Seroprevalence of SARS-CoV-2-specific antibodies among Australian blood donors, February–March 2022

The Australian COVID-19 Serosurveillance Network

Final report, 3 June 2022

Why did we do the survey?

- Routine surveillance based on reporting diagnosed cases provides an incomplete picture of SARS-CoV-2 infection in populations because of under-detection and under-reporting of cases. Estimation of the proportion of the population with SARS-CoV-2 antibodies (i.e., seroprevalence) can improve understanding of the cumulative population-level incidence of infection.

How did we do the survey?

- We used 5,185 de-identified Australian blood donor residual specimens to examine SARS-CoV-2 antibody prevalence approximately 6 weeks after the peak of the Omicron epidemic wave in January.
- Specimens were from blood donations received between 23 February and 3 March 2022 across all Australian states and territories and were tested on the Roche Elecsys anti-SARS-CoV-2 anti-spike and anti-nucleocapsid protein immunoassays.
- In the Australian setting, the presence of anti-spike antibodies indicates prior natural SARS-CoV-2 infection and/or vaccination against SARS-CoV-2. The presence of anti-nucleocapsid protein antibodies indicates prior natural infection, most likely within the recent past (i.e., 3-6 months).

What did we find?

- The prevalence of anti-spike antibodies was very high (98%) across all jurisdictions, with little variation by jurisdiction, age group and sex.
- The prevalence of anti-nucleocapsid antibodies was 17% overall and was highest in Queensland (26%), followed by Victoria (23%) and NSW (21%). Seroprevalence was lowest, at 0.5%, in WA.
- Anti-nucleocapsid seroprevalence was highest among donors aged 18–29 years at 27%, declining with increasing age to 6% in donors aged 70–89 years. These national age-specific patterns were also observed within Victoria, NSW, and Queensland. Seroprevalence was similar for males and females.

What does it mean?

- Anti-spike seropositivity was modestly higher than expected based on population vaccine coverage, possibly reflecting the presence of anti-spike antibodies induced following infection in those who have not been vaccinated. It may also be that donors are more likely to be vaccinated than the general population.
- The anti-nucleocapsid seroprevalence estimates suggest that at least one in five adults in NSW, Victoria, and Queensland may have contracted SARS-CoV-2 infection during the Omicron wave. This is consistent with the epidemiology of notified cases at the corresponding time period, with NSW, Victoria, and Queensland having had the largest SARS-CoV-2 outbreaks.
- Anti-nucleocapsid antibodies are produced at lower levels and wane faster in people who acquire infection following vaccination than in those not vaccinated. This means that the sensitivity of the serology assay to detect anti-nucleocapsid antibodies is reduced in settings with high vaccine coverage, such as Australia. Therefore, estimates of infection based on detecting nucleocapsid antibodies will underestimate the true cumulative SARS-CoV-2 infection rate.

What is next?

- The next blood donor serosurvey will commence in mid-June. This time point will estimate SARS-CoV-2 antibody prevalence following the spread of the Omicron BA.2 variant, the rapid rise in notified cases in WA, and capture any further surges leading up to winter.

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1. Background

Understanding the extent to which SARS-CoV-2 infection has been transmitted through the community has been critical to informing and evaluating infection control and prevention policies. Surveillance based on diagnosed cases is influenced by several factors, including testing capacity and access, test reliability, and health-seeking behaviour of the population. Also, many people infected with SARS-CoV-2 have few or no symptoms, particularly since effective vaccines have been available and may not even consider testing[1]. However, infection leaves an "immunological signal" in the form of anti-SARS-CoV-2 antibodies, which can be detected in blood specimens. Large-scale serosurveys of SARS-CoV-2 antibody prevalence conducted in the first year of the pandemic found very low levels in Australia, even after the so-called "second wave" in Victoria in 2020[2-5]. Until the emergence of Omicron, Australia had relatively low case numbers (and good case ascertainment) due to widely available testing, extensive contact tracing and isolation protocols. However, over a two-month period following the detection of the first Omicron case, cumulative case numbers had risen from 211,637 on 1 December 2021 to over 2.1 million by the end of January[6]. Omicron put considerable strain on the testing and contact tracing systems, leading to standard laboratory testing becoming less accessible due to lengthy wait times, expanded use of self-testing via rapid antigen tests, and the abandonment of most contact tracing efforts.

The serological picture of SARS-CoV-2 was complicated with the introduction of vaccines globally from late 2020 and in Australia from February 2021. The vaccines in widespread use in Australia generate an antibody response to the spike protein of the SARS-CoV-2 virus but not to other proteins found on the virus. Hence, the presence of anti-spike antibodies indicates prior vaccination against SARS-CoV-2 infection and/or natural infection, while the presence of anti-nucleocapsid protein antibodies indicates previous natural infection, most likely within the recent past. Vaccine-induced antibodies to nucleocapsid protein will be present following the use of vaccines that utilise inactivated whole virus (e.g., Sinopharm or Sinovac vaccines produced in China)[7]. However, currently, they are likely to have been used in only a very small proportion of the Australian population.

Serosurveys are now being utilised to generate important data on population exposure to both natural infection and vaccination[8, 9]. Following initial serosurveillance activities in 2020, the Australian COVID-19 Serosurveillance Network has embarked on a program of repeat surveys of blood donors. The program aims to estimate the prevalence of antibodies to SARS-CoV-2, whether derived from vaccination or natural infection and examine variations over time using repeat cross-sectional surveys of Australian blood donors. This report describes results from the first survey in this series conducted in late February to early March, approximately 6 weeks past the peak of the Omicron wave in NSW, ACT, Queensland, and Victoria and prior to substantial transmission in Western Australia (Figure 1).

2. Methods

Samples were collected from four Lifeblood processing centres located in NSW, Victoria, Queensland, and WA from any blood donations (plasmapheresis or whole blood) following routine screening prior to discarding. Donors aged 18 years or over who met routine donor eligibility criteria, as per the Australia Red Cross Lifeblood (https://www.lifeblood.com.au/blood/eligibility), were eligible for inclusion. Data on age, sex, and residential postcode were collected for each specimen.

