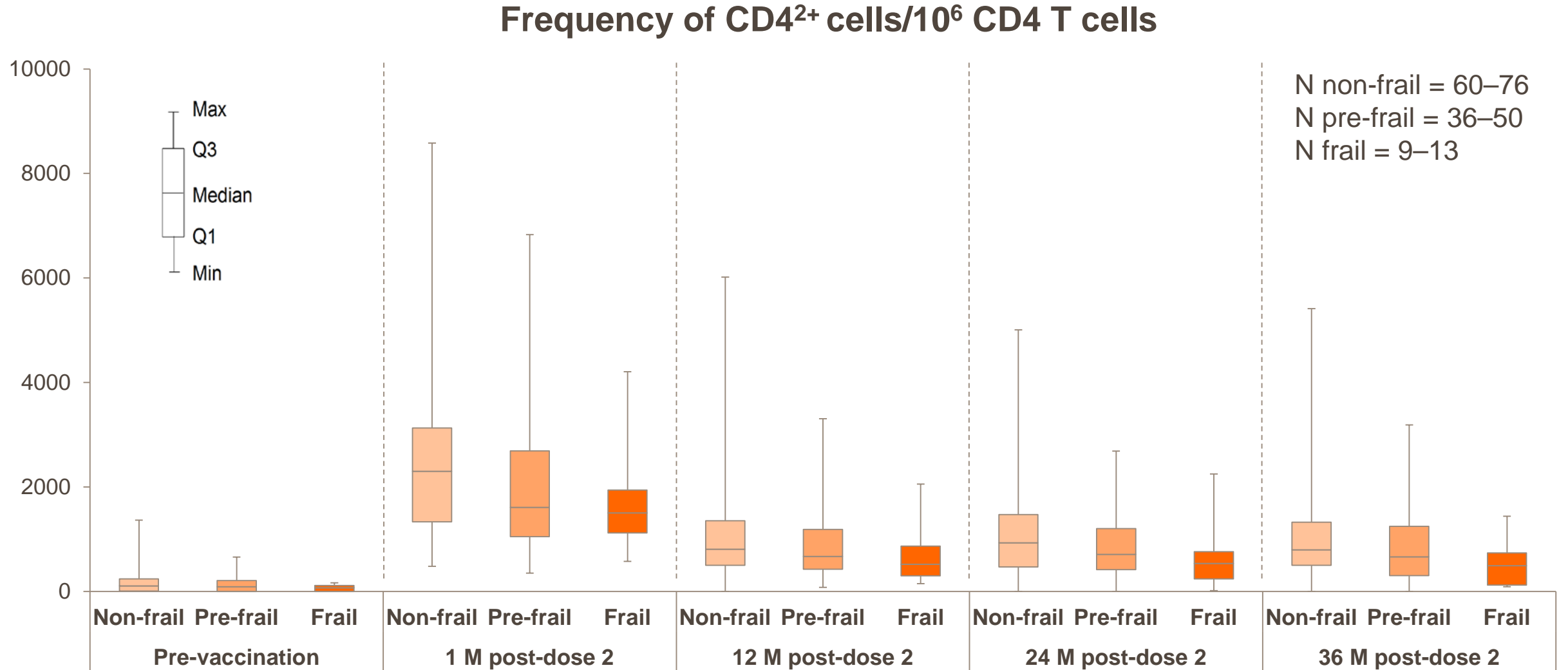


Results: RZV induced robust, persistent anti-gE antibody responses across frailty categories



