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Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted for Alternate Diagnoses

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Abstract:

Objectives: To determine the diagnostic yield of screening patients for SARS-CoV-2 who were admitted with a diagnosis unrelated to COVID-19, and identify risk factors for positive tests.

Design: Cohort from the Canadian COVID-19 Emergency Department Rapid Response Network (CCEDRRN) registry

Setting: 30 acute care hospitals across Canada

Participants: Patients hospitalized for non-COVID-19 related diagnoses who were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 1, and December 29, 2020

Main outcome: Positive nucleic acid amplification test (NAAT) for SARS-CoV-2

Outcome measure: Diagnostic yield

Results: We enrolled 15,690 consecutive eligible adults who were admitted to hospital without clinically suspected COVID-19. Among these patients, 122 tested positive for COVID-19, resulting in a diagnostic yield of 0.8% (95% CI 0.64% – 0.92%). Factors associated with a positive test included presence of a fever, being a healthcare worker, having a positive household contact or institutional exposure, and living in an area with higher 7-day average incident COVID-19 cases.

Conclusions: Universal screening of hospitalized patients for COVID-19 across two pandemic waves had a low diagnostic yield and should be informed by individual-level risk assessment in addition to regional COVID-19 prevalence.

Trial registration: NCT04702945

SUMMARY BOXES

Section 1: Universal screening of admitted patients for SARS-CoV-2 was implemented in many hospitals at the beginning of the pandemic. The Infections Diseases Society of America (IDSA) recommended avoiding universal screening of asymptomatic hospitalized patients in areas and times of low-COVID prevalence (defined as <2% prevalence) with very low certainty of evidence, based on studies of COVID-19 prevalence among asymptomatic individuals in the community.

Section 2: This study supports IDSA recommendations to avoid universal screening for COVID-19 in times and areas of low COVID prevalence and identifies patient-level risk factors strongly associated with positive testing that should be considered for screening.

Strengths and Limitations

- Pan-Canadian study including over 40 academic, non-academic, rural, and urban hospitals.
- Inclusion of patient partners, as well as public engagement, who assisted in the development and presentation of this manuscript.
- Inclusion of pertinent clinical variables, as well as relevant demographic and community-level variables.
- Exclusion of non-NAAT tests due to their infrequent use in the Canadian context.

INTRODUCTION

Healthcare institutions initiated widespread testing of admitted patients for coronavirus disease 2019 (COVID-19) in the spring of 2020 (1). Patients without any reported symptoms of COVID-19 were routinely tested even in jurisdictions where COVID-19 rates were low in order to identify asymptomatic carriers and prevent hospital outbreaks (2). Some jurisdictions have continued this practice without robust evidence to support this practice. An Alberta study of 3,375 patients admitted to hospital for alternate diagnoses during the first wave of the pandemic when COVID-19 prevalence was very low found that none of the patients tested positive (3). In contrast, other studies from times and regions with higher COVID-19 prevalence reported positive tests in between 2.6 and 15.5% of otherwise asymptomatic patients (4–8).

Universal testing has several potential downsides if diagnostic yield is low. First, it may worsen Emergency Department (ED) crowding, as admitted patients with pending COVID-19 tests are boarded in EDs until their test results are reported. While ED volumes were lower than usual in the early pandemic such that EDs could absorb this delay, high patient volumes have since returned, exacerbating the impact of this practice on hospital crowding (9). This in turn increases patient morbidity and mortality (10). In addition, diagnostic workups and therapeutic interventions may be delayed until COVID-19 test results are back, as it takes longer to move patients on isolation precautions through the system. This can further exacerbate patient outcomes and hospital crowding. Thirdly, diagnostic testing capacity may be limited, potentially delaying processing of tests for symptomatic patients. In addition, the use of Personal Protective Equipment (PPE) may be increased as institutions have placed patients with pending COVID-19 tests under isolation precautions. The use of PPE during resuscitation has been associated with worse patient outcomes (11). Lastly, there is also an opportunity cost for hospitals as money spent on universal testing could be allocated to other areas. These unintended consequences of liberal testing policies need to be weighed carefully against the anticipated diagnostic yield and potential benefits.

As for any diagnostic test, rational COVID-19 testing guidelines should be informed by the level of risk of the patient, such that testing is reduced in situations when risk is low, and more widespread when risk is high. Based on expert opinion, the Infectious Diseases Society of America (IDSA) recommended a testing strategy based on the prevalence of the disease in the community (12). They recommended universal testing of asymptomatic hospitalized patients in times and places of high disease prevalence defined as ≥10% or ≥10,000 active cases per 100,000 population and did not recommend universal testing in times and places of low prevalence, defined as under 2% prevalence of disease, or less than 2,000 active cases per 100,000. Most jurisdictions never met the proposed screening threshold as public health measures were enacted to reduce disease prevalence to avoid overwhelming hospital capacity. The IDSA was unable to provide further guidance due to lack of available evidence. Our aim was to determine the diagnostic yield of screening patients for SARS-CoV-2 who had been admitted with a diagnosis unrelated to COVID-19 and identify risk factors for positive tests.

METHODS

Study Design and Setting

The Canadian COVID ED Rapid Response Network (CCEDRRN, pronounced 'sedrin') is a pan Canadian population-based registry that has enrolled consecutive eligible patients presenting with suspected or confirmed COVID–19 from EDs across Canada starting on March 1, 2020. The study population, data collection, data quality assurance, management and governance structure are described in the network's methods paper (13). The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage. Thirty CCEDRRN sites in 7 provinces contributed data to this study (Appendix A).

Patient and Public Involvement

CCEDRRN has an active patient engagement committee with patient partners who have lived experience with COVID-19 from geographically representative areas of Canada. Patient partners provided input into the development of this research question and study protocol and the final manuscript.

Study Patients

Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study. Data from sites and periods that did not meet this quality threshold were excluded. We included consecutive eligible patients who were admitted to hospital and swabbed for SARS-CoV-2 using a nucleic acid amplification test (NAAT) within 24 hours of ED arrival. We enrolled patients between March 1, 2020 and December 29, 2020. To identify a population of admitted patients in whom COVID-19 disease was not suspected, we excluded patients with ED diagnoses that would have been clinically suspicious for COVID-19. These included all patients with ED diagnoses of suspected or confirmed COVID-19, influenza-like-illness (ILI), upper respiratory infections, and pneumonia or viral pneumonia for which testing would have been indicated based on clinical suspicion. We excluded patients who were discharged directly from the ED, diagnosed with COVID-19 before ED arrival (based on a NAAT done in the community), those whose first swab occurred more than 24 hours after their arrival, and repeat admissions. We also excluded patients in whom initial SARS-CoV-2 testing was negative and repeat testing became positive more than 5 days after arrival, as these patients could have contracted nosocomial COVID.

Data Collection

Trained research assistants collected data retrospectively from electronic and/or paper-based medical records into a central, web-based REDCap database (Vanderbilt University; Nashville, TN, USA). Research assistants captured demographics, infection risk, ED vital signs, presenting symptoms, comorbid conditions and the results of COVID-19 tests. The coordinating centre implemented regular data quality checks, including logic checks in REDCap as well as site-level record verifications for nonsensical or outlying values.

In addition to these clinical variables, we calculated the seven-day moving average incident COVID-19 case count for the health region of each participating site using publicly available epidemiological data (14). For each calendar day within each health region represented in the study, we calculated the average daily incident rate of new infections per 100,000 population over the preceding seven days. This seven-day moving average incidence was assigned to each patient based on the date of their index emergency department encounter and the health region of their postal code of residence. We allocated patients with no fixed address to the health region of the hospital in which they were tested. We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing), COVID-19 case data were not publicly available for the early pandemic. The seven-day moving average incident COVID-19 case count was categorized as 0 – 1.99 per 100,000 population, 2 – 7.99 per 100,000 population, and ≥8 per 100,000 population based on the relationship between incidence and COVID-19 positive results in a previous analysis (15).

Outcome:

The primary outcome was a positive NAAT for SARS-CoV-2 in patients admitted with non-COVID-related diagnoses.

Data Analysis:

We divided the cohort into two groups, those without symptoms of COVID-19 and those with symptoms compatible with COVID-19 that were attributed to an alternate diagnosis (i.e., CHF, COPD, Asthma, etc.). We considered cough, dyspnea, fever, general weakness, chest pain, diarrhea, nausea and vomiting, headache, chills, myalgia, sore throat, altered level of consciousness, and dysgeusia/anosmia to be COVID-19-compatible symptoms. We used descriptive statistics to describe the population. We calculated the diagnostic yield by dividing the number of positive NAATs over the total number of NAATs performed. We calculated the exact binomial proportion 95% confidence intervals (95% CI) for

all proportions and used the modified Clopper-Pearson interval for small samples. We completed a planned subgroup analyses for patients presenting with and without COVID compatible symptoms to determine associated factors for a positive test. The initial multivariable logistic regression model to identify factors associated with a positive NAAT considered candidate variables with a p-value cut-off point of 0.20 based on the Wald test from univariable analyses. From the full model, a step-down procedure reduced the model to key predictors based on Akaike's information criterion (AIC) scores (e.g., chose the model with the smallest AIC score). Candidate variables included seven-day moving average incident COVID-19 case count category, patient age, gender, infection risk, and presenting symptoms. We limited the number of predictor variables in the model to one variable for every 10 outcomes in our data to avoid overfitting. Statistical analysis was preformed using Stata (Version 16.1, StataCorp, College Station, Texas).

RESULTS

We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients. During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites.

We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1). Most patients arrived from home and were full code. The most common comorbidities were hypertension, diabetes and mental health illness. Of 3,113 patients admitted without COVID-19 compatible symptoms, 13 (0.4%, 95% CI 0.19% – 0.64%) tested positive for COVID-19. Of the 12,570 with COVID-19-

compatible symptoms, 109 patients (0.9%, 95% CI 0.70% – 1.03%) tested positive for COVID-19. Among the 122 individuals who tested positive for COVID-19, 33 (27.0%, 95% CI 19.0% - 35.0%) were from a geographic region that had a moving average daily incident rate of ≥8 infections per 100,000 population. The diagnostic yield of testing among patients with COVID-19 compatible symptoms admitted for alternative diagnoses did not vary substantially by presenting symptom (Figure 2) or ED diagnosis (Figure 3).

Table 1: Baseline Characteristics of admitted patients without clinical suspicion of COVID-19 (N=15,690)

	Patients without COVID-19 compatible symptoms (N=3,113)	**Patients with COVID-19 compatible symptoms attributed to an alternate diagnosis (N=12,570)**
Demographics		
Age (mean, SD)	57.6 (22.6)	64.6 (20.4)
Female (%)	1,418 (45.6)	5,924 (47.1)
Arrival From (%)		
Home	2,552 (82.0)	10,943 (87.0)
Long-term care or rehab facility	217 (7.0)	832 (6.6)
Unstable housing*	190 (6.1)	414 (3.3)
Corrections	7 (0.2)	14 (0.1)
Interfacility transfer	121 (3.9)	262 (2.1)
Risk for Infection (%)		
Travel	32 (1.0)	134 (1.1)
Institutional (LTC/prison)	231 (7.4)	721 (5.7)
Household contact	28 (0.9)	144 (1.1)
Occupational	10 (0.3)	38 (0.3)
Unknown	1,502 (48.2)	5,377 (42.8)
Pre-ED Goals of Care (%)		
Full code	2,946 (94.6)	11,259 (89.5)
Intermediate GOC	18 (0.6)	173 (1.4)
Do not resuscitate	149 (4.8)	1,142 (9.1)
Acuity		
Arrival by Ambulance (%)	1,724 (55.4)	7,189 (57.2)
CTAS 1 (Resuscitation)	241 (7.7)	1,053 (8.4)
CTAS 2 (Emergent)	1,000 (32.1)	5,786 (46.0)
CTAS 3 (Urgent)	1,527 (49.1)	5,086 (40.4)
CTAS 4 (Less Urgent)	295 (9.5)	572 (4.6)
CTAS 5 (Non Urgent)	40 (1.3)	59 (0.5)
Arrival Vital Signs, Mean (SD)		
Heart Rate, beats per min	91.2 (21.2)	95.5 (23.9)
Systolic BP, mm Hg	134.7 (25.1)	133.6 (27.9)

Oxygen saturation, (%)	96.6 (3.4)	95.7 (4.1)
Respiratory Rate, beats per min	18.6 (4.4)	21.2 (6.3)
Temperature, degrees Celsius	36.6 (0.6)	36.8 (0.9)
Comorbidities (%)		
Hypertension	951 (30.6)	5,321 (42.3)
Psychiatric Condition	728 (23.4)	2,134 (17.0)
Dyslipidemia	425 (13.6)	2,434 (19.4)
Diabetes	427 (13.7)	2,577 (20.5)
Chronic Neuro Disorder	322 (10.3)	1,406 (11.2)
Coronary Artery Disease	284 (9.1)	1,796 (14.3)
Rheumatologic Disorder	229 (7.4)	1,249 (9.9)
Dementia	199 (6.4)	696 (5.5)
Active Cancer	231 (7.4)	1,647 (12.9)
Chronic Kidney Disease	195 (6.3)	1,319 (10.5)
Chronic Lung Disease (not asthma)	199 (6.4)	1,691 (13.5)
Congestive Heart Failure	159 (5.1)	1,392 (11.1)
Asthma	125 (4.0)	712 (5.7)
Obesity	57 (1.8)	344 (2.7)
Symptoms (%)		
Cough	-	2,763 (22.0)
Dyspnea	-	4,757 (37.8)
Fever	-	2,531 (20.1)
General Weakness	-	3,183 (25.3)
Chest Pain	-	2,714 (21.6)
Diarrhea	-	1,339 (10.7)
Nausea/Vomiting	-	3,345 (26.6)
Headache	-	784 (6.2)
Chills	-	957 (7.6)
Myalgia	-	466 (3.7)
Sore Throat	-	374 (3.0)
Altered Consciousness	-	2,502 (19.9)
Dysgusea/Anosmia	-	41 (0.3)
Social Factors (%)		
Pregnant (%)	18 (0.6)	45 (0.4)
Tobacco use (%)	491 (15.8)	1,656 (13.2)
Illicit substance use (%)	421 (13.5)	967 (7.7)
ED Diagnosis (%)		
Respiratory Disease, not specified	8 (0.3)	118 (0.9)
COPD Exacerbation	11 (0.4)	648 (5.2)
Asthma Exacerbation	<5	97 (0.8)
Congestive Heart Failure	44 (1.4)	1,003 (8.0)
Shortness of Breath, NYD*	-	466 (3.6)
Cough, NYD*	-	63 (0.5)
Fever, NYD*	-	482 (3.8)
Outcome (%)		
Positive SARS-CoV-2 NAAT	13 (0.4)	109 (0.9)

*NYD denotes “not yet determined”

When examining the association between patient factors and screening positive self-reported fever, being a healthcare worker, having a positive household contact or institutional exposure, and being from an area where the seven-day moving average incident COVID-19 case count was ≥8 per 100,000 population were associate with a greater risk of testing positive (Table 2). The most important risk factor was reporting a household contact or being the caregiver of a known COVID-19 case.

