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Sociodemographic characteristics of SARS-CoV-2 serosurveillance studies with diverse recruitment strategies, Canada, 2020 to 2023

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Abstract

Background Serological testing was a key component of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) surveillance. Social distancing interventions, resource limitations, and the need for timely data led to serosurveillance studies using a range of recruitment strategies, which likely influenced study representativeness. Characterizing representativeness in surveillance is crucial to identify gaps in sampling coverage and to assess health inequities.

Methods We retrospectively analyzed three pre-existing longitudinal cohorts, two convenience samples using residual blood, and one de novo probabilistic survey conducted in Canada between April 2020 – November 2023. We calculated study specimen counts by age, sex, urbanicity, race/ethnicity, and neighborhood deprivation quintiles. We derived a 'representation ratio' as a simple metric to assess generalizability to a target population and various sociodemographic strata.

Results The six studies included 1,327,142 specimens. When stratifying by age group and sex, 67% of racialized minority subgroups were moderately underrepresented (representation ratio < 0.75). Representation was generally higher for older Canadians, urban neighborhoods, and neighborhoods with low material deprivation. Rural representation was highest in a study that used outpatient laboratory blood specimens. Racialized minority representation was highest in a de novo probabilistic survey cohort and an open longitudinal cohort recruited from an online polling panel.

Conclusion While no study had adequate representation of all subgroups, less traditional recruitment strategies were more representative of some population dimensions. Understanding demographic representativeness and barriers to recruitment are important considerations when designing population health surveillance studies.

Keywords Representativeness, Surveillance, COVID-19

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Introduction

Serological surveillance is a critical input to infectious disease control, including pandemic preparedness and response. In 2020, Canada launched the largest serological surveillance program in its history to monitor population immunity to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), informing COVID-19 epidemiology and antibody dynamics. Between April 2020 and February 2021, many studies began testing blood specimens for SARS-CoV-2 antibodies [1–6]. Challenged by social distancing measures, studies used diverse strategies to recruit participants or obtain blood samples. Recruitment strategy influences study population's characteristics and the extent to which participants represent the general population [7].

Serosurveillance studies can be broadly categorized as convenience samples, de novo probabilistic surveys, or pre-existing longitudinal cohorts. For SARS-CoV-2 serosurveillance, many countries used convenience samples of residual blood specimens due to low operational costs and ease of continued sample collection over time [1, 2, 8, 9]. Convenience samples may produce study populations that are unrepresentative of a target population, which may limit generalizability if traits that are unevenly represented correlate with seropositivity [1, 8, 10]. Probabilistic serosurveys, also deployed in many regions to monitor SARS-CoV-2, aim to improve generalizability using stratified, weight-based approaches to recruitment. De novo designs allow tailoring recruitment to study objectives [4, 5, 11–13]. However, probabilistic designs are time- and resource-intensive and are sometimes limited by low response rates [6, 14]. Sampling within pre-existing longitudinal cohorts can improve efficiency by leveraging an established sampling frame and study infrastructure. But this precludes tailoring the sampling frame to the current research question, and generalizability may be limited by inclusion criteria or attrition. Population estimates can be partially corrected to account for sample unrepresentativeness through post-hoc adjustments, for variables measured in the study population whose distribution (marginal or joint, depending on the method) is reliably estimated in the target population (e.g., by Census). Methods include post-stratification, iterative proportional fitting (raking), and regression with post-stratification [15]. Multilevel regression with post-stratification, when a multilevel regression model is fit using sociodemographic and/or geographic predictor variables and post-stratification weights are applied to the regression-based estimate for each strata, has been shown to perform better than traditional survey weighting approaches when modeling survey data with a non-negligible amount of participant non-response [16].

Multiple metrics have been developed to characterize the representativeness of a population. The average absolute relative bias (AARB) computes the difference in the proportion of a sample and the population of inference (often, estimated using Census counts) belonging to a variable category (e.g., female sex) and averages the absolute relative biases across all variable categories to generate a single numeric measure of representativeness [17]. Similarly, the Duncan dissimilarity index estimates the degree of separation, with respect to a categorical variable, between two populations as a sum of differences in proportions belonging to each variable level [18]. The representativeness indicator (R-indicator) compares participants to a sampling frame to assess non-response bias by quantifying the degree to which response probabilities vary across subgroups [19].

In this study, we introduce a simple metric for diagnosing the representativeness of subgroups within a study population. Using this metric, we evaluated the sociodemographic representativeness of six SARS-CoV-2 serosurveillance studies with diverse recruitment strategies by age, sex, race/ethnicity, urbanicity, and neighborhood measures of socioeconomic deprivation. Our findings can inform serosurveillance study design for diverse pathogens.

