THE EPIDEMIOLOGY OF SARS-COV-2 AND SEASONAL RESPIRATORY VIRUSES IN OTTAWA, ONTARIO DURING THE COVID-19 PANDEMIC

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ABSTRACT

This thesis aims to describe the epidemiology of SARS-CoV-2 and other seasonal respiratory viruses (SRV) in the Ottawa region and determine if there are demographic or occupational risk factors associated with viral infection. This was accomplished in three articles: a rapid review of the literature evaluating SARS-CoV-2 seroprevalence in transit users, an account of SRV activity in Ottawa, Ontario from August, 2018 to January, 2022, and an analysis of coronavirus (CoV) incidence and prevalence in several at risk groups. Results indicated a reduction in SRV incidence during the COVID-19 pandemic correlated with the introduction of non-pharmaceutical public health measures. SARS-CoV-2 seroprevalence indicative of natural infection was not greater in population groups hypothesized to be at greater risk of infection, such as transit users and those exposed to children. Lower socioeconomic status and racial or ethnic minority were consistently associated with higher SARS-CoV-2 seroprevalence. SRVs are expected to resurge and co-circulate with SARS-CoV-2. Results from this thesis suggest those of ethnic minority, low income or immunocompromised individuals may at greater risk.

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CHAPTER 1

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 700 million people and has caused over 6.9 million reported deaths [1]. Infection patterns of SARS-CoV-2 and other respiratory viruses has drastically changed over the course of the pandemic. Understanding the epidemiology of seasonal respiratory viruses (SRVs) in the context of the SARS-CoV-2 pandemic may provide insight into viral transmission patterns and aid in identifying vulnerable populations. This thesis aims to assess SARS-CoV-2 and SRV infection patterns among high-risk demographic groups and identify demographic risk factors for infection.

1.1 Objectives

1) Assess SARS-CoV-2 seropositivity and incidence of infection in high-risk groups including those that work or use public transit, those with high degree of exposure to children, and immunocompromised individuals.

2) Identify demographic variables associated with SARS-CoV-2 seroprevalence indicative natural infection.

3) Assess the effect of the COVID-19 pandemic on seasonal respiratory virus activity in the Ottawa region.

1.2 Description of each chapter

- Chapter 1 introduces the thesis topic and describes the objectives of this thesis.
- Chapter 2 represents the first article of the thesis, titled "SARS-CoV-2 Seroprevalence in Those Utilizing Public Transportation or Working in the Transportation Industry: A Rapid Review." This article is published in *International Journal of Environmental Research and Public Health.*
- Chapter 3 represents the second article of the thesis, titled "Seasonal respiratory virus circulation was diminished during the COVID-19 pandemic." This article is published in *Influenza and other Respiratory Viruses.*
- Chapter 4 represents the third article of the thesis, titled "Prevalence and incidence of coronavirus infections in high-risk population groups in Ottawa, Ontario, 2020-2022."
- Chapter 5 provides a summary of key findings from Chapters 2-4 and discusses potential implications and future directions of this thesis research.

1.3 Thesis organization

This thesis is composed of three component articles. Each article is represented by a Chapter of this thesis. A brief summary of each Chapter and how they are linked is provided below.

Chapter 2 represents a literature review that evaluates the seroprevalence of SARS-CoV-2 in those that use or work in the public transportation industry. This chapter addresses the first and second thesis objectives. While this chapter primarily assessed SARS-CoV-2 seroprevalence in those that use or work in public transit, it also highlights demographic characteristics and risk factors associated with seropositivity found in the literature. This chapter provides background information on what was known about SARS-CoV-2 seroprevalence in transit users at the time of publication and provides context for the analysis presented in Chapter 4.

Chapter 3 utilizes data from a laboratory in the Ottawa region to describe the activity of 15 common respiratory viruses over the course of the COVID-19 pandemic. This chapter addresses the third objective of this thesis; assessing the effect of the COVID-19 pandemic on seasonal respiratory virus activity. This chapter provides historical context on seasonal virus activity in Ottawa and illustrates how it was diminished during the pandemic. These findings were compared to the number of coronavirus (CoV) infections detected in the at-risk groups analyzed in Chapter 4.

Chapter 4 uses serology data to assess the incidence and prevalence of SARS-CoV-2 and seasonal coronaviruses (CoVs) in several high-risk groups including transit workers, those exposed to children, and immunocompromised individuals. The number of CoV and SARS-CoV-2 infections were compared between groups, and regression analyses were conducted to assess associations with antibody prevalence from natural infection and demographic characteristics. This chapter builds on contextual information provided by Chapters 2 and 3 and addresses all three thesis objectives.

1.4 References

1. World Health Organization. (n.d.). *Who coronavirus (COVID-19) dashboard*. World Health Organization. https://covid19.who.int/?adgroupsurvey=%7Badgroupsurvey%7D&gclid=EAIaIQobChMI88uApMfLgAMVIz4GAB3-bQPJEAAYASABEgK4BfD_BwE

CHAPTER 2

SARS-CoV-2 Seroprevalence in Those Utilizing Public Transportation or Working in the Transportation Industry: A Rapid Review

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Article preface: This chapter aims to summarize existing literature that assesses the seroprevalence of SARS-CoV-2 in those that use or work in public transit. It also identifies several demographic risk factors associated with higher burden of disease. The literature review represented in this chapter addresses the first and second thesis objective.

2.1 ABSTRACT

Proximity and duration of social contact while working or using public transportation may increase users' risk of SARS-CoV-2 exposure. This review aims to assess evidence of an association between use of public transportation or work in the transportation industry and prevalence of SARS-CoV-2 antibodies as well as to identify factors associated with seropositivity in transit users. A literature search of major databases was conducted from December 2019 to January 2022 using key worlds including "seroprevalence", "SARS-CoV-2", and "public transit". A narrative review of included studies was completed for the following categories: those working in the transportation industry, healthcare workers relying on public transit, and population-based studies. The association between work in the transit industry and seroprevalence varied based on location, demographic characteristics, and test sensitivities. No association was found in healthcare workers. Several population-based studies indicated higher seroprevalence in those using public transit. Overall seroprevalence estimates varied based on geographic location, population demographics, study methodologies, and calendar date of assessment. However, seropositivity was consistently higher in racial minorities and low-income communities.

2.2 INTRODUCTION

The coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains an international threat with over 550 million confirmed cases and 6 million deaths worldwide [1]. The virus has had a major impact on the transportation industry, shutting down international borders and influencing travel within municipalities. The drastic reduction in public transit ridership is a result of the introduction of remote work, switch to active transportation (i.e., walking or cycling), increased perception of risk associated with public transit use, and government and/or public health recommendations. However, public transit is an essential service with economic benefit that has been continuously relied on by many throughout the pandemic. The increased proximity and duration of social contact accompanying transit use may increase users' risk of SARS-CoV-2 infection. Racial minorities and those with lower education and income are at particular risk as they are over-represented in those continuing to use public transit during the pandemic and are already at increased risk for SARS-CoV-2 occupational exposure [2–4].

Serological testing provides a robust estimate of prior infection by capturing both symptomatic and asymptomatic individuals. This can provide information on virus transmission patterns, measure herd immunity, and predict the number of people susceptible to the virus. With the introduction of vaccinations and evolving variants, serosurveys can help identify gaps in immunity associated with demographic characteristics or risk factors and can focus vaccination programs on susceptible communities. Several systematic reviews have attempted to

consolidate and analyze results from hundreds of serosurveys world-wide to determine overall SARS-CoV-2 seroprevalence [5–7]. Many serosurveys report the prevalence of SARS-CoV-2 antibodies stratified by sex, gender, health status, and employment history with substantial heterogeneity of results. A systematic review and meta-analysis of 60 countries estimated that the pooled seroprevalence of SARS-CoV-2 was 9.47% as of 30 March 2021 [8]. Several seroprevalence studies have reported similar levels of exposure [9–11]; however, results varied by population. This indicates that at the time of study, most of the population had not been exposed to SARS-CoV-2. Seroprevalence is generally found to be similar among men and women [11,12]; however, some studies have found differences between the sexes [8,10]. A literature review of seroprevalence studies found that HCW are often considered a high-risk group; however, those that use adequate PPE are at no higher risk of infection than other groups [12]. Public transportation has been recognized as a high-risk environment for COVID-19 infection prompting the introduction of safety measures such as mask wearing, enhanced cleaning, and reduced capacity to promote physical distancing. Despite this, the risk of infection while using public transport is largely unknown with few studies focusing on this topic and even fewer that evaluate the risk of infection considering social determinants of health such as income and ethnicity. Our literature review aims to assess the prevalence of SARS-CoV-2 seropositivity associated with (1) employment in the transportation industry (e.g., pilots, bus drivers, or taxi drivers) and (2) use of public transportation. Secondary outcomes included identifying demographic characteristics and risk factors associated with seropositivity in these populations.

2.3 MATERIALS AND METHODS

A literature search of major databases including MEDLINE, Embase, PubMed, and Google Scholar, as well as the MEDRXIV and BIORXIV pre-print servers was performed. Databases were searched from December 2019 to January 2022. Studies were excluded if they were conducted when Omicron became the dominant variant in the Fall of 2021. Only studies that were written in English and incorporated demographic information were included. Populations of interest included those using public transportation and those working in occupations with high risk of exposure to SARS-CoV-2 (i.e., healthcare workers, taxi drivers, or bus operators). The search strategy included a combination of key words such as: “COVID-19” or “SARS-CoV-2”, “respiratory virus”, “seroprevalence”, “public transit”, “public transportation”, “transportation”, “demographic”, “COVID-19 antibodies”, and “socio-demographic”. Citation and reference tracking was performed and relevant materials manually searched. Databases were systematically reviewed. A risk of bias or quality assessment tool was not used; however, studies were informally assessed for limitations or aspects of the study that may have influenced results which were included in the narrative review. Data was extracted using Excel. Studies were organized in accordance with the Human Development Index (HDI) developed by United Nations [13]. This measure is a summary of average achievement in key dimensions such as length and quality of life, knowledge, and standard of living. On this scale, any country scoring higher than 0.8 in 2019 was considered to have very high human development, between 0.7 and 0.799 high human development, 0.55–0.699 medium human development, and less than 0.55 low human development. Outcomes of interest included the effect measure

(relative risk and mean difference) of the association between seroprevalence of antibodies to SARS-CoV-2 and any form of transit use and variables that were predictive of seropositivity.

2.4 RESULTS

Twenty-two relevant studies were identified and narratively reviewed. Publications were identified from African, European, North American, South American, and Asian countries. A list of included studies and their characteristics can be found in Table 2.1. A summary of findings from studies addressing the association between SARS-CoV-2 seropositivity and work in the transportation industry is presented in Table 2.2. Studies evaluating the association between SARS-CoV-2 seropositivity and use of public transportation were divided by population. Studies concentrating on healthcare workers and the risk associated with their commute to work are presented in Table 2.3. Those that focus on the risk associated with transit use in the general population are presented in Table 2.4.

Outcomes included point seroprevalence, prevalence ratios, odds ratios, relative risks, and associated confidence intervals. Key variables associated with SARS-CoV-2 seropositivity were documented.

Table 2.1. Characteristics of included studies from highest to lowest HDI.

Author	Location	HDI	Date	Type of Study	Study Population	# Participants	Serology			
							Assay	Target	Sensitivity (%)*	Specificity (%)*
Meylan	Lausanne, Switzerland	0.955	May 18-June 12-2020	Cross-sectional	Centre Hospitalier Universitaire Vaudois and Centre for Primary Care and Public Health staff	1874	Luminex-based assay (IgG)	S-protein	97	98
Pathela	New York City, USA	0.926	May 13-July 21, 2020	Cross-sectional	NYC adult resident; occupation subgroups	45,367	Liaison SARS-CoV-2 S1/S2	S1/S2 subunits of S protein	97.6	99.3
Soffin	New York City, USA	0.926	May 6, June 5, 2020	Cross-sectional	Surgeons and Anaesthesiologists at Hospital for Special Surgery	143	Abbott Architect SARS-CoV-2 IgG	Nucleocapsid	94-100[a]	99.4-100[a]
Venugopal	New York City, USA	0.926	May 2020	Cross sectional	Frontline HCWs of NYC hospitals	500	Abbott Architect IgG Assay	Nucleocapsid	100 (95%CICI 95.8-100%)	99.6 (95%CICI: 99-99.99%)
Feehan	Baton Rouge, USA	0.926	July 15-31, 2020	Cross sectional	Representative sample of residents	2138	Abbott Architect i2000SR IgG Assay	Not specified	Not specified	Not specified
Chan	Rhode Island, USA	0.926	May 5-22, 2020	Cross-sectional	Households, oversampled African Americans/Blacks and Hispanics/Latinos	1043	Not specified	Not specified	Not specified	Not specified

Mahajan	Connecticut, USA	0.926	June 4-July 29, 2020		Adults living in non- congregate settings (exclude those living in LTC homes, nursing homes, prisons); also oversampled non-Hispanic black and Hispanic individuals	567	Ortho-Clinical Diagnostics Vitros anti-SARS-CoV-2 IgG (some negative samples retested with Abbott Architect IgG – targeting nucleocapsid protein)	S-protein	90	100
Yamamoto	Toyama and Kohnoda, Japan	0.919	October-December, 2020	Repeated cross-sectional	National Center for Global Health and Medicine employees	2563	Abbott Architect (IgG); Roche Elecsys (total antibodies), confirmatory analysis of positive results using EUROIMMUN anti-S IgG immunoassay	Nucleocapsid protein	Not specified	Not specified
Nishida	Osaka Prefecture, Japan	0.919	June 12-19, 2020	Cross-sectional	Toyonaka Municipal Hospital employees	925	Abbott Architect SARS-COV-2 IgG Assay	Nucleocapsid	100	99.6

Pollan	Spain	0.904	April 27-May 11, 2020	Population-based cohort study	Spanish population	66,805	Orient Gene Biotech COVID-19 IgG/IgM Rapid Test Cassette (Point-of-Care Test);	RBD of S protein	IgG: 97.2; IgM: 87.9	100
							Abbott Architect IgG assay	Nucleoprotein	100[a]	99.6
Airoldi	Piedmont region, NorthWest Italy	0.892	April 28-August 7, 2020	Cross-sectional	Company workers thorugh screening program	23568	ZEUS ELISA SARS-CoV-2 IgG Test system	Not specified	93.3%(95%CI:78.7-98.2)	100% (95%CI:94.8-100)
Berselli	Emilia Romagna region,, Northern Italy	0.892	June 1-September 25, 2020	Cross-sectional	Company workers, self-referred individuals	7561	EUROIMMUNE ELISA anti-SARS-CoV-2 test for IgA and IgG	Not specified	100%[c]	92.5
							Roche Elecsys	Not specified	100[a]	99.8
							KHB SARS-CoV-2 IgM/IgG antibody Colloidal Gold	Not specified	98.81	98.02
Alsuwaldi	Abu, Dhabi, United Arab Emirates	0.890	July 19-August 14, 2020	Cross-sectional	Households in region; labour camps	8831 (households); 4855 (labour camp worker)	Roche Elecsys Anti-SARS-CoV-2	Nucleocapsid	100 (95%CI:88.1-100)[a]	99.8 (95%CI:99.6-99.1)
							LIAISON SARS-CoV-2 S1/S2 IgG Assay	S1 and S2 subunits of S protein	97.4 (95%CI: 86.6-99.5)[a]	98·5 (95% CI: 97·6–99·1)
Poustchi	18 Iranian Cities	0.783	April 17-June 2, 2020	Cross sectional	General population; high-risk occupations	8902	Pishtaz Teb SARS-CoV-2 ELISA IgG and IGM	Not specified	IgG: 94.1; IgM:79.4	IgG: 98.3; IgM: 97.3

Cruz-Arenas	Mexico City, Mexico	0.779	August 10-September 9, 2020	Cross-sectional	Instituto Nacional de Rehabilitación employees	300	LFA: IgG/IgM Rapid Test Cassette;	Not specified	79.5	100
							ELISA: Euroimmun Anti-SARS-CoV-2 NCP IgG Assay	Nucleocapsid protein	Not specified	Not specified
Colmenares-Mejía	Bucaramanga, Colombia	0.767	September 28-December 24, 2020	Cross-sectional	Workers from health, construction, public transportation, public force (army, police, transit officers), bike delivery messengers, independent or informal commercial (shopkeepers)	7045	Abbot ARC COV2 (IgG and IgM)	Not specified	85.2	97.3
De Oliveira	São Paulo, Brazil	0.765	March-July, 2020	Cross-sectional	Sírio-Libanês Hospital employees	1996	ELISA (IgG), unspecified	Nucleocapsid	86-95[a]	100[a]
Acurio-Paez	Cuenca, Ecuador	0.759	August 11-November 1, 2020	Cross sectional	Randomly selected inhabitants of Cuenca, Ecuador	2457	SD BIOSNSOR Standard Q Covid-19 IgG/IgM Plus	Not specified	94.3[b]	87.9[b]
Babu	Karnataka, India	0.645	September 3-16, 2020	Cross-sectional	Statewide population; risk subgroups	16,416	Covid Kavach Anti SARS-CoV-2 IgG antibody detection ELISA	Not specified	92.1	97.7

Gupta	New Delhi, India	0.645	June 22-July 24, 2020	Cross-sectional	HCW – All India Institute of Medical Sciences Staff	3739	ADVIA Centaur COV2T chemiluminescence IgG and IgM immunoassay	S-protein RBD	100[a]	99.8[a]
Naushin	India	0.645	August-September, 2020	Longitudinal, Cohort	Phenome-India Cohort	10,427	Roche Elecsys Anti-SARS-CoV-2; positive samples tested using GENScript cPass SARS-CoV-2 Neutralization Antibody Detection Kit	Nucleocapsid; S-protein	Undefined	Undefined
Halatoko	Lome, Togo	0.515	April 23, 2020 – May 8, 2020	Cross sectional	Occupational sectors: health care, air transport, police, road transport, informal (market sellers, craftsmen)	955	Lungene Rapid Test (IgG and IgM)	Not specified	72.9	85.0

S-protein: spike protein; RBD: receptor binding domain; ELISA: enzyme-linked immunosorbent assay; LFA: lateral flow assay.