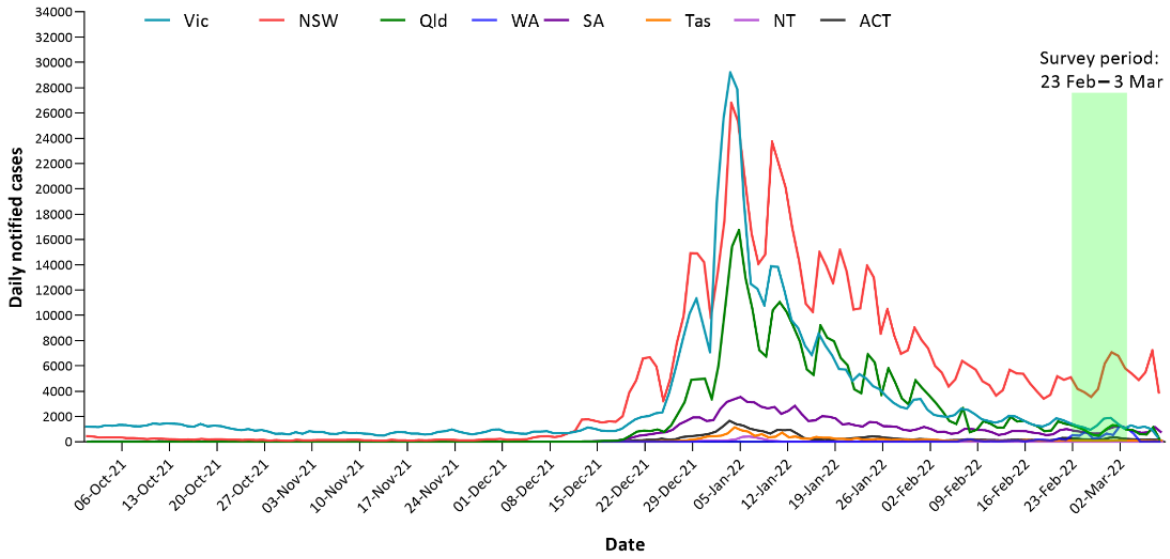
All samples were tested for the presence of antibodies to spike and nucleocapsid proteins using the Roche Elecsys Anti-SARS-CoV-2 anti-spike and anti-nucleocapsid immunoassays. These assays were selected for their high sensitivity, specificity, and throughput capacity[10, 11].

Population data were obtained from the Australian Bureau of Statistics 2021 mid-year estimated residential population (ERP), and blood donor panel statistics were obtained from Lifeblood.

Reported seroprevalence estimates and 95% confidence intervals (CIs) were based on crude seropositivity for anti-spike and anti-nucleocapsid, with 95% confidence intervals estimated by the exact binomial method. Estimates were presented stratified by age-groups, sex, and Statistical Area Level 4 (SA4). In sensitivity analyses, crude seropositivity age-standardised to the Australian ERP was also calculated by jurisdiction.

Ethics approvals were granted by the Sydney Children's Hospital Network Human Research Ethics Committee ([SCHN HREC] HREC 2022/ETH00187), Lifeblood Ethics Committee (2022#07) and UNSW HREC (2022/ETH00187).

Figure 1. Count of daily SARS-CoV-2 case notifications among adults aged 18–89 years by jurisdiction and timing of specimen collection*



*NT data to 10 Jan 2022 only

3. Results

3.1. Characteristics of the survey population

Results were available for 5,185 specimens collected, including 1,099 in Victoria, 1,155 in NSW, 1,135 in Queensland, 999 in WA, 205 in SA, 216 in Tasmania, 199 in NT, and 177 in ACT. The median age of donors whose specimens were included in the survey was 45 (interquartile range 31–58; range 18–83), and 58.2% were male (Supplementary Figure S1). A broad cross-section of SA4s were represented, with metropolitan SA4s slightly overrepresented in the sample (Supplementary Figure S2-S4).

3.2. Anti-spike protein seroprevalence

Prevalence of anti-spike antibodies was very high overall (98.1% [97.7–98.5]), ranging from 96.5% (95.2–97.5) in Queensland to 100% (97.9–100.0) in ACT (Figure 2A).

Prevalence of anti-spike antibodies was very high across all age groups nationally (Figure 2B), and within Victoria, NSW, Queensland, and WA (Figure 2C). Seroprevalence was similar for males (97.9%; 97.8–98.9) and females (98.4%; 97.8–98.9) (Supplementary Table S1).

The majority (>95%) of seropositive donors had high antibody titres (i.e., >250 U/ml), with little variation by jurisdiction (Figure 3A), and age-group (Figure 3B).

Figure 2: Crude SARS-CoV-2 anti-spike protein seroprevalence among Australian blood donors, by jurisdiction (A), age-groups (B), and age-groups within Victoria, NSW, Queensland, and WA (C)