Methods

Data

We assessed representativeness by analyzing demographic data from six Canadian study populations (Table 1). Here, we define a study to be representative if the sociodemographic composition of the study population matched the Census-based target population; we make no assumptions of the sampling mechanism or inferential validity. This similarity suggests the interpretation of an effect measure may be generalizable to the target population, but does not assume the effect estimate, within an uncertainty interval, will be identical between the study and target populations [20]. The six studies included one de novo cross-sectional probabilistic sample (the Canadian COVID-19 Antibody and Health Survey 1 [CCAHS-1]), one open longitudinal cohort recruited from a marketing research panel (Action to Beat Coronavirus study antibody cohort [Ab-C]), two pre-existing closed longitudinal cohorts (the Canadian Longitudinal Study on Aging COVID-19 Antibody Study [CLSA], the Canadian Partnership for Tomorrow's Health COVID-19 Antibody Study [CanPath]), and two serial cross-sectional convenience samples that used residual blood from blood donations (Canadian Blood Services [CBS]) and specimens collected for outpatient laboratory testing (Alberta Precision Laboratories [APL]). Specimen collection in the cohort studies occurred over one (CCAHS-1, CLSA) or multiple (Ab-C, CanPath) sampling phases, while both convenience samples tested specimens at either monthly or bimonthly intervals (CBS, APL). The

Table 1 Summary of SARS-CoV-2 serological study designs included in the study

Study	Design	Age	Region	Specimen type	Study time and size	De novo recruitment
Action to Beat Coronavirus (Ab-C)	Pre-existing longitudinal open research cohort	≥ 18	AB, BC, MB, NB, NL, NS, ON, PE, QC, SK, YT[a]	Dried blood spot	27,140 specimens from 10,621 participants May 2020 - April 2022	No
Alberta Precision Laboratories (APL)	Serial cross-sectional convenience sample	≥ 0	AB	Heparinized plasma Plasma Serum	210,906 specimens from 187,888 participants April 2020 - October 2022	No
Canadian Blood Services (CBS)	Serial cross-sectional random sample	≥ 18	AB, BC, MB, NB, NL, NS, ON, PE, SK	Serum	1,035,580 specimens from 446,187 participants May 2020 - November 2023	No
Canadian Covid-19 Antibody and Health Survey 1 (CCAHS-1)	Prospective cross-sectional cohort with direct (ages 1–24) or multi-stage (ages ≥ 25) sampling	≥ 1	AB, BC, MB, NB, NL, NT, NS, NU, ON, PE, QC, SK, YT	Dried blood spot	11,050 specimens from 11,050 participants November 2020 - April 2021	Yes
Canadian Longitudinal Study on Aging (CLSA)[b]	Pre-existing longitudinal closed research cohort	≥ 51	AB, BC, MB, NB, NL, NS, ON, PE, QC, SK	Dried blood spot Plasma	17,310 specimens from 17,310 participants October 2020 - August 2021	No
Canadian Partnership for Tomorrow's Health (CanPath)[c]	Pre-existing longitudinal closed research cohort	≥ 25	AB, BC, MB, NB, NL, NS, ON, PE, QC	Dried blood spot	25,156 specimens from 25,153 participants September 2020 - November 2021	No

Notes: [a]Five specimens were collected from Yukon territory and were excluded from all analyses. [b]Composed of comprehensive sub-cohort and tracking sub-cohort that recruited participants from seven and 10 provinces, respectively. [c]Composed of six distinct regional cohorts. AB: Alberta; BC: British Columbia; MB: Manitoba; NB: New Brunswick; NL: Newfoundland and Labrador; NT: Northwest Territories; NS: Nova Scotia; NU: Nunavut; ON: Ontario; PE: Prince Edward Island; QC: Quebec; SK: Saskatchewan; YT: Yukon

included studies tested specimens collected from April 2020 to November 2023 with sample sizes ranging from 11,050 (CCAHS-1) to 1,039,298 (CBS). Inclusion criteria and enrollment procedures have been described previously [1, 2, 6, 13, 21, 22]. This study was reported using the STrengthening the Reporting of OBservational studies in Epidemiology checklist for cross-sectional studies (see Supplementary Material 1) [23].

From each dataset, we extracted participants' age, sex, postal code, date of specimen collection, and self-reported race/ethnicity. We used postal code to classify participants' residence as urban or rural and to assign participants' neighborhood to a quintile of the Pampalon material and social deprivation indices [24]. Material deprivation is a composite measure of education, employment, and income reflecting access to essential material resources. Social deprivation is a composite measure of living alone, single-parent families, and people who are either separated, divorced, and/or widowed, reflecting the fragility of social networks. Both measures are derived from the 2016 Canadian Census [25]. We used the date of specimen collection as the sample date when available (CBS, APL); otherwise, we used the date of questionnaire completion (CanPath, CCAHS-1, CLSA) or specimen receipt (Ab-C).

Race/ethnicity information was unavailable for the APL study. Deprivation indices were available for the CBS, APL, CCAHS-1, and CLSA studies. Specimen counts for the CCAHS-1 study were rounded to base 2000 in accordance with data usage guidelines. Age was calculated as the age at specimen collection (Ab-C, APL, CBS) or questionnaire completion (CanPath, CLSA, CCAHS-1) and categorized as 0–17 years, 18–26 years, 27–36 years, 37–46 years, 47–56 years, or 57 years and older. For Ab-C specimens collected between December 2020 – April 2021 and July 2021 – September 2021, we used the 2019 baseline age since the age at current collection could not be calculated. We categorized sex as male or female and excluded participants who provided alternative responses ($n = 147$ [Ab-C]) from analyses involving participant sex. Because race/ethnicity data collection varied between studies and differed from Census categorization, we re-classified participants as 'white' and 'racialized minority' and did not analyze specific racialized minority groups (see Supplementary Tables S1-S2, Supplementary Material 2). For studies allowing multiple encounters with participants, we imputed missing variables when available for another encounter (CBS, APL, Ab-C, CLSA). We assumed CanPath participants missing province of residence data resided in the province of their regional cohort, but assessed the implications of this assumption in sensitivity analysis. We classified participants who identified as both white and a racialized minority as a racialized minority, and we considered Indigenous identities as a racialized minority but conducted sensitivity analyses with different classifications. Because only CCAHS-1 collected specimens from the capital cities of the Canadian territories, we restricted