*Does not include sensitivities and specificities from validation tests performed by authors.

[a] at least 14 days after symptom onset or positive RT-PCR test

[b] at least 15 days post infection

[c] at least 10 days after symptom onset

Table 2.2 Summary of findings from studies that assessed the association between seropositivity and work in the transportation industry from highest to lowest HDI.

Author	HDI Category	Outcome	Overall Seroprevalence (%)	Transit Outcomes		Variables associated with Seropositivity	Conclusion
				Seroprevalence (%)	Regression Analysis (i.e., OR, RR)		
Pathela	Very high	Seroprevalence (%), Poisson regression (RR; 95%CI)	23.6% (95%CI:23.2-24)	Air transport (n=137): 25%; Public transit, taxis and private drivers (n=479): 35%; Other transportation and warehousing (n=440) 27%	Essential worker (food services, construction, retail trade, transportation) compared to other industries RR: 1.63 (95%C: 1.5-1.7); Adjusted for sex at birth, age, borough, poverty level, working outside the home RR: 1.33 (95%CI:1.3-1.4)	Male sex, age 44-64, non-White race/ethnicity, living in a borough other than Manhattan or Staten Island, living in neighborhoods with high or very high poverty levels, employment in health care or essential worker category, not being unemployed at the time of serosurvey, working outside the home, having contact with someone with COVID-19, COVID-19 symptoms, being overweight or obese, increasing number of household members	Those working in the transportation industry more likely to have SARS-CoV-2 antibodies
Feehan	Very high	Seroprevalence (%), census weighted bivariate analysis (OR)	3.6 % (95%CI: 2.8-4.4)	N/A	Working in the transportation industry (n=11) compared to an office OR:6 (95%CI: 0.1-100)	Single marital status, public-facing job compared to office, healthcare career, black non-Hispanic race/ethnicity, younger than 29 years old	Work in the transportation industry comparable to risk associated with work in an office

Pollan	Very high	Seroprevalence (%) using two assays	POC test: 5% (95%CI:4.7-5.4); Immunoassay: 4.6% (95%CI:4.3-5.0)	POC test: (n=800); 5.9% (95%CI:3.9-8.7); Immunoassay (n=731): 5.8% (3.6-9.2)	N/A	Province, working in healthcare, confirmed COVID-19 case in household or among non-cohabitating family members and friends or among caregivers and cleaning staff or clients, COVID-19 symptoms	Seroprevalence of those working in the transport industry comparable to overall seroprevalence; comparable between tests
Airoldi	Very high	Seroprevalence (%)	4.97% (95%CI:4.69-5.25)	4.36% (95%CI:1.95-6.78)	N/A	Geographical location, those working in logistics or weaving factories	Seroprevalence in transportation industry workers comparable to general population
Berselli	Very high	Seroprevalence (%)	4.7%(95%CI:4.2-5.2)	1%	N/A	Seroprevalence higher in women, older age groups, HCW, dealers and vehicle repair workers, sport sector employees	No evidence of increased seroprevalence
Alsuwaldi - Household population*	Very high	Seroprevalence (%), bivariate model, multiple logistic regression model (OR)	10.4% (95%CI: 9.5-11.4)	20.8% (95%CI:15.9-26.7)	OR: 1.5 (95%CI:0.7-3.2) adjusted for age, sex, region, education, nationality, ethnicity, occupation, contact with someone diagnosed with COVID-19	Households: Region, education level, Asian ethnicity, not from UAE, contact with someone with COVID-19, COVID-19 symptoms	No association with transit use in multivariable analysis
Alsuwaldi - Labour camp population*	Very high	Seroprevalence (%), bivariate model, multiple logistic regression model (OR)	68.6% (95%CI: 61.7-74.7)	72.1% (95%CI:60.4-81.5)	OR: 2.7 (1.8-4.0) adjusted for age, sex, region, education, nationality, ethnicity, occupation, contact with someone diagnosed with COVID-19	Education, non-Arabic ethnicity, occupation, contact with someone with COVID-19, COVID-19 symptoms	Transit use and high-risk occupations associate with seropositivity

Poustchi	High	Seroprevalence (%) adjusted for population weighting and test performance	General population: 17.1% (95%CI: 14.6-19.5); High-risk population: 20% (95%CI:18.5-21.7)	Taxi drivers (n=718): 18.8% (95%CI: 14.7-23.2)	N/A	60 years or older, those in contact with someone with COVID-19, region, COVID-19 symptoms	Seroprevalence similar between high-risk occupations
Colmenares-Mejía	High	Seroprevalence (%) corrected for test performance and study design	19.5%(95%CI:18.6-20.4)	Commute to work: bike: 25.7% (95%CI: 16.6-34.8); public transportation: 23.9% (95%CI: 21.8-26); taxi 15.5% (95%CI: 12.3-18.7) Those working in the public transport industry: 16% (95%CI:11.7-20.3)	N/A	Occupational groups with multiple contacts with others during work hours, delivery drivers, grocery store tenants, informal commerce workers, those that used a bike, motorcycle, public transit than own car, COVID-19 symptoms	Similar seroprevalence in those working in the transportation industry and other high-risk occupations. Higher seroprevalence in those that use public transit to commute to work compared to those that use their own vehicle
Babu	Medium	Seroprevalence (%), generalized linear model-based multinomial regression (OR)	16.8% (95%CI: 15.5-18.1)	Bus conductors/auto drivers (n=1008): 16.1% (95%CI: 11.7-20.6);	Bus conductors/auto drivers compared to low-risk occupations: OR: 2.12 (95%CI:1.3-3.5)	Diarrhoea, chest-pain, rhinorrhea, fatigue, fever, professions who had more contact with the public, residence in containment zones, urbanisation level of the district	Those working in the transportation industry twice as likely to have SARS-CoV-2 antibodies

Halatoko	Low	Seroprevalence (%)	IgM or IgG: 0.9% (95%CI:0.4-1.8)	Air transport (n=212); IgM positive: 0.5% (95%CI: 0.01-2.6); IgG positive: 0.9% 95%CI: 0.1-3.4) Road Transport (n=122) IgM positive: 0% (95%CI: 0-2.9); IgG 0.8%95%CI: 0-4.5)	N/A	N/A	Low seroprevalence in general, similar among high-risk populations

RR: relative risk; OR: odds ratio; POC: point of care

*Alsuwaldi reported separate results for two different populations. Results varied by population so were presented as two separate studies.

Table 2.3. Summary of findings from studies that assessed the association between seropositivity and use of public transportation in healthcare workers from highest to lowest HDI.

Author	HDI Category	Outcome	Overall seroprevalence (%)	Transit Outcomes		Variables associated with seropositivity	Conclusions
				Seroprevalence (%)	Regression Analysis (i.e., OR, RR)		
Meylan	Very high	Seropositivity (%), multivariable logistic regression (OR)	10% (95%CI:8.7-11.5)	Frequency of transit use (# per week) 1 (n=104):7.7% (95%CI: 3.4-14.6); 2 (n=135): 9.6% (95%CI:5.2-15.9); 3 (n=148): 10.1% (95%CI: 5.8-16.2); 4 (n=199): 12.1 (95%CI: 7.9-17.4); 5 (n=275): 14.2% (95%CI: 10.3-18.9); >5 (n=220): 5.9% (95%CI:3.2-9.9); Use of face mask on public transport (n=151): 5.3% (95%CI: 2.3-10.2) Does not use face mask on public transport (n=930): 11.2% (95%CI: 9.2-13.4)	Use of mask at public transport compared to those that do not: OR=0.42 (95%CI:0.198-0.896) adjusted for daily contact w patients, work in ICU, COVID-19 case at home, and COVID-19 symptoms	Household contact with confirmed COVID-19, use of mask while using public transport, COVID-19 symptoms	Seropositivity increased with transit usage; face mask while using public transit reduced odds of seropositivity
Soffin	Very high	Seroprevalence (%), bivariate logistic regression (OR)	9.8%	N/A	OR: 1.48 (95%CI:0.2-6.3)	Fatigue, myalgia, fever, headache, spouse diagnosed with COVID-19	No association with mode of commute (public transport, walking/cycling, private)
Venugopal	Very high	Seroprevalence (%), bivariable, multivariable linear regression (OR)	27%	29%	Public transit compared to private OR: 1.3 (95%CI:0.9-2.0) Adjusted for ethnicity, symptoms, duration of symptoms: OR:0.84 (95%CI: 0.47-1.52)	Ethnicity other than Caucasian, living in an apartment/condo, walking to work, symptoms of COVID-19, community exposure	Type of transport to hospital not associated with seropositivity

Yamamoto	Very high	Seropositivity (%), Poisson regression (PR)	0.7% (95%CI:0.4-1.1)	N/A	Compared to those that used transit <1 time/week, those that used it 1 or more times/week prevalence ratio was 0.57 (95%CI:0.2-1.4)	Close contact with patients with COVID-19 at home and in the community	No association with transit
Nishida	Very high	Seropositivity (%)	IgG: 0.43% (95%CI:0.2-1.1)	0.76 % (n=396) (95%CI: 0.3-2.2)	N/A	No significant factors	No association with transit
Cruz-Arenas	High	Seropositivity (%), multiple logistic regression (OR)	LFA: 11% ELISA: (IgG only) 13%	N/A	Use of public transport for work commute OR: 1.62 95%CI: 0.82-3.21)	Olfactory alterations, security or janitorial occupations, education below a university degree increasing number of people in household	Type of transport to hospital not associated with seropositivity
De Oliveira	High	Prevalence (%), bivariate analysis, multivariate logistic regression (OR)	5.5%	N/A	Public transport (bus, metro): OR 1.17 (95%CI:0.79-1.75) Adjusted for gender, cleaning, working at COVID-19 units, type of transport OR: 1.103 (95%CI:0.731-1.665)	Professional category of cleaning and male gender	Type of transport to hospital not associated with seropositivity

Gupta	Medium	Seroprevalence (%)	13%	Public transit (n=235): 20%; Hospital transport (n=676): 16.9%; Own vehicle (n=1986): 12.4%; on foot (n=544): 11.2%; didn't declare (n=298): 6%	N/A	Contact with COVID positive individuals, COVID-19 symptoms, region of residence	Seroprevalence significantly higher in HCW that used public, or hospital transit compared to those that used other modes of commute ($p<0.05$)

OR: odds ratio; PR: prevalence ratio

Table 2.4. Summary of findings from studies that assessed the association between seropositivity and use of public transportation in population-based studies from highest to lowest HDI.

Author	HDI Category	Outcome	Overall Seroprevalence (%)	Transit Outcomes		Variables associated with seropositivity	Conclusions
				Seroprevalence (%)	Regression Analysis (I.e. OR, RR)		
Chan	Very high	Seroprevalence (%), age weighted	2.9% (95%CI: 1-6.2)	Public transportation/carpool (n=52): 6% (95%CI:0.1-20.5); own vehicle (n=920): 1.9% (95%CI:0.4-4.1); walking/biking (n=34): 2.8%(95%CI: 0-16.7)	N/A	Those living in a condo or apartment, those that rely on public transportation or carpool, race/ethnicity other than Caucasian, primary mode of transportation	Higher seroprevalence in transit users
Mahajan	Very high	Seroprevalence (%), weighted for non-response and population characteristics of Connecticut	General population: 4% (90%CI: 2-6); non-Hispanic black subpopulation: 6.4% (90%CI:0.9-11.9); Hispanic subpopulation: 19.9% (90%CI:13.2-26.6)	General population: 0% or too small to calculate Non-Hispanic Black subpopulation Airplane: 4 %(+/-4.8); public transportation: 23.7% (+/-7.5) Hispanic subpopulation Airplane: 4.8% (+/-3.3); public transportation: 13.1% (+/- 5.5)*	N/A	Race and ethnicity	No association with transit use in general population, seroprevalence significantly higher in transit users of ethnic minorities

Acurio-Paez	High	Seroprevalence (%), bivariate regression, multivariate regression (OR)	Maximum: 13.2% (95%CI: 12-14.6) (IgG or IgM); Minimum: 4% (95%CI:3.2-4.8) (IgG and IgM positive)	Foot (n=529): 12.5% (9.6-15.5); Bicycle/moto/trolley car (n=106): 11.3% (6.2-19.3); Private car (n=912): 11% (9.0-13.1); Public (bus/taxi) (n=742): 18.2%(15.5-21.2)	Public (bus/taxi) compared to private (own car, foot, bicycle) OR: 1.73 (95%CI:1.4-2.2) Adjusted for age, resources, COVID-19 in household, contact with flu like symptoms, number of people in household, physical contact with someone outside the household: 1.65 (95%CI: 1.28-2.14)	Age 35-49 years old, COVID-19 positive person in the home, using public transit, at least 6 people in a household, physical contact with a person outside the household, contact with someone with flu- like symptoms, not having enough resources for living	Those using public transit at increased risk of seropositivity
Nausin	Medium	Seropositivity (%), bivariate logistic regression (OR)	10.14% (95%CI: 9.6-10.7)	N/A	OR: 1.79 (95%CI:1.4-2.2) OR males: 1.91 (95%CI:1.44-2.55); OR females: 1.83 (95%CI:1.26-2.69)	Higher population density, high exposure work, those using public transit, non-smokers	Those using public transit at increased risk of seropositivity

* +/- margin of error at 90% CI

2.5 REVIEW

2.5.1 Transportation Industry

Essential workers in the transportation industry typically have a high number of social and professional contacts over a comparably large geographic distance which may increase their risk of SARS-CoV-2 exposure. Several serosurveys have purposely targeted industry workers thought to be at high risk of infection during the first wave of the COVID-19 pandemic [14–23]. The association between work in the transit industry and seroprevalence is far from clear with conflicting results found across numerous studies.

Very High HDI Countries

A population-based study in New York City during the first wave of the pandemic in Spring 2020 found that seroprevalence of SARS-CoV-2 antibodies was significantly higher in those working in the air (25.0%) and ground transportation (35.0%) industries compared to those who did not work outside the home during a government mandated stay at home order (22.2%) [14]. Of note, test validation was not reported. In contrast, another smaller American population-based study by Feehan et al. found no association [14]. This study population was 63.3% female and 66.9% white, with a small number or participants working in the transportation industry (n = 11) leading to broad confidence intervals and uncertainty in results [15]. A multivariate analysis was not included, so the effect of demographic and socioeconomic factors was unknown. In a

nation-wide longitudinal seroepidemiological study conducted during the first wave of the COVID-19 pandemic in Spain, Pollan et al. found no difference in seroprevalence between those working in the transportation industry and those working from home [16]. This analysis used sampling weights and post-stratification to adjust for selection probabilities and considered clustering by household and census tract when determining seroprevalence. A large representative sample including children, adolescents, and elderly largely of Spanish nationality were recruited. These subpopulations are unlikely to be employed in the transportation industry and could potentially introduce bias if included in the overall estimate of seroprevalence in transit workers. Both Feehan and Pollan found that the only occupation associated with higher seroprevalence was within healthcare. Two Italian studies targeted workers from a variety of occupational sectors to identify high-risk jobs during the first wave of the pandemic. Both studies had comparable overall seroprevalence at approximately 5% and found that work in the transportation industry was not associated with increased prevalence of antibodies to SARS-CoV-2. However, Airoldi et al. identified clusters of cases that were independent of a single industrial sector indicating that the safety measures initiated by corporations could affect the epidemic situation in each company [17]. PPE use and company policy was not measured in this study so authors were unable to explore this hypothesis. Although the overall sample size was large, the number of participants in each occupation group varied greatly. The sample size was small in several industry sectors resulting in broad confidence intervals which may impact the validity of results. Berselli et al.'s study focused on occupational risks and included mostly participants nominated by their employer, however also included self-referred individuals from whom occupational information was not collected [18].

Reason for self-referral and information on symptoms was not collected. Seroprevalence may have been overestimated if those with symptoms were more likely to participate. This study allowed participants to choose from qualitative tests, quantitative tests, or both. Summary results of each test were available, but results would have been strengthened if participants were randomly assigned a test group or if results were stratified by test. They also switched from testing for IgA and IgG using the EUROIMMUN anti-SARS-CoV-2 test to testing for IgG and IgM using the Roch Elecsys Anti-SARS-CoV-2 test kit for IgG and IgM halfway through the study. The reason for the switch was not indicated and could impact results, especially for IgM which was measured using two separate tests and presented as a single result. The United Arab Emirates has a large community of expatriates living and working in unregulated and often precarious conditions (e.g., construction). Alsuwaldi et al. sampled labor camp workers living in these congregate settings and random households after the first wave in Abu Dhabi, United Arab Emirates [19]. Labour camp workers have different socio-demographic characteristics and were analyzed separately from randomly sampled households representing the general population. They found work in the transportation industry was associated with seropositivity in labor camp workers (OR: 2.7; 95% CI: 1.8–4.0), but not in the general population (OR: 1.5; 95% CI: 0.7–3.2) compared to healthcare workers adjusted for age, sex, region, education, nationality, ethnicity, occupation, and contact with a person diagnosed with COVID-19. This may indicate that seropositivity was associated with labour camp conditions such as congregate living and eating in densely populated areas, and not work in the transportation industry itself.

