

SHIVERS

Risk factors and attack rates of seasonal influenza infection: results of the SHIVERS seroepidemiologic cohort study

Q Sue Huang, Don Bandaranayake, Tim Wood, E. Claire Newbern, Ruth Seeds, Jacqui Ralston, Ben Waite, Ange Bissielo, Namrata Prasad, Angela Todd, Lauren Jolley, Wendy Gunn, Anne McNicholas, Thomas Metz, Shirley Lawrence, Emma Collis, Amanda Retter, Sook-san Wong, Richard Webby, Judy Bocacao, Jennifer Haubrock, Graham Mackereth, Nikki Turner, Barbara McArdle, John Cameron, Gary Reynolds, Michael G. Baker, Cameron Grant, Colin McArthur, Sally Roberts, Adrian Trenholme, Conroy Wong, Susan Taylor, Paul Thomas, Jazmin Duque, Diane Gross, Mark G. Thompson, and Marc-Alain Widdowson, on behalf of the SHIVERS investigation team
Contact information: Q. Sue Huang* - Sue.Huang@esr.cri.nz

BACKGROUND

Understanding the attack rate of influenza infection and the proportion that become ill by risk group is key to implement cost-effective prevention measures. While population-based studies of anti-haemagglutinin antibody responses have been described previously, studies examining both anti-haemagglutinin and anti-neuraminidase antibodies are lacking.

METHODS

SHIVERS (Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance) sero-epidemiologic cohort study:

- Selected individuals (stratified by age and ethnicity) randomly from the patient population of representative general practices in Auckland, New Zealand in 2015.
- Tested paired sera of each participant for antibodies to haemagglutinin or neuraminidase using inhibition assays for 4 antigens (AH1, AH3, B/Yam, or B/Vic).
- Weekly follow-up (May-September) for all participants and collection of respiratory specimens from those reporting influenza-like illness (ILI) and testing these specimens for influenza by PCR.
- Rates of ILI and influenza-confirmed ILI were adjusted for non-reporting and non-swabbing.