our primary analysis to specimens collected from Canadian provinces but assessed territorial representativeness for CCAHS-1 separately. We excluded participants who did not meet the inclusion criteria of their respective study and who were missing province/territory of residence or serology test result data. In sensitivity analysis, we assessed representativeness for all Ab-C and CLSA questionnaire respondents, including those missing serology. For the CBS study, we did not assess the representativeness of the 0-17-year-old age group because there were no donors younger than 17. We calculated specimen counts using complete cases within each set of demographic strata (e.g., participants missing race/ethnicity were excluded when stratifying by age, sex, and race/ethnicity but not when stratifying by age, sex, and urbanicity).

Representation ratio analysis

To assess the representativeness of subgroups defined by one or more sociodemographic variable, we derived a *representation ratio* by dividing the proportion of study specimens in a sociodemographic subgroup by the proportion of participants in the subgroup from a target population. A representation ratio less than one indicates the group is underrepresented relative to the target population, and a ratio greater than one indicates overrepresentation. We defined the target subgroup distribution using weighted 2016 Canadian Census counts [25], rounding values to the nearest multiple of five. We restricted Census counts by age and province/territory to match studies' inclusion criteria (e.g., population counts from the province of Alberta were used to assess APL study representativeness). We calculated representation ratios on unweighted study populations to assess the unadjusted sociodemographic composition of each study except for CCAHS-1, due to guidelines restricting unweighted analyses [6]. We also computed the AARB [17] and Duncan dissimilarity index [18] of each study as compared to Census data (see Supplementary Methods, Supplementary Material 2). For the target distributions, race/ethnicity counts were derived using the Census population group variable and Indigenous-identifying respondents were classified as racialized minorities [25]. Indigenous-identifying Census respondents were classified as racialized minorities, but were excluded when generating ratios for CLSA and CanPath since Indigenous status was unavailable for most participants. We assessed the impact of excluding Indigenous-identifying Census respondents in a sensitivity analysis. We performed bootstrapping ($n = 5000$) to generate an uncertainty distribution for each representation ratio.

Sample count by strata analysis

In some cases, statistical adjustment or subsampling may allow derivation of representative population statistics from unbalanced study populations if there are sufficient samples from less represented strata [26]. The minimum number of observations per cell to produce reliable adjustment depends on many factors including the estimand, extent to which traits correlate with the estimand, target level of precision, and adjustment method. To inform whether adjustment might be feasible in our study populations, we assessed the number of strata with counts greater than 25 when grouped by age, sex, province of residence, urbanicity, race/ethnicity, and date of specimen collection binned into two-month intervals. All analyses were conducted in R version 4.3.1 [27].

Results

Study population

During data pre-processing, we excluded 64 observations for Ab-C (0.2%), 3,718 for CBS (0.4%), 3,870 for APL (1.8%), 822 for CanPath (3.16%), and 2,024 for CLSA (10.5%) due to missing data or failure to meet inclusion criteria. We analyzed the remaining 1,035,580 (CBS), 210,906 (APL), 27,140 (Ab-C), 25,156 (CanPath), 17,310 (CLSA), and 11,050 (CCAHS-1) observations (see Supplementary Table S3, Supplementary Material 2). For Ab-C, CLSA, and CanPath, the minimum age of participants included in our analysis (Table 1) was older than the minimum age specified in their inclusion criteria [13, 21, 22]. Across studies, the largest number of observations were in the 57 and older age group (34.4% [CCAHS-1] – 91.4% [CLSA]). Observations for the 18-26-year-old age group were generally low (0.0% [CanPath] – 5.6% [APL]) but were higher for CBS (10.6%) and CCAHS-1 (11.8%). Among studies for which neighborhood deprivation was available, specimen counts across social deprivation quintile were balanced, but only 8.3% (CBS), 8.4% (APL), 9.6% (CLSA), and 13.1% (CCAHS-1) of specimens were provided from the most materially deprived quintile of neighborhoods. Most studies skewed white (78.3% [Ab-C] – 94.7% [CLSA]) and female (52.3% [CLSA] – 64.8% [CanPath]), except CBS which skewed white (79.5%) and male (58.2%). Rural specimens accounted for 7.4% (CanPath) – 17.6% (CCAHS-1) of all specimens across studies. Convenience samples collected substantially more specimens for each demographic strata compared to other recruitment strategies (see Supplementary Figures S1-S4, Supplementary Material 2).

Average absolute relative bias analysis

There was moderate variability in the overall AARB between studies (Table 2). Study AARBs ranged from 18.19% (Ab-C open cohort) to 51.75% (CanPath closed cohort). Between closed longitudinal cohort studies, the

Table 2 Average absolute relative bias in SARS-CoV-2 serology studies

CBS	APL	CLSA	CanPath	Ab-C
20.23	31.22	29.76	51.75	18.19

estimated AARB of CanPath (51.75%) was notably larger than CLSA (29.76%). When plotting the AARB over time, there was at least one substantial increase in bias between consecutive months for each study (Fig. 1). Peaks tended to occur when monthly sample size was relatively low compared to other sampling months. Omitting months with disproportionately low sample sizes, the AARBs of both convenience samples remained fairly constant over time. AARB of the CanPath closed cohort increased moderately between November 2020 – June 2021, but dropped substantially in the following months. Monthly AARB was the most variable during the first Ab-C sampling wave (March 2020 – September 2020) compared to later months.