High HDI Countries

Poustchi et al. and Colmenares-Mejiad et al. both performed studies in countries with high HDI (Iran and Colombia, respectively) and found similar seroprevalences between transportation workers and other high-risk occupations (pharmacy workers, retail, health care workers, and other customer-facing staff) [20,21] indicating no increased risk of infection. Poustchi et al.'s study population was approximately 50% male, mostly between the ages of 30–49 and with no contact with confirmed COVID-19 patients. Serology results from a wide range of assays with differing sensitivities and specificities were reported across studies. Poustchi et al. used Pishtaz Teb SARS-CoV-2 ELISA kits which had not been fully assessed before this study and had the lowest sensitivity (66.9% in their validation study) compared to tests used in other included studies where the sensitivity was in the 90% range. Although they accounted for test performance in a sensitivity analysis, a low sensitivity could increase the number of false negatives and underestimate seroprevalence in this population. Tests with high sensitivity and specificity are required to ensure accurate estimation of seropositivity, especially when COVID-19 prevalence in the population is low. The median age of the study population used by Colmenares et al. was 37.4, 59.9% were female, and most were classified as having a socioeconomic status between 2–4 on a six-point scale. Almost all the studies focusing on the transportation industry were conducted in the first wave of the pandemic. However, Colemenares et al. performed their study during the transition period between the first and second waves in Colombia. They recruited participants over four months, a broad time frame during which transmission patterns and public health recommendations frequently changed. It

is possible that the staggered resumption of economic sectors and the effect of time could confound the effect of transportation use on seropositivity in this cross-sectional study.

Medium HDI Countries

In a state-wide survey of over 16,000 individuals in Karnataka, India, the population was divided into groups based on occupation risk [22]. Those that worked as bus conductors and auto drivers had twice the odds of seropositivity compared to low-risk individuals (e.g., those attending outpatient departments for minor ailments) (OR: 2.12; 95% CI: 1.28–3.51). The risk groups in this study were poorly defined and recruited from different populations. The low-risk group included only HCW and patients coming in for periodic care or visits to outpatient departments while the moderate and high-risk groups were chosen from the general population. This makes comparisons between groups challenging and reduces study generalizability.

Low HDI Countries

A Togolese study where almost 50% of the study participants worked in air or road transport found that there was no association between work in the transportation industry and seropositivity [23]. Most participants were male (71.6%), had a post-secondary education (51%), and were of Togolese nationality (98%). The overall seroprevalence in the study of 955

individuals was 0.9% (95% CI: 0.4–1.8). This sample size and low seroprevalence prohibited evaluation of the association with key variables.

Transportation Industry Trends

The majority of studies found that there was no association between work in the transportation industry and SARS-CoV-2 seroprevalence or that the risk of working in this industry was comparable to other occupations considered high risk. Of the studies conducted in countries with very high HDI, seroprevalence was only found to be associated with work in the transportation industry by one study [14] and those working in labour camps [19]. The economic inequality seen by those working in labour camps compared to the general population of Abu Dhabi may make this population more comparable with studies in the medium or low HDI category. Both studies conducted in countries with high HDI found seroprevalence was similar among high-risk occupations, while in countries with medium and low HDI results were inconsistent. The study population and restrictions imposed on economic sectors during the pandemic are key factors that should be considered when evaluating the transportation industry. Historically, the transportation industry has been male dominated which was reflected in several studies [19,23] and may limit generalizability of results. Public safety measures such as lockdowns and travel restrictions varied broadly between regions as the pandemic progressed and likely contributed to the heterogeneity of results. This also related to corporate policies as was noted by Airoldi where clusters of cases were found independent of a single industrial sector. Although some general trends were established,

results broadly varied between studies and no overall consensus was reached. This was likely implicated by the various study populations, sample methods, test specifications and timing of included studies.

2.5.2 Healthcare Workers

Healthcare worker (HCW) populations have been a focus of serosurveys due to their high rates of exposure to COVID-19 and the potential threat to patients and other healthcare workers if infected. Several studies have examined the occupational and environmental risks faced by HCW during the first wave of the COVID-19 pandemic, including commute via public transport with mixed results.

Very High HDI Countries

A cross-sectional study in a large group of HCW in Switzerland found a gradient of effect, where the proportion of individuals that tested positive for SARS-CoV-2 antibodies increased with the number of times they used public transit in a week. This study also found that wearing a mask while using public transit reduced the odds of seropositivity by 58.0% (OR: 0.42; 95% CI: 0.2–0.9) [24]. Soffin et al. found no association in one hundred forty-three surgeons and anesthesiologists in a specialty hospital in New York City [25]. The small sample included mostly young, white, educated males with few comorbidities which reflected a lower overall seroprevalence (9.8%) compared to other studies conducted in New York during this period

(27% and 23.6%; Venugopal and Pathela [14,26]). These results should be interpreted with caution as they may not be representative of the general population. A study evaluating a more representative population of HCW in New York during the same period identified a higher seroprevalence in those that walked to work compared to those that used private transportation. The study population included those over the age of 20, and had significant representation of Hispanic, Black, Asian, and Caucasian ethnicities. No association with mode of travel to work was identified when controlled for ethnicity, close contact with someone diagnosed or with symptoms of COVID-19, not wearing a face mask in healthcare or community setting, unprotected direct contact with infection secretions or excretions, and symptoms associated with COVID-19 infection (fever, cough, myalgia, ageusia, anosmia, nausea, diarrhea) [26]. This study also thoroughly described risk of exposure in concordance with CDC regulations [27], ensuring precise evaluation of risk. Two similar studies conducted in Japan following the first wave of the pandemic reported overall seroprevalence of less than 1% within their respective hospitals (0.7% Yamamoto; 0.43% Nishida) [28,29]. Although a large proportion of workers relied on public transit to travel to work, no association was found with mode of travel. Of note, seropositivity was lower in HCW compared to overall seropositivity measured in the public.

High HDI Countries

Two studies from high HDI countries were identified; both of which found no significant association between seropositivity and transit use in HCWs. The study populations were similar

where at least 60% were female and the majority were between 30–50 years of age. Cruz Arenas et al. performed their study in a private hospital not accepting COVID-19 patients, so it seems likely that the risk of exposure for HCW in this hospital would be lower than other locations accepting COVID-19 patients [30]. This evaluation had a relatively small sample size (n = 300) that was stratified into ten groups according to occupation thereby reducing statistical power compared to the other studies. De Olivieria et al. sampled primarily HCW working in COVID-19 units in São Paulo, Brazil [31]. However, did not clearly define risk of exposure according to frequency of contact with COVID-19 patients, instead classifying risk as high, medium, or low.

Medium HDI Countries

In contrast to the majority of studies focusing on HCWs, one prospective study conducted in India found seroprevalence was significantly higher in those that relied on public transportation (20.0%) or transportation provided by the hospital (16.9%) compared to private modes of transportation (12.0%). However, multivariate analysis was not conducted [32]. The authors speculated that seropositivity was highest in administrative staff and lowest in physicians due to better adherence to control practices. However, PPE use was measured by voluntary disclosure and not controlled for in a multivariate analysis.

Healthcare Worker Trends

All studies conducted in very high and high HDI countries found there was no association between mode of transport and seroprevalence in HCW, indicating that it is not a risk factor in these populations. It is possible that these regions have implemented effective emergency management procedures and PPE use that has protected employees from exposure. The single study that found an association with mode of transport in HCWs was conducted in India, a medium HDI country. This could be implicated with inefficient public transportation systems and mobility problems that are a product of India's increasing population density. This may lead to longer or more crowded commutes via public transit with increased risk of infection compared to studies conducted in other countries. There was consensus that seropositivity was higher in those with a household or community contact diagnosed with COVID-19 compared to those that encountered COVID-19 patients in the workplace, suggesting personal protective equipment (PPE) use and hospital policies have been effective in reducing the risk of infection in the workplace [25,27,28,31,32]. These combined findings could indicate HCW are diligently following mask wearing and physical distancing procedures while using public transit. However, this was not documented in most studies. All studies relied on retrospective self-reporting of symptoms associated with COVID-19 and PPE use which could introduce recall or reporting bias if participants do not report or are or unwilling to disclose any breach in protocol associated with PPE use. Similarly, the hospital disposition and number of COVID-19 patients accepted may impact risk of exposure and affect reported seroprevalence between studies. Reliance on

voluntary participation within hospitals could introduce response bias if those with higher risk of exposure are the ones volunteering to participate.

2.5.3 Population-Based Studies

Well-designed population-based serosurveys can offer more representative findings and more accurate estimate of overall and subgroup infection risk. Several national or state-wide serosurveys have been conducted at different stages of the pandemic to estimate the extent of infection and identify risk factors among the population, including use of public transit.

Very High HDI Countries

Two population-based studies of representative samples were conducted in the United States between May and July 2020, one in Rhode Island [33], and another in Connecticut [34]. Chan et al. found higher seroprevalence in those that relied on public transit (6.0%) compared to those that used a private vehicle (1.9%) and those that walked/biked (2.8%) [33]. Mahajan found no association between transit use and seropositivity in the general population. Of note, public transit use was low (3.4%). However, a greater proportion used public transit in a subgroup of non-Hispanic black and Hispanic participants and the seroprevalence was considerably higher (23.7%) in black transit users [34]. Non-response bias may threaten the validity of results given response rates as low as 11% and 7% in each study, respectively. Chan found response rates lower in men, those under the age of 35, and non-whites. Mahajan did not perform an analysis

on those that did not respond but did consider the nonresponse rate when weighting the sample. The potential to introduce bias is high if those that are more likely to test seropositive such as racial minorities have higher non-response rates.

High HDI Countries

A provincial-wide serosurvey in Ecuador during the same period determined that the odds of seropositivity associated with transportation use in a bivariate analysis was 1.73 (95% CI: 1.4–2.2) [35]. This study did not consider assay sensitivity/specificity but did adjust for key covariates (age, gender, having enough resources for living, household COVID-19 contact, contact with the flu, number of occupants in house, physical contact with someone with COVID-19), which did not change the results. In this study the seroprevalence was highest in those using public transit (bus/taxi) (18.2% (95% CI: 15.5–21.2)) compared to those who walked (12.5% (95% CI: 9.6–15.5)), used a bicycle/moto/trolley car (11.3% (95% CI: 6.2–19.3)), or private car (11.0% (95% CI: 9.0–13.1)).

Medium HDI Countries

A national scale study of over 10,000 participants assessed the spread of infection in India from August to September 2020 [36]. Results revealed that those using public transport were almost twice as likely to have antibodies to SARS-CoV-2 compared to those using private transport (OR 1.79; 95% CI: 1.4–2.2). However, the authors did not consider the sensitivity/specificity of the

antibody assays utilized or adjust for demographic characteristics which could affect validity of results.

Population-Based Study Trends

The two studies conducted in very high HDI countries had opposing results, likely a result of differing population demographics and test methods. Mahajan was the only study that found transit use was not associated with seropositivity in the general population, but did find SARS-CoV-2 seroprevalence considerably higher in black and Hispanic transit users [28]. Although conducted in two very different locations, the studies conducted in high and medium HDI countries both found that public transit users were almost twice as likely to have antibodies for SARS-CoV-2. This indicates that transit use is likely a risk factor for SARS-CoV-2 infection for the general population regardless of region. Most studies relied on random sampling weighted by census data to obtain a representative sample. It can be difficult to obtain a representative population sample of elderly and young adults using household surveys and census information. Young adults have higher mobility and may be officially registered to live in their parents' home but have relocated elsewhere. Public health measures and timing of lockdowns within communities may alter the estimated seroprevalence between studies. Acurio-Páez et al. performed their study while restrictions were relaxed and almost all activities were operating normally [35]. They reported over 90% adherence to physical distancing and mask wearing preventative measures, although reporting bias may be prevalent as adherence was measured by voluntary disclosure. In contrast, Chan et al. performed their study during a time of strict

lockdown with mandated mask use, where adherence to COVID-19 preventative measures was unknown or not reported [33]. Observing preventative safety measures and adhering to lockdown protocol has been proven to reduce SARS-CoV-2 transmission, and likely the risk of exposure to the public. This could explain why overall seropositivity measured by Acurio-Páez et al. was more than 10% higher than what was found by Chan.

2.5.4 Race and Ethnicity

Race and ethnicity are potential confounding variables when analyzing the relationship between transit use and seropositivity as there are complex interactions between occupational, social, and structural inequalities that increase the risk of COVID-19 in minority communities. Several studies examining socioeconomic factors and spatiotemporal transit use across neighborhoods have shown that decline in magnitude of ridership seen throughout the COVID-19 pandemic is much lower in people of color, those with less education, and lower income [2–4]. Black and Hispanic Americans make up a large proportion of the essential workforce, in jobs that require travel and public interaction (i.e., service industry, transportation, health care, cleaners, or seasonal workers) [37]. They are also less likely to own personal cars and require access to public transportation to get to school, work and access essential services such as childcare throughout the COVID-19 pandemic [38]. Several of the studies were conducted in a local population with low diversity [23,35] or did not report information on race or ethnicity [20–22,30–32,36]. Pollan et al. and Alsuwaldi et al. found that seroprevalence was lower in those of native nationality compared to other nationalities [16,19]. Five of the six studies

conducted in the United States sampled a diverse population and found that non-Hispanic black and Hispanic individuals had higher seroprevalence for SARS-CoV-2 antibodies compared to white individuals [14,15,26,33,34]. Venugopal et al. and Pathela et al. both conducted studies during the first wave of the pandemic in New York City and concluded that black and Hispanic individuals were almost twice as likely to have evidence of infection compared to white participants [14,26]. Pathela et al. estimated that the seropositivity in Hispanics was 35.3% (95% CI: 34.4–36.2) and 33.5% (95% CI: 32.0–35.1) in non-Hispanic black compared to non-Hispanic white 16.0% (95% CI: 15.5–16.6). In a regression analysis adjusted for sex, age, area of residence and level of poverty, the risk of seropositivity was almost twice as high in black and Hispanic individuals compared to non-Hispanic white individuals (RR: 1.83; 95% CI: 1.7–1.9 and RR: 1.84; 95% CI: 1.8–1.9), respectively [14]. Very similar results were found by Venugopal et al., where Hispanic and black individuals were more than twice as likely to test positive for SARS-CoV-2 antibodies compared to white participants in unadjusted OR of 2.42 (95% CI: 1.3–4.5) for Hispanics and 2.55 (95% CI: 1.3–5.0) for black participants [26]. These disparities disappear when added to a multivariate analysis that adjusts for ethnicity, mode of travel, moderate or high risk of community or occupational exposure, and symptoms attributable to COVID-19 infection.

2.6 FACTORS ASSOCIATED WITH SEROPOSITIVITY

Overall seroprevalence for SARS-CoV-2 antibodies varied geographically within single studies, where sampling techniques and testing procedures remained consistent. This indicates that regardless of methodology, risk of exposure, demographic variables, and population density likely contribute to risk of SARS-CoV-2 infection. The effect of population density was measured in several studies and revealed a clear relationship between increasing number of people in a region or household and seropositivity for SARS-CoV-2 antibodies. Similarly, higher seroprevalence was found in urban settings where quarantine and separation from household members may not be realistic. An association between flu-like symptoms and SARS-CoV-2 antibody prevalence was consistent across studies. Common symptoms included ageusia, anosmia, fever, diarrhea and olfactory alterations. Comparable to results found in more extensive systematic reviews [7,39], most studies found no association between sex and seropositivity for SARS-CoV-2 antibodies.

Inherent differences between countries with high and low HDI relate to how citizens are impacted by COVID-19 and contribute to the heterologous results of this evaluation. In countries with lower HDI, inadequate housing may make physical distancing and quarantine impractical. There is a large amount of informal economic activity where workers are paid on a daily wage, are self-employed or are involved in informal organizations [40]. A greater proportion of these workers have no choice but to work outside the home during the pandemic, often in hazardous conditions which could lead to greater seroprevalence for SARS-

CoV-2. Not all reviewed studies conducted in lower HDI countries reported higher seroprevalence. This could indicate lack of testing capacity or insufficient sampling techniques caused by lack of organization in informal industries. Countries with higher HDI generally experienced higher burdens of COVID-19 earlier in the pandemic [41]. These countries have greater contributions to the global economy encouraging business and tourism travellers that potentiate the spread of infectious disease. This was especially true early in the pandemic prior to the introduction of travel restrictions. Similarly, developed urban areas have widespread and efficient domestic transport systems that support connectivity but also facilitate COVID-19 transmission. Compared to lower HDI countries, higher HDI countries have a higher proportion of elderly people, putting them at greater risk of severe outcomes and mortality [42]. In Asian countries, masks are often worn during influenza season. This may have translated to greater adherence to COVID-19 public safety measures such as mask wearing during public transit use compared to other countries where mask wearing is a novelty. This might explain why COVID-19 seroprevalence was lower in Japanese studies.