RESULTS

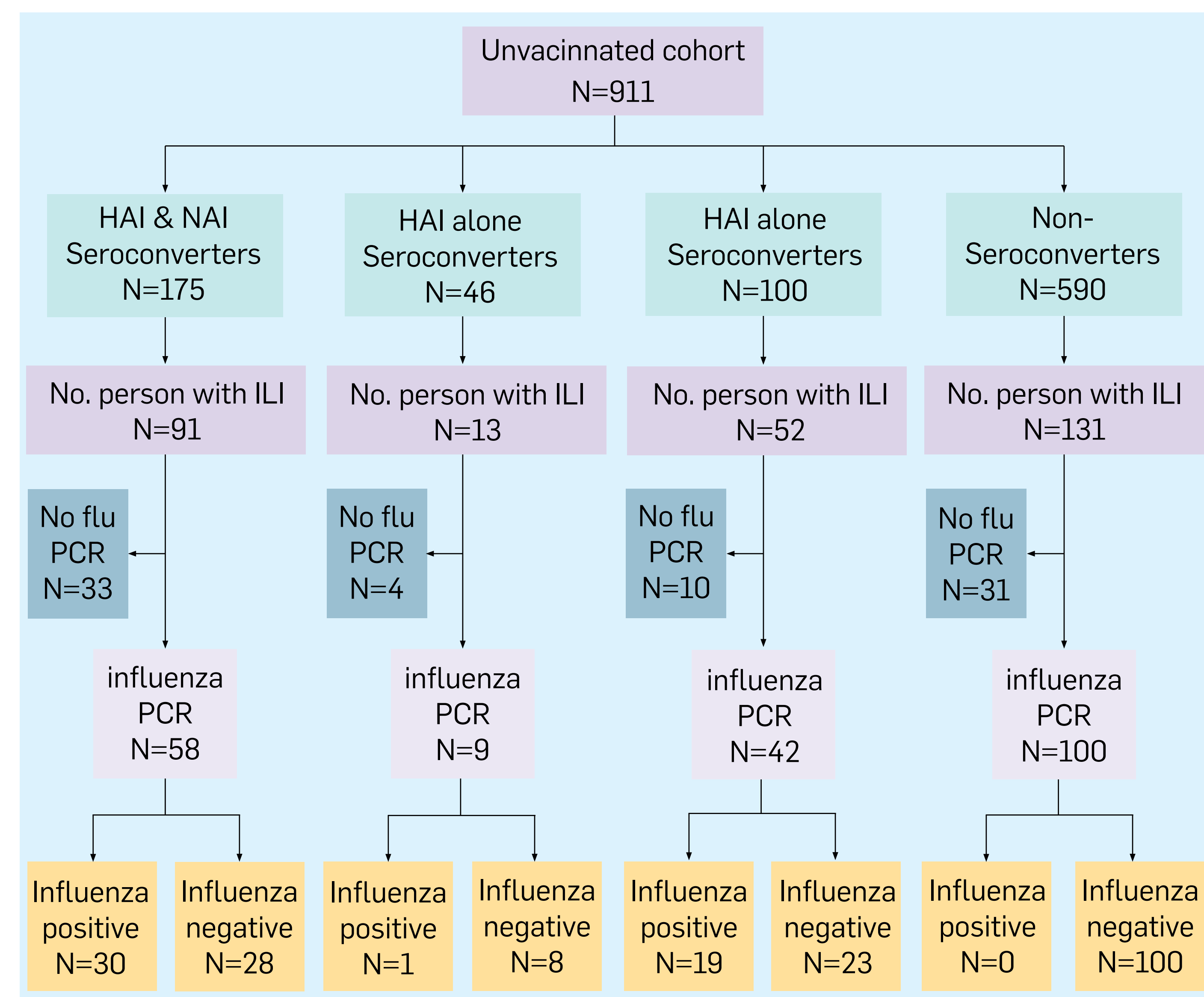


Figure 1. Flow diagram of HAI and NAI serology as well as PCR results among the unvaccinated cohort

Influenza infection and influenza-confirmed ILI attack rates (Figure 1):

- Of the 911 unvaccinated participants, 321 (35%) seroconverted to either HAI (haemagglutination-inhibition) or NAI (neuraminidase-inhibition) antibody.
- Of those serologically defined infections, an estimated 24% [76 (adjusted for non-reporting and non-swabbing)/321] would have experienced influenza-confirmed ILI (PCR positive)
- Of the influenza-confirmed ILI, an estimated 20% (15 (adjusted for non-reporting and non-swabbing)/76) would have sought medical care.