Representation ratio analysis

Studies had reasonable representation across sexes (representation ratio 0.7–1.3; Fig. 2) and, when available, by social deprivation (see Supplementary Figure S5, Supplementary Material 2). In all studies, racialized minority subgroups were underrepresented (representation ratio < 0.75) for some age and sex strata (Fig. 3). Racialized minority representation, while still low, was often better in older age groups (Ab-C, CanPath, and CLSA), but was better for younger age groups among women for CBS. Urban regions generally produced larger representation ratios by age and sex strata than rural regions in all studies (Figs. 2 and 3). While APL had reasonable representation of all material deprivation quintiles and rural residents (representation ratio 0.8–1.3), the CBS population skewed towards less materially deprived neighborhoods and urban regions (though male rural representation for CBS was higher than the three longitudinal cohort studies). 18-26-year-old males were underrepresented across most sex and urbanicity strata in all studies for which they were eligible to be sampled.

Among 18-46-year-olds, specimens from the Ab-C open cohort produced larger representation ratios across sex and urbanicity strata compared to CanPath (Fig. 3). Representation ratios of 18-46-year-old rural residents were generally larger across age and sex strata in CCAHS-1 than several studies with probabilistic recruitment strategies (Ab-C, CanPath). Of the two convenience samples, the CBS study was more representative of participants aged 18–46 across sex and urbanicity strata, whereas the APL study was more representative of individuals aged 47 and older. In CCAHS-1, the only study that sampled in the three Canadian territories, 0-17-year-olds were underrepresented across sexes in territorial specimens (see Supplementary Figure S6, Supplementary Material 2). Bootstrapping revealed low uncertainty in whether a representation ratio was greater or less than one for most subgroups (see Supplementary Figures S7-S13, Supplementary Material 2). Groups with representation ratios far from one tended to have high Duncan dissimilarity indices (see Supplementary Figure S14, Supplementary Material 2). Calculating representation ratios for Ab-C and CLSA participants who completed the questionnaire but did not provide a sample for serology, representativeness improved for several strata of middle-aged men among rural residents and racialized minorities in the Ab-C questionnaire cohort (see Supplementary Figure S15, Supplementary Material 2). This indicates that among those completing the questionnaire, women were more likely to also provide a sample for serological testing. Reclassifying mixed race/ethnicity participants as white had little impact except for the Ab-C cohort, for which 55% of racialized minorities were reclassified as white, leading to lower representation ratios (see

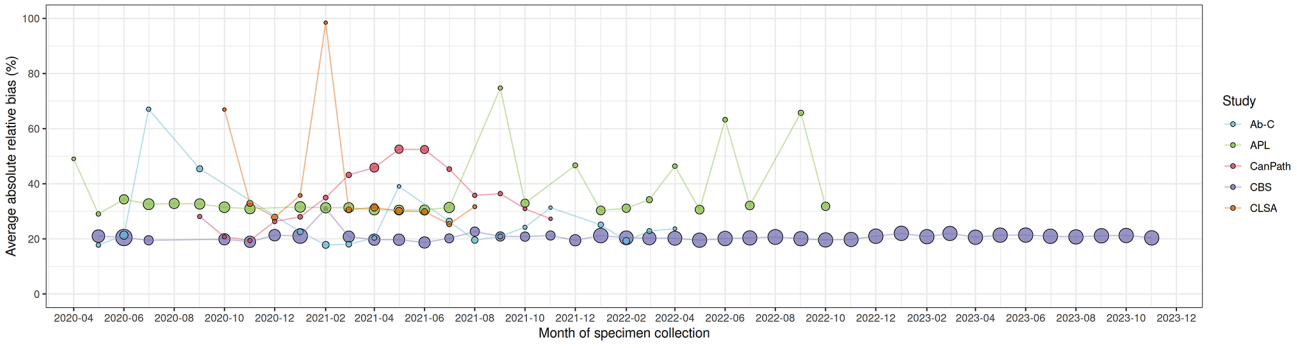

Fig. 1 Average absolute relative bias (AARB) in SARS-CoV-2 serology studies. AARB was calculated as the average absolute relative difference between proportion of monthly sample and Census-based population [25] belonging to a variable level across age group, sex, race/ethnicity, urbanicity, and neighborhood deprivation quintile (when available). Specimens with missing month of sample collection ($n = 1$ [0.0%, Ab-C], $n = 556$ [2.6%, CanPath]) were excluded from the analysis. Data point size is proportional to monthly sample size. AARB was not calculated for CCAHS-1 due to restricted data availability