2.7 STUDY LIMITATIONS

Several common limitations were observed across included studies. Most were observational cross-sectional studies. As such, they cannot be used to establish temporal association or causality. Cohort or longitudinal studies would be beneficial to analyze the change in seroprevalence and detect seroconversion that could be missed due to early testing or delayed antibody response. Longitudinal studies in particular are required to measure the effect of vaccination rates and introduction of new variants that were not captured in any of the included studies. Many of the studies relied on voluntary participation for recruitment. This method has the potential to introduce bias if those with COVID-19 symptoms are more likely to participate. This concern was evaluated by Pathela et al. who determined that 60% of participants had previous symptoms of COVID-19. Almost all studies relied on self-reported questionnaires to determine transit use and demographic characteristics. This method is prone to self-report bias as participants may provide inaccurate responses to preserve social desirability or control perception of themselves. Alternatively, if questions are ambiguous or wording is not inclusive to all reading levels, participants may interpret questions differently leading to inconsistencies in results. The validity of serosurveys has been questioned due to inconsistent sampling techniques and assay accuracy. High-quality serosurveys use validated tests, standardized lab methods and correct for demographic characteristics and test performance in seroprevalence estimates [43]. Several of the studies included in this analysis did not define the cut-off value used to estimate positivity, which could impact the calculated specificity and result in inaccurate seroprevalence estimates [44]. Similarly, an assortment of

serological tests with their own sensitivities and specificities were used to estimate seroprevalence making comparison between studies difficult. Furthermore, the lack of reference samples in the early days of the pandemic complicated assay calibration and standardization. Serosurveys may not capture all past infections due to variations in antibody kinetics such as time to seroconversion, duration of antibody response and rate of antibody waning. Cross-reactivity with common human coronavirus strains and other respiratory viruses is also a concern based on the assay and protein used and could impact seroprevalence results [45–47].

This rapid review has several limitations. Most included studies were conducted during the first wave of the pandemic. There are several reasons for this. Many seroprevalence studies were conducted at the beginning of the pandemic to better understand risk factors for this novel disease. Studies were also limited to only include those conducted before the emergence of the Omicron variant. Omicron has vastly different epidemiological characteristics and COVID-19 restrictions have changed with time, so these studies were excluded to improve comparability of results. Another limitation was the presence of several confounding factors that influenced the evaluation of the effect of public transportation use and seroprevalence of SARS-CoV-2. Results of seroprevalence studies are time-dependent and vary based on the location and type of test method. Therefore, conclusions from individual studies reflect the context of each region and may not be applicable to predict seroprevalence in neighboring regions. This limitation reflects the heterogeneity of findings found in this review and other seroprevalence studies worldwide and should be expected as a natural circumstance of the pandemic. Although

there are limitations, results from seroprevalence studies do show general trends in levels of population exposure and can help disentangle confounding factors to help identify risk factors as the pandemic evolves.

2.8 CONCLUSION

Most studies focusing on industry risk factors found no association between SARS-CoV-2 seroprevalence and work in the transportation industry, or that the risk of infection was no higher than other high-risk occupations. However, findings were not universal with conflicting results found in several studies. In HCWs, there was a consensus that mode of transport was not associated with SARS-CoV-2 seroprevalence. In population-based studies, use of public transit was generally associated with higher seropositivity and was implicated by race and ethnicity. A major limitation of these findings was that results could not be generalized due to the involvement of several confounding factors. Of the few studies that considered this topic, results varied based on study population, sociodemographic characteristics, type of assay used, sampling strategies, statistical analysis techniques, occupational hazards and timing of economic closures. However, several studies did report that SARS-CoV-2 seroprevalence was higher in transit users and results from these individual studies should be deliberated. Policy makers should consider transit use a risk factor when planning, implementing, monitoring, and improving strategies for reducing SARS-CoV-2 transmission. In regions where seroprevalence was associated with transit use in transportation workers, employers and policy makers may consider enforcing stricter adherence to public safety measures or implementing additional measures to protect employees. Similarly, across all studies seroprevalence was found to be higher in ethnic minorities and areas with lower socioeconomic status. Policy makers and practitioners should be aware that these populations may have higher rates of exposure and

may be more severely impacted by SARS-CoV-2. Further high-quality studies focused solely on this topic are required, as are longitudinal studies as the COVID-19 pandemic progresses.

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CHAPTER 3

Seasonal respiratory virus circulation was diminished during the COVID-19 pandemic

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Article preface: This article aims to assess the effect of the SARS-CoV-2 pandemic on seasonal respiratory virus activity in the Ottawa region and addresses the third thesis objective.

3.1 ABSTRACT

Measures introduced during the COVID-19 pandemic intended to address the spread of SARS-CoV-2 may also influence the incidence of other common seasonal respiratory viruses (SRV). This evaluation reports laboratory-confirmed cases of common SRV in a well-defined region of central Canada to address this issue. Surveillance data for common non-SARS-CoV-2 SRV in Ottawa, Canada, was provided by the Eastern Ontario Regional Laboratory Association (EORLA) reference virology lab. Weekly reports of the number of positive tests and the proportion that yielded positive results were analyzed from August 26, 2018, to January 2, 2022. A drastic reduction in influenza and other common SRV was observed during the 2020–2021 influenza season in the Ottawa region. Influenza was virtually undetected post-SARS-CoV-2 emergence. Rhinoviruses and enteroviruses were the only viruses that remained relatively unaffected during this period. We speculated that the introduction of nonpharmaceutical measures including masking to prevent SARS-CoV-2 transmission contributed to the near absence of SRV in the Ottawa region. These measures should remain a key component in addressing spikes in SRV activity and future pandemics.

3.2 INTRODUCTION

Since emerging in late 2019, SARS-CoV-2 has caused unprecedented morbidity and mortality worldwide. Public health policymakers have implemented nonpharmaceutical public health measures to mitigate SARS-CoV-2 spread including the use of face coverings, targeted lockdowns and stay-at-home orders, physical distancing, school closures, restricted international travel, mandated quarantine, and reduced close contacts. In Ontario, most of these measures were put into place from March 12 to 30, 2020. Testing regulations and access to testing varied by stage of the pandemic and availability of tests. Influenza, RSV, and other common respiratory viruses typically follow predictable seasonal patterns with high activity levels in the winter months. Australia and New Zealand saw a 98% decrease in influenza incidence during the 2020 peak influenza or “flu” season. Reduced activity was also reported for common respiratory illnesses such as the respiratory syncytial virus (RSV); seasonal human coronaviruses (HCoV); parainfluenza virus types 1, 2, 3, and 4 (PIVs); and human metapneumovirus (HMPV). Irregular seasonal behavior was observed in enteroviruses (EV), adenoviruses (AV), and rhinoviruses (RV) throughout the Southern Hemisphere [1,2]. Similar patterns were observed throughout the winter influenza season in the Northern Hemisphere. Minimal influenza and RSV activity were reported during peak seasons in the UK and Europe, where most respiratory illness-related healthcare visits were accredited to COVID-19 [3]. Surveillance data from the United States showed that influenza and RSV were circulating at historically low levels from March 2020 to May 2021. HCoV, PIV, and HMPV activity decreased in March 2020 and remained low through May 2021, after which HCoV and PIV rose to

prepandemic levels. The increase in HCoV, RSV, and PIV in the spring of 2021 was inconsistent with historical seasonal peaks usually observed in the winter months. RV and EV activity decreased in March 2020 but returned to pre-pandemic levels in May 2020 [4]. A study utilizing Canadian surveillance data reported an absence of most respiratory viruses including influenza A, influenza B, and RSV during 2020–2021. The exception was enteroviruses and rhinoviruses, which were continuously detected throughout the pandemic [5]. This evaluation utilized surveillance data to evaluate the effect of SARS-CoV-2 pandemic countermeasures on seasonal respiratory virus circulation in the Ottawa region. Ottawa is a diverse city consisting of a broad spectrum of communities and socioeconomic conditions. Consequently, we believe that our results are broadly applicable to developed world settings.

3.3 METHODS

Design and setting

This observational study was conducted using publicly available surveillance data from the Ottawa region. The catchment area included the 1.3 million people living in the Champlain region, Ontario's most eastern Local Health Integrated Network (LHIN). The Champlain region population is concentrated in the city of Ottawa and also spans east and west sharing a 465 km border with Quebec. This region is ethnically and linguistically diverse; 19.8% identify French as their first language, and at least 2.8% are recent immigrants [6]. The vast majority of samples were obtained from patients assessed at The Ottawa Hospital and Children's Hospital of Eastern Ontario (CHEO) there by capturing both adult and pediatric population data.

Data sources

Specimens were collected from the Champlain region population and submitted to the Eastern Ontario Regional Laboratory Association (EORLA) regional reference virology lab based at CHEO. These data are in the public domain and circulated weekly to several sources including the Public Health Agency of Canada (PHAC) as part of the Respiratory Virus Detection Surveillance System and FluWatch report [7]. All data included in this analysis were obtained from publicly available de-identified datasets. As such, ethics board and laboratory approval were not required.

Measures/variables

Respiratory viruses of interest included: influenza A, influenza B, respiratory syncytial virus, parainfluenza viruses 1–4, human metapneumovirus, seasonal human coronaviruses (HCoV-229E, HCoV-OC42, HCoV-NL63, and HCoV-HKU1), adenovirus, enterovirus, rhinovirus, and SARS-CoV-2. Health Canada-approved assays were used for viral detection. Almost all tests were multiplex reverse transcriptase real-time PCR assays, except for one SARS-CoV-2 assay that was a TMA-based nucleic acid amplification assay. Most samples were collected using nasopharyngeal swabs or bronchoalveolar lavage (BAL). The cycle threshold (Ct) value and gene target varied by test. A description of the tests used for each virus can be found in Table 3.1. Data from non-SARS-CoV-2 respiratory virus activities were reported weekly from August 26, 2018, to December 26, 2021. SARS-CoV-2 data were reported from August 26, 2020, to December 26, 2021. Influenza season was defined as from the beginning of November to the end of April. A case was defined as a laboratory confirmed positive test foreach respiratory virus. Percent positive values were calculated as the number of tests that yielded positive results divided by the total number of tests performed for a given week expressed as a percentage for each virus.

Table 3.1. Types of tests used to measure the seroprevalence of each respiratory virus. Location of where testing was performed within the catchment area and contextual factors and restrictions in place that may have impacted the measured seroprevalence of SARS-CoV-2 and common respiratory viruses in the Ottawa region.

Virus	Type of test used	Location	Testing Restrictions
Influenza A Influenza B RSV	-Hologic FluA/B/RSV assay -Luminex Aries FluA/B/RSV assay	-Testing performed for some of the community hospitals (QCH, Montfort, Glengarry, Cornwall, Hawkesbury, Renfrew) in addition to TOH and CHEO	-Largely unrestricted. Testing was almost always performed if it is requested.
HMPV Endemic HCOVs Enterovirus Rhinovirus Adenovirus Parainfluenza viruses (1-4)	-Allplex respiratory virus panel 2 -Allplex respiratory virus panel 3	->99% of requests are from TOH and CHEO	-Mid 2020 onwards, most hospitalized patients were not tested for respiratory viruses other than influenza A, influenza B, RSV, SARS-CoV-2 -Testing was restricted and must be approved by a microbiologist unless ordered by ID
SARS-CoV-2	-Allplex 2019-n CoV assay -Cobas SARS-CoV-2 assay -Aptima SARS-CoV-2 assay -Fusion SARS-CoV-2 assay	-Entire catchment area	-Subject to local and provincial guidelines

CHEO: Children's Hospital of Eastern Ontario; HCoV: Human coronavirus; HMPV: Human metapneumovirus; QHC: Queensway Carleton Hospital; RSV: Respiratory syncytial virus; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; TOH: The Ottawa Hospital

Statistical methods

The number of positive laboratory results and the percent positive value of each virus were summarized using combination line and bar graphs. Enterovirus and rhinovirus data were reported as a single value. Data for parainfluenza virus types 1–4 were combined and presented in one chart due to the trivial number of reported cases.

3.4 RESULTS

An overview of the number of non-SARS-CoV-2 specimens submitted to the EORLA laboratory for testing and the number of positive results for each virus from 2018 to 2021 is provided in Figure 3.1. From the beginning of November to the end of April, approximately 7300 specimens were tested in the 2018–2019 season, 1800 in 2019–2020, and 9800 in 2020–2021. Viral peaks largely consisting of influenza and RSV occurred from November to February of the 2018–2019 and 2019–2020 winter season. An obvious absence of viral respiratory illness was reported from March 2020 onward including during the typical flu season of 2020–2021. Enterovirus and rhinovirus returned to endemic levels in August 2020, whereas viral activity for other respiratory illnesses remained low. RSV resumed prepandemic activity levels in September 2021. The number of positive specimens and the percent of specimens that tested positive for each respiratory virus are described in Figure 3.2. Influenza A was dominant in the 2018–2019 winter season and both influenza A and B were prominent in the winter of 2019–2020. Influenza activity was negligible following the onset of the COVID-19 pandemic in March 2020 (Figure 3.2a). The RSV season in Ontario and North America in general usually starts between November and January and generally lasts 3–4 months [8]. Besides an absence of activity in 2020–2021, standard RSV seasonality was observed throughout the study period (Figure 3.2b). HMPV was observed at consistently low levels from December 2018 to June2019 and December 2019 to February 2020. No activity was observed in March 2020 and one spike in detection was recorded in February 2021 (Figure 3.2c). Typical endemic coronavirus seasonality consistent with pre-COVID-19 seasonal norms occurred in the 2018–2019 season with a peak from

December to February and continued activity into early spring of 2019. Reduced incidence was detected the following winter with few positive cases and no activity identified over the 2020–2021 winter. Following several atypically early cases of HCoV in the spring of 2021, HCoV began to increase to prepandemic levels in the winter of 2021–2022 (Figure 3.2d). Enterovirus and rhinovirus activity remained largely unchanged by the COVID-19 pandemic aside from a brief period from March 2020 to July 2020, in which few cases were detected. A spike of positive specimens in August 2020 preceded a return to prepandemic levels of viral activity (Figure 3.2e). Two positive cases of adenovirus were detected from March 2020 to September 2020, after which approximately one case was found every few weeks, analogous to prepandemic incidence rates (Figure 3.2f). In 2018–2019, parainfluenza activity was highest from February to June. Reduced activity was seen in the 2019–2020 season, with no positive cases detected in the peak 2020–2021 winter season. Parainfluenza activity returned to prepandemic levels in June of 2021 (Figure 3.2g). The reduction in common respiratory virus activity coincided with an increase in SARS-CoV-2 activity that began in August 2020 (Figure 3.2h).

