Impact of dried blood spot sample collection on SARS-CoV-2 antibody test results in a serological study of older Canadians

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# Letter

Over the past decades, serosurveillance has proven to be cost-effective to monitor the prevalence of infectious diseases, when compared to various forms of laboratory tests [1–3]. One traditional method of blood sample collection involves venous blood sampling (VBS), which requires participants to visit a testing center in person and provide their blood samples through venous extraction [4]. Instead of VBS, studies estimating population prevalence of infectious disease markers in blood sometimes ask participants to self-collect and mail a dried blood spot (DBS) for laboratory testing, instead of having a venous blood samples collected by a trained health professional [5]. DBS has gained increasing popularity in recent years due to its convenience and many SARS-CoV-2 serological studies have used DBS [5–7]. However, limited data are available on evaluating its validity and whether DBS changes laboratory findings.

In a national SARS-CoV-2 serological study of older Canadians, participants could choose whether to mail a DBS sample or provide a venous sample at a testing center [8]. Upon the study data with both anti-N and anti-S assay results available (N=7,230), we developed a propensity score model to examine the association of demographics, geography, and health-related factors with the choice of DBS or venous sample. We applied propensity score weighting (weighting method: inverse probability of treatment weighting (IPTW)) to adjust for potential confounding variables and compare SARS-CoV-2 Anti-N and Anti-S assay results when using the same assay on DBS or venous samples.

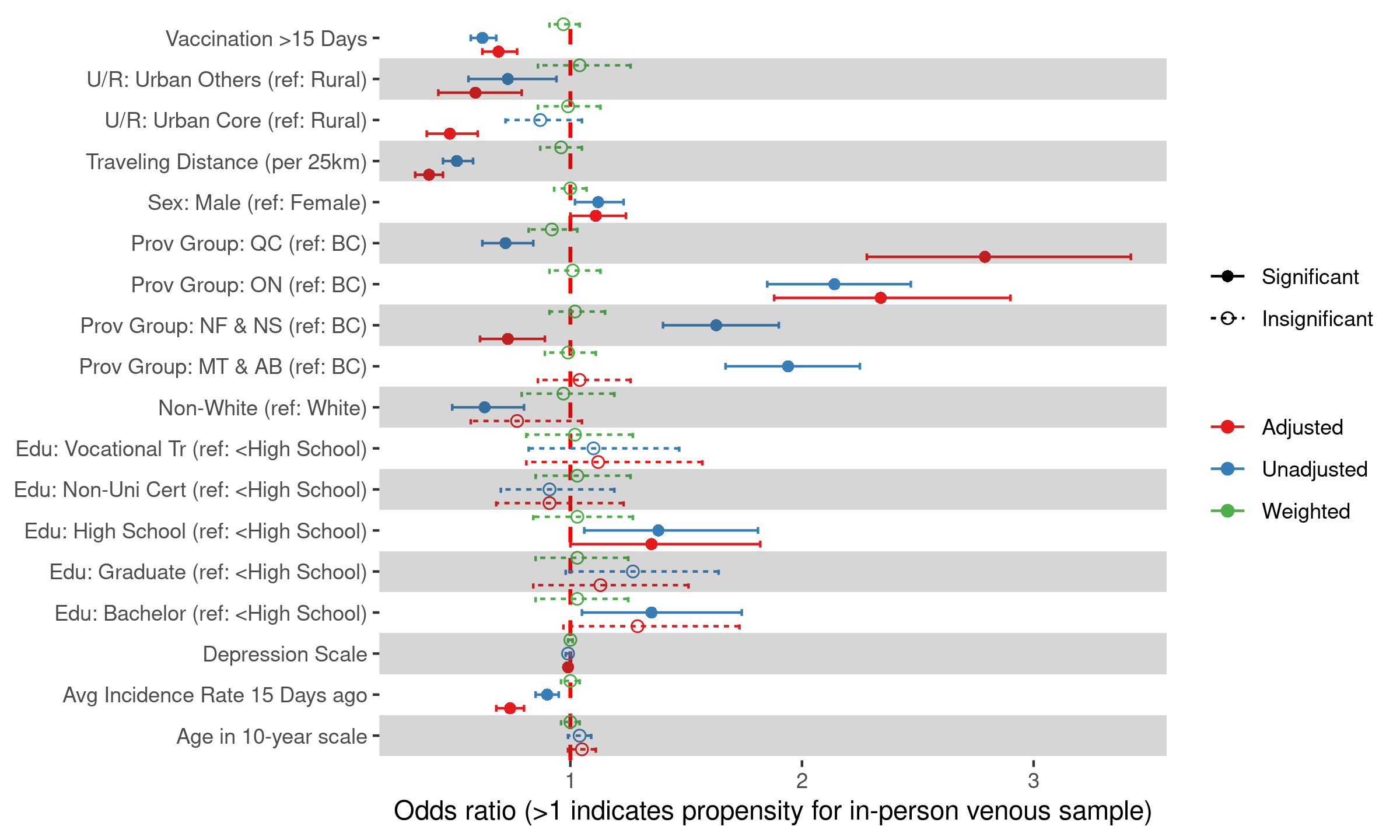
Participants choosing to provide in-person venous samples were more likely to be male, white, unvaccinated, and living in an urban area (**Fig. 1**). After propensity score weighting with balance achieved, venous samples were 223% more likely to be Anti-N positive (OR: 3.33, 95% CI: 2.78 - 4.01) and 27% more likely to be Anti-S positive (OR: 1.27, 95% CI: 1.08 - 1.49). Among Anti-S antibody positive samples, venous samples had significantly higher quantitative anti-S levels (**Fig. 2**), which is tested using Kolmogorov-Smirnov (KS) Test.