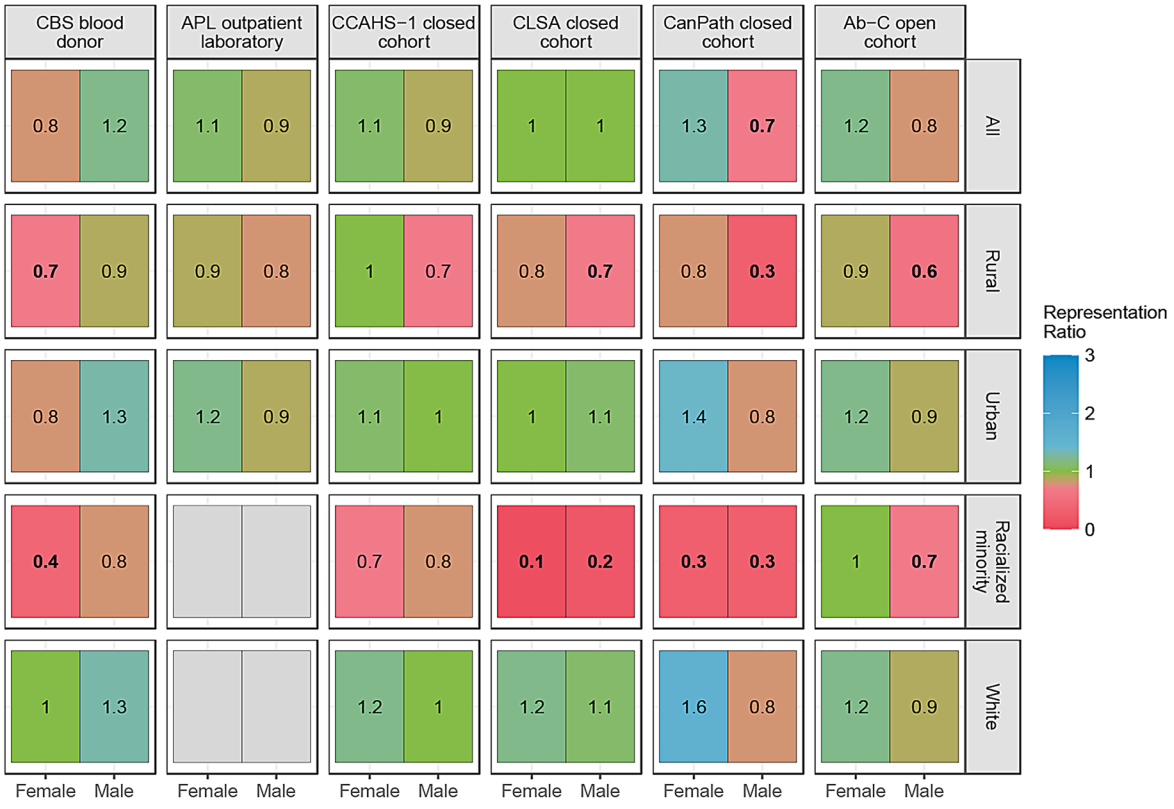

Fig. 2 SARS-CoV-2 serological study representativeness by sex, urbanicity, and racial/ethnic identity. Representativeness was calculated by dividing the proportion of study specimens collected from a subgroup by the proportion of general population in the subgroup. Total population counts were estimated using the 2016 Canadian Census [25]. Bolded representation ratios indicate greater than 95% of subgroup bootstrap replicates produced representation ratios below 0.75. Bootstrapping was not performed for studies with weighted counts (CCAHS-1)

Supplementary Figures S16-S17, Supplementary Material 2). Including Indigenous-identifying individuals as racialized minorities in the representation ratio denominator for studies for which data were unavailable (CLSA and CanPath) had little impact on findings (see Supplementary Figure S18, Supplementary Material 2). A sensitivity analysis revealed representation ratios were nearly identical between the CanPath cohort with imputed province versus a dataset where participants with missing province were excluded.

Sample count analysis

The convenience samples with large overall sample size produced substantially more cells with counts greater than 25 across 4 levels of stratification compared to all other study designs in the primary analysis (Table 3) and sensitivity analysis (see Supplementary Table S4, Supplementary Material 2). Pre-existing closed probabilistic cohorts (CLSA, CanPath) produced a greater proportion of cells with counts greater than 25 than other probabilistic recruitment strategies (Ab-C, CCAHS-1) for all strata.

Discussion

In this study, we developed a simple method for characterizing study population representativeness and applied it to describe the variability in sociodemographic representativeness across six SARS-CoV-2 serosurveillance studies with diverse recruitment strategies. No study was adequately representative of all sociodemographic subgroups.

Representation ratios are a flexible diagnostic measure for characterizing study populations. Ratios can consider any combination of characteristics for which reliable estimates of their distribution in a target population are available. Ratios can be used to compare study populations, even when target populations differ, and can be estimated before and after application of sample weights. Representation ratios can complement existing metrics related to study population representativeness. AARB and Duncan dissimilarity index are both convenient aggregate measures of a study population's representativeness. While convenient, these metrics do not give insights into the specific populations that are under- or over-represented, which our representation ratio can. Unlike the AARB and our representation ratio, the Duncan dissimilarity index can be computed between