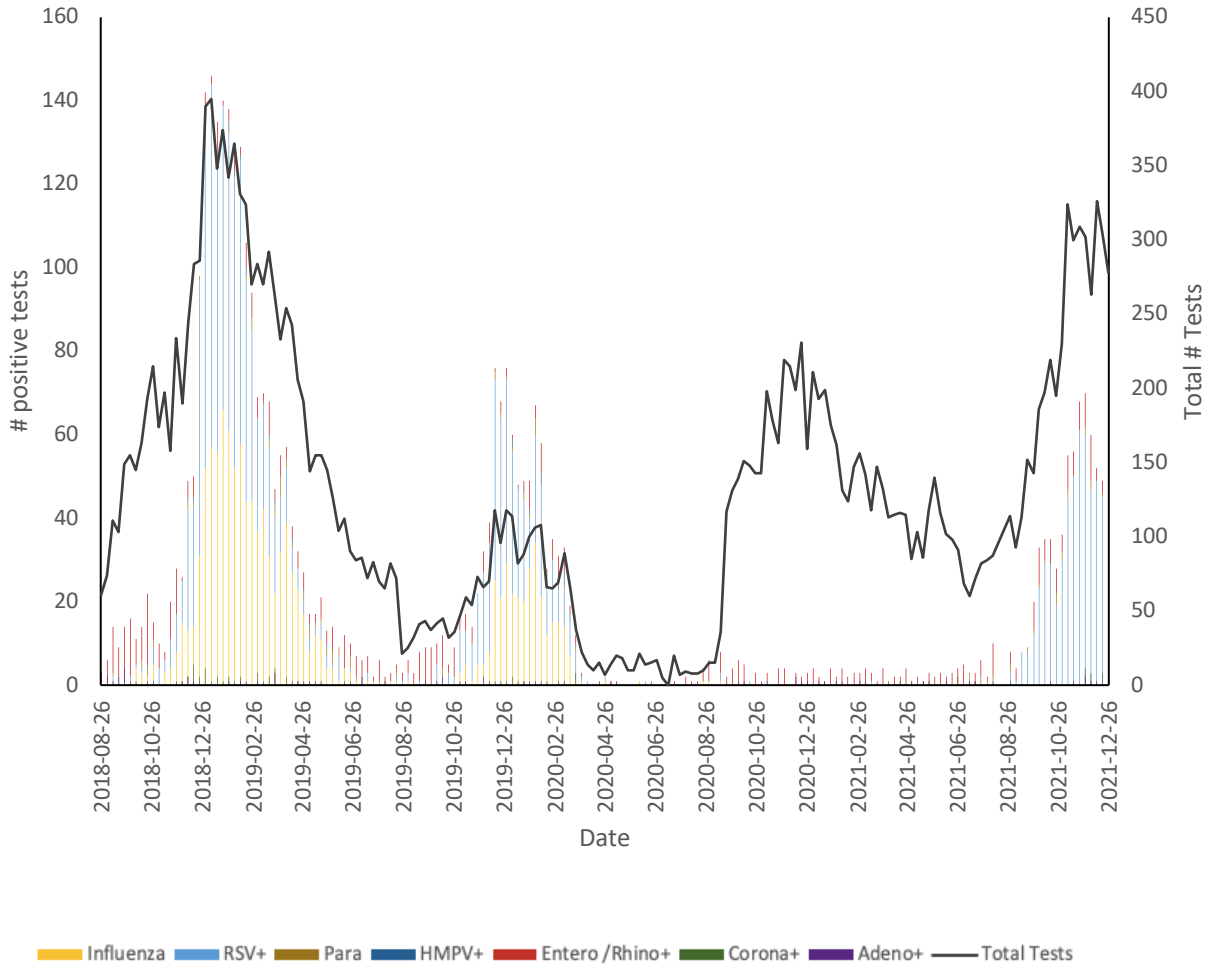
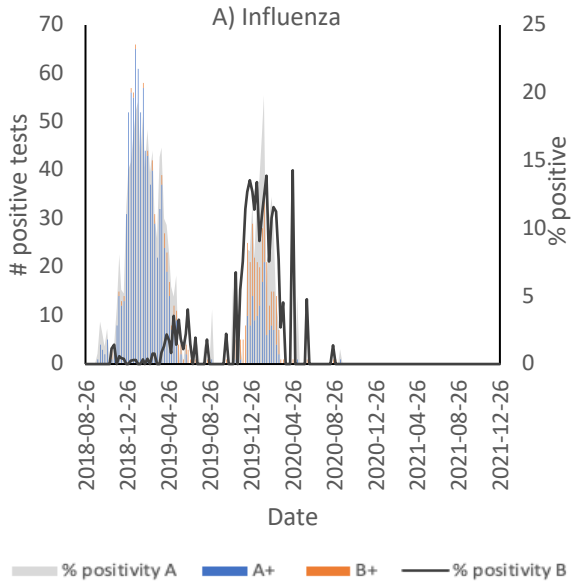
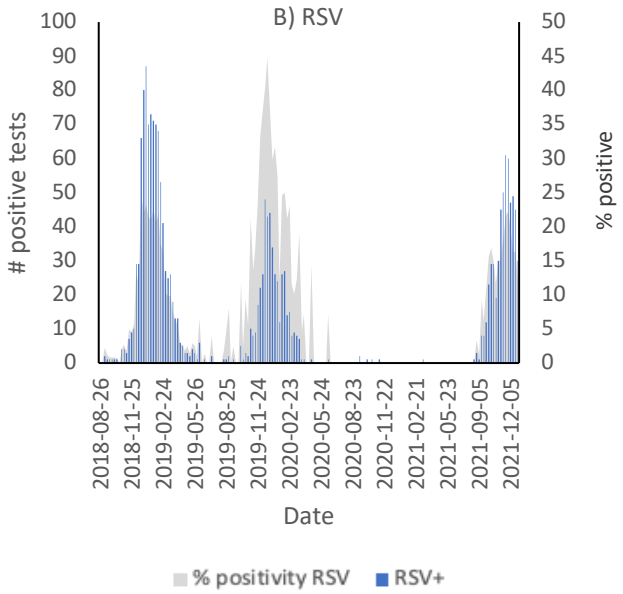
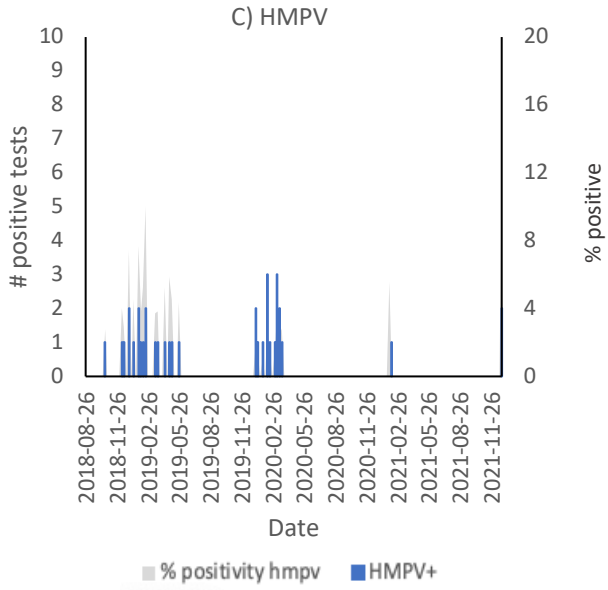
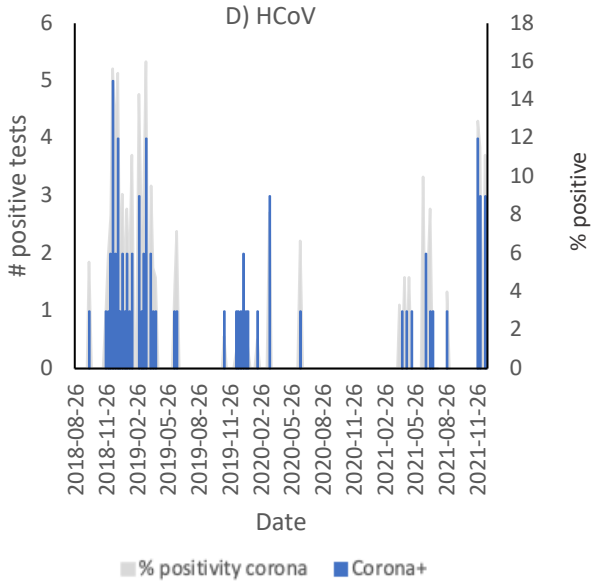


Figure 3.1. Total number of tests performed and number of positive common respiratory virus cases collected weekly in the Ottawa region.


A) Influenza
positive tests
% positive
Date
% positivity A
A+
B+
% positivity B


B) RSV
positive tests
% positive
Date
% positivity RSV
RSV+


C) HMPV
positive tests
% positive
Date
% positivity hmpv
HMPV+


D) HCoV
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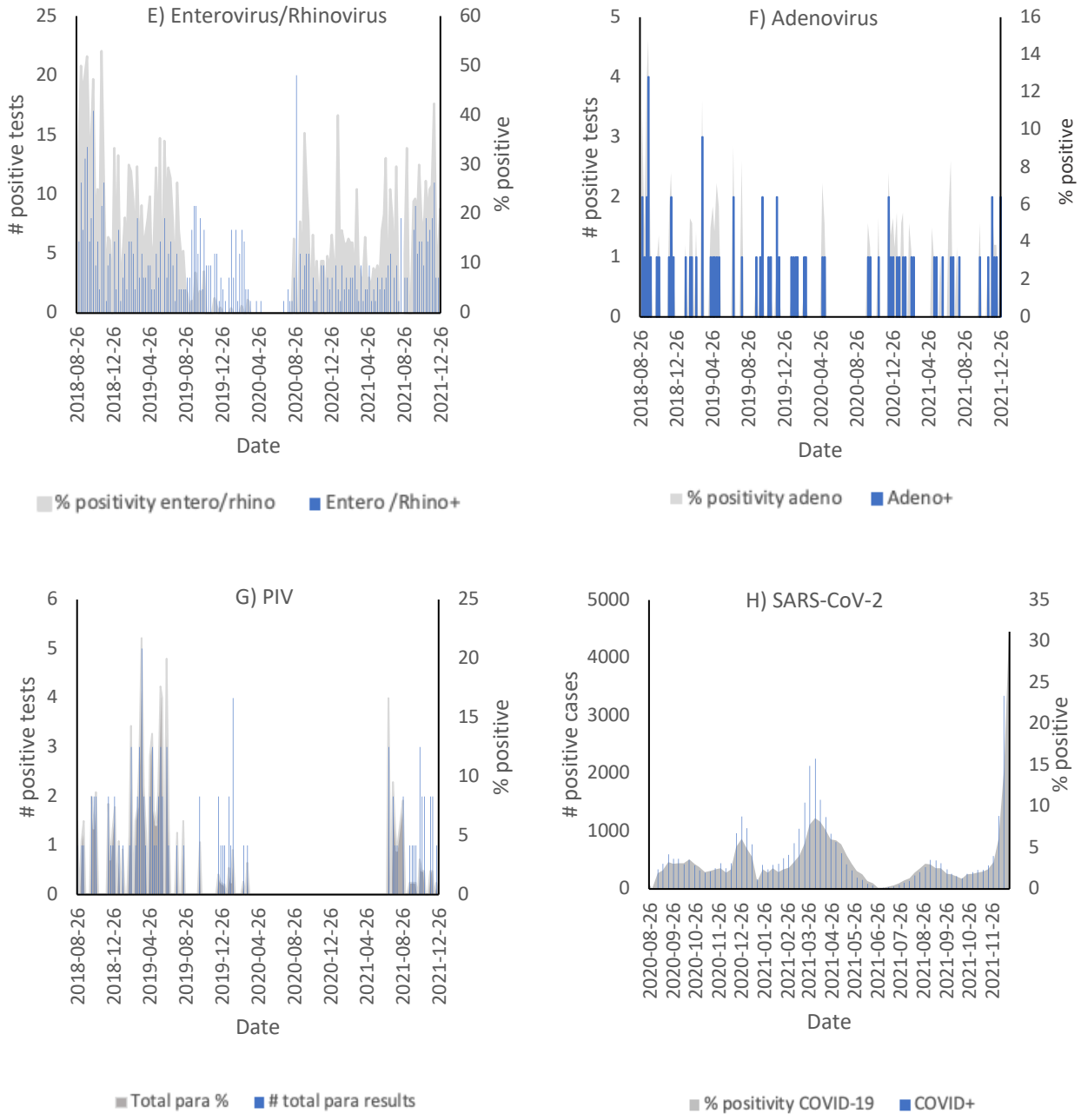

Figure 3.2: Number of positive tests and proportion of submitted tests that yielded positive results for influenza A and B, respiratory syncytial virus, human metapneumovirus, endemic human coronaviruses, entero/rhinoviruses, adenoviruses, parainfluenzas 1-4, and COVID-19 collected weekly from the Ottawa region. The shaded regions and line (3.2a) represent the test positivity as a percent. The bars represent the number of positive test results reported each week.

3.5 DISCUSSION

A clear absence of surveyed non-SARS-CoV-2 activity was observed beginning in March 2020, which lasted until August 2021. This timeline coincides with the introduction of public health measures in the Ottawa region and suggests that these measures implemented to mitigate SARS-CoV-2 transmission effectively reduced cases of seasonal respiratory viruses in the region. Consistent with trends observed worldwide [2,5,9,10] influenza and RSV saw the greatest decline in activity. Influenza has been practically undetected in the region since the onset of the COVID-19 pandemic. RSV was absent during the 2020–2021 season but returned to pre-pandemic levels the following season. There are several reasons as to why COVID-19 mitigation measures have proven to be highly effective against common respiratory viruses such as influenza compared to SARS-CoV-2. Although influenza and SARS-CoV-2 are both spread through droplet transmission, influenza has lower transmissibility (R0=1.3) compared to the ancestral strain of SARS-CoV-2 (R0=2.0–4.0) [11]. Consequently, measures including mask wearing and physical distancing may be more efficient at preventing influenza transmission [4]. Further, a degree of immunity to common respiratory viruses is already present in the population. A higher dose exposure and persistent viral load may be required for common respiratory infections to flourish compared to the novel SARS-CoV-2, which may have a competitive advantage in an immunologically naïve population [3]. In accordance with other jurisdictions, our evaluation also observed atypical HCoV and PIV activity. Children have been known to propagate respiratory illness to their households and communities, so it is possible that school closures may have blunted viral outbreaks that usually occur in the fall and winter

[4,12]. Reopening of schools is likely a key explanation for the reappearance of RSV to pre-pandemic levels in the fall of 2021. Rhinoviruses, adenoviruses, and enteroviruses remained relatively unaffected by the COVID-19 pandemic in this study and worldwide [3–5,9]. This persistence may be attributed to varied modes of transmission compared to SARS-CoV-2, higher survival time on surfaces, or lack of envelope, which could provide protection against sanitizing and handwashing behaviors. Although there is compelling evidence that public health measures have reduced seasonal respiratory virus activity alternative hypotheses should be considered. Additional theories include the vast immunologic naivety of the host population and the capabilities of SARS-CoV-2 as a pathogenic competitor. Interferon-stimulated immunity caused by a viral infection can provide nonspecific interference, deferring other viruses from establishing in a population [13–15] Interference is thought to limit coinfection rates and contributes to the seasonality of common respiratory viruses including influenza [8]. It is possible that the presence of SARS-CoV-2 is outcompeting other viruses in the respiratory tract, delaying future outbreaks of respiratory viruses. However, these theories require more robust research in the application to SARS-CoV-2. Seasonal coronaviruses and SARS-CoV-2 share over 30% sequence homology in the S2 subunit, which may result in overlapping immune epitopes [16]. Some studies have indicated that previous infection by seasonal HCoVs reduces the risk of infection and severity of SARS-CoV-2 [16–18]. Other studies have suggested that vaccination or natural infection by SARS-CoV-2 may boost antibodies and protect against endemic coronaviruses [18–25]. These views are not universal and conflicting findings argue that antibodies may be increased but do not provide protection from infection or hospitalization [26]. Frequent recombination [27,28] and waning natural immunity [29] characteristic of the

HCoV family suggest that any cross-immunity provided by infection or vaccination will not be strong enough to prevent future infections or inhibit seasonal HCoV circulation. Data from this study support the hypothesis that cocirculation of endemic coronaviruses and SARS-CoV-2 is possible, as seasonal HCoV activity returned to the Ottawa area in April 2021 despite ongoing waves of COVID-19 infection. However, atypical seasonality was observed, which may reflect the effects of cross-protection or viral interference. Further studies will hopefully fully elucidate the effect of SARS-CoV-2 on seasonal HCoV circulation and the complex immunological interactions between the two.

As measures are relaxed and vaccination is increasingly relied upon to control COVID-19, the resurgence of respiratory viruses is expected and already occurring in some locations [1]. Reduced transmission over the past 2 years has distorted the pool of susceptible individuals and may change the epidemiology of respiratory viruses for years to come. Early exposure and frequent stimulations early in life train the immune system to effectively respond to threats and have been linked to a fortified immune response in adulthood. Lack of immune stimulation caused by nonpharmaceutical public health measures over the past 2 years may result in immune deficits in children with negative consequences when the pandemic resolves [30]. Opening international borders and increasing human mobility may also stimulate viral circulation as influenza transmission and seasonality have been partially attributed to international travel [31]. Although rare, co-infection by influenza and SARS-CoV-2 has been shown to result in an increased risk of severe illness and death (RR:5.92; 95%CI:3.21–10.91) compared to patients with neither [14]. Testing for influenza and other respiratory viruses

should remain a priority. The COVID-19 pandemic has demonstrated that nonpharmaceutical interventions are an important component in controlling viral transmission that may also be applied to seasonal respiratory virus outbreaks. Reinstating mask mandates or social distancing during influenza season or in high-risk environments such as schools is anticipated to reduce transmission or even prevent future outbreaks of common respiratory viruses. The pandemic has also illustrated that remote work or school is feasible in some industries and supports social distancing theories. Now that the infrastructure is available, employees and students may be encouraged to stay home if they are feeling ill, reducing the risk of viral outbreaks in schools or workplaces. Clinicians should also be aware of an increase in respiratory virus activity that does not follow recurrent norms and encourage influenza vaccination.

This analysis is subject to several limitations. Due to the ecological nature of this study causation cannot be inferred. However, these findings are substantiated by a growing body of evidence that has documented similar patterns and suggest that public health measures meant to prevent SARS-CoV-2 transmission have interfered with seasonal respiratory virus activity worldwide [2–5,9,10]. It is possible that reduced testing and redirected patient flow underestimated viral activity. Those experiencing viral respiratory illness may have been sent to COVID-19-specific test sites instead of usual care where surveillance occurs. There was a short period during the summer of 2020 when testing using the extended respiratory virus panel (extended respiratory panel of all viruses excluding SARS-CoV-2, influenza A, influenza B, and RSV) was suspended to cope with COVID-19. This may have resulted in an underestimation of the true number of cases. More detailed information on contextual factors that may have

influenced the number of tests completed can be found in Table 3.1. Others may have been hesitant or incapable of accessing usual care or testing services amid lockdowns and COVID-19 precautions. CHEO received 34% more specimens in the 2020–2021 influenza season compared to the 2018–2019 influenza season, so it is unlikely that testing capacity largely underestimated viral activity for influenza A, influenza B, or RSV. No seasonal spikes in influenza incidence, RSV hospital, and ICU admissions were observed, which also supports the proposal that findings truly represent reduced community circulation. Relatedly, Australia had more liberal testing criteria than Canada and still found only 33 positive influenza tests out of 60,031 tested specimens during peak season [2]. Another limitation was that the influenza vaccination rate was not measured in this evaluation. Findings from the 2020–2021 Canadian Seasonal Influenza Vaccination Coverage Survey indicated that influenza vaccination coverage in the 2020–2021 season (40%) was slightly reduced to the 2019–2020 season (42%) and 2018–2019 season (42%) [32]. The COVID-19 pandemic has enforced pre-existing preferences and trepidations surrounding influenza vaccination [33]. Misinformation and spill-over of COVID-19 vaccine hesitancy may have reduced influenza vaccination rates [33-35]. Additionally, COVID-19 vaccine fatigue defined as an individual's inaction towards vaccine information is due to perceived burden or burnout [36] may impact influenza vaccination rates. As vaccination rates were not measured in this study, the exact proportion of the population vulnerable to infection is unknown and may have affected reported influenza infection rates. Finally, the surveillance data used in this analysis may not be fully representative of the Ottawa population at risk for RV infection as not all viral testing occurred at the CHEO virology laboratory. Individuals tested for SRVs through the Public Health Ontario Laboratory were not captured in these data.