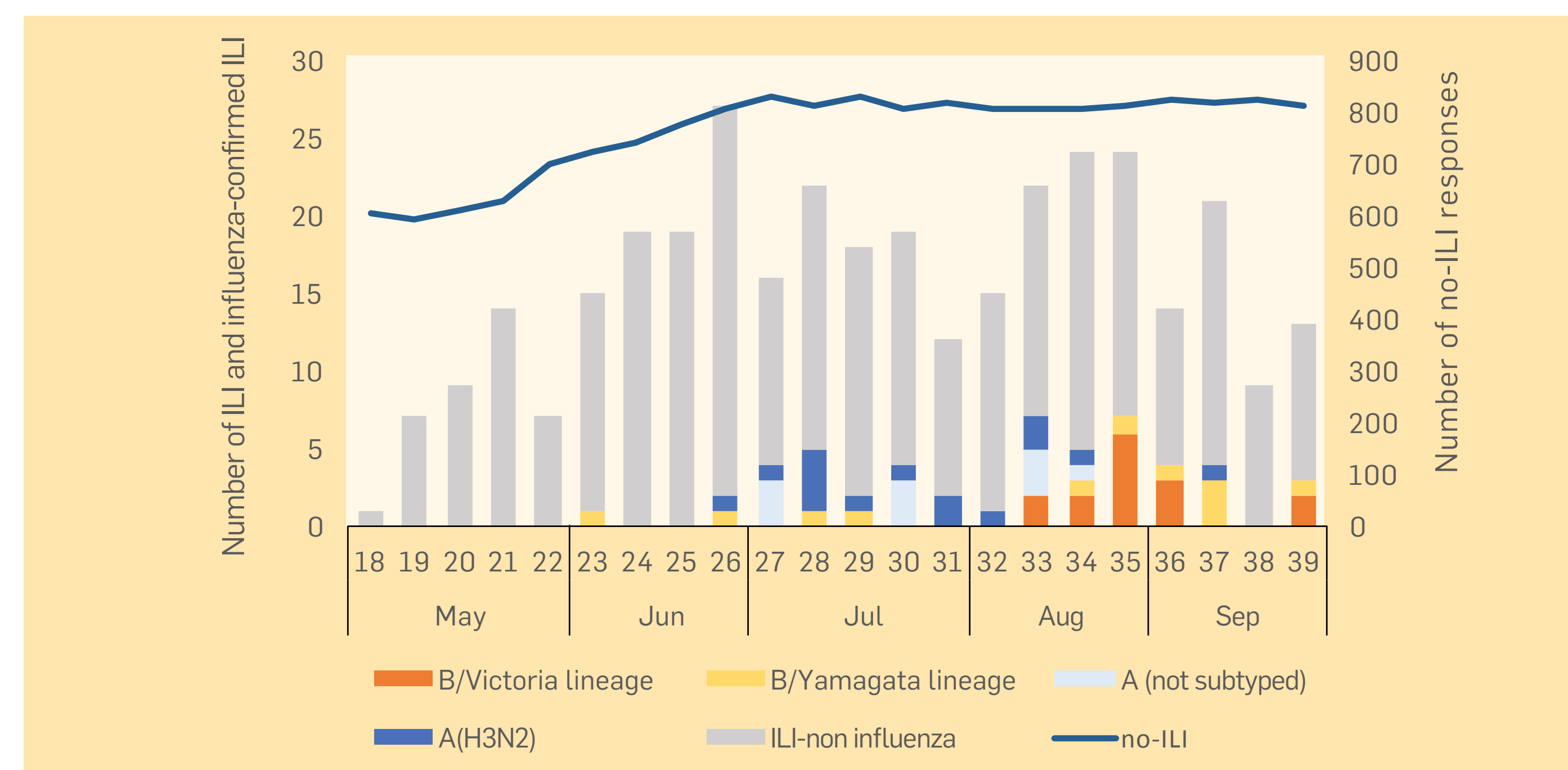


Figure 2. Temporal distribution of influenza-like illness (ILI) and influenza-confirmed ILI and no-ILI among the cohort during 27 April to 27 September 2015.

Influenza activity in NZ in 2015 was at the moderate level. Two distinct circulation patterns: A(H3N2) predominated during weeks 26-33 and influenza B (mainly B/Victoria predominated during weeks 34-39).