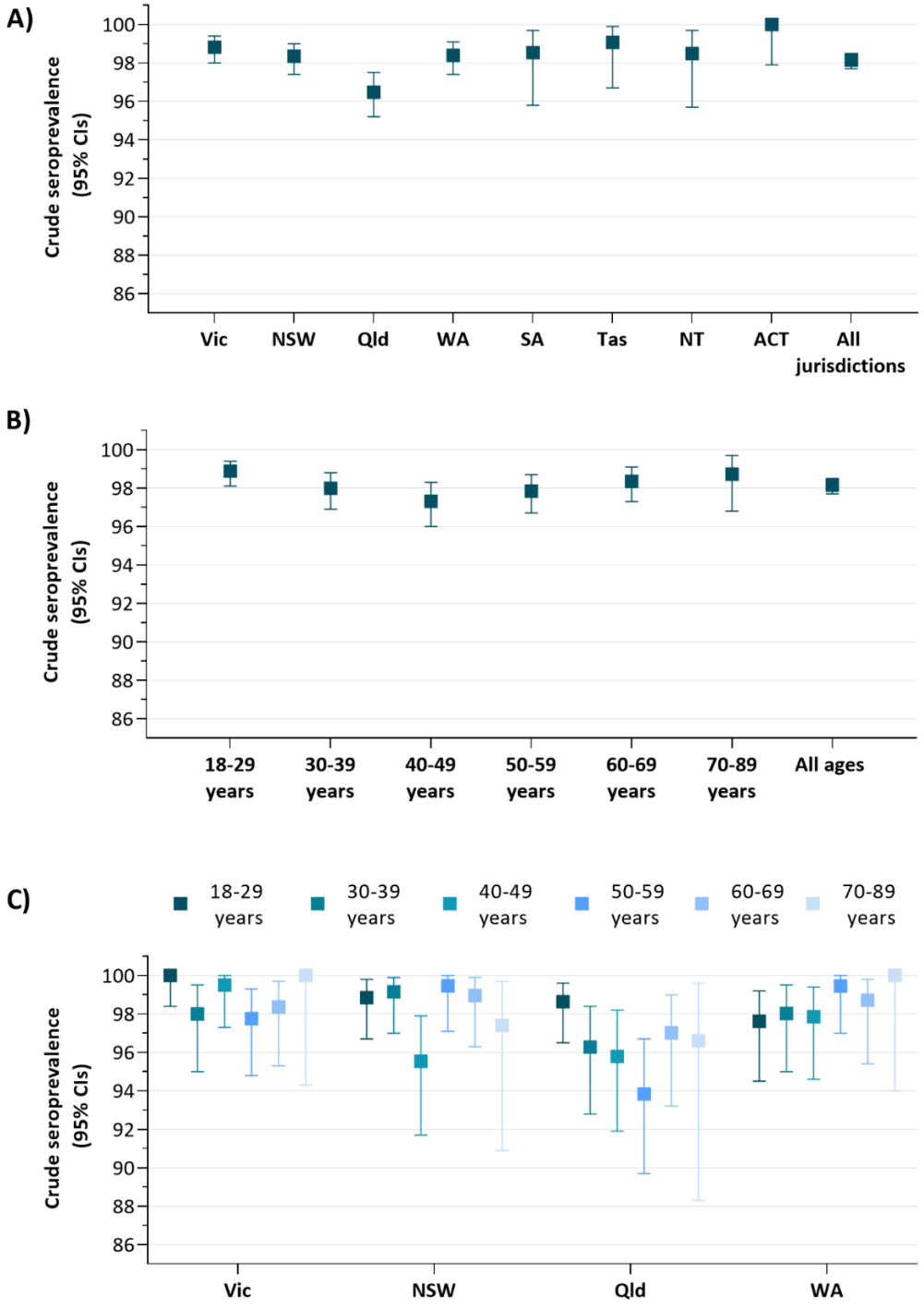
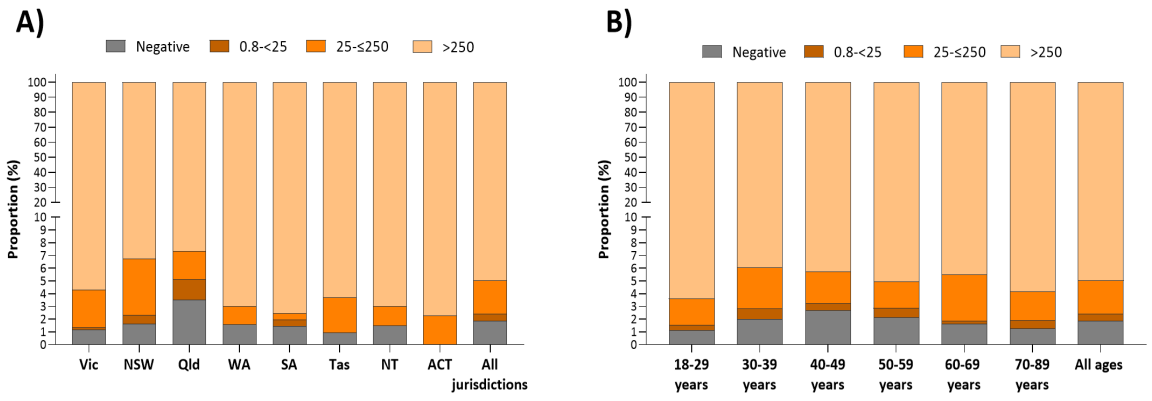


Figure 3: SARS-CoV-2 anti-spike protein antibody concentration levels among Australian blood donors, by jurisdiction (A) and age-groups (B)



3.3. Anti-nucleocapsid protein seroprevalence

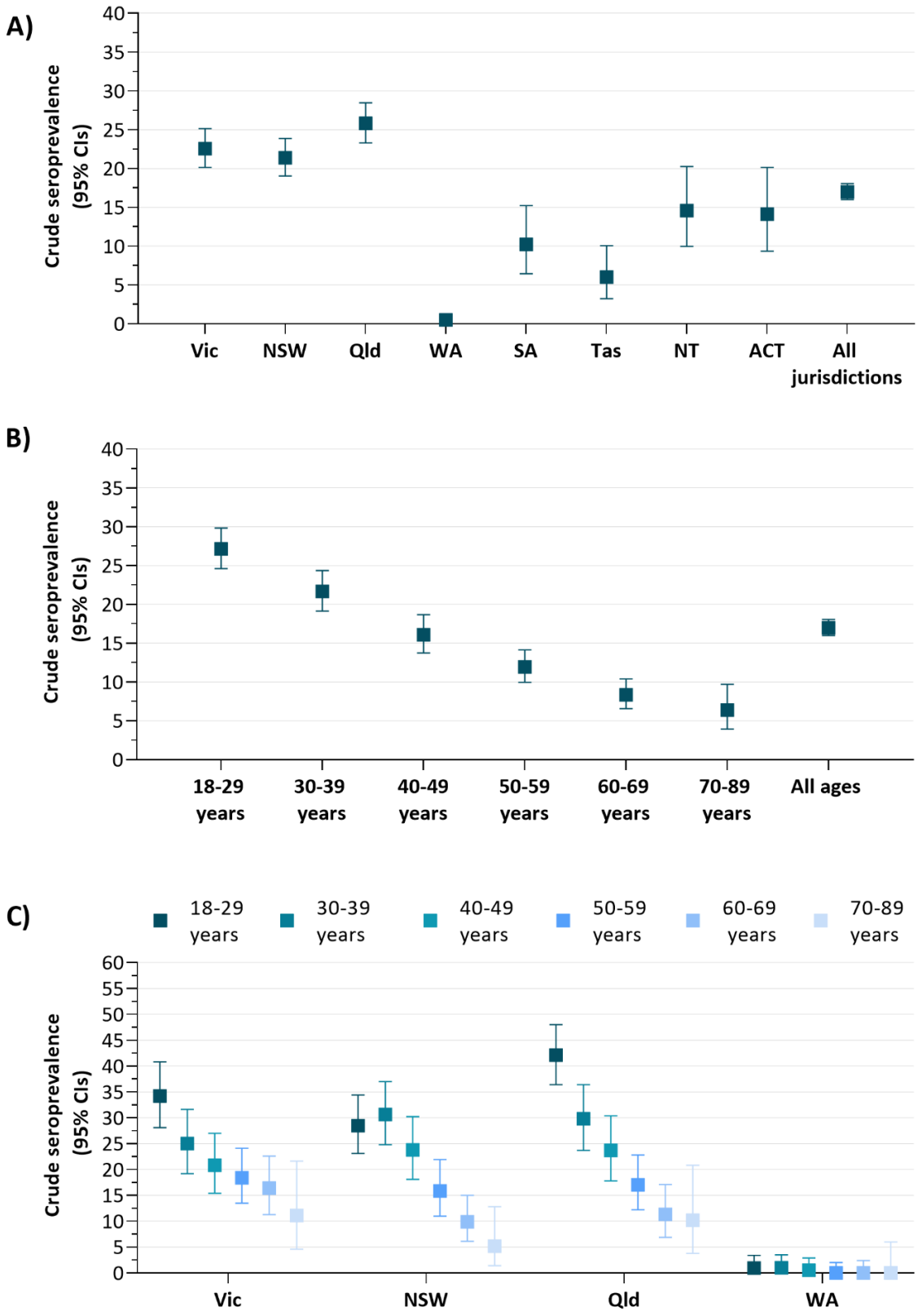
Prevalence of anti-nucleocapsid antibodies was 17.0% (16.0–18.0) overall. Seroprevalence was highest in Queensland (25.8%; 23.3–28.5), followed by Victoria (22.6%; 20.1–25.2) and NSW (21.4%; 19.1–23.9). Seroprevalence was lowest, at 0.5% (0.2–1.2) in WA (Figure 4A). No differences in seroprevalence across jurisdictions were observed following age adjustment compared with unadjusted seroprevalence (data not shown).

