

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
<input type="checkbox"/>	<input checked="" type="checkbox"/> The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
<input type="checkbox"/>	<input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
<input type="checkbox"/>	<input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
<input checked="" type="checkbox"/>	<input type="checkbox"/> A description of all covariates tested
<input checked="" type="checkbox"/>	<input type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
<input type="checkbox"/>	<input checked="" type="checkbox"/> A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
<input type="checkbox"/>	<input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
<input type="checkbox"/>	<input checked="" type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
<input checked="" type="checkbox"/>	<input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
<input checked="" type="checkbox"/>	<input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	No software was used to collect the data.
Data analysis	Analyses were conducted in R Studio Version 2024.12.1+563 (2024.12.1+563). Code used to conduct analysis and generate manuscript figures is publicly available at https://github.com/sbents/serology_SA_KC .

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The King County serological data used in this study have been deposited at https://github.com/sbents/serology_SA_KC. The King County RHINO surveillance data are available under restricted access for privacy laws, and access can be obtained by request through Dr. Kacey Potis at kacey.potis@doh.nih.gov. The serological

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	Age
Recruitment	King County study participants were sampled from residual samples and existing clinical data from Seattle Children's Hospital. Recruitment for South Africa data involved recruiting households until a sample size of 110 households was reached. In the rural setting, households were selected from the HDSS, and in the urban site households were selected randomly using global positioning system coordinates. More information can be found here: 10.1016/S2214-109X(21)00141-8. No known biases in the data were reported.
Ethics oversight	The King County sample collection and this study were approved by the Institutional Review Board of Seattle Children's Hospital. This study was granted a waiver of consent since it used residual clinical samples and existing clinical data (attached in submission). Authors did not have access to identifiable information. The South Africa PHIRST protocol was approved by the University of the Witwatersrand Human Research Ethics Committee (Reference 150808) and the US CDC's Institutional Review Board relied on the local review (#6840). The protocol was registered on http://clinicaltrials.gov in 2015 (Reference NCT02519803) and participants provided individual written consent or assent prior to enrollment. The authors did not have access to identifiable information.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample size calculations were not conducted as these analyses focused on secondary data. The King County serology sampled from 1,508 individuals and the South Africa serological data sampled from 1,028 individuals. Including analysis from two serological datasets allowed us to assess whether our findings were robust in two different populations with varying level of vaccination uptake and in pandemic vs non-pandemic contexts. In addition to these two large serological surveys, representative age-specific flu hospitalization data from King County was utilized. This provided an observed hospitalization dataset to relate influenza-specific serological findings to.
Data exclusions	Data were not excluded.
Replication	Authors could not replicate the findings of the experimental results as only secondary data analysis was conducted.
Randomization	Randomization is not relevant to this study as it is focused on age-specific immunological dynamics and there is no treatment group of interest.
Blinding	Blinding is not relevant to this study as it is focused on age-specific immunological dynamics and there is no treatment for blinding to occur.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	<p>South Africa serology: Antibody levels were measured using hemagglutinin inhibition assays against influenza strains: A/South Africa/2517/2016 EPI_ISL_230453, A/Singapore/INFIMH-16-0019/2016 EPI_ISL_225834, B/South Africa/R3037/2016 EPI_ISL_231726, and B/South Africa/R5631/17 EPI_ISL_17008503.</p> <p>King County serology: Meso Scale Discovery (MSD) electrochemiluminescence immunoassay and laboratory analysis was performed at the Fred Hutchinson Cancer Center. We used the V-PLEX COVID-19 Respiratory Panel 3 IgG Kit to analyze antibody concentration in arbitrary units [AU] per milliliter against Flu A/Hong Kong/2014 H3, Flu A/Michigan/2015 H1, Flu A/Shanghai/2013 H7, Flu B/Brisbane/2008 HA, Flu B/Phuket/2013 HA, HCoV-229E Spike, HCoV-HKU1 Spike, HCoV-NL63 Spike, HCoV-OC43 Spike, MERS-CoV Spike, RSV Pre-Fusion F, SARS-CoV-1 Spike, SARS-CoV-2 N, SARS-CoV-2 S1 RBD, and SARS-CoV-2 Spike antigens (SARS-CoV-2 based on ancestral strain).</p>
Validation	<p>Validation information for the V-PLEX COVID-19 Respiratory Panel 3 IgG Kit can be found at: https://www.mesoscale.com/products/v-plex-covid-19-respiratory-panel-3-igg-kit-5-pl-k15403u/. Hemagglutination inhibition (HAI) assays using turkey red blood cells were performed to determine serological reactivity titres for serum samples against influenza. More information can be found at: 10.1111/irv.12881 and https://iris.who.int/bitstream/handle/10665/44518/9789241548090_eng.pdf.</p>

Plants

Seed stocks	<i>Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.</i>
Novel plant genotypes	<i>Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.</i>
Authentication	<i>Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.</i>