Table 2: Multivariable analysis of factors associated with positive SARS-CoV-2 NAATs (N=15,690)

	Univariate analysis odds ratio (95% CI)	**Final model with fully adjusted odds ratio (95% CI)[1]**	**P-value**
Sex			
Male	*Reference*	*Reference*	0.18
Female	0.84 (0.59 – 1.21)	0.78 (0.54 – 1.12)	
Age			
	1.00 (1.00 – 1.02)	1.00 (0.99 – 1.01)	0.27
7-day average incident COVID-19 cases			
0 – 1.99 daily cases per 100,000 population	*Reference*	*Reference*	< 0.001
2 to 7.99 daily cases per 100,000 population	1.42 (0.91 – 2.22)	1.47 (0.94 – 2.31)	
≥8 daily cases per 100,000 population	2.99 (1.95 – 4.59)	3.17 (2.05 – 4.89)	
COVID-19 compatible symptoms present			
No	*Reference*	*Reference*	0.08
Yes	2.08 (1.71 – 3.71)	1.65 (0.90 – 3.00)	
Self-reported fever, or temperature ≥ 37.5 °C			
No	*Reference*	*Reference*	< 0.001
Yes	2.72 (1.89 – 3.90)	2.53 (1.74 – 3.67)	
Diarrhea present			
No	*Reference*	*Reference*	0.11
Yes	1.74 (1.04 – 2.92)	1.57 (0.93 – 2.67)	
Healthcare worker			
No	*Reference*	*Reference*	< 0.001
Yes	5.62 (1.35 – 23.43)	4.67 (1.05 – 20.54)	
Household contact or caregiver			
No	*Reference*	*Reference*	< 0.001
Yes	9.48 (5.01 – 17.96)	7.74 (3.98 – 15.04)	
Institutional exposure			
No	*Reference*	*Reference*	< 0.001
Yes	3.46 (2.17 – 5.52)	3.39 (2.10 – 5.47)	
Dysgeusia or anosmia present			

No	*Reference*	-
Yes	3.21 (0.43 – 23.52)	-
Dyspnea present		
No	*Reference*	-
Yes	1.16 (0.80 – 1.70)	-
Nausea or vomiting present		
No	*Reference*	-
Yes	0.81 (0.51 – 1.29)	-

[1] Final model determined by including variables with a p-value of p<0.20 during the sex and age adjusted analysis and using the Akaike Information Criterion (AIC) to determine additional variables to exclude from the final model. Variables adjusted for all other variables present in the final model

DISCUSSION

Our aim was to evaluate the diagnostic yield of screening non-COVID-19 admissions for SARS-CoV-2 across Canada in 2020 and identify patient-level risk factors for positive tests. The diagnostic yield of screening patients with non-COVID-19 related ED diagnoses who were admitted to hospital was low overall, and extremely low in patients without COVID compatible symptoms. The most important patient factors associated with a positive test were having a positive household contact, being a healthcare worker, or having had an institutional exposure to COVID-19. Those factors were more important that a high (≥8 daily cases per 100,000 population) 7-day moving average incident COVID-19 case count.

Our study has several strengths. We used data from a large pan-Canadian registry that enrolls from large geographically and culturally diverse areas and is one of the largest registries in the world. CCEDRRN's patient enrolment and data verification protocols are rigorous, ensuring consecutive eligible patients and high-quality clinical data (13). We have previously demonstrated the inter-rater reliability for our data collection methods, including for symptoms (13).

Prior studies have examined the diagnostic yield of universal screening in single centers with varied diagnostic yield estimates between 0 and 15.5% (3–8). Many of these were case series with limited methods from the early pandemic. There is one known multi-center study which examines the benefit of universal screening for elective and emergent surgical admissions at 14 centers in the Netherlands (1). Like our study, the authors found that the overall COVID-19 NAAT positivity varied with community

prevalence. Our finding that positive SARS-CoV-2 tests were associated with self-reported or measured fever is in keeping with a prior Cochrane systematic review that noted considerable variability in COVID-19 associated symptoms (17).

Our study is interesting in the context of the IDSA recommendations which were based on expert opinion and of "very low certainty" (12). The IDSA panel recommended avoiding universal screening for COVID-19 in times and areas of low COVID prevalence, defined as a disease prevalence of under 2% , or fewer than 2,000 active cases per 100,000 population, a threshold so high that it was never met at any of our study sites, even though multiple sites were in COVID-19 hotspots in 2020 (12). This threshold would have equated to over 6 million cases of active COVID-19 infection in the United States at any given time, which would have vastly overwhelmed hospital capacity, and thus represents an untenable threshold for hospitals. It is therefore not surprising that the prevalence of COVID-19 during the study period was far below the IDSA recommended threshold for initiating screening. While the number needed to screen to identify one positive case among admitted patients in our study was between 110 and 250 among unvaccinated patients, we propose that the IDSA screening threshold likely needs to be adopted.

A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield. While our study is based on a Canadian population without international sites, we believe our findings are generalizable given their wide geographic spread, and the cultural and racial diversity of our patient population. Finally, as data becomes available on the fourth wave of the pandemic, a future study should examine the impact of widespread vaccination on the yield of screening. As a larger proportion of the population is protected from severe disease and death through vaccination, decision makers should carefully consider the low diagnostic yield of a universal testing strategy going forward.

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COMPETING INTERESTS

None identified.

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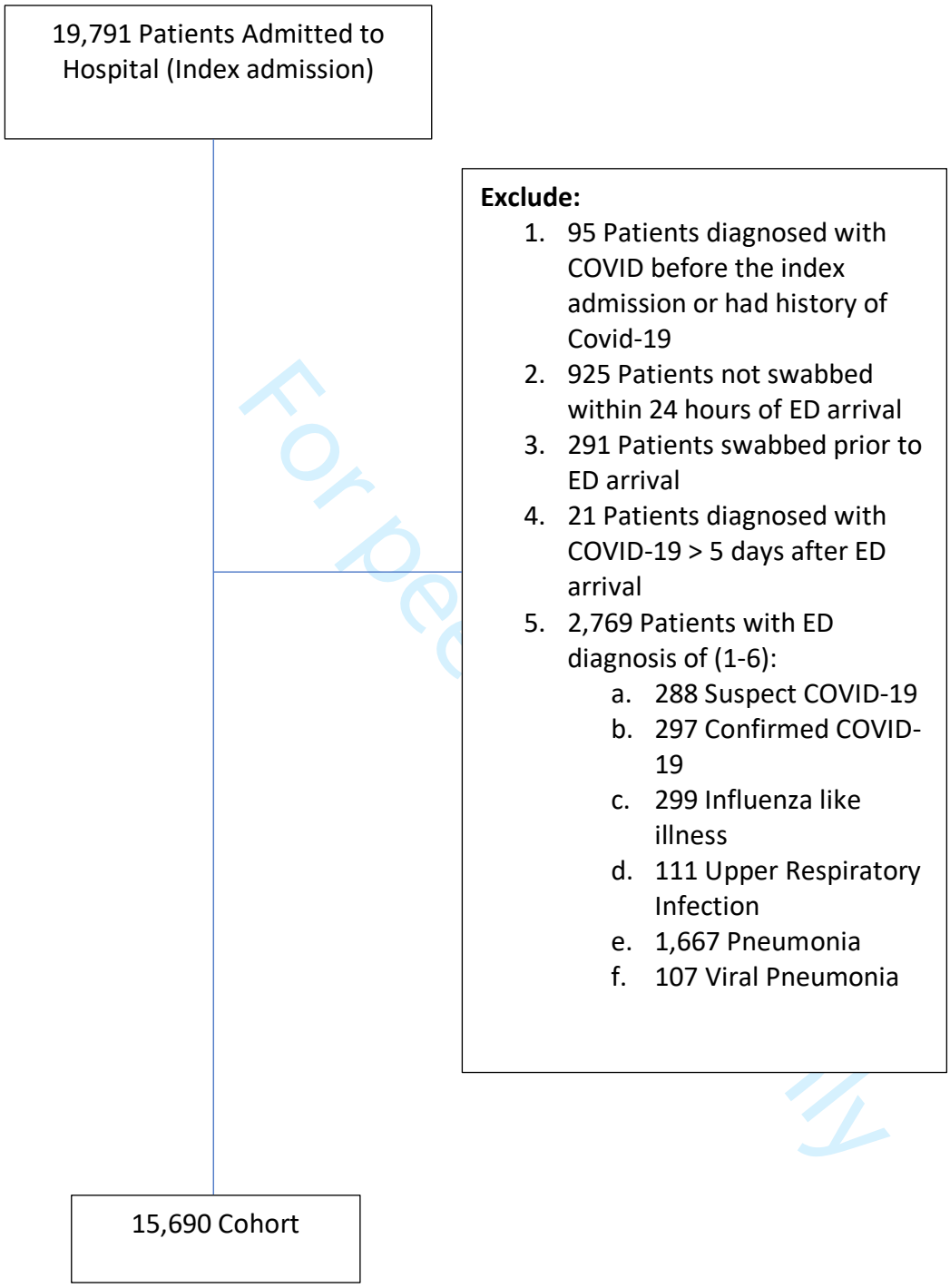
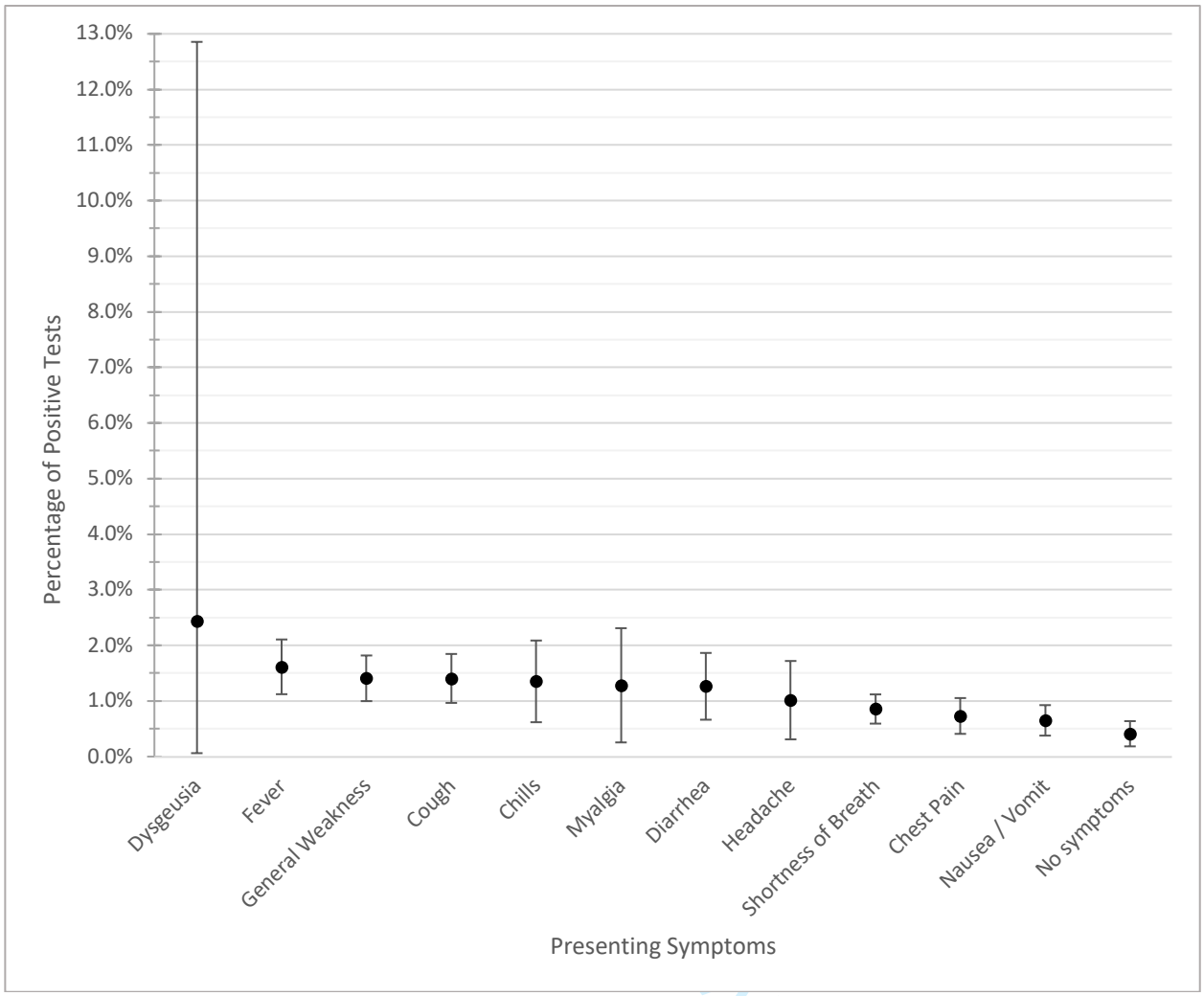
FIGURE CAPTIONS