Anti-nucleocapsid seroprevalence was highest among donors aged 18–29 years at 27.2% (24.6–29.8), declining with increasing age to 6.4% (3.9–9.7) in donors aged 70–89 years (Figure 4B), consistent with age-specific rates of case notifications. These age-specific patterns were also observed within Victoria, NSW, and Queensland (Figure 4C). In WA, seroprevalence was extremely low across all age-groups (Figure 4C). Seroprevalence was similar for males (16.5%; 15.2–17.9) and females (17.6%; 16.0–19.3) (Supplementary Table S2).

The proportion of anti-spike seropositive samples that were negative for anti-nucleocapsid antibodies was 77.5% in Victoria, 78.3% in NSW, 73.6% in Queensland, 89.6% in SA, 93.9% in Tasmania, 85.2% in NT, 99.5% in WA, and 85.9% in ACT.

Anti-nucleocapsid seroprevalence was compared with cumulative case notifications (aged 18–89 years, as a proportion of the state/territory population of the same age) reported up to 14 days prior to the median date of collection. Seroprevalence was higher than cumulative notifications for all jurisdictions: cumulative case notifications were 10.9% in NSW, 9.8% in Vic, 7.3% in Qld, 0.1% in WA, 6.3% in SA, 3.4% in Tas, 7.5% in ACT; NT excluded as data only available to 10 January 2022.

Figure 4. Crude SARS-CoV-2 anti-nucleocapsid protein seroprevalence among Australian blood donors, by jurisdiction (A), age group (B) and age-groups within Victoria, NSW, Queensland, and WA (C)



4. Interpretation

- Seroprevalence of anti-spike antibody was very high (>98.0%) across all jurisdictions, with little variation by age group and sex. These estimates are modestly higher than what would be expected in the general population based on vaccine coverage rates[12].
- The very high prevalence of anti-spike antibodies likely reflects a combination of vaccine recipients and natural infection among the small minority of donors who had not been vaccinated. The vaccines used in Australia and natural infection with SARS-CoV-2 produce spike antibody responses indistinguishable using routinely available assays.
- Blood donors may be more highly vaccinated than the general population. It is well recognised that blood donors have a higher average income and education level and are healthier than the general population[13, 14]. These factors have been shown to impact health-seeking behaviour, including being associated with higher uptake of COVID-19 vaccination[15-17].
- The anti-nucleocapsid seroprevalence estimates suggest that at least one in five adults in NSW, Victoria, and Queensland may have contracted SARS-CoV-2 infection during the Omicron wave. This is consistent with the epidemiology of notified cases at the corresponding time period, with NSW, Victoria, and Queensland having had the largest SARS-CoV-2 outbreaks. Seroprevalence was very low in WA, which is consistent with the limited community transmission of SARS-CoV-2 in the state at the time.
- Anti-nucleocapsid seroprevalence was higher than cumulative case notifications for all jurisdictions. This was expected as routine surveillance does not capture all people infected with SARS-CoV-2 because some are asymptomatic, not diagnosed, or not reported.
- Evidence suggests that anti-nucleocapsid antibodies are produced at lower levels and wane faster in people who acquire infection following vaccination than those who have not been vaccinated[18, 19]. This means that the sensitivity of the serology assay to detect anti-nucleocapsid antibodies is reduced in settings with high vaccine coverage, and estimates of the cumulative number of recent infections based on detecting nucleocapsid antibodies will underestimate recent (e.g., past 3-6 months) cumulative SARS-CoV-2 attack rate in the population.
- Available local data shows that the sensitivity of the Roche assay to detect anti-nucleocapsid antibodies in vaccinated persons with breakthrough Omicron infections is 78%. This means that approximately 20% of infections may be missed by these seroprevalence estimates.
- In the UK and USA, crude seroprevalence estimates (i.e., without adjustment for sensitivity and specificity of the assay) have been used to track changes in infection rates over time using the Roche assay. Steady increases in anti-nucleocapsid seroprevalence have been reported, consistent with the reported trends in SARS-CoV-2 infection occurrence in these countries[8, 9, 20].
- The next round of the blood donor serosurvey will commence in mid-June 2022. This time point will provide an estimate of SARS-CoV-2 antibody prevalence following the spread of the Omicron BA.2 variant and rapid rise in notified cases in WA and capture any further surges leading up to winter.