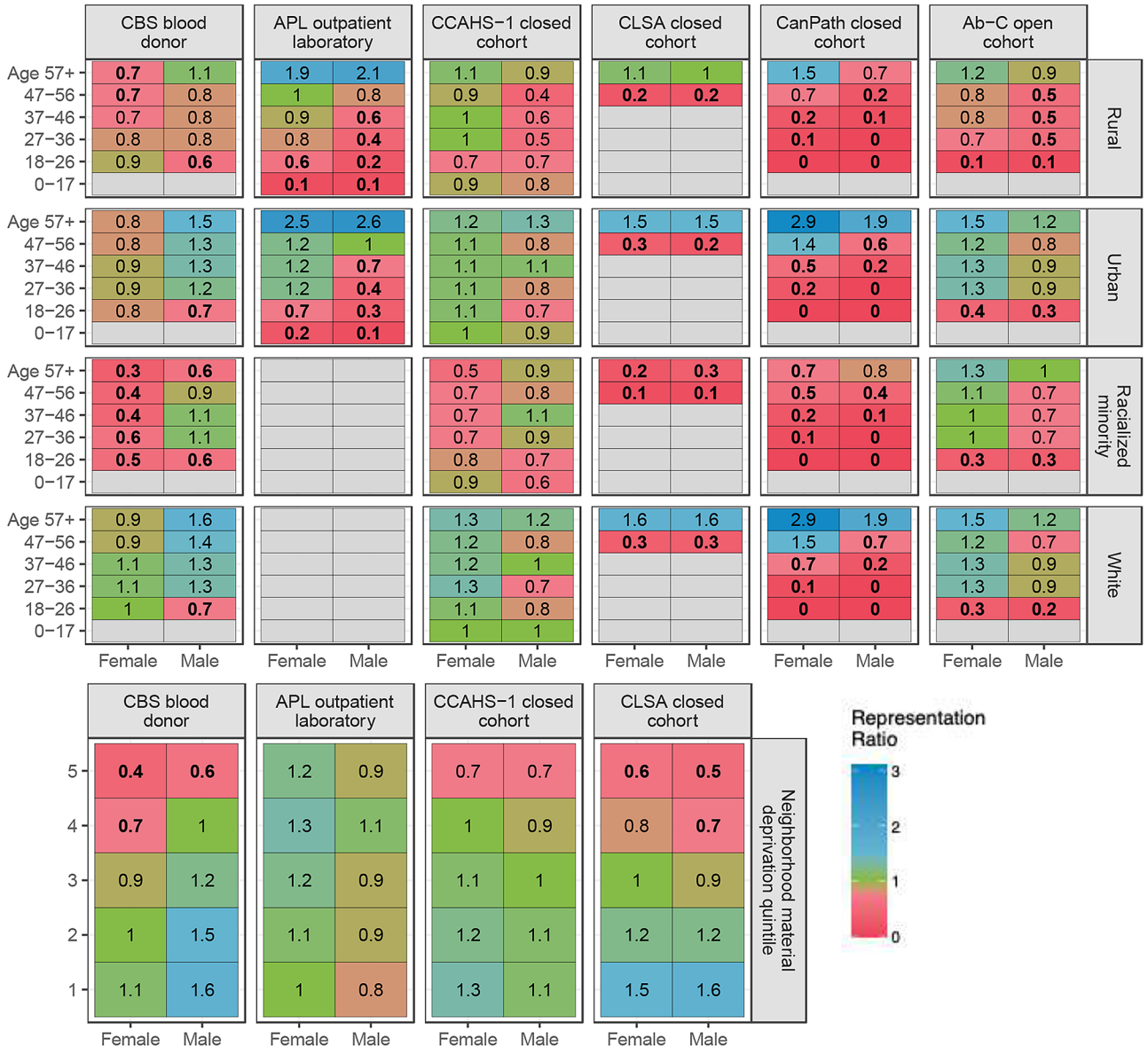

Fig. 3 SARS-CoV-2 serological study representativeness by age group, sex, urbanicity, racial/ethnic identity, and material deprivation quintile. Representativeness was calculated by dividing the proportion of study specimens collected from a subgroup by the proportion of general population in the subgroup. Total population counts were estimated using the 2016 Canadian Census [25]. Material deprivation scores were not available for Ab-C and CanPath studies. Bolded representation ratios indicate greater than 95% of subgroup bootstrap replicates produced representation ratios below 0.75. Bootstrapping was not performed for studies with weighted counts (CCAHS-1)

Table 3 Percentage of SARS-CoV-2 serology study demographic subgroups with greater than 25 collected specimens

		Demographic subgroups			
Study (specimen count)	**Months sampled**	**Age, Sex, Province, Month**	**Age, Sex, Province, Urban, Month**	**Age, Sex, Province, Race/Ethnicity, Month**	**Age, Sex, Province, Race/Ethnicity, Urban, Month**
CBS blood donor (1,035,580)	41	92%	74%	70%	51%
APL outpatient laboratory (210,906)	27	94%	84%	NA	NA
Ab-C open cohort (27,140)	18	32%	21%	21%	14%
CanPath closed cohort (25,156)	15	40%	31%	33%	26%
CLSA closed cohort (17,310)	11	50%	36%	34%	27%
CCAHS-1 closed cohort (11,050)	6	33%	20%	21%	13%

Notes: Date of sample collection was binned into 2-month intervals for each level of stratification. All specimen counts were unweighted

any two surveys in the same target population using any covariates measured in both surveys without a reference database; however, such an implementation does not give insights into which survey is more representative. Notably, representation ratios do not provide insights into the relationship between participant characteristics and a study's estimand, and do not address unmeasured confounding within subgroups. For instance, if the proportion of respondents within strata who are unvaccinated or essential workers (two traits that are associated with higher seropositivity) differs from the general population, post-hoc adjustment would not remove bias from estimated seropositivity [28, 29]. It is therefore recommended to collect data on potential confounders, either through participant questionnaires or linking participant records to administrative databases, and to consider these variables in post-hoc adjustment when auxiliary data are available [10].