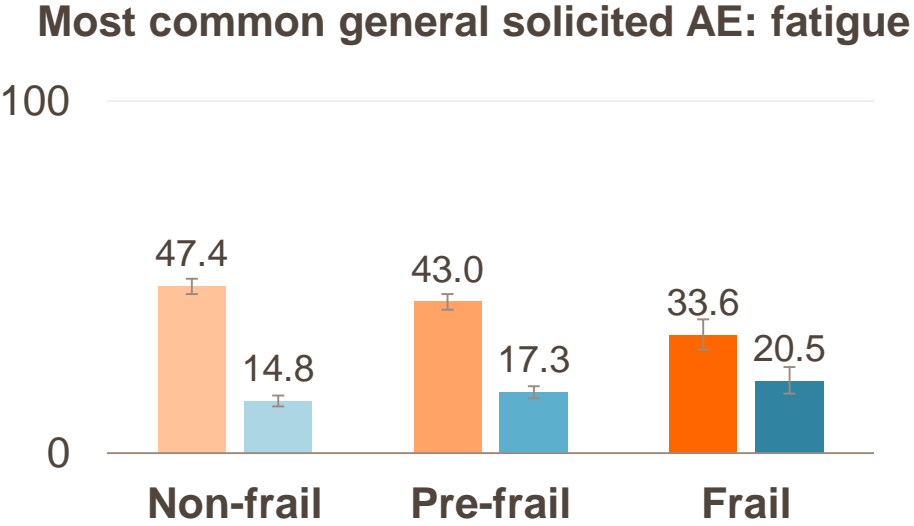
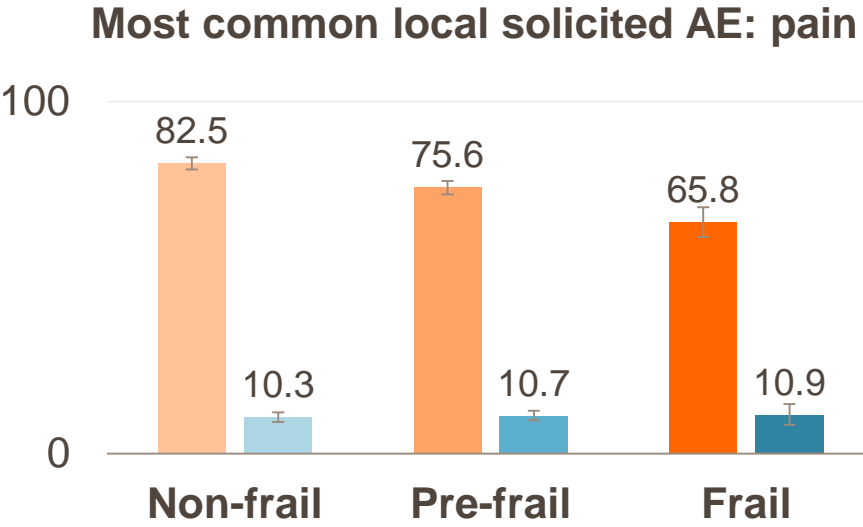
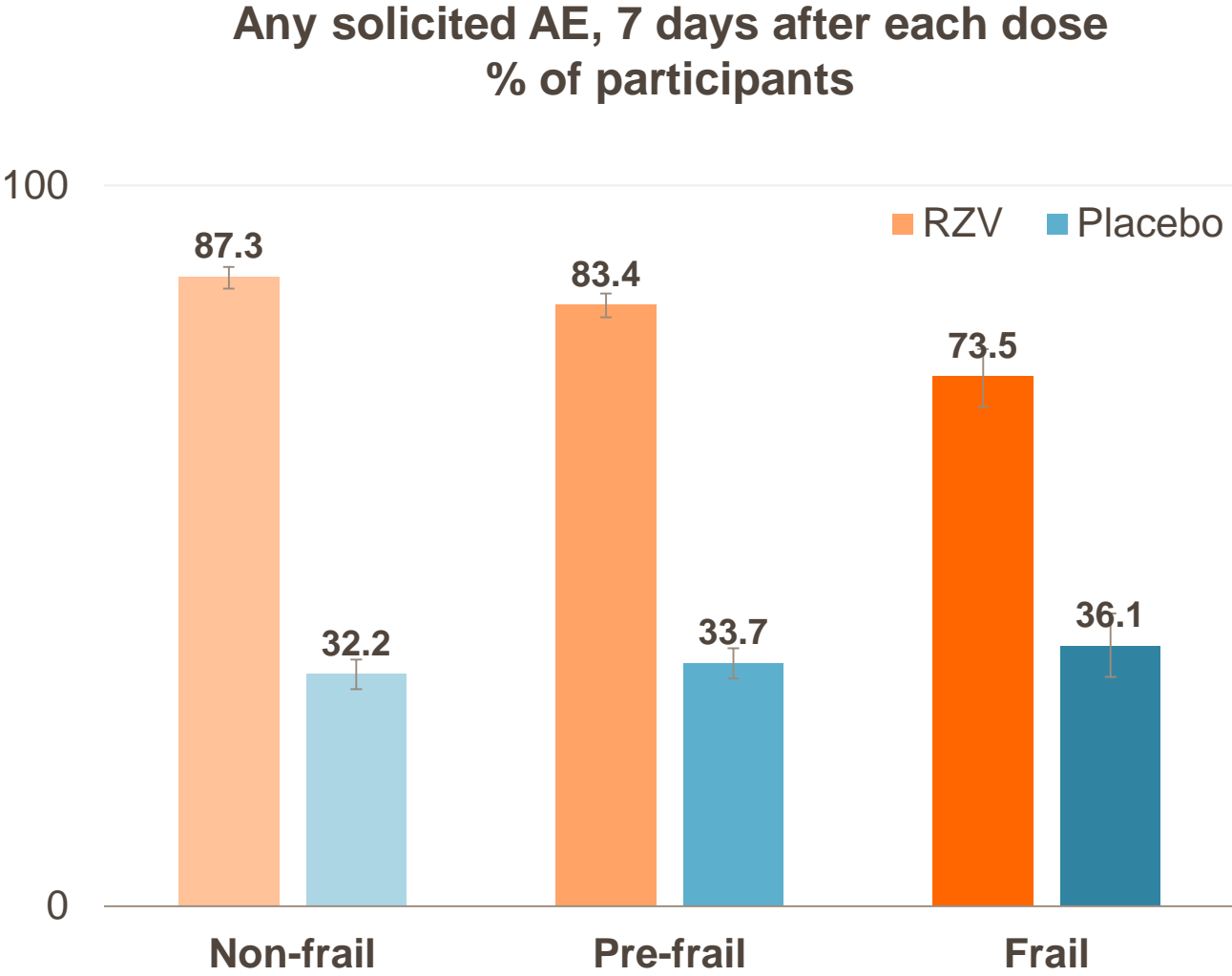
Adapted according-to-protocol cohort for immunogenicity – humoral. **GMC**, geometric mean concentration; **CI**, confidence interval; **M**, months.