5. Supplementary data

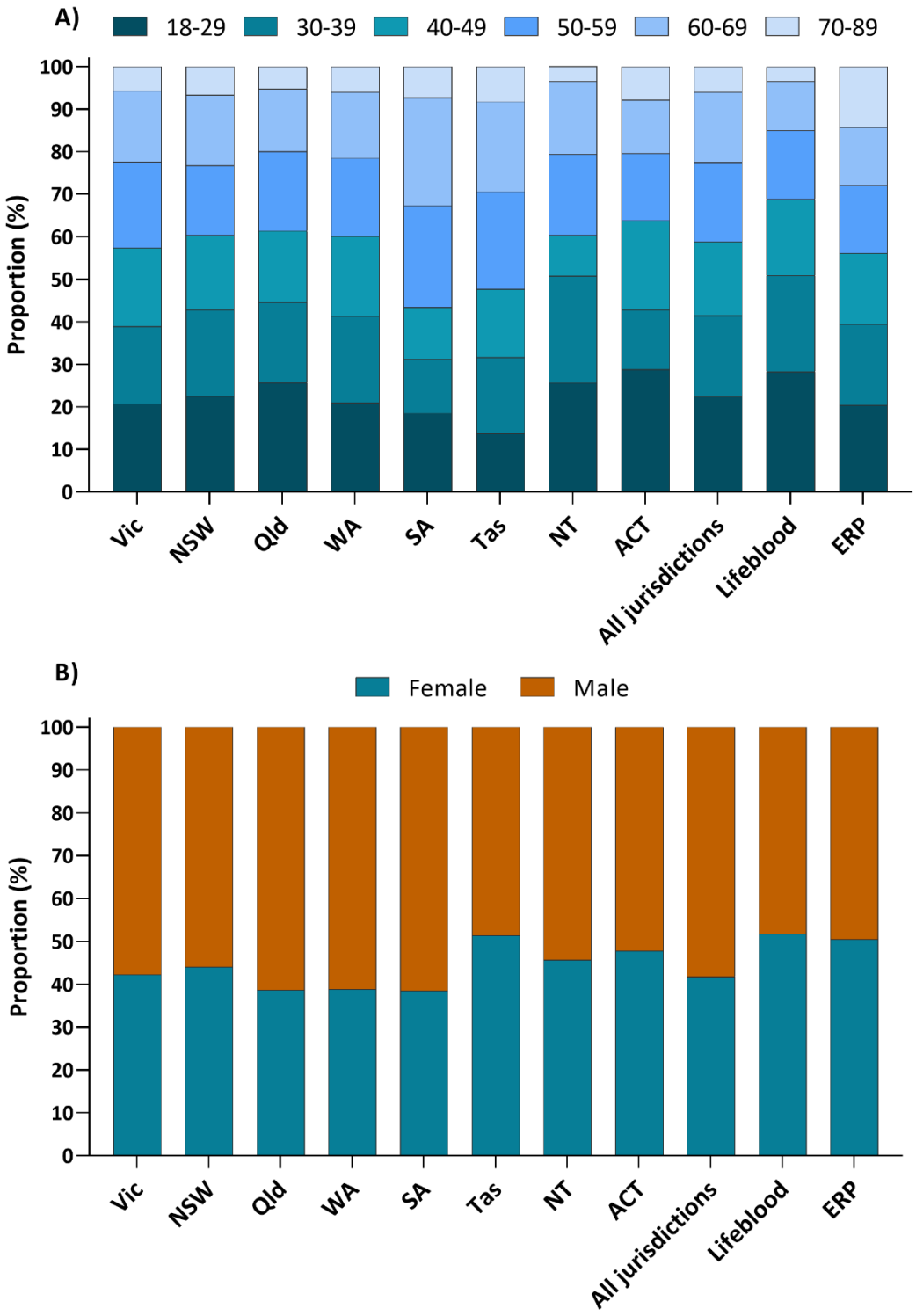
Table S1. Crude SARS-CoV-2 anti-spike protein seroprevalence among Australian blood donors by jurisdiction, age group and sex

	Overall n/N (%; 95% CI)	**Victoria** n/N (%; 95% CI)	**NSW** n/N (%; 95% CI)	**Queensland** n/N (%; 95% CI)	**WA** n/N (%; 95% CI)	**SA** n/N (%; 95% CI)	**Tasmania** n/N (%; 95% CI)	**NT** n/N (%; 95% CI)	**ACT** n/N (%; 95% CI)
Overall	5089/5185 (98.1; 97.7–98.5)	1086/1099 (98.8; 98.0–99.4)	1136/1155 (98.4; 97.4–99.0)	1095/1135 (96.5; 95.2–97.5)	983/999 (98.4; 97.4–99.1)	202/205 (98.5; 95.8–99.7)	214/216 (99.1; 96.7–99.9)	196/199 (98.5; 95.7–99.7)	177/177 (100; 97.9–100)
Age group (years)									
18–29	1147/1160 (98.9; 98.1–99.4)	228/228 (100; 98.4–100)	257/260 (98.8; 96.7–99.8)	288/292 (98.6; 96.5–99.6)	205/210 (97.6; 94.5–99.2)	37/38 (97.4; 86.2–99.9)	30/30 (100; 88.4–100)	51/51 (100; 93.0–100)	51/51 (100; 93.0–100)
30–39	973/993 (98.0; 96.9–98.8)	196/200 (98.0; 95.0–99.5)	233/235 (99.1; 97.0–99.9)	207/215 (96.3; 92.8–98.4)	199/203 (98.0; 95.0–99.5)	25/26 (96.2; 80.4–99.9)	39/39 (100; 91.0–100)	49/50 (98.0; 89.4–99.9)	25/25 (100; 86.3–100)
40–49	871/895 (97.3; 96.0–98.3)	201/202 (99.5; 97.3–100)	193/202 (95.5; 91.7–97.9)	182/190 (95.8; 91.9–98.2)	183/187 (97.9; 94.6–99.4)	25/25 (100; 86.3–100)	32/33 (97.0; 84.2–99.9)	18/19 (94.7; 74.0–99.9)	37/37 (100; 90.5–100)
50–59	951/972 (97.8; 96.7–98.7)	218/223 (97.8; 94.8–99.3)	188/189 (99.5; 97.1–100)	198/211 (93.8; 89.7–96.7)	183/184 (99.5; 97.0–100)	49/49 (100; 92.7–100)	49/50 (98.0; 89.4–99.9)	38/38 (100; 90.7–100)	28/28 (100; 87.7–100)
60–69	838/852 (98.4; 97.3–99.1)	180/183 (98.4; 95.3–99.7)	190/192 (99.0; 96.3–99.9)	163/168 (97.0; 93.2–99.0)	153/155 (98.7; 95.4–99.8)	51/52 (98.1; 89.7–100)	46/46 (100; 92.3–100)	33/34 (97.1; 84.7–99.9)	22/22 (100; 84.6–100)
70–89	309/313 (98.7; 96.8–99.7)	63/63 (100; 94.3–100)	75/77 (97.4; 90.9–99.7)	57/59 (96.6; 88.3–99.6)	60/60 (100; 94.0–100)	15/15 (100; 78.2–100)	18/18 (100; 81.5–100)	7/7 (100; 59.0–100)	14/14 (100; 76.8–100)
Sex									
Male	2955/3017 (97.9; 97.4–98.4)	625/634 (98.6; 97.3–99.3)	635/646 (98.3; 97.0–99.1)	667/696 (95.8; 94.1–97.2)	604/611 (98.9; 97.7–99.5)	123/126 (97.6; 93.2–99.5)	102/104 (98.1; 93.2–99.8)	103/104 (99.0; 94.8–100)	96/96 (100; 96.2–100)
Female	2134/2168 (98.4; 97.8–98.9)	461/465 (99.1; 97.8–99.8)	501/509 (98.4; 96.9–99.3)	428/439 (97.5; 95.6–98.7)	379/388 (97.7; 95.6–98.9)	79/79 (100; 95.4–100)	112/112 (100; 96.8–100)	93/95 (97.9; 92.6–99.7)	81/81 (100; 95.5–100)