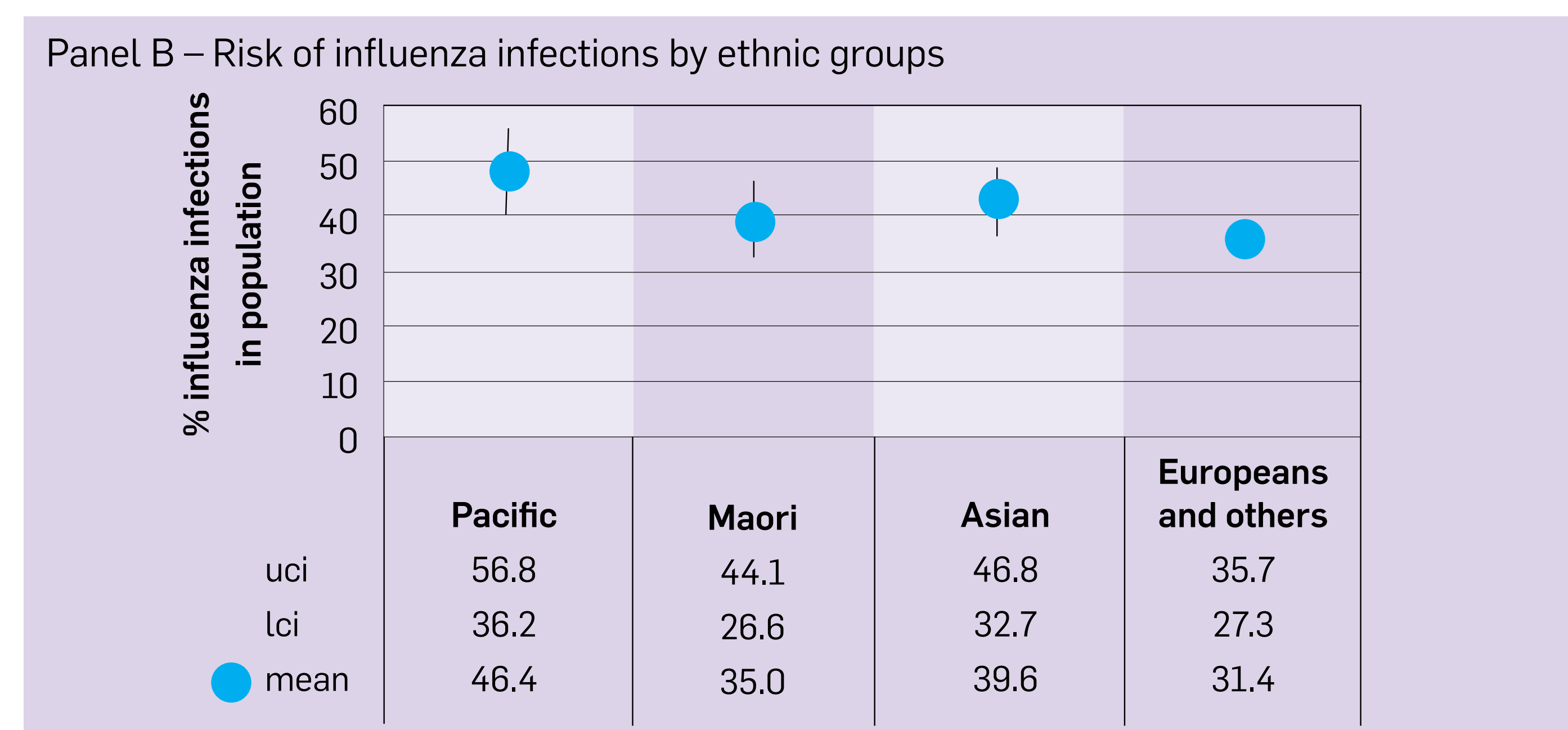