Probabilistic surveys have traditionally been considered the 'gold standard' for obtaining representative samples [7]. Use of administrative datasets to construct sampling frames often provides superior population coverage compared to non-probability samples that rely on participant self-selection. The statistical framework also permits estimation of sampling errors and characteristics associated with non-response [30]. While resource constraints may limit the ability of probabilistic designs to perform repeated specimen collection, non-probability sampling within continuous streams of residual blood specimens, such as blood donors, may be more feasible for modelling longitudinal trends, which can also incorporate complex geographic structures [31]. The generalizability of probabilistic designs may also be limited if differences between respondents and non-respondents are non-random [7]. Bias may be introduced via a 'healthy volunteer' effect whereby cohort participants are healthier than the general population [32], similar to the 'healthy donor' bias documented in blood donor research cohorts [33]. Where available, response rates of the included studies were fairly low (23% [CCAHS-1], 25% [Ab-C] [6, 13]; these response rates exclude individuals who completed a questionnaire but did not provide a blood sample). This suggests non-response bias could partially explain some of the observed differences in representativeness between study designs. The above response rates are consistent with other probabilistic serosurveys [12], although response rates as high as 69% have been reported [11].

Many large-scale SARS-CoV-2 studies relied on blood donor and healthcare patient populations for serology specimens [30, 34]. Blood donors have been discounted as a population for public health surveillance, while the potential for expanded screening of residual outpatient laboratory samples remains unclear. However, we found the representativeness of these convenience populations compared favorably to other designs for some sociodemographic dimensions. For low- and middle-income countries with limited operational resources, leveraging residual blood samples may provide a cost-effective avenue to obtain representative data. Future studies should evaluate the potential of linkage to administrative datasets to better characterize representativeness and derive statistical weights for adjustment. Gaps in demographic representation may be overcome by synthesizing data from multiple surveillance streams, though differences in choice of assay, use of venous blood draws or dried blood samples, and the format or availability of variables can curtail the ability to synthesize data across studies [35, 36].

Racialized minorities were underrepresented across all studies. Language barriers and skepticism of research or medical institutions may contribute to poor representation of some minority groups [37, 38]. While use of stratified random sampling or sampling weights may improve sample representativeness, they do not address the underlying individual and societal factors governing participation in health research. Direct engagement and collaboration with community members throughout the research cycle may mitigate recruitment barriers by facilitating trust, reducing misinformation, and ensuring study materials are accessible [38, 39]. Racialized minorities may be better represented in healthcare cohorts like APL [39], though a lack of race-based data in Canadian administrative healthcare datasets may make this difficult to measure [40]. Notably, representation of racialized minorities improved as age increased in most studies requiring participant opt-in (Ab-C, CLSA, CanPath), but young minorities exhibited better representativeness compared to older subgroups in CBS. Lack of a standardized definition of participant race/ethnicity impeded comparison across studies and prevented assessment of representativeness by specific minority group.

Several other dimensions of representativeness varied across studies. The Ab-C open cohort was substantially more representative of 18-46-year-olds across sex and urbanicity strata compared to the CanPath longitudinal closed cohort (Fig. 3). CLSA and CanPath recruited participants aged 45–85 in 2010 and 35–74 in 2009, respectively, leading to older age distributions for their COVID-19 sub-studies [21, 22]. Between convenience samples, individuals residing in the most materially deprived areas were underrepresented when using blood donations (representation ratio 0.4–0.6), but not when using outpatient labs (representation ratio 0.9–1.2). Donor eligibility criteria, along with the 'healthy donor effect' or other unmeasured socioeconomic factors, may homogenize the demographic composition of the sampled donor pool [33]. Rural regions were consistently underrepresented compared to urban counterparts in all

studies, which may be due to urban-centric recruitment patterns or willingness to travel for specimen collection (Figs. 2 and 3).

We did not observe a consistent increase in AARB over time for any study (Fig. 1). Bias tended to increase when monthly sample size was low, except for CanPath where months with larger sample sizes tended to have greater AARBs. Participant attrition can cause shifts in study population composition over time [41], and may contribute to biased estimates if dropout is related to the outcome of interest. For example, an online mental health survey conducted during the SARS-CoV-2 pandemic found participants with anxiety or depression symptoms were less likely to complete multiple survey waves, resulting in under-estimation of symptom prevalence [42]. However, the presence of attrition does not always lead to biased study estimates [43].