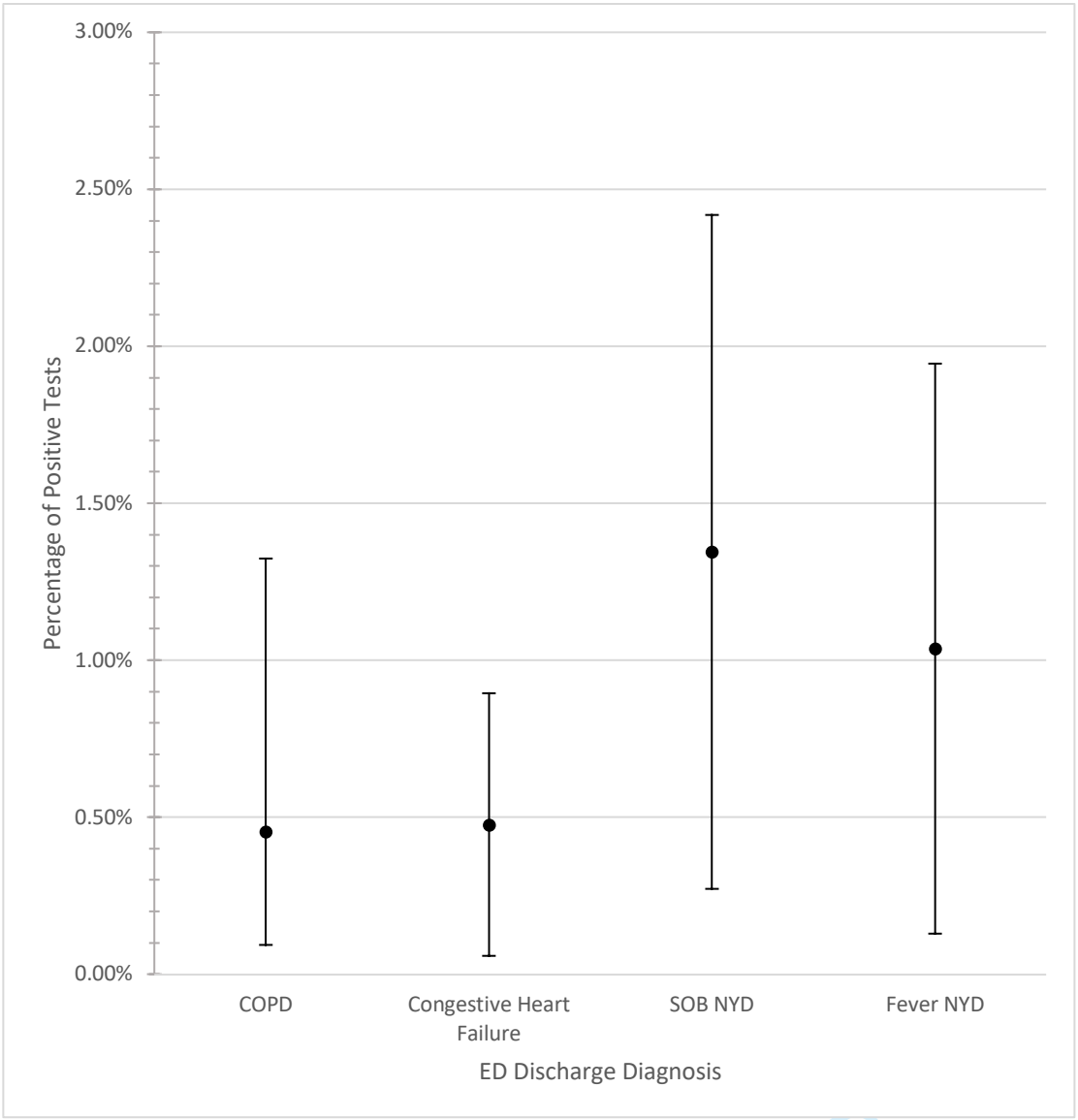
Figure 1. Patient Flow Diagram

Figure 2. Diagnostic Yield by Presenting Symptoms with 95% confidence intervals

Figure 3. Diagnostic Yield by ED Diagnosis with 95% confidence intervals.







SUPPLEMENT

Supplement Table 1. Network coordinating center staff at the University of British Columbia

Name	Roles	Contributions
Jeffrey Hau	Data manager	REDCap, data processing and analysis for manuscripts.
Vi Ho	National coordinator	Coordinate with provincial coordinators and training/onboarding of research assistants.
Serena Small	Research coordinator	Ethics & privacy reviews, data management plan, privacy impact assessment, and qualitative analyses
Amber Cragg	Research manager	Data and manuscript management
Wei Zhao	Data analyst	Data processing and analysis for manuscripts.
Vicky Wu	Data analyst	Data processing and analysis for manuscripts.
Elnaz Bodaghkhani	Research associate	Data and manuscript management

Supplement Table 2. Provincial Coordinators

Name	Province	Institutional affiliation	Contributions to CCEDRRN
Corinne DeMone	NS	Dalhousie University, Halifax, Nova Scotia	Research ethics board submission, manages research assistants, data cleaning and quality.
Jacqueline Fraser	NB	Dalhousie University, St. John New Brunswick	Site coordinator as well as research assistant.
Martyne Audet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis	Provincial research coordinator, translation of research material to French, ethics management.
Connie Taylor	ON	Queen's University, Kingston	Coordination of research assistants in Ontario, maintenance of REB applications for the province
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg	Lead RA for the province

Aimee Goss	SK	University of Saskatchewan, Saskatoon	Screens records in Saskatoon, data/extraction and entry, coordinates research assistants.
Hina Walia	AB	University of Calgary, Calgary	Provincial coordinator lead for Alberta, oversight of all Alberta sites.
Josie Kanu	BC	University of British Columbia, Vancouver	Provincial coordinator lead for BC, oversight of all BC sites.

Supplement Table 3. Institutional research assistant (RA) leads

Name	Province	Institutional affiliation(s)
Corinne DeMone	NS	Dartmouth General Hospital, Cobequid Community Health Centre, Hants Community Hospital Secondary Assessment Centers of the Dartmouth General Hospital, and Halifax Infirmary, Halifax
Jacqueline Fraser	NB	Saint John Regional Hospital, Saint John
Alexandra Nadeau	QC	CHU de Québec Université Laval, Quebec City
Audrey Nolet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis
Xiaoqing Xue	QC	Jewish General Hospital, Montréal
David Iannuzzi	QC	McGill University Health Center, Montréal
Chantal Lanthier	QC	Hôpital du Sacré-Cœur de Montréal, Montréal
Konika Nirmalanathan	ON	University Health Network, Toronto
Vlad Latiu	ON	Kingston General Hospital, Hotel Dieu Hospital, Kingston
Joanna Yeung	ON	Sunnybrook Health Sciences Center, Toronto
Natasha Clayton	ON	Hamilton General Hospital, Juravinski Hospital, Hamilton
Tom Chen	ON	London Health Sciences Centre, London
Jenna Nichols	ON	Health Sciences North, Sudbury
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg
Aimee Goss	SK	St. Paul's Hospital, Royal University Hospital, Saskatoon City Hospital, Saskatoon
Stacy Ruddell	AB	Foothills Medical Centre, Peter Lougheed Centre, Rockyview General Hospital, South Health Campus, Calgary
Natalie Runham	AB	University of Alberta Hospital, Edmonton
Karlin Su	AB	Royal Alexandra Hospital/Northeast Community Health Center, Edmonton
	BC	St. Paul's Hospital, Mount Saint Joseph, Vancouver
Bernice Huynh	BC	Abbotsford Regional Hospital and Cancer Center, Abbotsford
Amanda Swirhun	BC	Royal Columbian Hospital, New Westminster

Name	Province	Institutional affiliation(s)
Tracy Taylor	BC	Eagle Ridge Hospital and Health Care Centre, Port Moody
Mai Hayashi	BC	Royal Inland Hospital, Kamloops
Mackenzie Cheyne	BC	Kelowna General Hospital, Kelowna
Sarim Asim	BC	Surrey Memorial Hospital, Surrey
Katherine Lam	BC	Vancouver General Hospital, Vancouver
Kelsey Compagna	BC	Lions Gate Hospital, Vancouver

Supplement Table 4. Contributing Study Sites and Investigators

Lead Investigator	Contributing Site / Code	Member Investigators
Maritime		
Patrick Fok		
Nova Scotia		
Hana Wiemer	Halifax Infirmary/ 902	Patrick Fok
	Dartmouth General Hospital/ 903	Hana Wiemer
	Hants Community Hospital/ 904	Samuel Campbell
	Cobequid Community Health Centre/ 905	Kory Arsenault
	Secondary Assessment Centers of Dartmouth General and Halifax Infirmary/ 908	Tara Dahn
New Brunswick		
Kavish Chandra	Saint John Regional Hospital/ 901	Kavish Chandra
Quebec		
Patrick Archambault	Hotel-Dieu de Lévis/ 701	Patrick Archambault
	Jewish General Hospital/ 702	Joel Turner
	Centre Hospitalier de l'Université Laval (CHU de Québec)/ 703	Éric Mercier
	L'hôpital Royal Victoria - Royal Victoria Hospital/ 705	Greg Clark
	Hôpital de l'Enfant-Jésus,CHU de Québec/ 706	Éric Mercier
	Hôpital du Saint-Sacrement, CHU de Québec/ 707	Éric Mercier
	Hôpital Saint-François d'Assise, CHU de Québec/ 708	Éric Mercier
	Hôtel-Dieu de Québec,CHU de Québec/ 709	Éric Mercier
	IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec/ 710	Sébastien Robert
	Hôpital du Sacré-Coeur de Montreal/ 711	Raoul Daoust
Ontario		
Laurie Morrison & Steven Brooks	Sunnybrook/ 401	Ivy Cheng
	The Ottawa Hospital - Civic Campus/ 403	Jeffrey Perry
	The Ottawa Hospital - General Campus/ 404	Jeffrey Perry
	Kingston/Queens/ 406	Steven Brooks
	Hamilton General Hospital/ 407	Michelle Welsford
	Health Science North, Sudbury Ontario/ 408	Rob Ohle
	University Hospital – LHSC/ 409	Justin Yan
	North York General Hospital, Toronto/ 410	Rohit Mohindra
	Victoria Hospital – LHSC/ 412	Justin Yan
	Toronto Western Hospital/ 414	Megan Landes
Manitoba		
Tomislav Jelic	Health Sciences Centre/ 307	Tomislav Jelic
Saskatchewan		
Phil Davis	St Paul's Hospital, Saskatoon/ 303	Phil Davis
	Royal University, Saskatoon/ 304	Phil Davis

	Saskatoon City Hospital, Saskatoon/ 305	Phil Davis
Alberta		
Andrew McRae	University of Alberta Hospital, Edmonton/ 201	Brian Rowe
	Foothills, Calgary/ 202	Katie Lin
	Rockyview, Calgary/ 203	Andrew McRae
	Peter Lougheed Centre/ 204	Andrew McRae
	South Campus, Calgary/ 205	Stephanie VandenBerg
	Northeast Community Health Centre, Edmonton/ 206	Jake Hayward, Jaspreet Khangura
	Royal Alexandra Hospital, Edmonton/ 306	Jake Hayward, Jaspreet Khangura
British Columbia		
Corinne Hohl	Vancouver General Hospital/ 101	Daniel Ting
	Lions Gate Hospital/ 102	Maja Stachura
	Saint Paul's Hospital/ 103	Frank Scheuermeyer
	Mount St Joseph's/ 104	Frank Scheuermeyer
	Surrey Memorial Hospital/ 105	Balijeet Braar
	Royal Columbian Hospital/ 106	John Taylor
	Abbotsford Regional Hospital/ 107	Ian Martin
	Eagle Ridge Hospital/ 108	Sean Wormsbecker
	Royal Inland Hospital/ 112	Ian Martin
	Kelowna General / Hospital/ 115	Lee Graham

Appendix A: List of hospital sites, with an inclusion start and end date for this study.

Site Name	Province	Start Date	End Date
Vancouver General Hospital	British Columbia	1-Mar-2020	31-Aug-2020
Lions Gate Hospital	British Columbia	1-Mar-2020	29-Apr-2020
Saint Paul's Hospital	British Columbia	1-Mar-2020	23-May-2020
Mount Saint Joseph Hospital	British Columbia	1-Mar-2020	24-Mar-2020
Surrey Memorial Hospital	British Columbia	19-Mar-2020	30-Apr-2020
Royal Columbian Hospital	British Columbia	1-Mar-2020	31-May-2020
Abbotsford Regional Hospital	British Columbia	20-Apr-2020	15-Jul-2020
University of Alberta Hospital	Alberta	8-Apr-2020	7-May-2020
Foothills Medical Centre	Alberta	1-Mar-2020	7-Apr-2020
Rockyview General Hospital	Alberta	1-Mar-2020	7-Apr-2020
Peter Lougheed Centre	Alberta	1-Mar-2020	12-Dec-2020
South Health Campus	Alberta	1-Mar-2020	12-Dec-2020
St Paul's Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Royal University Hospital	Saskatchewan	17-Mar-2020	31-Oct-2020
Saskatoon City Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Sunnybrook Health Sciences Centre	Ontario	14-May-2020	31-Oct-2020
The Ottawa Hospital - Civic Campus	Ontario	14-May-2020	31-May-2020
Health Science North	Ontario	14-May-2020	29-Dec-2020
Toronto Western Hospital	Ontario	1-Sep-2020	31-Sep-2020
Hotel-Dieu de Lévis	Quebec	4-May-2020	18-May-2020
Jewish General Hospital	Quebec	1-Mar-2020	4-Jun-2020
Hôpital de l'Enfant-Jésus,CHU de Québec	Quebec	4-May-2020	23-Jul-2020
IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec	Quebec	4-May-2020	13-May-2020

Hôpital du Sacré-Coeur de Montreal	Quebec	4-May-2020	18-May-2020
Saint John Regional Hospital	New Brunswick	12-Mar-2020	12-Apr-2020
Halifax Infirmary	Nova Scotia	5-Apr-2020	15-Apr-2020
Dartmouth General Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Hants Community Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Cobequid Community Health Centre	Nova Scotia	5-Apr-2020	15-Apr-2020
Secondary Assessment Centers of Dartmouth General and Halifax Infirmary	Nova Scotia	26-Mar-2020	15-May-2020

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2 (abstract)	"Cohort from the CCEDRRN registry"
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Included within the results and conclusions of the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	Relevant scientific literature has been cited and the rationale for the study is outlined.
Objectives	3	State specific objectives, including any prespecified hypotheses	5	"Our aim was to determine the diagnostic yield of screening patients admitted to hospital with a diagnosis unrelated to COVID-19 for SARS-CoV-2 in 2020, and identify risk factors for a positive test"
Methods				
Study design	4	Present key elements of study design early in the paper	5	The Study Design and Setting is outlined early in the Methods Section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Included in "Study Design and Setting" sub-section.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	Included in the "Study Patients" sub-section. Eligibility, sources and methods of selection are described.