Results: RZV induced robust, persistent gE-specific CD4²⁺ responses across frailty categories



Adapted according-to-protocol cohort for immunogenicity – cell-mediated immunity. **M**, months; **Q1–Q3**, interquartile range.

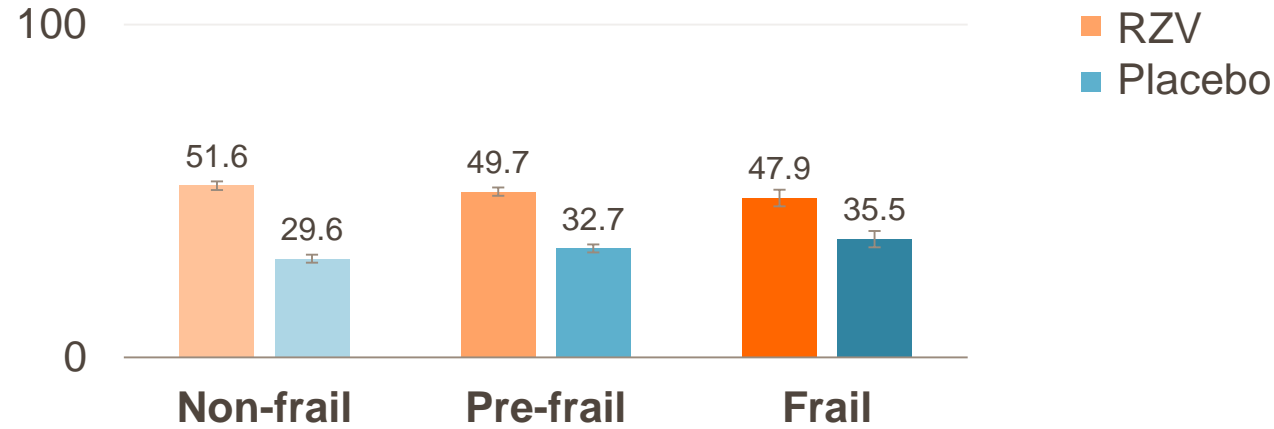
Results: Reactogenicity decreased with increasing frailty in RZV recipients



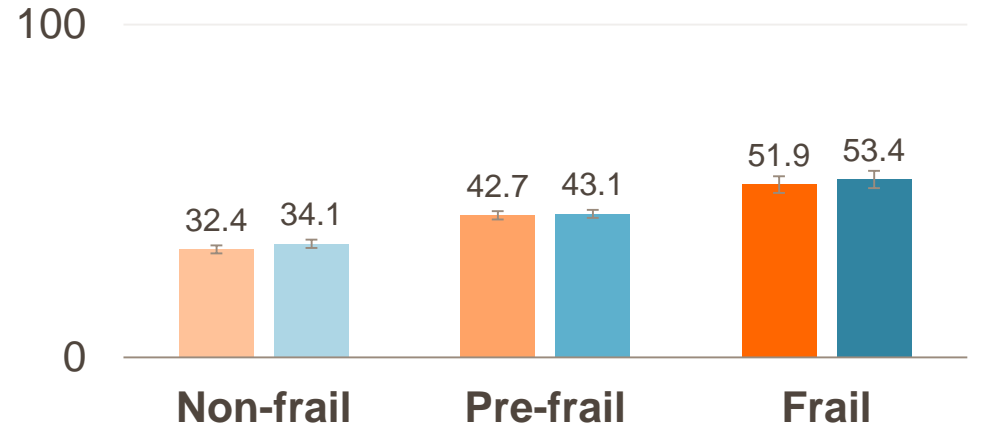
Total vaccinated cohort, diary card subset. AE, adverse event.