3.6 CONCLUSION

This study describes a near absence of seasonal respiratory viruses in the Ottawa region for the 2020/2021 respiratory virus season. Findings from this study add to a growing body of evidence that suggests that public health measures introduced to prevent the spread of SARS-CoV-2 have also reduced laboratory-confirmed seasonal respiratory virus infections. These measures should continue to be strategically utilized to prevent, or at least diminish, the burden of future seasonal respiratory virus spikes and in response to further pandemics.

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CHAPTER 4

Reduced seasonal coronavirus incidence in high-risk population groups during the COVID-19 pandemic

Article preface: The aims of this study were to examine the incidence and prevalence of SARS-CoV-2 and seasonal coronaviruses in at risk groups, and to identify demographic risk factors associated with antibody prevalence indicative of infection. This chapter addresses all three thesis objectives. An appendix with supplementary material can be found immediately following this chapter (page 122).

4.1 ABSTRACT

Background: Epidemiological data on seasonal coronaviruses (sCoVs) may provide insight on transmission patterns and demographic factors that favour coronaviruses (CoVs) with greater disease severity. This study describes the incidence of CoVs in several high-risk groups in Ottawa, Canada from October 2020 to March 2022.

Methods: Serological assays quantified IgG and IgM antibodies to SARS-CoV-2, HCoV-OC43, HCoV-NL63, HCoV-HKU1, and HCoV-229E. Incident infections were compared between four population groups: individuals exposed to children, transit users, immunocompromised, and controls. Associations between antibody prevalence indicative of natural infection and demographic variables were assessed using regression analyses.

Results: Transit users and those exposed to children were at no greater risk of infection compared to the control group. Fewer infections were detected in the immunocompromised group ($p=0.03$). SARS-CoV-2 seroprevalence was greater in individuals with low income and within ethnic minorities.

Conclusions: Our findings suggest that non-pharmaceutical interventions intended to reduce SAR-CoV-2 transmission protected populations at high risk of exposure. The re-emergence of sCoVs and other common respiratory viruses alongside SARS-CoV-2 may alter infection patterns and increase the risk in vulnerable populations.

4.2 INTRODUCTION

The impact of SARS-CoV-2 has been experienced worldwide and resulted in more than 6.9 million deaths [1]. The pandemic has focused attention on the antigenically diverse coronavirus family. Seasonal coronaviruses (sCoVs) typically circulate at high levels in the community and are associated with 15-30% of common cold cases [2]. Understanding the epidemiological data related to sCoVs may help identify factors that favour infection and inform surveillance and control strategies [3].

The relatively high recombination and mutation rate of human coronaviruses (HCoVs) has resulted in great genetic diversity and unpredictable changes in virulence [4]. The emergence of cross-species transmission events observed with SARS-CoV-1, MERS-CoV and SARS-CoV-2 has shown that CoVs represent an ongoing threat of emergence from multiple existing animal reservoirs. Humans are routinely infected by two genera of coronaviruses: alphacoronaviruses (HCoV-229E and HCoV-NL63) and betacoronaviruses (HCoV-OC43, HCoV-HKU1, SARS-CoV-1, MERS-CoV and SARS-CoV-2). Seasonal coronaviruses (HCoV-OC43, HCoV-NL63, HCoV-229E, HCoV-HKU1) are omnipresent and typically circulate in the winter months. Reinfections are a common characteristic of seasonal coronaviruses. Adults are typically infected every 2 to 3 years but reinfection can occur within months of initial infection [5,6]. Typical symptoms of sCoVs include rhinitis, headache, fever, and cough. Severe disease and lower respiratory tract illness such as pneumonia and bronchitis are rare but more likely to occur in children, elderly, and immunocompromised individuals [4].

Pre-existing immunity to SARS-CoV-2 from previous seasonal coronavirus infection has been reported [7-9]. However, the translation of neutralizing capabilities and durable cross-immunity between sCoVs and pandemic coronaviruses is not fully understood. Pre-existing immunity from sCoVs in the form of antibodies or B and T cell memory may enhance immune response to SARS-CoV-2 and reduce COVID-19 severity [7, 10]. Correlates of immunity are further complicated by cross-reactivity among coronaviruses with antigenically related epitopes. Predictably, cross-reactivity is more likely to occur with a more conserved antigen [11,12]. Prior sCoV exposures may negatively impact the immune response to SARS-CoV-2 infection. Boosted antibodies may not be associated with protection or neutralization and have reduced affinity towards the novel SARS-CoV-2 virus. This suggests immune imprinting or original antigenic sin (OAS) and has been associated with negative clinical outcomes [13-15]. The relationship between SARS-CoV-2 and sCoV antibodies and immunity is unclear but does impact vaccination strategies and disease outcomes.

SARS-CoV-2 seroprevalence is highly variable among studies and is dependent on demographic characteristics, variant of concern, assay type, and public health measures in place at the time of evaluation. Ottawa, Canada, is an economically affluent city and the headquarters of multiple federal government departments and home of multiple technology companies. Almost 20% of citizens used public transit prior to the COVID-19 pandemic placing it fourth among Canadian cities for proportion of usage [16]. The culturally and linguistically diverse population with high reliance on public transit makes Ottawa an ideal location to assess respiratory virus

infection and immunity. As in most other settings, the SARS-CoV-2 wild-type was the primary local variant until March 2021. Thereafter, the alpha variant and to a lesser extent the delta variant became prominent in Ontario [17]. Key public health measures in place during the study period included closure or reduced capacity in public areas, limits on close contacts, stay-at-home orders, masking, utilization of remote school modalities and reduced class sizes, vaccination requirements and travel restrictions which all impacted population exposure risk.

Understanding of sCoV epidemiology can serve as an informative model for what may be expected of SARS-CoV-2 or other emerging CoVs in a post-pandemic setting. Identifying demographic groups and risk factors associated with infection can be used to inform intervention methods and protect vulnerable populations. This study aimed to describe the incidence of SARS-CoV-2 and seasonal coronavirus infection in several high-risk groups in Ottawa, Ontario from October 2020 to March 2022. We also aimed to identify demographic risk factors associated with coronavirus antibody prevalence acquired from natural infection.

4.3 METHODS

4.3.1 SSO

Study participants were enrolled in the Stop the Spread Ottawa Study (SSO). SSO is a prospective, longitudinal cohort that tracking SARS-CoV-2 antibody trends and investigating variants of concern [18]. All participants provided informed consent. SSO is approved by the Ottawa Health Science Network Research Ethnics Board (#2020-0481-01H). Individuals in the Ottawa region were eligible if they were 18 years of age or older, at risk of SARS-CoV-2 exposure due to occupation (i.e. healthcare, long-term care facilities, teachers, air travel cabin crew) or pre-existing health condition, or if they had a history of SARS-CoV-2 infection confirmed by PCR test. Participants were followed for 10 months with the option to extend for an additional 24 months. Those with a history of SARS-CoV-2 infection at baseline were allocated to the convalescent cohort for longitudinal sampling and participants without SARS-CoV-2 infection were included in the surveillance cohort. Those testing positive for SARS-CoV-2 by RT-PCR or rapid antigen test (RAT) or receiving SARS-CoV-2 vaccine(s) were asked to cross-over from the surveillance cohort to the convalescent cohort [19]. An electronic questionnaire was administered at baseline, and at three- and ten-months following enrolment to capture demographics, medical history, COVID-19 infection(s) and associated symptoms, and exposure risk factors as well as socioeconomic and psychosocial impacts of COVID-19. Blood samples for serum and peripheral blood mononuclear cell (PBMC) isolation was collected at baseline for all participants. During the initial 10 months, monthly serum and bimonthly PBMC draws were

completed for the convalescent cohort. Blood specimens were provided monthly for those that participated in the extension.

4.3.2 Substudy

Of the 1112 participants enrolled in the initial SSO study, 245 were selected for the substudy analysis described hereafter (Figure 4.1). Participants were prioritized for inclusion if they had plasma samples available from three separate time points: baseline, month 3 and month 10. If samples were unavailable from these timepoints, the sample collected closest to the timepoint of interest was selected. All visits occurred between October 22, 2020 and February 28, 2022. Covariates suspected to influence SARS-CoV-2 seroprevalence were determined *a priori*. Missing demographic variables from participant questionnaires were verified using medical records where available and by participant call-back. Ethnicity was classified as either white or other due to small sample sizes of non-white populations within the SSO cohort. Smoking status was defined as those that are current smokers or those that currently do not smoke. Both education and income were included as indicators of socioeconomic status. Education was categorized as those that did not complete high school, those that completed a trade, college or university degree below a bachelors, and those that achieved a graduate degree or higher. Income was defined as those with a household income less than $59,999, those with a household income between $60,000-$119,999 and those with a household income greater than $120,000. The main outcome of interest was incident HCoV-OC43, HCoV-NL63, HCoV-229E, HCoV-HKU1 and SARS-CoV-2 infections (Appendix Table 4.1). Incident infections were

compared between population groups of interest. We also assessed associations between demographic characteristics and antibody prevalence. Seasonal coronavirus IgG titres were used to assess associations with demographic variables because all participants were seropositive at baseline. Serology methodology, infection definitions and cut-off point definitions can be found in section 4.3.5.

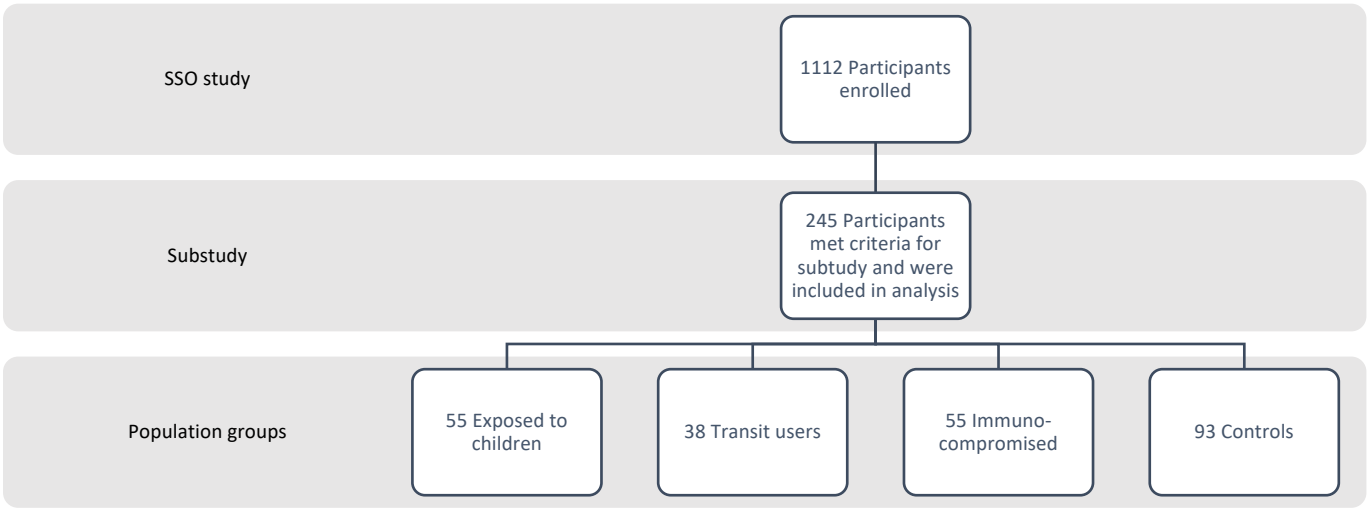

Figure 4.1. Flow diagram of participants selected for substudy

4.3.3 Population Groups

Participants were selected for this study if they met the criteria for one of three population groups of interest: high level of exposure to children at home or in the workplace, transit users or those that work in the public transportation industry, or immunocompromised individuals. Participants were categorized into the group exposed to children if they worked in a school or daycare or lived with one or more children in their household. Participants were classified in the transit user group they used public transportation at least once a week on average across follow-up or worked in the public transportation industry (i.e. city bus operator, lightrail operator, taxi driver). Participants were classified as immunocompromised if they had a primary or secondary immunodeficiency or required immunomodulatory treatment incorporating a range of conditions such as multiple sclerosis, rheumatoid arthritis, cancer, diabetes, HIV, asthma or COPD requiring medication, and organ/bone marrow transplant recipients. A control group of healthy individuals with minimal to no exposure to transit or children was included. Participants that met inclusion criteria for more than one group were categorized into the group with greater hypothesized exposure. Those exposed to children and transit users were hypothesized to be at greater risk of exposure compared to the control group. Children are frequently identified as the index case of respiratory disease in households and are known to be the primary drivers of viral transmission in the community increasing exposure in this group [20, 21]. Use of or work in the public transportation industry involves prolonged social contact in an enclosed space which has historically been assumed to increase the risk of respiratory virus transmission [22]. If a participant was both exposed to children and a transit user, they

were categorized as a transit user. Immunocompromised individuals were hypothesized to be at reduced risk as we assumed they would take more precautions to avoid exposure. Sensitivity analyses were conducted removing participants that met criteria for more than one group.

4.3.4 Statistical Power

Prevalence of antibodies against sCoVs was estimated at 85% in the control group and 95% in the groups exposed to children and transit users. A sample size of 245 was calculated to be sufficient to detect a difference in proportions of 10% between the high-risk groups and the control group using a two-tailed test with 80% power and a 0.05 significance level. The immunocompromised group was expected to have lower antibody prevalence estimated at 65%. The proposed sample size of 245 was projected to be sufficient to detect a 20% difference in proportions between the immunocompromised and control groups. Ultimately, sample size was dictated by sample availability across timepoints and budget constraints.

4.3.5 Laboratory Methods

Immunoglobulin G (IgG) titres (BAU/mL) against SARS-CoV-2 spike (S), receptor binding domain (RBD) and nucleocapsid (N) proteins in participant serum were quantified using a high throughput chemiluminescent direct ELISA as described before [23]. Incident COVID-19 infections were identified through serology and self-report of positive PCR and rapid antigen test (RAT). Self-reported positive results were validated using medical records where possible. Natural immunity was defined if a participant was positive (signal-to-cut-off (SCO)>1) for anti-N IgG and either anti-S or anti-RBD IgG. Thresholds were established at a 3% false discover rate (FDR) from the density distribution of pre-pandemic sera. In the event of indiscriminate positive serum samples for those with no self-reported test results, natural immunity was determined by examining the signal strength (magnitude of SCO) and the preceding and subsequent serum results [19]. Participants with an infection confirmed by PCR or positive serology prior to baseline visit were considered SARS-CoV-2 seropositive at baseline.

Plasma IgG and IgM titres (relative luminescent units [RLU]) against HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63 spike proteins were quantified using a chemiluminescent ELISA. Both IgG and IgM were measured at a single dilution and data was scaled to account for inter-plate variability. This assay was modified from previously described assays [23, 24]. The distribution of fold changes for each sCoV were evaluated separately. It was assumed that in most cases there would be limited CoV infection during the period of evaluation, so any changes in antibody titre caused by infection would appear as an outlier [6]. A 2-fold increase in

titre between paired samples was used to define IgG seroconversion. Acute infection was defined if the IgM titre was greater than the mean +(3SD/2SD). Examination of IgG and IgM titres over time was used to verify infection in all instances where either IgG or IgM seroconversion was observed. Serology results where a participant tested positive for more than one seasonal coronavirus at a single timepoint was assumed to indicate cross-reactivity rather than a co-infection. It was assumed the infection was caused by the most prevalent seasonal coronavirus in the Ottawa region. Infections were classified using the following hierarchal ranking system from highest to lowest expected prevalence: OC43>NL63>HKU1>229E [25-28].

4.3.6 Statistical Analysis

Categorical or dichotomous variables were presented as proportions. Continuous variables with a normal distribution were presented as means with standard deviation. Normality of data was assessed using Q-Q plots and histograms. Linearity was assessed through visual inspection of scatter plots. Differences between categorical or dichotomous variables was assessed using chi-square tests. Differences between continuous variables was assessed using Student's t-test. The number of incident infections were compared between groups using the chi-square test and Fisher's exact test for small cell sizes. The groups exposed to children and public transit were combined and classified as a high-risk group where sample size was a concern. SARS-CoV-2 seropositivity resulting from natural infection was used as the dependent variable in logistic regression. HCoV-NL63, HCoV-OC43, HCoV-HKU1 and HCoV-229E IgG antibody titres were used

as dependent variables in generalized linear models. A univariate regression analysis was performed as part of an exploratory analysis for all variables to determine associations between SARS-CoV-2 seroprevalence and sCoV antibody titres and demographic variables. Variables that were significant using a cut-off of 0.2 or were determined clinically important a priori were added to a multivariable model. Likelihood ratio tests were used to assess the fit of nested models. Logistic regression model fit was evaluated using the Hosmer-Lemeshow test and ROC statistics. Results were presented as odds ratios and 95% confidence intervals (CIs). Residual plots were used to assess model fit of linear models. Variable estimates and p values were presented. Sensitivity analyses were conducted removing participants that fit the criteria for more than one population group. The significance level was defined at $p<0.05$. All analyses were conducted using SAS Analytics Software.