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7	Variables are outlined in the "Data Collection" sub-section.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7	Data sources and methods of assessment are outlined in the "Study Design and Setting" and "Data Collection" sub-sections.
Bias	9	Describe any efforts to address potential sources of bias	6-7	Described within the "Study Patients" and the "Data Collection" sub-sections.
Study size	10	Explain how the study size was arrived at	6	Described within the "Study Patients" sub-section.

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8	Included within the "Data Collection" and "Data Analysis" sub-sections.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8	Descriptive statistics, sub-group analyses, and regression models were used. Confounding was addressed via multivariable regression.
		(*b*) Describe any methods used to examine subgroups and interactions	8	Sub-group analyses were planned for patients presenting with and without COVID compatible symptoms.
		(*c*) Explain how missing data were addressed	6-7	"Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study" "We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing)"
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7-8	Loss to follow-up was not an issue. Study enrolled consecutive patients who met the inclusion/exclusion criteria and data collected through chart review.
		(*e*) Describe any sensitivity analyses	N/A	Not performed.
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically

				suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients."
		(b) Give reasons for non-participation at each stage	N/A	Study was based on chart review.
		(c) Consider use of a flow diagram	Figure 1	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9	Paragraph 2 of the results includes the descriptive summaries.
		(b) Indicate number of participants with missing data for each variable of interest	N/A	See methods.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020".
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8	"During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites."
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A	
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9	Descriptive results and comparative findings are described in the latter 2 paragraphs of the "Results"
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9	Follows the sentence "We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1)."
Discussion				
Key results	18	Summarise key results with reference to study objectives	9-10	The study objective is recalled and situated within the context of the results.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11	"A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield."
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	Key references are recalled, and the study results are situated with these references.
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11	"While our study is based on a Canadian population without international sites, we believe our

				findings are likely generalizable given the wide geographic spread of our study sites."
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11	Included under "Funding" Section.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

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Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Infectious diseases
Keywords:	COVID-19, EPIDEMIOLOGY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Diagnostic microbiology < INFECTIOUS DISEASES

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Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

Phil Davis[1], Rhonda J. Rosychuk[2], Jeffrey P Hau[3,14], Ivy Cheng[4,5], Andrew D. McRae[6], Raoul Daoust[7], Eddy Lang[8], Joel Turner[9], Jaspreet Khangura[10], Patrick T. Fok[11], Maja Stachura[12], Baljeet Brar[13], and Corinne Hohl[14] **on behalf of the CCEDRRN investigators, and for the Network of Canadian Emergency Researchers and the Canadian Critical Care Trials Group**

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Word count (excluding title page, abstract, references, figures, and tables): 2282

Keywords: screening, COVID-19, coronavirus disease, health services utilization, diagnostic testing, pandemic

Abstract:

Objectives: To determine the diagnostic yield of screening patients for SARS-CoV-2 who were admitted with a diagnosis unrelated to COVID-19, and identify risk factors for positive tests.

Design: Cohort from the Canadian COVID-19 Emergency Department Rapid Response Network (CCEDRRN) registry

Setting: 30 acute care hospitals across Canada

Participants: Patients hospitalized for non-COVID-19 related diagnoses who were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 1, and December 29, 2020

Main outcome: Positive nucleic acid amplification test (NAAT) for SARS-CoV-2

Outcome measure: Diagnostic yield

Results: We enrolled 15,690 consecutive eligible adults who were admitted to hospital without clinically suspected COVID-19. Among these patients, 122 tested positive for COVID-19, resulting in a diagnostic yield of 0.8% (95% CI 0.64% – 0.92%). Factors associated with a positive test included presence of a fever, being a healthcare worker, having a positive household contact or institutional exposure, and living in an area with higher 7-day average incident COVID-19 cases.

Conclusions: Universal screening of hospitalized patients for COVID-19 across two pandemic waves had a low diagnostic yield and should be informed by individual-level risk assessment in addition to regional COVID-19 prevalence.

Trial registration: NCT04702945

Strengths and Limitations

- Pan-Canadian study including over 40 academic, non-academic, rural, and urban hospitals.
- Inclusion of patient partners, as well as public engagement, who assisted in the development and presentation of this manuscript.
- Inclusion of pertinent clinical variables, as well as relevant demographic and community level variables.
- Exclusion of non-NAAT tests due to their infrequent use in the Canadian context.

INTRODUCTION

Healthcare institutions initiated widespread testing of admitted patients for coronavirus disease 2019 (COVID-19) in the spring of 2020 (1). Patients without any reported symptoms of COVID-19 were routinely tested even in jurisdictions where COVID-19 rates were low in order to identify asymptomatic carriers and prevent hospital outbreaks (2). Some jurisdictions have continued this practice without robust evidence to support this practice. An Alberta study of 3,375 patients admitted to hospital for alternate diagnoses during the first wave of the pandemic when COVID-19 prevalence was very low found that none of the patients tested positive (3). In contrast, other studies from times and regions with higher COVID-19 prevalence reported positive tests in between 2.6 and 15.5% of otherwise asymptomatic patients (4–8).

Universal testing has several potential downsides if diagnostic yield is low. First, it may worsen Emergency Department (ED) crowding, as admitted patients with pending COVID-19 tests are boarded in EDs until their test results are reported. While ED volumes were lower than usual in the early pandemic such that EDs could absorb this delay, high patient volumes have since returned, exacerbating the impact of this practice on hospital crowding (9). This in turn increases patient morbidity and mortality (10). In addition, diagnostic workups and therapeutic interventions may be delayed until COVID-19 test results are back, as it takes longer to move patients on isolation precautions through the system. This can further exacerbate patient outcomes and hospital crowding. Thirdly, diagnostic testing capacity may be limited, potentially delaying processing of tests for symptomatic patients. In addition, the use of Personal Protective Equipment (PPE) may be increased as institutions have placed patients with pending COVID-19 tests under isolation precautions. The use of PPE during resuscitation has been associated with worse patient outcomes (11). Lastly, there is also an opportunity cost for hospitals as money spent on universal testing could be allocated to other areas. These unintended consequences of liberal testing policies need to be weighed carefully against the anticipated diagnostic yield and potential benefits.

As for any diagnostic test, rational COVID-19 testing guidelines should be informed by the level of risk of the patient, such that testing is reduced in situations when risk is low, and more widespread when risk is high. Based on expert opinion, the Infectious Diseases Society of America (IDSA) recommended a testing strategy based on the prevalence of the disease in the community (12). They recommended universal testing of asymptomatic hospitalized patients in times and places of high disease prevalence defined as ≥10% or ≥10,000 active cases per 100,000 population and did not recommend universal testing in times and places of low prevalence, defined as under 2% prevalence of disease, or less than 2,000 active cases per 100,000. Most jurisdictions never met the proposed screening threshold as public health measures were enacted to reduce disease prevalence to avoid overwhelming hospital capacity. The IDSA was unable to provide further guidance due to lack of available evidence. Our aim was to determine the diagnostic yield of screening patients for SARS-CoV-2 who had been admitted with a diagnosis unrelated to COVID-19 and identify risk factors for positive tests.

METHODS

Study Design and Setting

The Canadian COVID ED Rapid Response Network (CCEDRRN, pronounced 'sedrin') is a pan Canadian population-based registry that has enrolled consecutive eligible patients presenting with suspected or confirmed COVID–19 from EDs across Canada starting on March 1, 2020. The study population, data collection, data quality assurance, management and governance structure are described in the network's methods paper (13). The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015). Thirty CCEDRRN sites in 7 provinces contributed data to this study (Appendix A). Data are available upon reasonable request and can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Patient and Public Involvement

CCEDRRN has an active patient engagement committee with patient partners who have lived experience with COVID-19 from geographically representative areas of Canada. Patient partners provided input into the development of this research question and study protocol and the final manuscript.

Study Patients

Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study. Data from sites and periods that did not meet this quality threshold were excluded. We included consecutive eligible patients who were admitted to hospital and swabbed for SARS-CoV-2 using a nucleic acid amplification test (NAAT) within 24 hours of ED arrival. We enrolled patients between March 1, 2020 and December 29, 2020. To identify a population of admitted patients in whom COVID-19 disease was not suspected, we excluded patients with ED diagnoses that would have been clinically suspicious for COVID-19. These included all patients with ED diagnoses of suspected or confirmed COVID-19, influenza-like-illness (ILI), upper respiratory infections, and pneumonia or viral pneumonia for which testing would have been indicated based on clinical suspicion. We excluded patients who were discharged directly from the ED, diagnosed with COVID-19 before ED arrival (based on a NAAT done in the community), those whose first swab occurred more than 24 hours after their arrival, and repeat admissions. We also excluded patients in whom initial SARS-CoV-2 testing was negative and repeat testing became positive more than 5 days after arrival, as these patients could have contracted nosocomial COVID.

Data Collection

Trained research assistants collected data retrospectively from electronic and/or paper-based medical records into a central, web-based REDCap database (Vanderbilt University; Nashville, TN, USA). Research assistants captured demographics, infection risk, ED vital signs, presenting symptoms, comorbid conditions and the results of COVID-19 tests. The coordinating centre implemented regular

data quality checks, including logic checks in REDCap as well as site-level record verifications for nonsensical or outlying values.

In addition to these clinical variables, we calculated the seven-day moving average incident COVID-19 case count for the health region of each participating site using publicly available epidemiological data (14). For each calendar day within each health region represented in the study, we calculated the average daily incident rate of new infections per 100,000 population over the preceding seven days. This seven-day moving average incidence was assigned to each patient based on the date of their index emergency department encounter and the health region of their postal code of residence. We allocated patients with no fixed address to the health region of the hospital in which they were tested. We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing), COVID-19 case data were not publicly available for the early pandemic. The seven-day moving average incident COVID-19 case count was categorized as 0 – 1.99 per 100,000 population, 2 – 7.99 per 100,000 population, and ≥8 per 100,000 population based on the relationship between incidence and COVID-19 positive results in a previous analysis (15).

Outcome:

The primary outcome was a positive NAAT for SARS-CoV-2 in patients admitted with non-COVID-related diagnoses.

Data Analysis:

We divided the cohort into two groups, those without symptoms of COVID-19 and those with symptoms compatible with COVID-19 that were attributed to an alternate diagnosis (i.e., CHF, COPD, Asthma, etc.). We considered cough, dyspnea, fever, general weakness, chest pain, diarrhea, nausea and vomiting, headache, chills, myalgia, sore throat, altered level of consciousness, and dysgeusia/anosmia to be COVID-19-compatible symptoms. We used descriptive statistics to describe the population. We

calculated the diagnostic yield by dividing the number of positive NAATs over the total number of NAATs performed. We calculated 7-day average of NAAT positivity over the study period by dividing the number of positive NAATs over all tests performed and averaging over a 7-day period. We calculated the exact binomial proportion 95% confidence intervals (95% CI) for all proportions and used the modified Clopper-Pearson interval for small samples. We completed a planned subgroup analyses for patients presenting with and without COVID compatible symptoms to determine associated factors for a positive test. The initial multivariable logistic regression model to identify factors associated with a positive NAAT considered candidate variables with a p-value cut-off point of 0.20 based on the Wald test from univariable analyses. From the full model, a step-down procedure reduced the model to key predictors based on Akaike's information criterion (AIC) scores (e.g., chose the model with the smallest AIC score). Candidate variables included seven-day moving average incident COVID-19 case count category, patient age, gender, infection risk, and presenting symptoms. We limited the number of predictor variables in the model to one variable for every 10 outcomes in our data to avoid overfitting. Statistical analysis was preformed using Stata (Version 16.1, StataCorp, College Station, Texas).

RESULTS

We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients. During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites. The 7-day average diagnostic test positivity varied between 0 and 2.9% across sites during the study period (Figure 2).

We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1). Most patients arrived from home and were full code. The most common comorbidities were hypertension, diabetes and mental health illness.

Of 3,113 patients admitted without COVID-19 compatible symptoms, 13 (0.4%, 95% CI 0.19% – 0.64%) tested positive for COVID-19. Of the 12,570 with COVID-19-compatible symptoms, 109 patients (0.9%, 95% CI 0.70% – 1.03%) tested positive for COVID-19. Among the 122 individuals who tested positive for COVID-19, 33 (27.0%, 95% CI 19.0% - 35.0%) were from a geographic region that had a moving average daily incident rate of ≥8 infections per 100,000 population. The diagnostic yield of testing among patients with COVID-19 compatible symptoms admitted for alternative diagnoses did not vary substantially by presenting symptom (Figure 3) or ED diagnosis (Figure 4).

When examining the association between patient factors and screening positive self-reported fever, being a healthcare worker, having a positive household contact or institutional exposure, and being from an area where the seven-day moving average incident COVID-19 case count was ≥8 per 100,000 population were associate with a greater risk of testing positive. The most important risk factor was reporting a household contact or being the caregiver of a known COVID-19 case.