We observed significant differences in sampling method preferences across provinces. Compared to British Columbia (BC), participants in Ontario (ON) and Quebec (QC) preferred in-person venous sampling. In the Atlantic provinces, however, there was a preference for at-home DBS sampling over the venous sampling approach. Stratified analysis by province revealed that these trends were mostly consistent with national-level data analysis, except for QC. In QC, higher average COVID-19 incidence (per 100,000 participants) was associated with increased propensity (OR: 1.05, 95% CI: 1.02 - 1.09) for in-person venous sampling, unlike other provinces.

Our findings contrast with prior reports that serological tests perform similarly in DBS and venous samples [5–7] and suggest that more work is needed to understand how different assays perform on DBS samples, and the provincial variations in choosing sampling methods at the behavioral level.

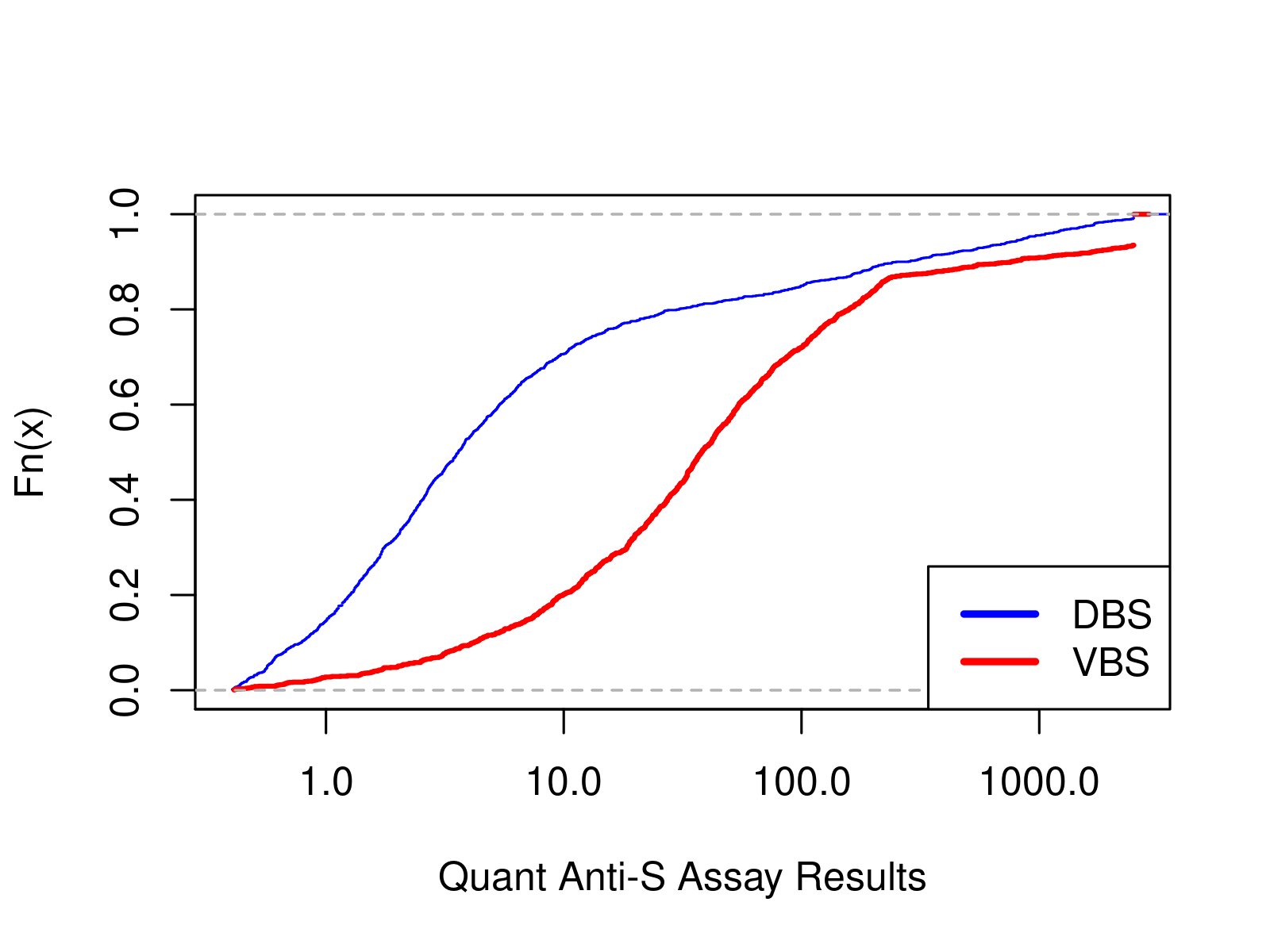
# Figure

**Figure 1**: Odds ratios from the propensity score model predicting who is more likely to give an in-person venous sample vs. mailed DBS sample



1. Adjusted: Odds ratios from the propensity score model, which is a multivariate logistic regression model.
2. Unadjusted: Odds ratios from each simple logistic regression model, regressing on venous blood sampling against DBS sampling.
3. Weighted: Odds ratios from simple logistic regression models comparing the difference between two sampling groups, using weights from IPTW.

**Figure 2**: Empirical cumulative distribution function for the quantitative Anti-S level among participants who tested positive on the Anti-S assay. Venous samples tended to have higher Anti-S levels compared to DBS. 8.43% of venous samples were above the assay’s upper limit of detection, compared to 0% of DBS.



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