4.4 RESULTS

4.4.1 Participant Characteristics

Two-hundred and forty-five participants were included in the analysis. Fifty-five were identified as exposed to children, 38 were classified as transit users, 59 were immunocompromised, and 93 served as controls. The demographic characteristics of all participants are reported in Table 4.1. Across all participants, the average age was 50 years, 54.7% were women, 91.0% were white, and 63.6% had at least a university degree. A comparison of demographic characteristics between each population group of interest and the control group revealed transit users and those exposed to children to be younger ($p<0.01$, $p<0.01$), and that those exposed to children have a higher household income ($p<0.01$). The immunocompromised group were older ($p=0.02$) and more likely to be male compared to the control group ($p=0.02$).

Table 4.1. Characteristics of 245 participants stratified into population groups of interest. Continuous variables are presented as mean (SD) and categorical variables presented as N (%). Differences between groups were assessed using student t-tests for continuous variables and chi-square tests for categorical variables.

Characteristic	All participants (n=245)	Population Group				P-value
		Exposed to children (n=55)	Transit user (n=38)	Immuno-compromised (n=59)	Control (n=93)	
Sex (n, %)						
Female	134 (54.69)	34 (61.82)	23 (60.53)	23 (38.98)	54 (58.06)	0.047
Male	111 (45.31)	21 (38.18)	15 (39.47)	36 (61.02)	39 (41.94)	
Age (mean, SD)	50 (14.21)	46 (9.15)	42 (14.06)	57 (12.18)	51 (15.71)	<0.001
Income (n, %)						
<$59,999	40 (16.33)	3 (5.45)	8 (21.05)	16 (27.12)	13 (13.98)	<0.001
$60,000-89,999	44 (17.96)	3 (5.45)	9 (23.68)	14 (23.73)	18 (19.35)	
$90,000-119,999	43 (17.55)	14 (25.45)	5 (13.16)	11 (20)	13 (13.98)	
>$120,000	93 (37.96)	34 (61.82)	13 (34.21)	18 (19.35)	34 (36.56)	
No response	25 (10.20)	1 (1.82)	3 (7.89)	6 (10.17)	15 (16.13)	
Ethnicity (n, %)						
White	223 (91.02)	50 (90.91)	34 (89.47)	51 (86.44)	88 (94.62)	0.214**
Other*	22 (8.98)	5 (9.10)	4 (10.53)	8 (13.56)	5 (5.38)	
Education (n, %)						
Highschool or less	20 (8.16)	3 (5.45)	6 (15.79)	4 (6.78)	7 (7.53)	0.557**
Trade/college	62 (25.31)	10 (18.18)	9 (23.68)	20 (33.90)	23 (24.73)	
Bachelor's degree	100 (40.82)	26 (47.27)	12 (31.58)	22 (37.29)	40 (43.01)	
Graduate or higher	56 (22.86)	16 (29.09)	10 (26.32)	10 (16.95)	20 (21.51)	
No response	7 (2.86)	0	1 (2.7)	3 (5.45)	3 (2.94)	
Smoking status (n,%)						
Current smokers	14 (5.71)	2 (3.64)	3 (7.89)	6 (10.17)	3 (3.23)	0.216**
Non-smokers	231 (94.29)	53 (96.36)	35 (92.11)	53 (89.83)	90 (96.77)	

*Ethnicity was classified as either white or other due to small number of non-white participants. The "other" category included the following ethnicities: South Asian (n=5), West Asian (n=4), Filipino (n=2), Latin American (n=2) Indigenous (n=2), Black (n=1), Chinese (n=1), and Other (n=5).

**Groups exposed to children and transit user combined to account for small cell sizes

4.4.2 Incident Infections

Among the 245 participants, 34 (13.9%) had antibody titres to SARS-COV-2, HCoV-OC43, HCoV-NL63, HCoV-E229, or HCoV-HKU1 over the 16-month follow-up period suggestive of recent infection. Incident SARS-CoV-2 infections were identified in 12 (4.9%) participants and 23 (9.4%) participants were infected by at least one sCoV (Table 4.2). HCoV-HKU1 was the most common sCoV identified [proportion with an infection: 5.3% (n=13)], followed by HCoV-OC43 [3.3% (n=8)], and HCoV-NL63 [0.8% (n=2)]. No HCoV-229E infections were detected. Among the population groups of interest, the proportion with sCoV infection was greatest among the control group [14.0% (n=13)], followed by those exposed to children [9.1% (n=5)], transit users [7.9% (n=3)], and immunocompromised participants [3.4% (n=2)] (Table 4.2). The proportion of participants with sCoV infection(s) did not differ between those exposed to children, transit users, and our control group. Considerably fewer infections were observed in those with an immune compromising condition compared to the control group (p=0.03). At baseline, all 245 participants had elevated plasma IgG for HCoV-229E, HCoV-NL63, HCoV-HKU1, and HCoV-OC43 and 70 (28.6%) of participants were seropositive for SARS-CoV-2, denoting a prior infection. The control group had the greatest number SARS-CoV-2 anti-N seropositive participants [44.0% (n=41)], followed by those exposed to children [30.9%(n=17)], transit users [18.4% (n=7)] and immunocompromised individuals [8.5%(n=5)] (Table 4.3).

Table 4.2. Number of coronavirus infections detected among 245 participants from October 22, 2020, to February 28, 2022 stratified by population group. Comparisons between those exposed to children, transit user, immunocompromised groups to the control group were conducted using Fisher's exact test. Results are presented as number of participants that were infected by each virus (N) and the proportion of the group infected (%).

		Participant Group			
Virus	Total Participants (n=245)	Control (n=93)	Exposed to children (n=55)	Transit (n=38)	Immuno-compromised (n=59)
SARS-CoV-2	12 (4.9)	5 (5.38)	4 (7.27)	1 (2.63)	2 (3.39)
HCoV-HKU1	13 (5.31)	9 (9.68)	2 (3.64)	1 (2.63)	1 (1.69)
HCoV-OC43	8 (3.27)	3 (3.23)	3 (5.45)	2 (5.26)	0 (0)
HCoV-NL63	2 (0.82)	1 (1.08)	0 (0)	0	1 (1.08)
HCoV-229E	0 (0)	0 (0)	0 (0)	0	0 (0)
Total sCoV^	23 (9.39)	13 (13.98)	5 (9.09)**	3 (7.89)	2 (3.39)*
Total CoV^^	34 (13.88)	18 (19.35)	8 (14.55)**	4 (10.53)	4 (6.78)*

* Significant at $p<0.05$

**Chi-square test used.

^ Number (%) of participants that tested positive for HCoV-NL63, HCoV-OC43, HCoV-HKU1, or HCoV-229E.

^^ Number (%) of participants that tested positive for HCoV-NL63, HCoV-OC43, HCoV-HKU1, HCoV-OC43 and SARS-CoV-2. A participant in the group with exposure to children tested positive for SARS-CoV-2 and HCoV-OC43 so sCoV and SARS-CoV-2 infections do not sum to the total in the "Total Participants" and "Exposed to children" columns.

Table 4.3. Demographic variables of 245 participants stratified by SARS-CoV-2 seropositivity status indicative of prior natural infection. Continuous variables are presented as mean (SD) and categorical variables presented as number of seropositive participants divided by the number of participants in that group (%). Multivariate logistic regression was used to assess associations between SARS-CoV-2 seroprevalence and demographic variables at baseline presented as odds ratios (OR) and 95% confidence intervals (CIs). Significant associations are highlighted.

Variable	SARS-CoV-2 Seropositive (n=70)	SARS-CoV-2 Seronegative (n=175)	OR	95%CI
Population group				
Exposed to children	17/55 (30.90)	38/55 (69.09)	0.81	0.35-1.86
Transit User	7/38 (18.42)	31/38 (81.58)	**0.35**	**0.13-0.96**
Immunocompromised	5/59 (8.47)	54/59 (91.53)	**0.05**	**0.02-0.17**
Control	41/93 (44.09)	52/93 (55.91)	Ref	Ref
Sex				
Male	34/111 (30.63)	77/111 (69.37)	Ref	Ref
Female	36/134 (26.87)	98/134 (73.13)	0.58	0.29-1.16
Ethnicity				
White	59/223 (26.46)	164/223 (73.54)	Ref	Ref
Other	11/22 (50.0)	11/22 (50.0)	**6.73**	**2.06-21.94**
Age	53.04 (SD: 15.29)	48.77 (13.60)	**1.04**	**1.02-1.07**
Smoking status				
Smoker	1/14 (7.14)	13/14 (92.86)	0.25	0.03-2.38
Non-smoker	69/231 (29.87)	162/231 (70.13)	Ref	Ref
Education				
Highschool or less	7/27 (25.93)	20/27 (74.07)	0.77	0.21-2.78
Trade/college	13/62 (20.97)	49/62 (79.03)	0.59	0.22-1.58
Bachelor's degree	34/100 (34.0)	66/100 (66.0)	1.24	0.53-2.89
Masters' or higher	16/56 (28.57)	40/56 (71.43)	Ref	Ref
Income				
<$59,999	13/20 (65.0)	7/20 (35.0)	**3.14**	**1.06-9.27**
$60,000-$89,999	10/44 (22.72)	34/44 (77.27)	0.96	0.35-2.64
$90,000-$120,000	8/43 (18.60)	35/43 (81.40)	0.76	0.27-2.10
+$120,000	28/93 (30.11)	65/93 (69.89)	Ref	Ref

4.4.3 Risk Factor Analysis

SARS-CoV-2 seropositivity suggestive of natural infection was greater in older participants, those with a household income less than $59,999 and those of ethnic minority in a multivariable logistic regression analysis (Table 4.3). The odds of seropositivity was no greater in those exposed to children compared to our control group. Immunocompromised individuals were less likely to have anti-N SARS-CoV-2 antibodies at baseline (OR: 0.05; 95%CI:0.02-0.17) compared to our control group. Increasing age had a small positive association with SARS-CoV-2 antibody prevalence (OR:1.04; 95%CI:1.02-1.07). The odds of seropositivity were more than 6 times greater in those of ethnic minority compared to white participants (OR: 6.73, 95%CI: 2.06-21.94). The odds of seropositivity increased 3-fold in those with a household income less than $59,999 compared to those reporting a household income greater than $120,000 (OR:3.14; 95%CI:1.06-9.27). Increasing number of children in the household and level of public transportation use was not associated with SARS-CoV-2 seroprevalence (Appendix Table 4.2).

Few associations were found between anti-sCoV IgG antibody titres and demographic characteristics in multivariate linear regression models adjusted for age, sex, smoking status, income, education and ethnicity (Table 4.4). Of consequence, smokers were found to have higher anti-HCoV-HKU1 antibody titres compared to non-smokers (p=0.03). Those that used public transportation daily or worked in the transportation industry were found to have higher anti-HCoV-HKU1 antibody titres compared to those that did not use public transit, but this result was not consistent across the four sCoVs. Increasing number of children in the household was not associated with sCoV antibody titres (Appendix Table 4.2). Sensitivity analyses

excluding participants that may have been categorized in more than one population group (n=28) showed no appreciable change in results, with limited changes in p-values and magnitude of effect (Appendix Table 4.3).

Table 4.4. Associations between demographic risk factors and coronavirus antibody titres for 245 participants at baseline. Multivariate linear regression analysis was used to assess associations. Separate models were used for each virus. Results significant at the p<0.05 level are highlighted.

	HKU1		OC43		NL63		229E	
Variable	Estimate	P-value	Estimate	P-value	Estimate	P-value	Estimate	P-value
Population group								
Control	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Exposed to children	0.06	0.38	0.01	0.89	-0.01	0.99	0.03	0.77
Transit Users	0.10	0.17	0.02	0.85	-0.08	0.35	-0.06	0.48
Immunocompromised	-0.08	0.20	-0.13	0.13	-0.06	0.42	-0.08	0.34
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.05	0.80	<0.01	0.95	0.02	0.72	-0.07	0.25
Age	0.001	0.53	<0.01	0.80	<-0.01	0.88	<-0.01	0.28
Non-smoker	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Current smoker	**0.11**	**0.03**	0.05	0.71	-0.20	0.12	-0.15	0.26
Household income								
+$120,000	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<$59,999	-0.14	0.06	-0.05	0.65	-0.03	0.72	0.01	0.91
$60,000-$89,999	-0.03	0.69	-0.08	0.42	-0.07	0.40	-0.11	0.20
$90,000-$120,000	-0.02	0.76	-0.10	0.30	-0.09	0.31	-0.03	0.74
Education								
Masters or higher	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Highschool or less	-0.04	0.66	-0.06	0.64	-0.16	0.19	-0.18	0.14
Trade/college	-0.06	0.39	-0.10	0.31	-0.06	0.50	0.04	0.67
Bachelor's degree	<-0.01	0.99	0.03	0.73	-0.07	0.38	-0.11	0.15
White ethnicity	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Non-white ethnicity	0.08	0.34	0.18	0.12	0.08	0.45	0.03	0.72

4.5 DISCUSSION

The proportion of the study population with incident sCoV infections was 9.4%. Similar values were reported in the Ottawa region by the Eastern Ontario Regional Laboratory Association (EORLA) regional reference laboratory lab, where sCoV percent positivity ranged from 0-10% from October 2020 to December 2021 [29]. Given the ubiquitous nature of seasonal coronaviruses and high frequency of reinfections [5], under normal circumstances it is expected that most participants would experience a sCoV infection within the follow-up period. A dramatic decline in common respiratory viruses such including influenza, RSV, parainfluenza viruses (PIV), rhinovirus, and sCoVs was observed worldwide following the introduction of SARS-COV-2 [30-32]. This phenomenon has been partially attributed to government mandated non-pharmaceutical COVID-19 interventions initiated to slow SARS-CoV-2 transmission. These measures appear to have been effective in reducing sCoV transmission as well, contributing to the low number of incident infections observed in this observation period. As SARS-CoV-2 transitions from pandemic to endemic classification, sCoV and other respiratory virus activity is expected return to pre-pandemic levels. Co-circulating viruses including sCoVs, influenza and RSV can lead to a wide range of clinical symptoms that overlap with COVID-19. Misdiagnosis or underdiagnosis is more likely to occur if coinfections are present or if settings do not have the capacity for multiplexed testing [3].

The prevalence of anti-N SARS-CoV-2 antibodies was 28.0% at baseline, slightly higher than the average estimated seroprevalence during this period in Ontario measured between 0.9%-15.0% [33, 34]. SARS-CoV-2 seroprevalence is expected to be higher in this study as participants were

recruited if they had experienced SARS-CoV-2 infection or were at higher risk of infection. Therefore, the reported seroprevalence is not representative of the general population but does provide insight into the level of exposure among high-risk population groups.

While children have been documented to have lower prevalence and severity of COVID-19 [35, 36], they still play an important role in SARS-CoV-2 transmission. Hundreds of students mix in an often crowded and poorly ventilated indoor school environment facilitating transmission [37]. Additionally, children are more likely to have mild or asymptomatic infections and unknowingly propagate outbreaks among households and communities [36]. In contrast to our analysis, a higher risk of SARS-CoV-2 infection has been reported in adults living with children in the US [38] and the UK [39]. Other studies in North America have found that SARS-CoV-2 infection was no greater among school staff than in the community and that most COVID-19 cases among students and teachers were acquired outside the school environment [40-42]. One of these studies was conducted in Ontario during the first wave of the pandemic [41]. As with our cohort, participants in this study were subject to similar community-based nonpharmaceutical public health interventions. Thus, we believe it is appropriate to compare results between studies. A possible explanation for the discrepancy between the above-mentioned studies is the substantial amount of time schools were closed in Ontario. Ontario schools were closed for a total of 20 weeks (March 14 to May 15, 2021), a period longer than in any other Canadian province or territory [43]. Intermittent school closures and shifts to online learning likely reduced exposure in this group and contributed to the reduced number of infections detected in SSO. Pre-existing immunity caused by frequent respiratory infections has

been proposed as a mechanism to explain lower susceptibility to SARS-CoV-2 infection in children [39, 44]. A similar mechanism may explain why adults exposed to children experienced fewer SARS-CoV-2 infections during the observation period. Adults living with children have been shown to experience more frequent respiratory infections than those that do not live with children, which may provide a greater degree of immune mediated protection against SARS-CoV-2 [45].

The proportion of transit users with CoV infections was comparable to our control group despite hypothesized increased risk of exposure. The small number of CoV infections detected in transit users may be a consequence of effective public health measures implemented at the start of the pandemic to protect both transit users and operators. This included frequent cleaning and disinfection of facilities and high touch surfaces, limited capacity, and installation of physical barriers [46, 47]. The considerable decline in transit ridership observed in Canada and worldwide throughout the pandemic [22, 48] may also explain why fewer infections were observed in transit users. The reduction in transit usership was partially attributed to reduced travel demand in response to stay-at home orders [48] and the greater perception of SARS-CoV-2 transmission risk associated with public transit use [22]. The restrictions on capacity and reduced ridership limited crowding and allowed those that continued to use public transit during the pandemic adequate space to maintain physical distancing recommendations. Similarly, the perception of increased risk may have encouraged adherence to recommended public health protocols. The light rail transit system in Ottawa was also shut down for several months during the study period for mechanical issues which may have altered transit usage.