DISCUSSION

Our aim was to evaluate the diagnostic yield of screening non-COVID-19 admissions for SARS-CoV-2 across Canada in 2020 and identify patient-level risk factors for positive tests. The diagnostic yield of screening patients with non-COVID-19 related ED diagnoses who were admitted to hospital was low overall, and extremely low in patients without COVID compatible symptoms. The most important patient factors associated with a positive test were having a positive household contact, being a healthcare worker, or having had an institutional exposure to COVID-19. Those factors were more important than a high (≥8 daily cases per 100,000 population) 7-day moving average incident COVID-19 case count.

Our study has several strengths. We used data from a large pan-Canadian registry that enrolls from large geographically and culturally diverse areas and is one of the largest registries in the world. CCEDRRN's patient enrolment and data verification protocols are rigorous, ensuring consecutive eligible patients and high-quality clinical data (13). We have previously demonstrated the inter-rater reliability for our data collection methods, including for symptoms (13).

Prior studies have examined the diagnostic yield of universal screening in single centers with varied diagnostic yield estimates between 0 and 15.5% (3–8). Many of these were case series with limited methods from the early pandemic. There is one known multi-center study which examines the benefit of universal screening for elective and emergent surgical admissions at 14 centers in the Netherlands (1). Like our study, the authors found that the overall COVID-19 NAAT positivity varied with community prevalence. Our finding that positive SARS-CoV-2 tests were associated with self-reported or measured fever is in keeping with a prior Cochrane systematic review that noted considerable variability in COVID-19 associated symptoms (16).

Our study is interesting in the context of current IDSA recommendations which were based on expert opinion and of "very low certainty" (12). The IDSA panel recommended avoiding universal screening for COVID-19 in times and areas of low COVID prevalence, defined as a disease prevalence of under 2% , or fewer than 2,000 active cases per 100,000 population, a threshold so high that it was never met at any of our study sites, even though multiple sites were in COVID-19 hotspots in 2020 (12). The IDSA threshold would have equated to over 6 million cases of active COVID-19 infection in the United States at any given time, which would have vastly overwhelmed hospital capacity, and thus represents an untenable threshold for hospitals. It is therefore not surprising that the prevalence of COVID-19 during the study period was far below the IDSA recommended threshold for initiating screening. While the number needed to screen to identify one positive case among admitted patients in our study was between 110 and 250 among unvaccinated patients, we propose that new screening thresholds need to be adopted which would ideally be based on readily available measures of local incident cases or test positivity.

A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield. Additionally, our study was performed before the newer COVID-19 variants, such as Omicron, circulated widely. However, our methods are easily replicated, and we intend to repeat our study in a recent dataset reflective of new COVID-19 variants. While our study is based on a Canadian population without international sites, we believe our findings are generalizable given their wide geographic spread, and the cultural and racial diversity of our patient population. Finally, as data becomes available on the fourth wave of the pandemic, a future study should examine the impact of widespread vaccination on the yield of screening. As a larger proportion of the population is protected from severe disease and death through vaccination, decision makers should carefully consider the low diagnostic yield of a universal testing strategy going forward.

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Thank you to all of our patient partners who shared their lived experiences and perspectives to ensure that the knowledge we co-create addresses the concerns of patients and the public. Creating the largest network of collaboration across Canadian Emergency Departments would not have been feasible without the tireless efforts of Emergency Department Chiefs, and research coordinators and research assistants at participating sites. Finally, our most humble and sincere gratitude to our colleagues in medicine, nursing,

and the allied health professions who have been on the front lines of this pandemic from day one staffing our ambulances, Emergency Departments, hospitals and ICUs bravely facing the risks of COVID-19 to look after our fellow citizens and after one another. We dedicate this network to you.

COMPETING INTERESTS

None identified.

FUNDING

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AUTHOR CONTRIBUTION STATEMENT

All authors conceived and planned the study together, and iteratively refined the study objectives and analytic plan. PH, RJR, ADM, EL and CMH obtained funding for the study. PD, IC, ADM, RD, JT, JK, PRF, MS and BB supervised data collection. JPH analyzed the data under the supervision of RJR. All authors interpreted the analysis. PD drafted the manuscript. All authors were actively involved in reporting out work by revising the manuscript for content. All authors take responsibility for the manuscript as a whole.

DATA SHARING

Data are available upon reasonable request. They can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Table 1: Baseline Characteristics of admitted patients without clinical suspicion of COVID-19 (N=15,690)

	Patients without COVID-19 symptoms (N=3,113)	Patients with COVID-19 compatible symptoms attributed to an alternate diagnosis (N=12,570)
Demographics		
Age (mean, SD)	57.6 (22.6)	64.6 (20.4)
Female (%)	1,418 (45.6)	5,924 (47.1)
Pregnant (%)	18 (0.6)	45 (0.4)
Tobacco use (%)	491 (15.8)	1,656 (13.2)
Illicit substance use (%)	421 (13.5)	967 (7.7)
Arrival by Ambulance (%)	1,724 (55.4)	7,189 (57.2)
Arrival From (%)		
Home	2,552 (82.0)	10,943 (87.0)
Long-term care or rehab facility	217 (7.0)	832 (6.6)
Unstable housing*	190 (6.1)	414 (3.3)
Corrections	7 (0.2)	14 (0.1)
Interfacility transfer	121 (3.9)	262 (2.1)
Risk for Infection (%)		
Travel	32 (1.0)	134 (1.1)
Institutional (LTC/prison)	231 (7.4)	721 (5.7)
Household contact	28 (0.9)	144 (1.1)
Occupational	10 (0.3)	38 (0.3)
Unknown	1,502 (48.2)	5,377 (42.8)
Pre-ED Goals of Care (%)		
Full code	2,946 (94.6)	11,259 (89.5)
Intermediate GOC	18 (0.6)	173 (1.4)
Do not resuscitate	149 (4.8)	1,142 (9.1)
Acuity		
CTAS 1 (Resuscitation)	241 (7.7)	1,053 (8.4)
CTAS 2 (Emergent)	1,000 (32.1)	5,786 (46.0)
CTAS 3 (Urgent)	1,527 (49.1)	5,086 (40.4)
CTAS 4 (Less Urgent)	295 (9.5)	572 (4.6)
CTAS 5 (Non Urgent)	40 (1.3)	59 (0.5)
Arrival Vital Signs, Mean (SD)		
Heart Rate, beats per min	91.2 (21.2)	95.5 (23.9)
Systolic BP, mm Hg	134.7 (25.1)	133.6 (27.9)
Oxygen saturation, (%)	96.6 (3.4)	95.7 (4.1)
Respiratory Rate, beats per min	18.6 (4.4)	21.2 (6.3)
Temperature, degrees Celsius	36.6 (0.6)	36.8 (0.9)
Comorbidities (%)		
Hypertension	951 (30.6)	5,321 (42.3)
Psychiatric Condition	728 (23.4)	2,134 (17.0)
Dyslipidemia	425 (13.6)	2,434 (19.4)
Diabetes	427 (13.7)	2,577 (20.5)
Chronic Neuro Disorder	322 (10.3)	1,406 (11.2)

Coronary Artery Disease	284 (9.1)	1,796 (14.3)
Rheumatologic Disorder	229 (7.4)	1,249 (9.9)
Dementia	199 (6.4)	696 (5.5)
Active Cancer	231 (7.4)	1,647 (12.9)
Chronic Kidney Disease	195 (6.3)	1,319 (10.5)
Chronic Lung Disease (not asthma)	199 (6.4)	1,691 (13.5)
Congestive Heart Failure	159 (5.1)	1,392 (11.1)
Asthma	125 (4.0)	712 (5.7)
Obesity	57 (1.8)	344 (2.7)
Symptoms (%)		
Cough	-	2,763 (22.0)
Dyspnea	-	4,757 (37.8)
Fever	-	2,531 (20.1)
General Weakness	-	3,183 (25.3)
Chest Pain	-	2,714 (21.6)
Diarrhea	-	1,339 (10.7)
Nausea/Vomiting	-	3,345 (26.6)
Headache	-	784 (6.2)
Chills	-	957 (7.6)
Myalgia	-	466 (3.7)
Sore Throat	-	374 (3.0)
Altered Consciousness	-	2,502 (19.9)
Dysgusea/Anosmia	-	41 (0.3)
ED Diagnosis (%)		
Respiratory Disease, not specified	8 (0.3)	118 (0.9)
COPD Exacerbation	11 (0.4)	648 (5.2)
Asthma Exacerbation	<5	97 (0.8)
Congestive Heart Failure	44 (1.4)	1,003 (8.0)
Shortness of Breath, NYD*	-	466 (3.6)
Cough, NYD*	-	63 (0.5)
Fever, NYD*	-	482 (3.8)
Outcome (%)		
Positive SARS-CoV-2 NAAT	13 (0.4)	109 (0.9)

*NYD denotes “not yet determined”

Table 2: Multivariate analysis of factors associated with positive SARS-CoV-2 nucleic tests (N=15,690)

	Univariate analysis odds ratio (95% CI)	Final model with fully adjusted odds ratio (95% CI)[1]	P-value
Sex			
Male	*Reference*	*Reference*	0.18
Female	0.84 (0.59 – 1.21)	0.78 (0.54 – 1.12)	
Age			
	1.00 (1.00 – 1.02)	1.00 (0.99 – 1.01)	0.27
7-day average incident COVID-19 cases			
0 – 1.99 daily cases per 100,000 population	*Reference*	*Reference*	< 0.001
2 to 7.99 daily cases per 100,000 population	1.42 (0.91 – 2.22)	1.47 (0.94 – 2.31)	
≥8 daily cases per 100,000 population	2.99 (1.95 – 4.59)	3.17 (2.05 – 4.89)	
COVID-19 compatible symptoms present			
No	*Reference*	*Reference*	0.08
Yes	2.08 (1.71 – 3.71)	1.65 (0.90 – 3.00)	
Self-reported fever, or temperature ≥ 37.5 °C			
No	*Reference*	*Reference*	< 0.001
Yes	2.72 (1.89 – 3.90)	2.53 (1.74 – 3.67)	
Diarrhea present			
No	*Reference*	*Reference*	0.11
Yes	1.74 (1.04 – 2.92)	1.57 (0.93 – 2.67)	
Healthcare worker			
No	*Reference*	*Reference*	0.06
Yes	5.62 (1.35 – 23.43)	4.67 (1.05 – 20.54)	
Household contact or caregiver			
No	*Reference*	*Reference*	< 0.001
Yes	9.48 (5.01 – 17.96)	7.74 (3.98 – 15.04)	
Institutional exposure			
No	*Reference*	*Reference*	< 0.001
Yes	3.46 (2.17 – 5.52)	3.39 (2.10 – 5.47)	
Dysgeusia or anosmia present			
No	*Reference*	-	
Yes	3.21 (0.43 – 23.52)	-	
Dyspnea present			
No	*Reference*	-	
Yes	1.16 (0.80 – 1.70)	-	
Nausea or vomiting present			
No	*Reference*	-	
Yes	0.81 (0.51 – 1.29)	-	

[1] Final model determined by including variables with a p-value of p<0.20 during the sex and age adjusted analysis, and using the Akaike Information Criterion (AIC) to determine additional variables to exclude from the final model. Variables adjusted for all other variables present in the final model

Figure 1: Patient Flow Diagram

Figure 2: 7-day working average of COVID-19 NAAT positivity over the study period across sites.

Figure 3: Diagnostic Yield by Presenting Symptoms

Figure 4: Diagnostic Yield by ED Diagnosis

ETHICAL APPROVAL STATEMENT

The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015).

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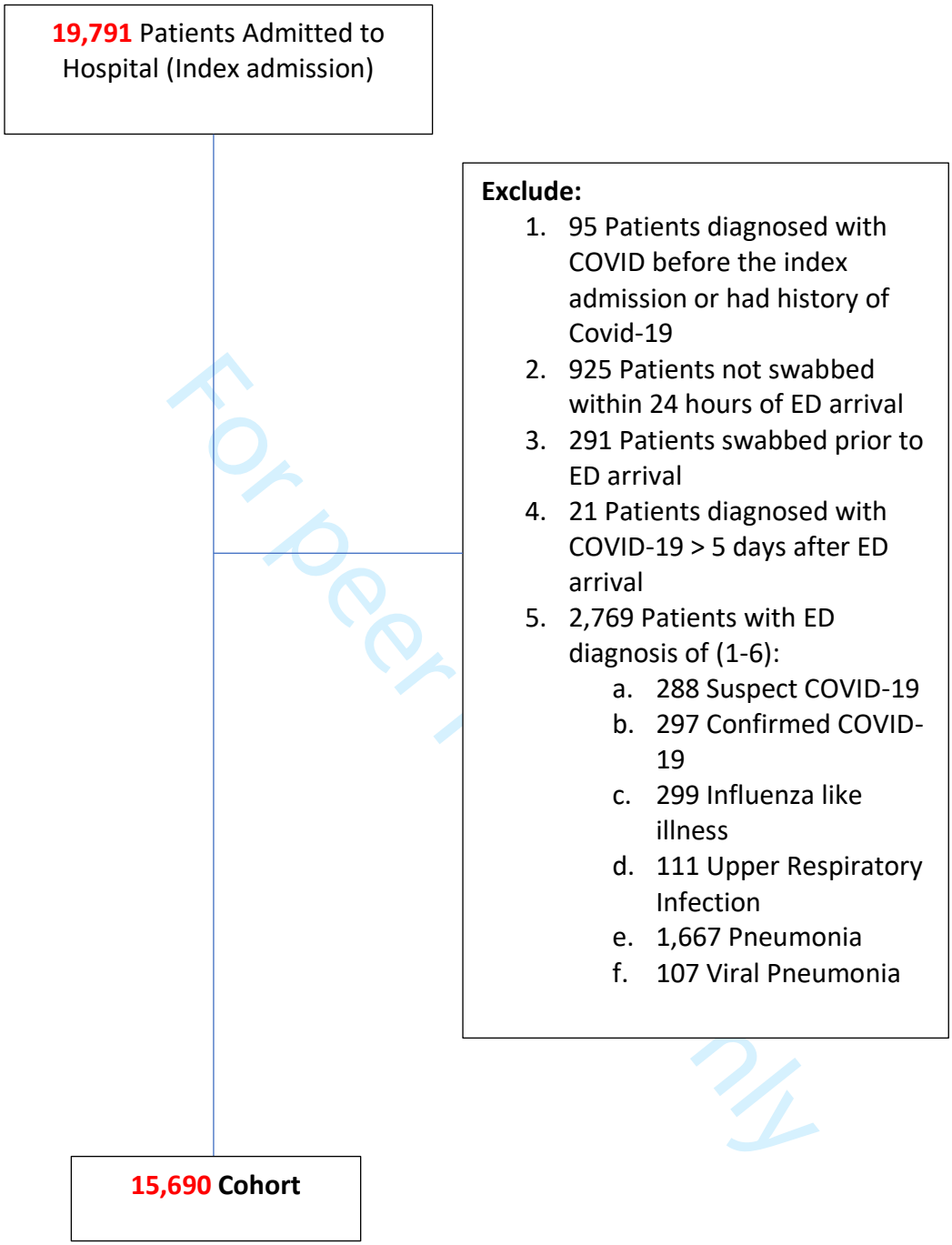