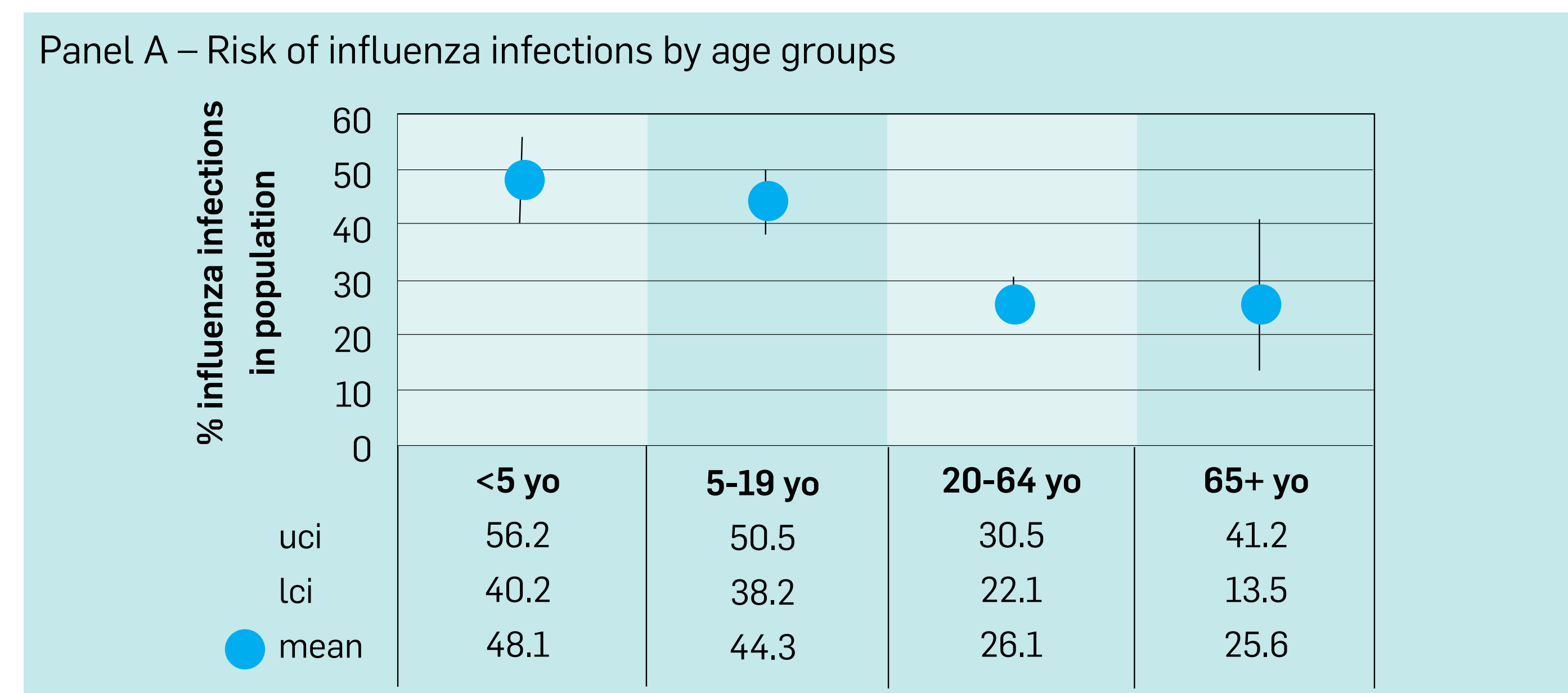