The study had several limitations. First, our analysis considered representativeness by age, sex, race/ethnicity, urbanicity, and neighborhood deprivation. Many other sociodemographic dimensions are important considerations for representativeness in serosurveillance studies, particularly those related to health and disability. We hypothesize a 'healthy participant' sampling bias may have led to underrepresentation of individuals with poor health and/or disability in all study populations except outpatient laboratories [32, 33]. Prior analyses of the pre-existing longitudinal cohorts included in our study indicated participants are more educated and/or have higher income than the general population [13, 21, 22], as are blood donors in the United States [44]. Second, the measurement of race/ethnicity differed between studies. Race/ethnicity options for CBS included four mutually exclusive categories, while the Ab-C, CCAHS-1, CanPath, CLSA, and Census datasets permitted selection of multiple racial/ethnic identities. This necessitated dichotomizing the race/ethnicity variable as white or racialized minority and may have biased the CBS representation estimate if individuals who identified as mixed race/ethnicity selected their race/ethnicity as white during donation. Additionally, due to unavailable Indigenous identity data, we modified our representation assessment for the CLSA and CanPath studies by omitting Indigenous-identifying individuals from the Census dataset. Our sensitivity analysis suggests this did not substantially impact our findings (see Supplementary Figure S16, Supplementary Material 2). Third, we restricted our analysis to SARS-CoV-2 serostudies conducted within a single country and used an acceptability level of underrepresentation that is context-specific and open to interpretation. We focused on strata with fewer than 25 samples in our cell count analysis, but this threshold was arbitrary. No general rule of thumb exists for minimum observations for post-hoc adjustment; it depends on the estimand, extent to which traits correlate with the estimand, target level of precision, and the post-hoc adjustment method. Simple post-stratification requires observations in strata defined by all combination of traits (though analysts can collapse strata to achieve this) [45, 46]. Iterative proportional raking and regression-based approaches can be used with empty strata, but tend to poorly with unbalanced representation [47]. With MrP, generalizability can be reasonable with many empty strata defined using all participant characteristics if there are sufficient observations when stratifying by the covariate used in the second level (e.g., if the second level of the model is geographic region, generalizability may be possible even if people with certain characteristics are not represented in all areas) [48]. While MrP is fairly robust to model misspecification, performance is reduced when using misspecified models [49] or if sample coverage is poor and there are a moderate number of sparse or empty strata. Fourth, we did not analyze factors shaping the sociodemographic composition of each study, including intentional oversampling. For example, CCAHS-1 used a stratified random sampling strategy that oversampled geographic regions with greater COVID-19 prevalence and less populated regions to improve estimate precision. Less populated areas of Canada often have fewer racialized minorities, which likely contributes to lower representation ratios [6]. Understanding the causes and consequences of each study's sociodemographic composition requires more detailed analysis than is presented here. Fifth, our assessment of representativeness by material and social deprivation quintile may be prone to misclassification bias. Both indices are estimated at the smallest standard geographic unit of the Canadian Census that generally contains 400 to 700 people (dissemination area), and are linked to participant postal code. Such area-level proxy measures of deprivation may not reflect the individual deprivation status of study participants [24]. Finally, our study is not a comprehensive assessment of all SARS-CoV-2 serology studies conducted in Canada. Demographic groups excluded here were evaluated elsewhere [50].

Understanding variability in demographic representation between study designs is an important consideration when planning serosurveillance studies, which increasingly leverage pre-existing samples or cohorts. This study provides a simple metric to evaluate and compare the representativeness of study populations. We found that underrepresentation of racialized minorities and younger age groups was common and not restricted to convenience samples, which had better representation for some sociodemographic strata. This suggests that representative estimates could be obtained in resource-constrained settings by leveraging lower-cost approaches, such as existing blood or laboratory services, compared

to large-scale probabilistically sampled serosurveys. Identifying coverage barriers is vital to support adequate representation and detection of disease trends within demographic subgroups. We also observed differences in the measurement of participant race/ethnicity between studies. This highlights the necessity for consistent, and sufficient, measurement of sociodemographic variables, along with the need to adopt a standardized approach to the measurement of self-identified race/ethnicity in Canada.

Abbreviations

AARB	Average Absolute Relative Bias
Ab-C	Action to Beat Coronavirus
APL	Alberta Precision Laboratories
CanPath	Canadian Partnership for Tomorrow's Health
CBS	Canadian Blood Services
CCAHS-1	Canadian COVID-19 Antibody and Health Survey 1
CLSA	Canadian Longitudinal Study on Aging
MrP	Multilevel Regression with Post-stratification
R-indicator	Representativeness indicator
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22975-y.

Supplementary Material 1: STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist for cross-sectional studies

Supplementary Material 2: Supplementary figures and tables to support the main manuscript. We report the results of sensitivity analyses and additional sub-analyses of serological study representativeness. The bootstrap distributions for the representation ratios shown in Figures 2 and 3 are provided. We also summarize variable missingness, specimen counts by sociodemographic strata, and the classification of participant self-reported racial/ethnic identities.

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Author contributions

MJK and WAR designed the study with input from DLB, SFO, and CC. MJK, YY, and JC contributed to data analysis. MJK and WAR drafted the initial manuscript. All authors revised the manuscript and approved the final version.

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Data availability

The authors are not authorized to share individual-level data from any study. Processes are available for researchers to request access to datasets for studies that have undergone institutional ethical approval. Data from Canadian Blood Services and Alberta Precision Laboratories may be made available upon request, subject to internal review, privacy legislation, data sharing agreements, and research ethics approval. The CCAHS-1 study by Statistics Canada can be analyzed for approved projects at Research Data Centres located across Canada (https://www.statcan.gc.ca/en/microdata/data-centres/access). Data are available from the Canadian Longitudinal Study on Aging (www.clsa-elcv.ca) for researchers who meet the criteria for access to de-identified CLSA data. Access to the Ab-C study data can be requested through the COVID-19 Immunity Task Force Databank (https://portal.citf.mcgill.ca/). Access to the CanPath data can be requested through the CanPath data portal (https://portal.canpath.ca/). Analytical code will be available in a public repository upon publication.

Declarations

Ethics approval and consent to participate

This secondary analysis of de-identified demographic data was approved by the McGill University Faculty of Medicine and Health Sciences Research Ethics Board (study number 22-03-077) and conducted in accordance with the Declaration of Helsinki. The Research Ethics Board waived the need to obtain informed consent to participate from study participants for this secondary analysis. The six studies that collected primary data analyzed in this report were each approved by one or more Research Ethics Board or Institutional Review Board of a Canadian institution, as previously reported. All experiments were conducted in compliance with the relevant guidelines and regulations.

Consent for participation

Not applicable.

Competing interests

The authors declare no competing interests.

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