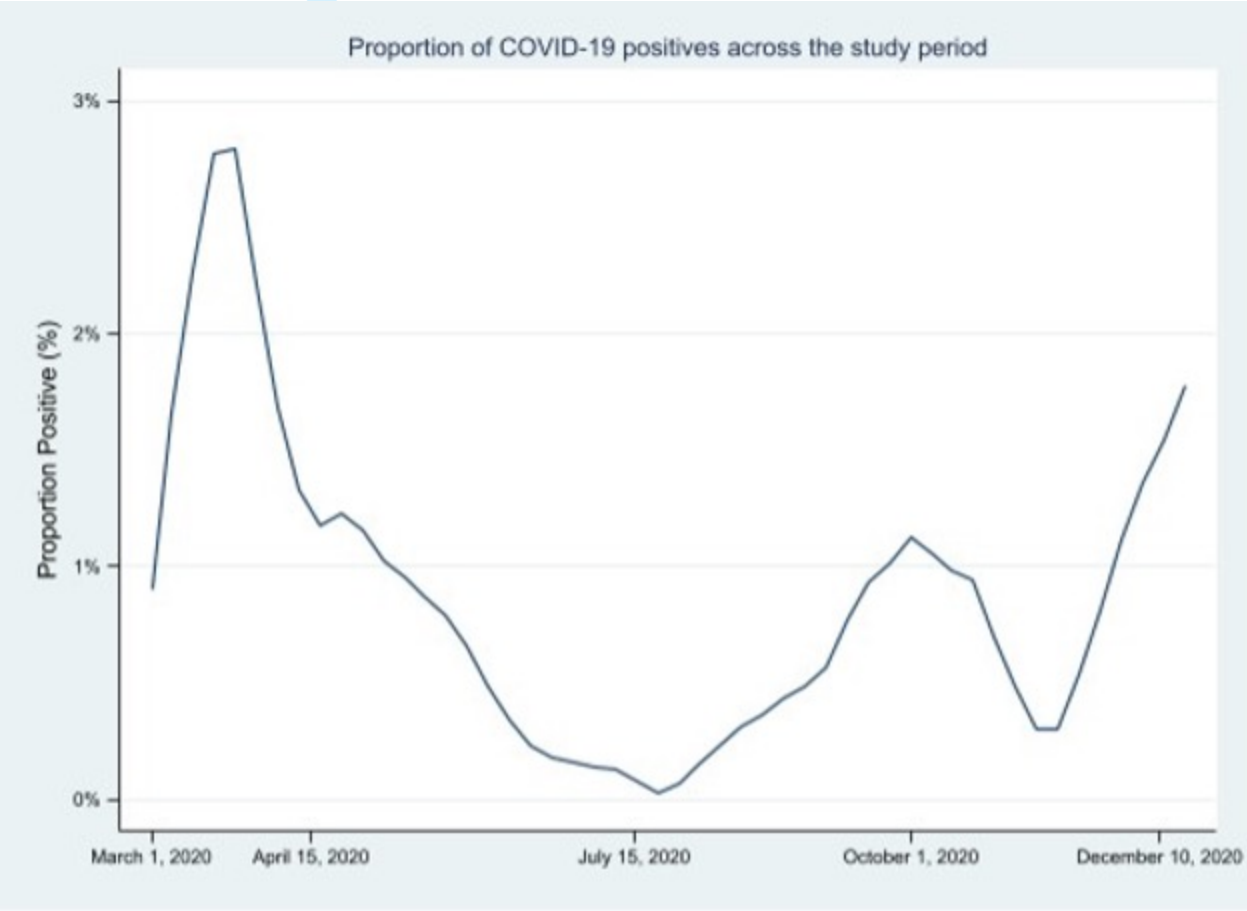

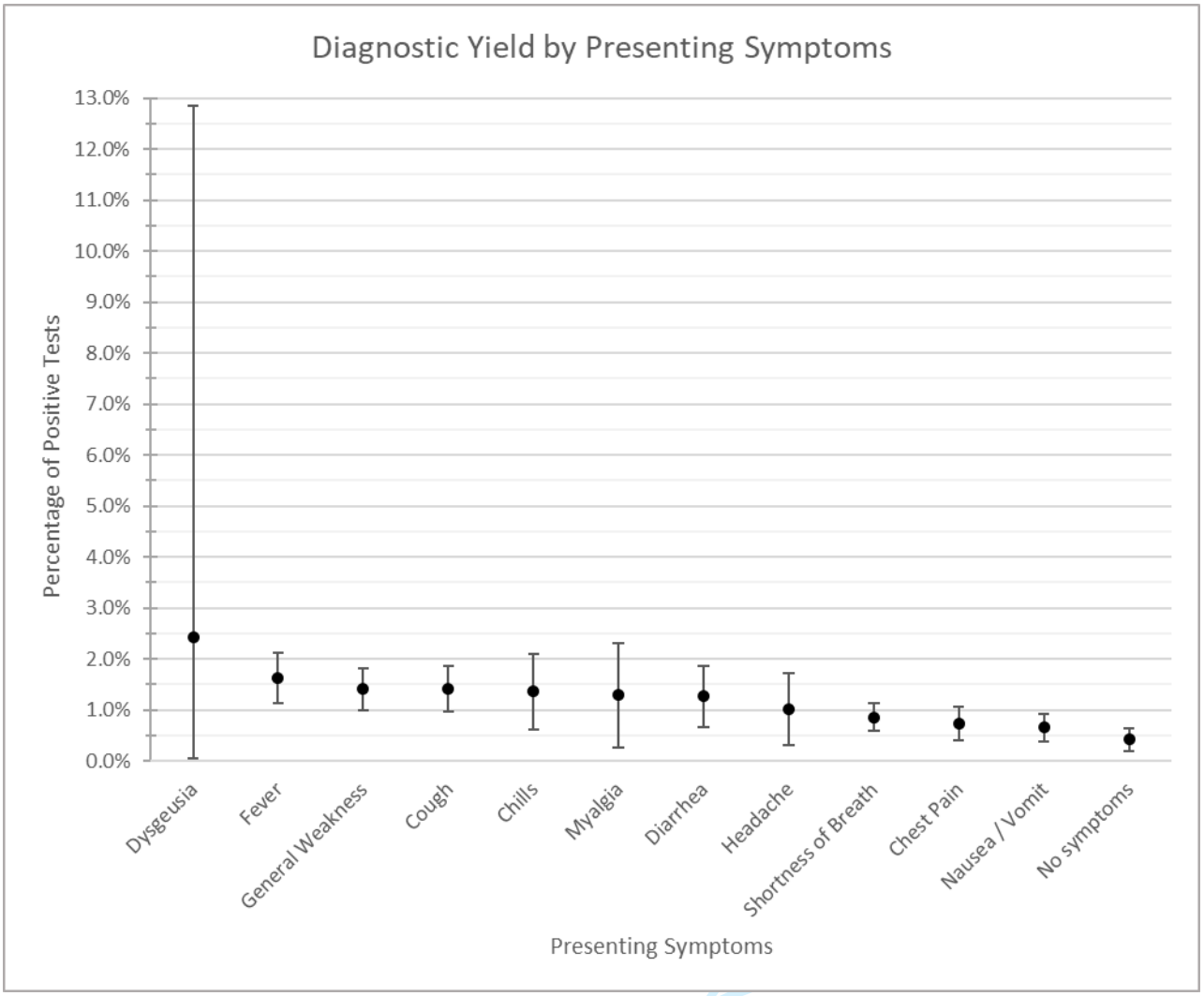

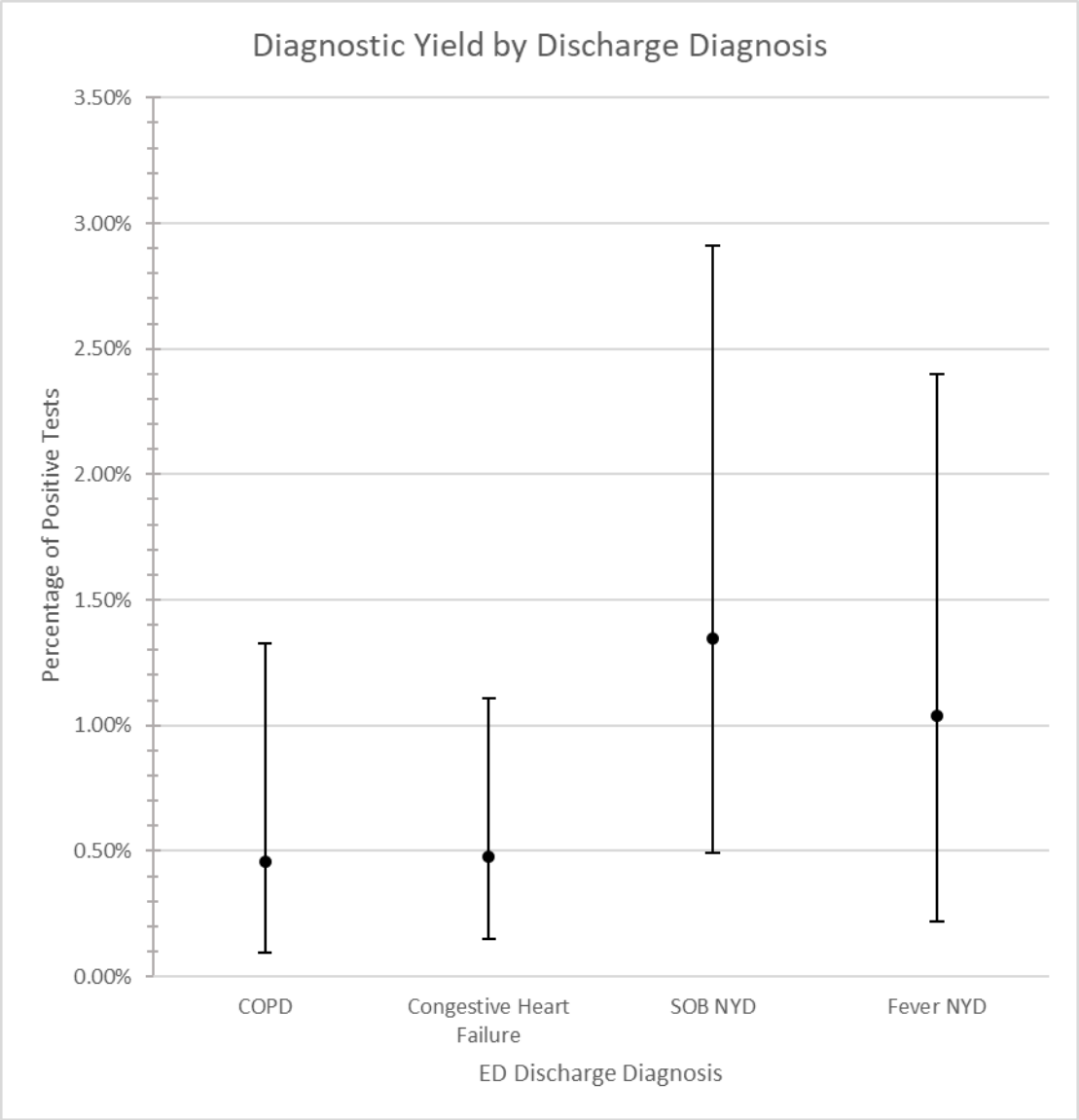

*NYD denotes “not yet determined”

APPENDIX & SUPPLEMENT

Appendix A: List of hospital sites, with an inclusion start and end date for this study.