Figure 3: Age distribution among serologically defined influenza infections. The highest attack rates of influenza infection were in children aged <5 years and Pacific peoples.

SOUTHERN HEMISPHERE INFLUENZA AND VACCINE EFFECTIVENESS RESEARCH & SURVEILLANCE

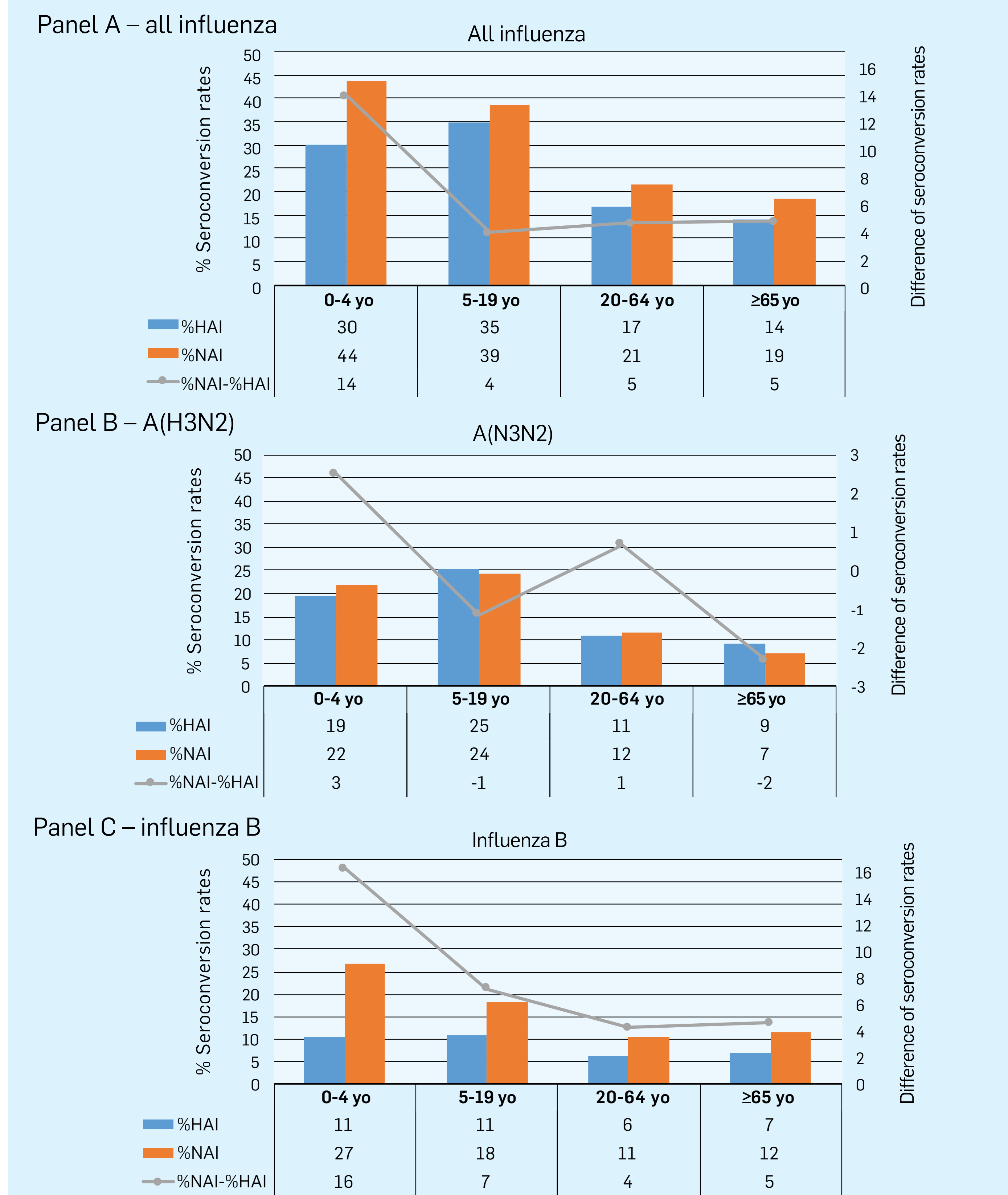


Figure 4 Proportions and differences of HAI and NAI seroconversion by age groups and viruses. Seroconversion to NAI alone was significantly higher among children aged <5 years vs those aged ≥5 years (14% vs 4%; p<0.001) and among those with influenza B virus vs A(H3N2) virus infections (7% vs 0.3%; p<0.001).

CONCLUSIONS

- One of the largest and most comprehensive sero-epidemiologic cohort studies for all ages.
- The first report to quantify attack rates of seasonal influenza infections by measuring seroconversion against both haemagglutinin and neuraminidase antigens and 31% infections identified through seroconversion with anti-neuraminidase antibodies alone.
- Children and Pacific peoples had the highest rates of influenza infection and influenza-confirmed ILI.
- Our study highlighted the importance of measuring serologically defined infections against not just haemagglutinin but also neuraminidase antigens to understand the true epidemiology and immunology of influenza and guiding countermeasure strategies.

Conflicts of Interest: Conflicts of Interest: Of the listed study authors, A Trenholme receives funding for non-SHIVERS projects from Wyeth and Novavax and GlaxoSmithKline and Paul Thomas receives funding from Genentech and GlaxoSmithKline.