SARS-CoV-2 transmission risk while using public transit has been correlated with exposure time [49]. While this occurrence was not consistently observed in this study, those that used public transit at least several times a week had higher anti-HKU1 IgG antibody titres compared to those that did not use public transit at all (Appendix Table 4.2). We were unable to assess for similar trends with HCoV-OC43, HCoV-NL63 and HCoV-229E due to low incidence.

Immunocompromised individuals had reduced odds of SARS-CoV-2 seropositivity from natural infection at baseline and fewer CoV infections over the period of observation compared to our controls. Insufficient serological response to COVID-19 vaccination has also been observed in solid organ transplant (SOT) recipients receiving immunosuppressive agents [50]. Disparities in antibody kinetics may explain why fewer infections were observed in the immunocompromised individuals. These individuals may develop fewer antibodies in response to natural infection or vaccination or experience rapid antibody waning. Alternatively, immunocompromised individuals and those with a higher burden of comorbidities are at greater risk of severe disease if infected by SARS-CoV-2 or other common respiratory viruses. These individuals may have taken more precautions during the COVID-19 pandemic to avoid exposure such as limiting close contacts, avoiding crowds, and adhering more strictly to public health measures. As public health restrictions are removed, policy makers and healthcare professionals should be aware that this population remains at risk and may require continued special measures.

Few demographic variables were correlated with baseline IgG titres against HCoV-HKU1, HCoV-NL63, HCoV-229E and HCoV-OC43. The high prevalence these viruses resulted in antibody titres

being consistently high among all individuals, leading to difficulties in detecting any titre differences between groups. By contrast, most of the population was naïve to SARS-CoV-2, enabling detection of difference in levels of exposure between demographic groups. The odds of seroprevalence were greater in those with a low household income and of ethnic minority. Our findings add to extensive evidence showing the burden of SARS-CoV-2 is greater among minority groups and those of low socioeconomic status [33, 51]. Many factors may contribute to demonstrated inequities, such as living in more crowded households, education and finances, language or cultural barriers, and increased work in an environment that required in-person presence during the pandemic.

The strengths of this study include well characterized reports of clinical and self-reported data. We were able to analyze multiple serial blood samples for each participant with a low attrition rate over time. The combined use of serology, self-reported PCR and RAT tests and clinical symptoms reduce misclassification of COVID-19 infections. The shifting landscape of public health measures and emerging variants of concern complicates the interpretation of SARS-CoV-2 seroprevalence in other studies. This issue was less impactful with SSO as almost all samples were collected prior to the arrival of the Omicron variant.

This study is subject to several limitations. The study cohort consisted of highly educated, high income individuals with limited ethnic diversity which limited our ability to infer associations within lower socioeconomic groups and reduced generalizability of results. Several factors complicate the interpretation of sCoV serology results. The World Health Organization does not

have standardized guidelines for units, controls or recommended thresholds when reporting sCoV serology results so determining a threshold of infection can be challenging. Similarly, almost all individuals have detectable antibodies indicating a prior infection so obtaining a true negative control is difficult. Evaluation of IgG and IgM titres over time were used to verify infection. However, in some cases samples were not available from all desired timepoints and the interval between available samples was too broad to detect a rise in antibody titres. For this reason, sCoV infection incidence is likely underreported and we were not always able to determine when a seasonal coronavirus infection occurred with precision. Longitudinal antibody kinetics and serologic response to infection vary by individual and are dependent on many factors including demographics, comorbidities, and disease severity [52]. The heterogeneity in antibody response may underestimate the number of detected infections. Several participants tested positive for more than one coronavirus and one participant tested positive for all four sCoVs (Appendix Table 4.4). Cross-reactivity among CoVs is a well-documented concern with CoV serology [10, 11] and simultaneous infection for all viruses is highly improbable. Unfortunately, only one antigen was used in the serological assay and acute infection were not diagnosed by PCR so we are unable to corroborate assay results. Future studies may consider the use of multiple antigens to improve the reliability of sCoV results. Analysis of other common respiratory viruses including influenza and RSV in at risk-populations would enhance our coronavirus-specific observations.

4.6 CONCLUSION

This analysis demonstrates that CoV incidence was reduced in immunocompromised individuals and similar between those exposed to children, transit users, and controls. Non-pharmaceutical public health interventions likely reduced viral transmission. Relaxation of these measures has resulted in a return of sCoV and other common respiratory viruses including influenza and RSV. The reappearance of seasonal respiratory viruses may have a greater impact on individuals of non-white ethnicity, those of low socioeconomic status, and those with an immunocompromising condition. The lasting presence of SARS-CoV-2 in a post-pandemic era may continue to alter seasonal respiratory virus circulation and have consequences for population susceptibility to disease.

4.7 REFERENCES

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Chapter 4 Appendix

Appendix Table 4.1. Type of test used and definition of infection for SARS-CoV-2 and seasonal coronaviruses.

Virus	Test	Antigen	Immunoglobulin	Infection Definition	Infection Validation
SARS-CoV-2	Chemiluminescent direct ELISA	S, RBD, N	IgG	SCO>1 for anti-N IgG and either anti-S or anti-RBD IgG	SCO of preceding and subsequent serum samples
	PCR	N/A	N/A	Self-reported infection*	Medical records, participant follow-up
	Rapid tests	N/A	N/A	Self-reported infection*	Medical records, participant follow-up
HCoV-NL63, HCoV-OC43, HCoV-229E, HCoV-HKU1	Chemiluminescent ELISA	S	IgG	2-fold IgG titre increase between subsequent visits	Examination of IgG and IgM titre response over time
	Chemiluminescent ELISA	S	IgM	Above the mean titre +(3SD/2SD)	Examination of IgG and IgM titre response over time

*Target or cut-off information not collected for self-reported infections.

Appendix Table 4.2. Multivariate regression results measuring the magnitude of effect of increasing exposure to public transit and number of children in the household adjusted for ethnicity, sex, income, education, age, smoking status, and comorbidities. Multivariate logistic regression analysis used to assess the odds of SAR-CoV-2 seropositivity indicative of natural infection at baseline. Linear regression analysis used to assess seasonal coronavirus antibody titres at baseline. Separate models were fit for each virus.

Demographic variable	HKU1		OC43		NL63		229E		SARS-CoV-2	
(reference category)	Estimate	P-value	Estimate	P-value	Estimate	P-value	Estimate	P-value	OR	95% CI
Other ethnicity (v. white)	0.06	0.50	0.17	0.13	0.05	0.62	0.19	0.11	**4.55**	**1.59-13.0**
Female sex (v.male)	0.04	0.42	0.02	0.76	0.04	0.56	-0.04	0.54	0.74	0.39-1.43
Income (v. +$120,000)										
<$59,999	0.01	0.87	0.19	0.12	0.14	0.19	-0.09	0.47	2.74	0.90-8.33
$60,000-$89,999	-0.10	0.18	-0.01	0.94	0.02	0.83	-0.03	0.75	1.81	0.67-4.92
$90,000-$120,999	-0.03	0.71	-0.06	0.53	-0.05	0.57	<-0.03	0.98	0.80	0.31-2.05
Prefer to not answer	-0.02	0.72	-0.10	0.29	-0.08	0.36	-0.03	0.73	0.56	0.21-1.49
Education (v.master's)										
High school or less	-0.14	0.14	-0.16	0.19	**-0.25**	**0.03**	-0.12	0.34	0.86	0.25-2.99
Trade/college	-0.09	0.21	-0.11	0.24	-0.07	0.41	-0.04	0.69	0.64	0.25-1.66
Bachelor's degree	-0.01	0.83	<-0.01	0.99	-0.07	0.36	-0.06	0.48	1.18	0.52-2.67
Age	<0.02	0.30	<0.01	0.81	<-0.01	0.96	<-0.01	0.76	**1.04**	**1.01-1.07**
Smoking (v. non-smoking)	**0.23**	**0.03**	0.03	0.81	-0.20	0.11	0.13	0.36	0.20	0.02-1.74
Number of children*	0.03	0.22	-0.04	0.26	<0.01	0.99	0.02	0.67	0.88	0.60-1.28
Transit Use (v. never)										
Once a week	-0.02	0.83	-0.17	0.21	-0.09	0.48	-0.07	0.62	0.35	0.08-1.49
A few times a week	0.08	0.54	-0.11	0.50	-0.28	0.06	-0.09	0.61	0.31	0.03-2.74
Daily	**0.30**	**<0.03**	0.04	0.75	0.11	0.37	0.08	0.55	0.27	0.05-1.51
Number of comorbidities**	**-0.03**	**0.05**	**-0.06**	**0.01**	-0.03	0.10	-0.04	0.08	**0.70**	**0.56-0.89**

*Number of children living in household

**Included cancer, diabetes, HIV, primary immunodeficiency, neurological impairment/disease, organ or bone marrow transplant, or chronic heart, lung, liver or kidney disease

Appendix Table 4.3. Sensitivity analysis removing all participants that met criteria for more than one population group of interest (n=217). Multivariate logistic regression analysis used to assess the odds of SAR-CoV-2 seropositivity indicative of natural infection at baseline. Linear regression analysis used to assess seasonal coronavirus antibody titres at baseline. Separate models were fit for each virus.

	HKU1		OC43		NL63		E229		SARS-CoV-2	
Variable	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value	OR	95%CI
Control	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Exposed to children	<-0.01	0.98	0.02	0.86	-0.03	0.72	-0.01	0.89	0.89	0.34-2.10
Transit User	<-0.02	0.98	0.03	0.76	-0.04	0.69	-0.08	0.47	0.45	0.15-1.35
Immunocompromised	-0.08	0.25	-0.09	0.34	-0.07	0.46	-0.03	0.75	**0.06**	**0.02-0.20**
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.03	0.62	-0.02	0.82	0.02	0.72	-0.02	0.75	0.50	0.26-1.04
Age	<0.01	0.44	<0.01	0.73	<-0.01	0.99	<-0.01	0.61	1.04	0.05-1.04
Non-smoker	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Smoker	**0.24**	**0.03**	-0.01	0.95	-0.21	0.11	0.13	0.37	0.21	0.08-0.21
>$120,000	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<$59,999	-0.13	0.12	-0.02	0.86	-0.03	0.77	-0.02	0.87	3.65	1.17-11.40
$60,000-$89,999	-0.03	0.75	-0.04	0.74	-0.04	0.69	-0.04	0.74	0.97	0.33-2.90
$90,000-$120,000	-0.01	0.91	-0.10	0.30	-0.09	0.31	-0.04	0.68	0.79	0.28-2.21
Graduate or higher	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Highschool or less	-0.16	0.10	-0.11	0.39	**-0.27**	**0.03**	-0.14	0.32	0.87	0.23-3.33
Trade/college	-0.09	0.23	-0.08	0.42	-0.08	0.38	-0.07	0.49	0.61	0.21-1.73
Bachelor's degree	-0.02	0.73	0.02	0.86	-0.09	0.30	-0.09	0.33	1.32	0.54-3.18
White ethnicity	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Other	0.16	0.12	0.24	0.08	0.12	0.32	0.21	0.12	**6.81**	**1.82-25.57**

Appendix Table 4.4. Classification for participants that tested positive for more than one coronavirus (n=7). Serology results where a participant tested positive for more than one seasonal coronavirus at a single time point was thought to be a result of cross-reactivity. It was assumed the infection was caused by the most prevalent seasonal coronavirus. Infections were classified using the hierarchal ranking system from highest to lowest expected prevalence: OC43>NL63>HKU1>229E.

Participant	Positive serology result					Infection classification
	HKU1	OC43	NL63	229E	SARS-CoV-2	
SSO0033		Yes		Yes		OC43
SSO0082	Yes	Yes	Yes	Yes		OC43
SSO0221		Yes	Yes	Yes	Yes	OC43, SARS-CoV-2
SSO0551			Yes	Yes		NL63
SSO0611	Yes	Yes				OC43
SSO0612		Yes	Yes	Yes		OC43
SSO0810	Yes		Yes	Yes		NL63

CHAPTER 5

The final chapter of this thesis summarizes key findings from the three articles (Chapters 2 through 4) and describes how results address the objectives outlined on page 1. This chapter also discusses areas of future research and implications for practice and policy.

5.1 SUMMARY OF KEY FINDINGS

5.1.1 SARS-CoV-2 seroprevalence in high-risk groups

SARS-CoV-2 seroprevalence indicative of natural infection was expected to be greater in Individuals that used public transit and those with high levels of exposure to children. Most of the population-based studies assessed in the literature review presented in Chapter 2 found SARS-CoV-2 seroprevalence was greater among transit users. This finding contrasts with what was found in Chapter 4 where SARS-CoV-2 seroprevalence was comparable between transit users, those with high levels of exposure to children and a control group. Disparity in results is likely caused by varying population demographics, assay type and methodology, and timing of study. The study population in Chapter 4 was largely white, older, highly educated and with high household income. In comparison, many of the studies in Chapter 2 that found greater seroprevalence in transit users were conducted in areas with high population density or included a more diverse study population which may have increased seroprevalence.

This thesis also evaluated SARS-CoV-2 seroprevalence in high-risk occupations including transportation workers and teachers. Chapter 4 found no association between SARS-CoV-2 infection and working with children, while Chapters 2 and 4 both found no association with SARS-CoV-2 infection and work in the transportation industry. A systematic review evaluating the risk of SAR-CoV-2 seroprevalence in different occupations had similar findings, estimating SARS-CoV-2 seroprevalence to be 5.07% for education, training, and library occupations and 3.5% for those in the transportation and material moving occupations [1]. Some studies have also found that most documented SARS-CoV-2 cases in essential workers were acquired in the community or from someone in the household rather than in the workplace [2-7].
These findings suggest pharmaceutical interventions such as lockdowns, travel restrictions, school closures, improved ventilation systems and enhanced surface cleaning in schools and transit environments were effective in reducing transmission.

While findings from this thesis did not consistently find greater SARS-CoV-2 infection in high-risk groups or occupations, the high level of exposure and proximity to others does increase the risk of respiratory virus transmission in the transit and school environments. Policy makers and public health officials should be cognizant of these populations and ensure proper protective measures are in place in the event of future outbreaks.

Findings from Chapter 4 indicated immunocompromised individuals had fewer CoV infections compared to immunocompetent individuals. Although this population group was only studied

in one article, existing studies have also found low prevalence of SARS-CoV-2 antibodies indicative of natural infection in those with immunocompromising conditions [8-10]. There are several possible explanations for this finding. The strength and duration of antibody response after infection may be weaker in immunocompromised individuals, contributing to the low antibody prevalence. Alternatively, increased risk of severe disease in immunocompromised individuals may have initiated protective behavioural changes such as physical distancing and reducing number of close contacts. As most SARS-CoV-2 public health measures are eliminated, the low levels of infection acquired immunity detected in this population suggest they may be at greater risk of infection. Vaccine campaigns and protective strategies should be targeted towards these susceptible individuals.

5.1.2 Demographic factors associated with seropositivity

Chapters 2 and 4 both found that the burden of disease was higher in those of low socioeconomic status or those of racial or ethnic minority. Similar conclusions were frequently cited in the literature and related to disparities in access to healthcare, limited resources, and high housing density among other factors [11,12]. While this thesis found SARS-CoV-2 seroprevalence was lower in high-risk groups, it was consistently high in those of low socioeconomic status and ethnic or racial minorities. This may suggest sociodemographic factors were greater determinants of seroprevalence than occupational or behavioural factors such as transit use. A recent study found bus drivers had higher SARS-CoV-2 seroprevalence than the general population but was unable to determine if occupational hazards or

sociodemographic factors were the primary determinants of seroprevalence as most bus drivers had lower wages and were of racial or ethnic minority [13]. These findings indicate socioeconomic status, race and ethnicity are confounding variables that must be considered when estimating respiratory virus seroprevalence. Results from this thesis suggest low income and minority groups may be more susceptible to future outbreaks. Policy makers and government officials should recognize the disproportionate burden of disease and concentrate resources and surveillance efforts in vulnerable populations.

5.1.3 Seasonal respiratory virus incidence during the COVID-19 pandemic

Chapters 3 and 4 found few individuals were infected with sCoVs during the COVID-19 pandemic in the Ottawa region. Chapter 3 also found a reduction in activity of 11 other common respiratory viruses, including influenza and RSV. Results from this thesis were consistent with studies conducted worldwide, suggesting non-pharmaceutical interventions in place to reduce SARS-CoV-2 transmission were also effective against SRVs [14-18]. Low viral activity over the last few years suggests population immunity to SRVs may be low. This finding has major implications as the elimination of public health measures is expected to cause a resurgence of SRVs. Co-circulation of SRVs and SARS-CoV-2 with a larger number of susceptible individuals may alter infection patterns and increase the severity of disease for unexpected population groups. Future studies investigating the incidence of all common respiratory viruses longitudinally is essential in identifying infection dynamics between viruses and predicting long-term viral transmission risk among population groups.

5.2 CONCLUSION

This thesis described the epidemiology of SARS-CoV-2 and SRVs in several at risk groups. An overall reduction in seasonal respiratory virus incidence was observed during the COVID-19 pandemic, and high-risk population groups were not found to be at greater risk of infection. SRVs are expected to resurge and co-circulate posing greater risk for susceptible populations. Findings from this thesis suggest those of ethnic or racial minority, low socioeconomic status, and presence of an immunocompromising condition may be at greater risk. Constant monitoring of SARS-CoV-2 and SRV incidence and infection patterns will be required as SARS-CoV-2 transitions to an endemic threat.

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