Site Name	Province	Start Date	End Date
Vancouver General Hospital	British Columbia	1-Mar-2020	31-Aug-2020
Lions Gate Hospital	British Columbia	1-Mar-2020	29-Apr-2020
Saint Paul's Hospital	British Columbia	1-Mar-2020	23-May-2020
Mount Saint Joseph Hospital	British Columbia	1-Mar-2020	24-Mar-2020
Surrey Memorial Hospital	British Columbia	19-Mar-2020	30-Apr-2020
Royal Columbian Hospital	British Columbia	1-Mar-2020	31-May-2020
Abbotsford Regional Hospital	British Columbia	20-Apr-2020	15-Jul-2020
University of Alberta Hospital	Alberta	8-Apr-2020	7-May-2020
Foothills Medical Centre	Alberta	1-Mar-2020	7-Apr-2020
Rockyview General Hospital	Alberta	1-Mar-2020	7-Apr-2020
Peter Lougheed Centre	Alberta	1-Mar-2020	12-Dec-2020
South Health Campus	Alberta	1-Mar-2020	12-Dec-2020
St Paul's Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Royal University Hospital	Saskatchewan	17-Mar-2020	31-Oct-2020
Saskatoon City Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Sunnybrook Health Sciences Centre	Ontario	14-May-2020	31-Oct-2020
The Ottawa Hospital - Civic Campus	Ontario	14-May-2020	31-May-2020
Health Science North	Ontario	14-May-2020	29-Dec-2020
Toronto Western Hospital	Ontario	1-Sep-2020	31-Sep-2020
Hotel-Dieu de Lévis	Quebec	4-May-2020	18-May-2020
Jewish General Hospital	Quebec	1-Mar-2020	4-Jun-2020
Hôpital de l'Enfant-Jésus,CHU de Québec	Quebec	4-May-2020	23-Jul-2020
IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec	Quebec	4-May-2020	13-May-2020
Hôpital du Sacré-Coeur de Montreal	Quebec	4-May-2020	18-May-2020
Saint John Regional Hospital	New Brunswick	12-Mar-2020	12-Apr-2020
Halifax Infirmary	Nova Scotia	5-Apr-2020	15-Apr-2020
Dartmouth General Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Hants Community Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Cobequid Community Health Centre	Nova Scotia	5-Apr-2020	15-Apr-2020
Secondary Assessment Centers of Dartmouth General and Halifax Infirmary	Nova Scotia	26-Mar-2020	15-May-2020

Supplement Table 1. Network coordinating center staff at the University of British Columbia

Name	Roles	Contributions
Jeffrey Hau	Data manager	REDCap, data processing and analysis for manuscripts.
Vi Ho	National coordinator	Coordinate with provincial coordinators and training/onboarding of research assistants.
Serena Small	Research coordinator	Ethics & privacy reviews, data management plan, privacy impact assessment, and qualitative analyses
Amber Cragg	Research manager	Data and manuscript management
Wei Zhao	Data analyst	Data processing and analysis for manuscripts.
Vicky Wu	Data analyst	Data processing and analysis for manuscripts.
Elnaz Bodaghkhani	Research associate	Data and manuscript management

Supplement Table 2. Provincial Coordinators

Name	Province	Institutional affiliation	Contributions to CCEDRRN
Corinne DeMone	NS	Dalhousie University, Halifax, Nova Scotia	Research ethics board submission, manages research assistants, data cleaning and quality.
Jacqueline Fraser	NB	Dalhousie University, St. John New Brunswick	Site coordinator as well as research assistant.
Martyne Audet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis	Provincial research coordinator, translation of research material to French, ethics management.
Connie Taylor	ON	Queen's University, Kingston	Coordination of research assistants in Ontario, maintenance of REB applications for the province
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg	Lead RA for the province
Aimee Goss	SK	University of Saskatchewan, Saskatoon	Screens records in Saskatoon, data/extraction and entry, coordinates research assistants.
Hina Walia	AB	University of Calgary, Calgary	Provincial coordinator lead for Alberta, oversight of all Alberta sites.
Josie Kanu	BC	University of British Columbia, Vancouver	Provincial coordinator lead for BC, oversight of all BC sites.

Supplement Table 3. Institutional research assistant (RA) leads

Name	Province	Institutional affiliation(s)
Corinne DeMone	NS	Dartmouth General Hospital, Cobequid Community Health Centre, Hants Community Hospital Secondary Assessment Centers of the Dartmouth General Hospital, and Halifax Infirmary, Halifax
Jacqueline Fraser	NB	Saint John Regional Hospital, Saint John
Alexandra Nadeau	QC	CHU de Québec Université Laval, Quebec City
Audrey Nolet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis
Xiaoqing Xue	QC	Jewish General Hospital, Montréal
David Iannuzzi	QC	McGill University Health Center, Montréal
Chantal Lanthier	QC	Hôpital du Sacré-Cœur de Montréal, Montréal
Konika Nirmalanathan	ON	University Health Network, Toronto
Vlad Latiu	ON	Kingston General Hospital, Hotel Dieu Hospital, Kingston
Joanna Yeung	ON	Sunnybrook Health Sciences Center, Toronto
Natasha Clayton	ON	Hamilton General Hospital, Juravinski Hospital, Hamilton
Tom Chen	ON	London Health Sciences Centre, London
Jenna Nichols	ON	Health Sciences North, Sudbury
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg
Aimee Goss	SK	St. Paul's Hospital, Royal University Hospital, Saskatoon City Hospital, Saskatoon
Stacy Ruddell	AB	Foothills Medical Centre, Peter Lougheed Centre, Rockyview General Hospital, South Health Campus, Calgary
Natalie Runham	AB	University of Alberta Hospital, Edmonton
Karlin Su	AB	Royal Alexandra Hospital/Northeast Community Health Center, Edmonton
	BC	St. Paul's Hospital, Mount Saint Joseph, Vancouver
Bernice Huynh	BC	Abbotsford Regional Hospital and Cancer Center, Abbotsford
Amanda Swirhun	BC	Royal Columbian Hospital, New Westminster
Tracy Taylor	BC	Eagle Ridge Hospital and Health Care Centre, Port Moody
Mai Hayashi	BC	Royal Inland Hospital, Kamloops
Mackenzie Cheyne	BC	Kelowna General Hospital, Kelowna
Sarim Asim	BC	Surrey Memorial Hospital, Surrey
Katherine Lam	BC	Vancouver General Hospital, Vancouver
Kelsey Compagna	BC	Lions Gate Hospital, Vancouver

Supplement Table 4. Contributing Study Sites and Investigators

Lead Investigator	Contributing Site / Code	Member Investigators
Maritime		
Patrick Fok		
Nova Scotia		
Hana Wiemer	Halifax Infirmary/ 902	Patrick Fok
	Dartmouth General Hospital/ 903	Hana Wiemer
	Hants Community Hospital/ 904	Samuel Campbell
	Cobequid Community Health Centre/ 905	Kory Arsenault
	Secondary Assessment Centers of Dartmouth General and Halifax Infirmary/ 908	Tara Dahn
New Brunswick		
Kavish Chandra	Saint John Regional Hospital/ 901	Kavish Chandra
Quebec		
Patrick Archambault	Hotel-Dieu de Lévis/ 701	Patrick Archambault
	Jewish General Hospital/ 702	Joel Turner
	Centre Hospitalier de l'Université Laval (CHU de Québec)/ 703	Éric Mercier
	L'hôpital Royal Victoria - Royal Victoria Hospital/ 705	Greg Clark
	Hôpital de l'Enfant-Jésus,CHU de Québec/ 706	Éric Mercier
	Hôpital du Saint-Sacrement, CHU de Québec/ 707	Éric Mercier
	Hôpital Saint-François d'Assise, CHU de Québec/ 708	Éric Mercier
	Hôtel-Dieu de Québec,CHU de Québec/ 709	Éric Mercier
	IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec/ 710	Sébastien Robert
	Hôpital du Sacré-Coeur de Montreal/ 711	Raoul Daoust
Ontario		
Laurie Morrison & Steven Brooks	Sunnybrook/ 401	Ivy Cheng
	The Ottawa Hospital - Civic Campus/ 403	Jeffrey Perry
	The Ottawa Hospital - General Campus/ 404	Jeffrey Perry
	Kingston/Queens/ 406	Steven Brooks
	Hamilton General Hospital/ 407	Michelle Welsford
	Health Science North, Sudbury Ontario/ 408	Rob Ohle
	University Hospital – LHSC/ 409	Justin Yan
	North York General Hospital, Toronto/ 410	Rohit Mohindra
	Victoria Hospital – LHSC/ 412	Justin Yan
	Toronto Western Hospital/ 414	Megan Landes
Manitoba		
Tomislav Jelic	Health Sciences Centre/ 307	Tomislav Jelic
Saskatchewan		
Phil Davis	St Paul's Hospital, Saskatoon/ 303	Phil Davis
	Royal University, Saskatoon/ 304	Phil Davis

	Saskatoon City Hospital, Saskatoon/ 305	Phil Davis
Alberta		
Andrew McRae	University of Alberta Hospital, Edmonton/ 201	Brian Rowe
	Foothills, Calgary/ 202	Katie Lin
	Rockyview, Calgary/ 203	Andrew McRae
	Peter Lougheed Centre/ 204	Andrew McRae
	South Campus, Calgary/ 205	Stephanie VandenBerg
	Northeast Community Health Centre, Edmonton/ 206	Jake Hayward, Jaspreet Khangura
	Royal Alexandra Hospital, Edmonton/ 306	Jake Hayward, Jaspreet Khangura
British Columbia		
Corinne Hohl	Vancouver General Hospital/ 101	Daniel Ting
	Lions Gate Hospital/ 102	Maja Stachura
	Saint Paul's Hospital/ 103	Frank Scheuermeyer
	Mount St Joseph's/ 104	Frank Scheuermeyer
	Surrey Memorial Hospital/ 105	Balijeet Braar
	Royal Columbian Hospital/ 106	John Taylor
	Abbotsford Regional Hospital/ 107	Ian Martin
	Eagle Ridge Hospital/ 108	Sean Wormsbecker
	Royal Inland Hospital/ 112	Ian Martin
	Kelowna General / Hospital/ 115	Lee Graham

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2 (abstract)	"Cohort from the CCEDRRN registry"
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Included within the results and conclusions of the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	Relevant scientific literature has been cited and the rationale for the study is outlined.
Objectives	3	State specific objectives, including any prespecified hypotheses	5	"Our aim was to determine the diagnostic yield of screening patients admitted to hospital with a diagnosis unrelated to COVID-19 for SARS-CoV-2 in 2020, and identify risk factors for a positive test"
Methods				
Study design	4	Present key elements of study design early in the paper	5	The Study Design and Setting is outlined early in the Methods Section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Included in "Study Design and Setting" sub-section.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	Included in the "Study Patients" sub-section. Eligibility, sources and methods of selection are described.

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7	Variables are outlined in the "Data Collection" sub-section.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7	Data sources and methods of assessment are outlined in the "Study Design and Setting" and "Data Collection" sub-sections.
Bias	9	Describe any efforts to address potential sources of bias	6-7	Described within the "Study Patients" and the "Data Collection" sub-sections.
Study size	10	Explain how the study size was arrived at	6	Described within the "Study Patients" sub-section.

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8	Included within the "Data Collection" and "Data Analysis" sub-sections.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8	Descriptive statistics, sub-group analyses, and regression models were used. Confounding was addressed via multivariable regression.
		(*b*) Describe any methods used to examine subgroups and interactions	8	Sub-group analyses were planned for patients presenting with and without COVID compatible symptoms.
		(*c*) Explain how missing data were addressed	6-7	"Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study" "We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing)"
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7-8	Loss to follow-up was not an issue. Study enrolled consecutive patients who met the inclusion/exclusion criteria and data collected through chart review.
		(*e*) Describe any sensitivity analyses	N/A	Not performed.
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically

				suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients."
		(b) Give reasons for non-participation at each stage	N/A	Study was based on chart review.
		(c) Consider use of a flow diagram	Figure 1	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9	Paragraph 2 of the results includes the descriptive summaries.
		(b) Indicate number of participants with missing data for each variable of interest	N/A	See methods.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020".
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8	"During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites."
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A	
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9	Descriptive results and comparative findings are described in the latter 2 paragraphs of the "Results"
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9	Follows the sentence "We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1)."
Discussion				
Key results	18	Summarise key results with reference to study objectives	9-10	The study objective is recalled and situated within the context of the results.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11	"A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield."
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	Key references are recalled, and the study results are situated with these references.
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11	"While our study is based on a Canadian population without international sites, we believe our

				findings are likely generalizable given the wide geographic spread of our study sites."
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11	Included under "Funding" Section.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

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Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

Phil Davis[1], Rhonda J. Rosychuk[2], Jeffrey P Hau[3,14], Ivy Cheng[4,5], Andrew D. McRae[6], Raoul Daoust[7], Eddy Lang[8], Joel Turner[9], Jaspreet Khangura[10], Patrick T. Fok[11], Maja Stachura[12], Baljeet Brar[13], and Corinne Hohl[14] **on behalf of the CCEDRRN investigators, and for the Network of Canadian Emergency Researchers and the Canadian Critical Care Trials Group**

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Keywords: screening, COVID-19, coronavirus disease, health services utilization, diagnostic testing, pandemic

Abstract:

Objectives: To determine the diagnostic yield of screening patients for SARS-CoV-2 who were admitted with a diagnosis unrelated to COVID-19, and identify risk factors for positive tests.

Design: Cohort from the Canadian COVID-19 Emergency Department Rapid Response Network (CCEDRRN) registry

Setting: 30 acute care hospitals across Canada

Participants: Patients hospitalized for non-COVID-19 related diagnoses who were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 1, and December 29, 2020

Main outcome: Positive nucleic acid amplification test (NAAT) for SARS-CoV-2

Outcome measure: Diagnostic yield

Results: We enrolled 15,690 consecutive eligible adults who were admitted to hospital without clinically suspected COVID-19. Among these patients, 122 tested positive for COVID-19, resulting in a diagnostic yield of 0.8% (95% CI 0.64% – 0.92%). Factors associated with a positive test included presence of a fever, being a healthcare worker, having a positive household contact or institutional exposure, and living in an area with higher 7-day average incident COVID-19 cases.

Conclusions: Universal screening of hospitalized patients for COVID-19 across two pandemic waves had a low diagnostic yield and should be informed by individual-level risk assessment in addition to regional COVID-19 prevalence.

Trial registration: NCT04702945

Strengths and Limitations

- Pan-Canadian study including over 40 academic, non-academic, rural, and urban hospitals.
- Inclusion of patient partners, as well as public engagement, who assisted in the development and presentation of this manuscript.
- Inclusion of pertinent clinical variables, as well as relevant demographic and community level variables.
- Exclusion of non-NAAT tests due to their infrequent use in the Canadian context.

INTRODUCTION

Healthcare institutions initiated widespread testing of admitted patients for coronavirus disease 2019 (COVID-19) in the spring of 2020 (1). Patients without any reported symptoms of COVID-19 were routinely tested even in jurisdictions where COVID-19 rates were low in order to identify asymptomatic carriers and prevent hospital outbreaks (2). Some jurisdictions have continued this practice without robust evidence to support this practice. An Alberta study of 3,375 patients admitted to hospital for alternate diagnoses during the first wave of the pandemic when COVID-19 prevalence was very low found that none of the patients tested positive (3). In contrast, other studies from times and regions with higher COVID-19 prevalence reported positive tests in between 2.6 and 15.5% of otherwise asymptomatic patients (4–8).