Table S2. Crude SARS-CoV-2 anti-nucleocapsid protein seroprevalence among Australian blood donors by jurisdiction, age group and sex

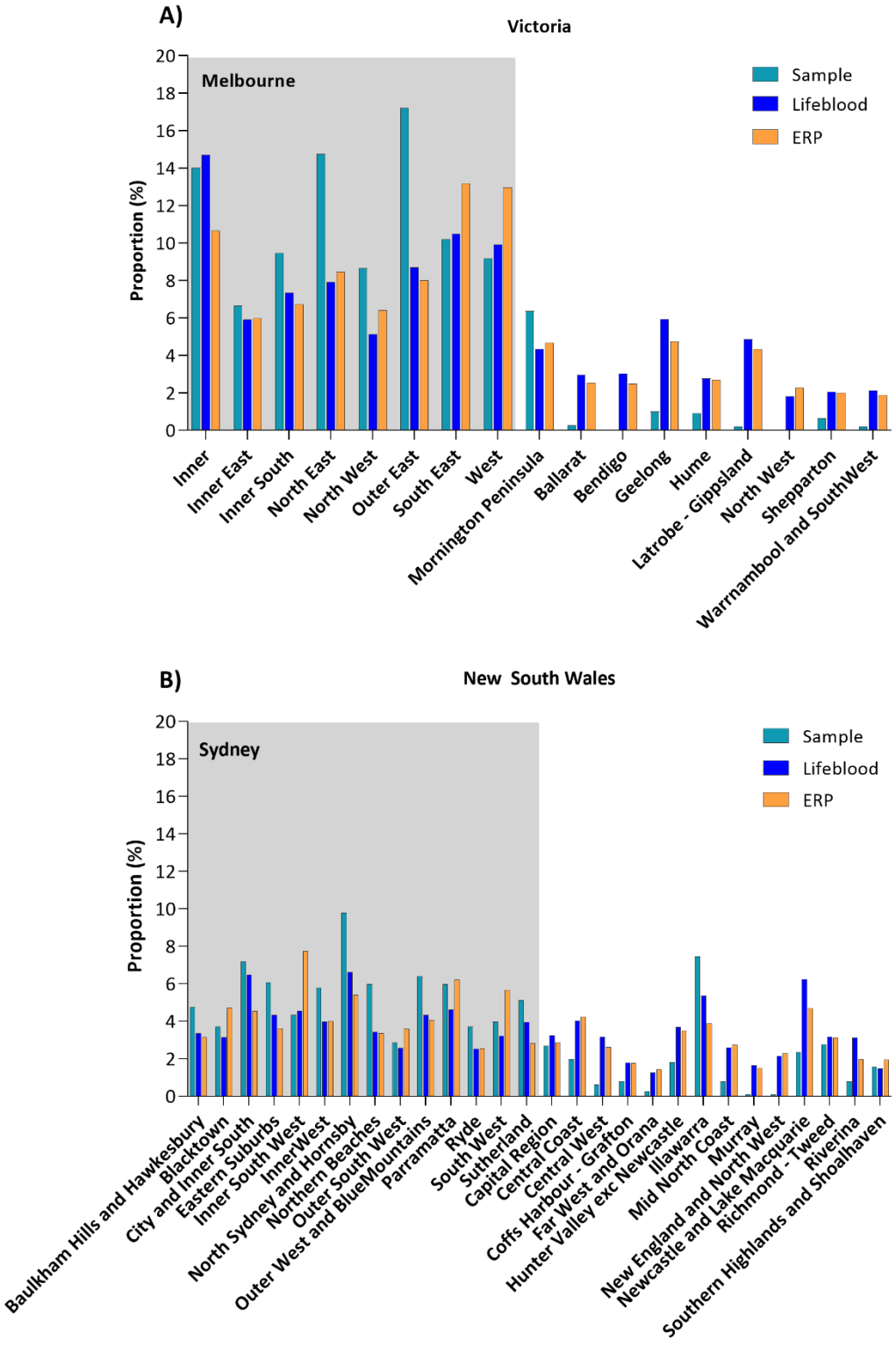
	Overall n/N (%; 95% CI)	**Victoria** n/N (%; 95% CI)	**NSW** n/N (%; 95% CI)	**Queensland** n/N (%; 95% CI)	**WA** n/N (%; 95% CI)	**SA** n/N (%; 95% CI)	**Tasmania** n/N (%; 95% CI)	**NT** n/N (%; 95% CI)	**ACT** n/N (%; 95% CI)
Overall	881/5185 (17.0; 16.0–18.0)	248/1099 (22.6; 20.1–25.2)	247/1155 (21.4; 19.1–23.9)	293/1135 (25.8; 23.3–28.5)	5/999 (0.5; 0.2–1.2)	21/205 (10.2; 6.5–15.2)	13/216 (6.0; 3.2–10.1)	29/199 (14.6; 10.0–20.3)	25/177 (14.1; 9.4–20.1)
Age group (years)									
18–29	315/1160 (27.2; 24.6–29.8)	78/228 (34.2; 28.1–40.8)	74/260 (28.5; 23.1–34.4)	123/292 (42.1; 36.4–48.0)	2/210 (1.0; 0.1–3.4)	8/38 (21.1; 9.6–37.3)	7/30 (23.3; 9.9–42.3)	11/51 (21.6; 11.3–35.3)	12/51 (23.5; 12.8–37.5)
30–39	215/993 (21.7; 19.1–24.3)	50/200 (25.0; 19.2–31.6)	72/235 (30.6; 24.8–37.0)	64/215 (29.8; 23.7–36.4)	2/203 (1.0; 0.1–3.5)	3/26 (11.5; 2.4–30.2)	3/39 (7.7; 1.6–20.9)	16/50 (32.0; 19.5–46.7)	5/25 (20.0; 6.8–40.7)
40–49	144/895 (16.1; 13.7–18.7)	42/202 (20.8; 15.4–27.0)	48/202 (23.8; 18.1–30.2)	45/190 (23.7; 17.8–30.4)	1/187 (0.5; 0–2.9)	3/25 (12.0; 2.5–31.2)	0/33 (0; 0–10.6)	0/19 (0; 0–17.6)	5/37 (13.5; 4.5–28.8)
50–59	116/972 (11.9; 10.0–14.1)	41/223 (18.4; 13.5–24.1)	30/189 (15.9; 11.0–21.9)	36/211 (17.1; 12.2–22.8)	0/184 (0; 0–2.0)	4/49 (8.2; 2.3–19.6)	2/50 (4.0; 0.5–13.7)	1/38 (2.6; 0.1–13.8)	2/28 (7.1; 0.9–22.8)
60–69	71/852 (8.3; 6.6–10.4)	30/183 (16.4; 11.3–22.6)	19/192 (9.9; 6.1–15.0)	19/168 (11.3; 6.9–17.1)	0/155 (0; 0–2.4)	1/52 (1.9; 2.3–19.6)	0/46 (0; 0–7.7)	1/34 (2.9; 0.1–15.3)	1/22 (4.5; 0.1–22.8)
70–89	20/313 (6.4; 3.9–9.7)	7/63 (11.1; 4.6–21.6)	4/77 (5.2; 1.4–12.8)	6/59 (10.2; 3.8–20.8)	0/60 (0; 0–6.0)	2/15 (13.3; 1.7–40.5)	1/18 (5.6; 0.1–27.3)	0/7 (0; 0–41.0)	0/14 (0; 0–23.2)
Sex									
Male	499/3017 (16.5; 15.2–17.9)	143/634 (22.6; 19.4–26.0)	134/646 (20.7; 17.7–24.1)	170/696 (24.4; 21.3–27.8)	4/611 (0.7; 0.2–1.7)	13/126 (10.3; 5.6–17.0)	4/104 (3.8; 1.1–9.6)	14/104 (13.5; 7.6–21.6)	17/96 (17.7; 10.7–26.8)
Female	382/2168 (17.6; 16.0–19.3)	105/465 (22.6; 18.9–26.7)	113/509 (22.2; 18.7–26.1)	123/439 (28.0; 23.9–32.5)	1/388 (0.3; 0–1.4)	8/79 (10.1; 4.5–19.0)	9/112 (8.0; 3.7–14.7)	15/95 (15.8; 9.1–24.7)	8/81 (9.9; 4.4–18.5)