Results: Unsolicited medically attended visits and serious adverse events increased with frailty and were balanced between placebo and RZV groups

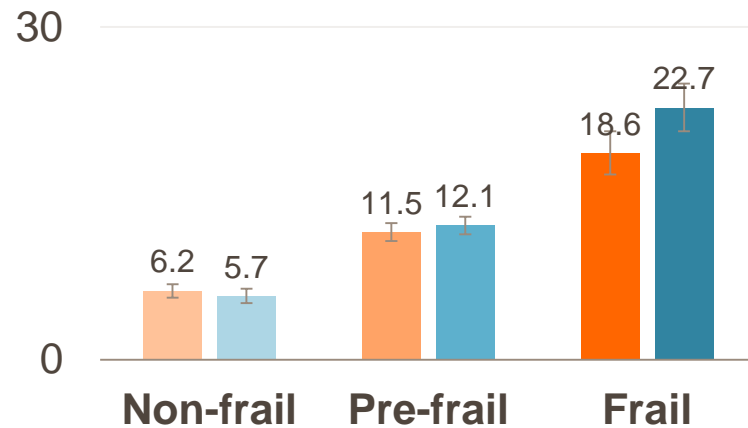
Unsolicited AEs, 30 days after each dose



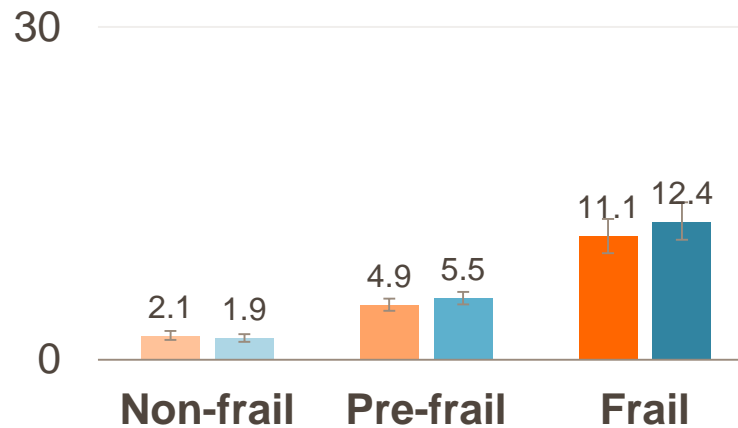
Medically attended visits, 8 months post-dose-1



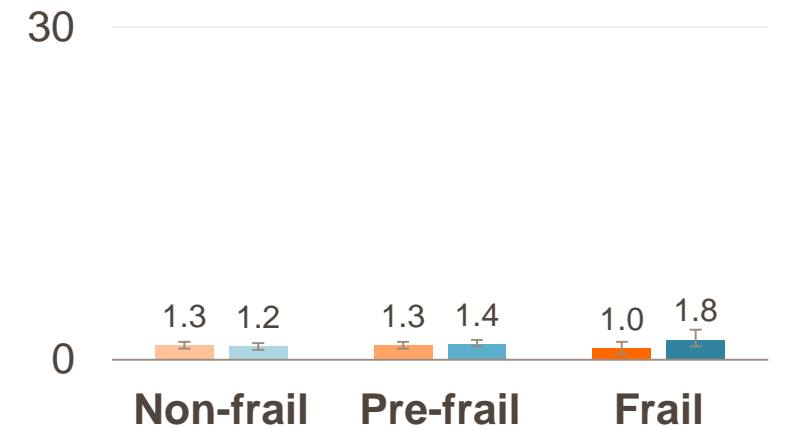
SAEs, 14 months post-dose 1



Deaths, entire study



pIMDs, entire study

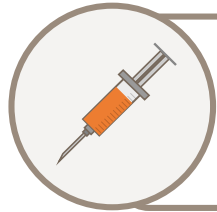


Total vaccinated cohort. (S)AE, (serious) adverse event; pIMD, potential immune-mediated disease.

Conclusions



The relatively nonrestrictive in/exclusion criteria in the parent ZOE studies resulted in a range of participants that included frail and pre-frail older adults.



Vaccine efficacy was high (>90%) across frailty subgroups. Immunogenicity was robust and there was no safety signal in relation to frailty.



RZV significantly reduces the risk of herpes zoster and is safe to use across the spectrum of frailty.



A frailty index was readily calculated based on data sometimes collected in randomized trials for vaccines and other interventions. Frailty could thus be considered retrospectively in other studies even where a frailty measure was not included up front.

Thank you!