Figure S1. Distribution of demographic characteristics, age group (A) and sex (B) for each jurisdiction, compared with all jurisdictions combined, the broader blood donor population[1] and Estimated Residential Population (ERP)[2]



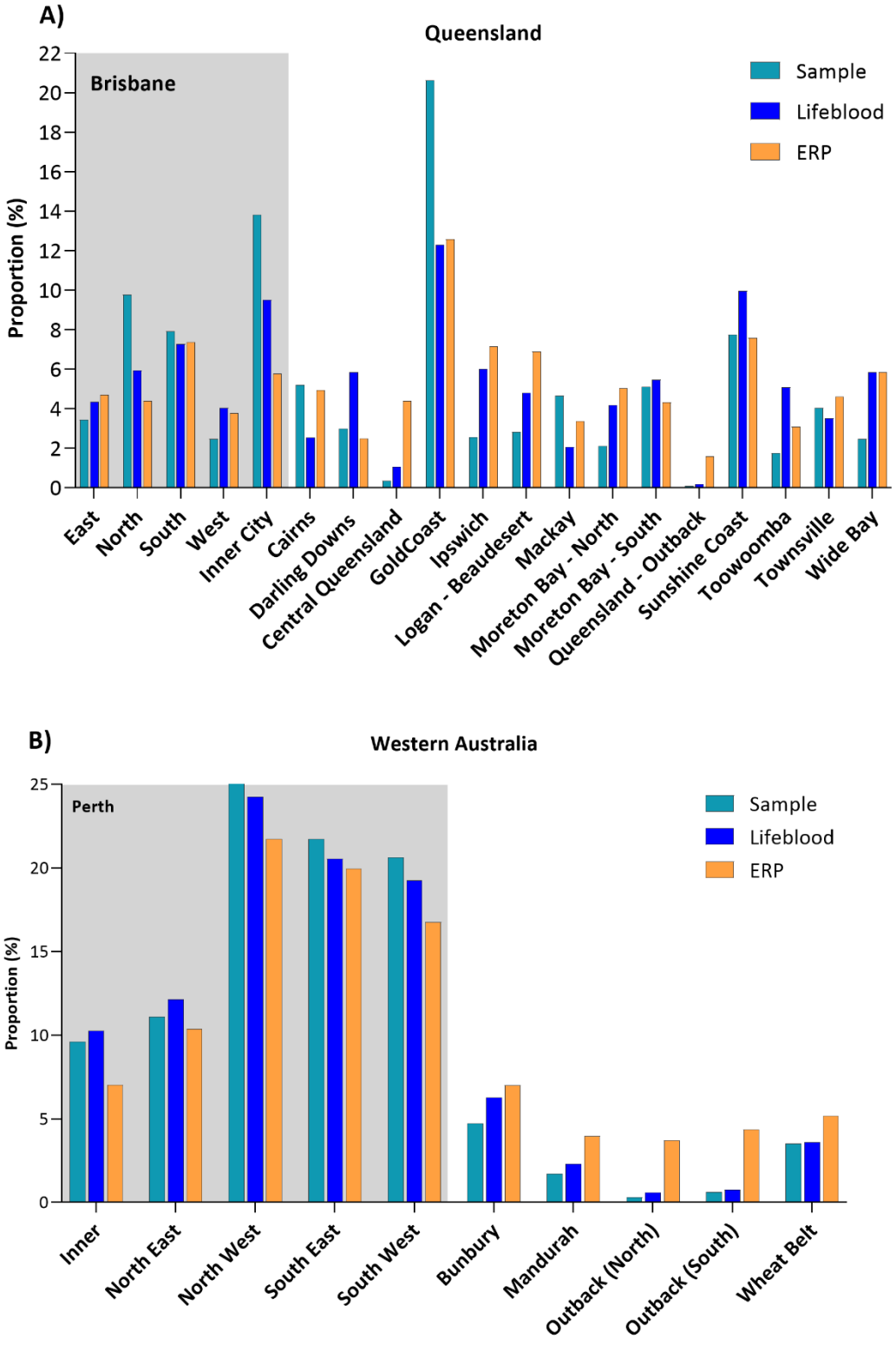
1: All persons donating blood to Australian Lifeblood between 1 January 2021–31 December 2021.
2: ABS data on the estimated residential population of persons aged 18–89 years in Australia (excluding Other Territories) as of 30 June 2021.

Figure S2. Distribution of demographic characteristics by Statistical Area Level 4 (SA4), for Victoria (A) and New South Wales (B), compared with the broader blood donor population[1] and Estimated Residential Population (ERP)[2]



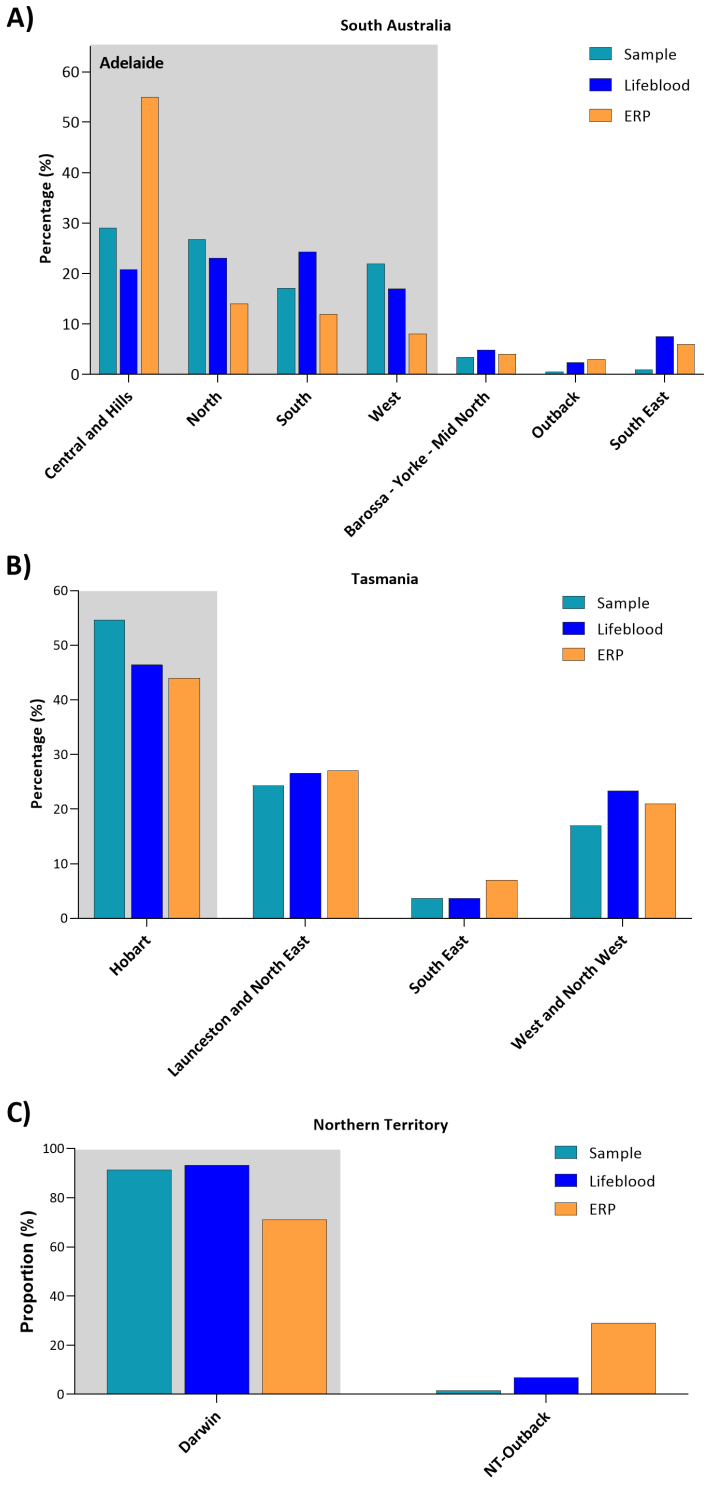
1: All persons donating blood to Australian Lifeblood between 1 January 2021–31 December 2021.
2: ABS data on the estimated residential population of persons aged 18–89 years in Australia (excluding Other Territories) as of 30 June 2021.

Figure S3. Distribution of demographic characteristics by Statistical Area Level 4 (SA4), for Queensland (A) and Western Australia (B), compared with the broader blood donor population[1] and Estimated Residential Population (ERP)[2]



1: All persons donating blood to Australian Lifeblood between 1 January 2021–31 December 2021.
2: ABS data on the estimated residential population of persons aged 18–89 years in Australia (excluding Other Territories) as of 30 June 2021.

Figure S4. Distribution of demographic characteristics by Statistical Area Level 4 (SA4), for South Australia (A), Tasmania (B) and the Northern Territory (C), compared with the broader blood donor population[1] and Estimated Residential Population (ERP)[2]



1: All persons donating blood to Australian Lifeblood between 1 January 2021–31 December 2021.
2: ABS data on the estimated residential population of persons aged 18–89 years in Australia (excluding Other Territories) as of 30 June 2021. The Australian Capital Territory is made up of a single SA4 hence not presented.

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