Universal testing has several potential downsides if diagnostic yield is low. First, it may worsen Emergency Department (ED) crowding, as admitted patients with pending COVID-19 tests are boarded in EDs until their test results are reported. While ED volumes were lower than usual in the early pandemic such that EDs could absorb this delay, high patient volumes have since returned, exacerbating the impact of this practice on hospital crowding (9). This in turn increases patient morbidity and mortality (10). In addition, diagnostic workups and therapeutic interventions may be delayed until COVID-19 test results are back, as it takes longer to move patients on isolation precautions through the system. This can further exacerbate patient outcomes and hospital crowding. Thirdly, diagnostic testing capacity may be limited, potentially delaying processing of tests for symptomatic patients. In addition, the use of Personal Protective Equipment (PPE) may be increased as institutions have placed patients with pending COVID-19 tests under isolation precautions. The use of PPE during resuscitation has been associated with worse patient outcomes (11). Lastly, there is also an opportunity cost for hospitals as money spent on universal testing could be allocated to other areas. These unintended consequences of liberal testing policies need to be weighed carefully against the anticipated diagnostic yield and potential benefits.

As for any diagnostic test, rational COVID-19 testing guidelines should be informed by the level of risk of the patient, such that testing is reduced in situations when risk is low, and more widespread when risk is high. Based on expert opinion, the Infectious Diseases Society of America (IDSA) recommended a testing strategy based on the prevalence of the disease in the community (12). They recommended universal testing of asymptomatic hospitalized patients in times and places of high disease prevalence defined as ≥10% or ≥10,000 active cases per 100,000 population and did not recommend universal testing in times and places of low prevalence, defined as under 2% prevalence of disease, or less than 2,000 active cases per 100,000. Most jurisdictions never met the proposed screening threshold as public health measures were enacted to reduce disease prevalence to avoid overwhelming hospital capacity. The IDSA was unable to provide further guidance due to lack of available evidence. Our aim was to determine the diagnostic yield of screening patients for SARS-CoV-2 who had been admitted with a diagnosis unrelated to COVID-19 and identify risk factors for positive tests.

METHODS

Study Design and Setting

The Canadian COVID ED Rapid Response Network (CCEDRRN, pronounced 'sedrin') is a pan Canadian population-based registry that has enrolled consecutive eligible patients presenting with suspected or confirmed COVID–19 from EDs across Canada starting on March 1, 2020. The study population, data collection, data quality assurance, management and governance structure are described in the network's methods paper (13). The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015). Thirty CCEDRRN sites in 7 provinces contributed data to this study (Appendix A). Data are available upon reasonable request and can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Patient and Public Involvement

CCEDRRN has an active patient engagement committee with patient partners who have lived experience with COVID-19 from geographically representative areas of Canada. Patient partners provided input into the development of this research question and study protocol and the final manuscript.

Study Patients

Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study. Data from sites and periods that did not meet this quality threshold were excluded. We included consecutive eligible patients who were admitted to hospital and swabbed for SARS-CoV-2 using a nucleic acid amplification test (NAAT) within 24 hours of ED arrival. We enrolled patients between March 1, 2020 and December 29, 2020. To identify a population of admitted patients in whom COVID-19 disease was not suspected, we excluded patients with ED diagnoses that would have been clinically suspicious for COVID-19. These included all patients with ED diagnoses of suspected or confirmed COVID-19, influenza-like-illness (ILI), upper respiratory infections, and pneumonia or viral pneumonia for which testing would have been indicated based on clinical suspicion. We excluded patients who were discharged directly from the ED, diagnosed with COVID-19 before ED arrival (based on a NAAT done in the community), those whose first swab occurred more than 24 hours after their arrival, and repeat admissions. We also excluded patients in whom initial SARS-CoV-2 testing was negative and repeat testing became positive more than 5 days after arrival, as these patients could have contracted nosocomial COVID.

Data Collection

Trained research assistants collected data retrospectively from electronic and/or paper-based medical records into a central, web-based REDCap database (Vanderbilt University; Nashville, TN, USA). Research assistants captured demographics, infection risk, ED vital signs, presenting symptoms, comorbid conditions and the results of COVID-19 tests. The coordinating centre implemented regular

data quality checks, including logic checks in REDCap as well as site-level record verifications for nonsensical or outlying values.

In addition to these clinical variables, we calculated the seven-day moving average incident COVID-19 case count for the health region of each participating site using publicly available epidemiological data (14). For each calendar day within each health region represented in the study, we calculated the average daily incident rate of new infections per 100,000 population over the preceding seven days. This seven-day moving average incidence was assigned to each patient based on the date of their index emergency department encounter and the health region of their postal code of residence. We allocated patients with no fixed address to the health region of the hospital in which they were tested. We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing), COVID-19 case data were not publicly available for the early pandemic. The seven-day moving average incident COVID-19 case count was categorized as 0 – 1.99 per 100,000 population, 2 – 7.99 per 100,000 population, and ≥8 per 100,000 population based on the relationship between incidence and COVID-19 positive results in a previous analysis (15).

Outcome:

The primary outcome was a positive NAAT for SARS-CoV-2 in patients admitted with non-COVID-related diagnoses.

Data Analysis:

We divided the cohort into two groups, those without symptoms of COVID-19 and those with symptoms compatible with COVID-19 that were attributed to an alternate diagnosis (i.e., CHF, COPD, Asthma, etc.). We considered cough, dyspnea, fever, general weakness, chest pain, diarrhea, nausea and vomiting, headache, chills, myalgia, sore throat, altered level of consciousness, and dysgeusia/anosmia to be COVID-19-compatible symptoms. We used descriptive statistics to describe the population. We

calculated the diagnostic yield by dividing the number of positive NAATs over the total number of NAATs performed. We calculated 7-day average of NAAT positivity over the study period by dividing the number of positive NAATs over all tests performed and averaging over a 7-day period. We calculated the exact binomial proportion 95% confidence intervals (95% CI) for all proportions and used the modified Clopper-Pearson interval for small samples. We completed a planned subgroup analyses for patients presenting with and without COVID compatible symptoms to determine associated factors for a positive test. The initial multivariable logistic regression model to identify factors associated with a positive NAAT considered candidate variables with a p-value cut-off point of 0.20 based on the Wald test from univariable analyses. From the full model, a step-down procedure reduced the model to key predictors based on Akaike's information criterion (AIC) scores (e.g., chose the model with the smallest AIC score). Candidate variables included seven-day moving average incident COVID-19 case count category, patient age, gender, infection risk, and presenting symptoms. We limited the number of predictor variables in the model to one variable for every 10 outcomes in our data to avoid overfitting. Statistical analysis was preformed using Stata (Version 16.1, StataCorp, College Station, Texas).

RESULTS

We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients. During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites. The 7-day average diagnostic test positivity varied between 0 and 2.9% across sites during the study period (Figure 2).

We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1). Most patients arrived from home and were full code. The most common comorbidities were hypertension, diabetes and mental health illness.

Of 3,113 patients admitted without COVID-19 compatible symptoms, 13 (0.4%, 95% CI 0.19% – 0.64%) tested positive for COVID-19. Of the 12,570 with COVID-19-compatible symptoms, 109 patients (0.9%, 95% CI 0.70% – 1.03%) tested positive for COVID-19. Among the 122 individuals who tested positive for COVID-19, 33 (27.0%, 95% CI 19.0% - 35.0%) were from a geographic region that had a moving average daily incident rate of ≥8 infections per 100,000 population. The diagnostic yield of testing among patients with COVID-19 compatible symptoms admitted for alternative diagnoses did not vary substantially by presenting symptom (Figure 3) or ED diagnosis (Figure 4).

When examining the association between patient factors and screening positive self-reported fever, being a healthcare worker, having a positive household contact or institutional exposure, and being from an area where the seven-day moving average incident COVID-19 case count was ≥8 per 100,000 population were associate with a greater risk of testing positive (Table 2). The most important risk factor was reporting a household contact or being the caregiver of a known COVID-19 case.

DISCUSSION

Our aim was to evaluate the diagnostic yield of screening non-COVID-19 admissions for SARS-CoV-2 across Canada in 2020 and identify patient-level risk factors for positive tests. The diagnostic yield of screening patients with non-COVID-19 related ED diagnoses who were admitted to hospital was low overall, and extremely low in patients without COVID compatible symptoms. The most important patient factors associated with a positive test were having a positive household contact, being a healthcare worker, or having had an institutional exposure to COVID-19. Those factors were more important than a high (≥8 daily cases per 100,000 population) 7-day moving average incident COVID-19 case count.

Our study has several strengths. We used data from a large pan-Canadian registry that enrolls from large geographically and culturally diverse areas and is one of the largest registries in the world. CCEDRRN's patient enrolment and data verification protocols are rigorous, ensuring consecutive eligible patients and high-quality clinical data (13). We have previously demonstrated the inter-rater reliability for our data collection methods, including for symptoms (13).

Prior studies have examined the diagnostic yield of universal screening in single centers with varied diagnostic yield estimates between 0 and 15.5% (3–8). Many of these were case series with limited methods from the early pandemic. There is one known multi-center study which examines the benefit of universal screening for elective and emergent surgical admissions at 14 centers in the Netherlands (1). Like our study, the authors found that the overall COVID-19 NAAT positivity varied with community prevalence. Our finding that positive SARS-CoV-2 tests were associated with self-reported or measured fever is in keeping with a prior Cochrane systematic review that noted considerable variability in COVID-19 associated symptoms (16).

Our study is interesting in the context of current IDSA recommendations which were based on expert opinion and of "very low certainty" (12). The IDSA panel recommended avoiding universal screening for COVID-19 in times and areas of low COVID prevalence, defined as a disease prevalence of under 2% , or fewer than 2,000 active cases per 100,000 population, a threshold so high that it was never met at any of our study sites, even though multiple sites were in COVID-19 hotspots in 2020 (12). The IDSA threshold would have equated to over 6 million cases of active COVID-19 infection in the United States at any given time, which would have vastly overwhelmed hospital capacity, and thus represents an untenable threshold for hospitals. It is therefore not surprising that the prevalence of COVID-19 during the study period was far below the IDSA recommended threshold for initiating screening. While the number needed to screen to identify one positive case among admitted patients in our study was between 110 and 250 among unvaccinated patients, we propose that new screening thresholds need to be adopted which would ideally be based on readily available measures of local incident cases or test positivity.

A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield. Additionally, our study was performed before the newer COVID-19 variants, such as Omicron, circulated widely. However, our methods are easily replicated, and we intend to repeat our study in a recent dataset reflective of new COVID-19 variants. While our study is based on a Canadian population without international sites, we believe our findings are generalizable given their wide geographic spread, and the cultural and racial diversity of our patient population. Finally, as data becomes available on the fourth wave of the pandemic, a future study should examine the impact of widespread vaccination on the yield of screening. As a larger proportion of the population is protected from severe disease and death through vaccination, decision makers should carefully consider the low diagnostic yield of a universal testing strategy going forward.

ACKNOWLEDGEMENTS

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Thank you to all of our patient partners who shared their lived experiences and perspectives to ensure that the knowledge we co-create addresses the concerns of patients and the public. Creating the largest network of collaboration across Canadian Emergency Departments would not have been feasible without the tireless efforts of Emergency Department Chiefs, and research coordinators and research assistants at participating sites. Finally, our most humble and sincere gratitude to our colleagues in medicine, nursing,

and the allied health professions who have been on the front lines of this pandemic from day one staffing our ambulances, Emergency Departments, hospitals and ICUs bravely facing the risks of COVID-19 to look after our fellow citizens and after one another. We dedicate this network to you.

COMPETING INTERESTS

None identified.

FUNDING

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AUTHOR CONTRIBUTION STATEMENT

All authors conceived and planned the study together, and iteratively refined the study objectives and analytic plan. PH, RJR, ADM, EL and CMH obtained funding for the study. PD, IC, ADM, RD, JT, JK, PRF, MS and BB supervised data collection. JPH analyzed the data under the supervision of RJR. All authors interpreted the analysis. PD drafted the manuscript. All authors were actively involved in reporting out work by revising the manuscript for content. All authors take responsibility for the manuscript as a whole.

DATA SHARING

Data are available upon reasonable request. They can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Table 1: Baseline Characteristics of admitted patients without clinical suspicion of COVID-19 (N=15,690)

	Patients without COVID-19 symptoms (N=3,113)	Patients with COVID-19 compatible symptoms attributed to an alternate diagnosis (N=12,570)
Demographics		
Age (mean, SD)	57.6 (22.6)	64.6 (20.4)
Female (%)	1,418 (45.6)	5,924 (47.1)
Pregnant (%)	18 (0.6)	45 (0.4)
Tobacco use (%)	491 (15.8)	1,656 (13.2)
Illicit substance use (%)	421 (13.5)	967 (7.7)
Arrival by Ambulance (%)	1,724 (55.4)	7,189 (57.2)
Arrival From (%)		
Home	2,552 (82.0)	10,943 (87.0)
Long-term care or rehab facility	217 (7.0)	832 (6.6)
Unstable housing*	190 (6.1)	414 (3.3)
Corrections	7 (0.2)	14 (0.1)
Interfacility transfer	121 (3.9)	262 (2.1)
Risk for Infection (%)		
Travel	32 (1.0)	134 (1.1)
Institutional (LTC/prison)	231 (7.4)	721 (5.7)
Household contact	28 (0.9)	144 (1.1)
Occupational	10 (0.3)	38 (0.3)
Unknown	1,502 (48.2)	5,377 (42.8)
Pre-ED Goals of Care (%)		
Full code	2,946 (94.6)	11,259 (89.5)
Intermediate GOC	18 (0.6)	173 (1.4)
Do not resuscitate	149 (4.8)	1,142 (9.1)
Acuity		
CTAS 1 (Resuscitation)	241 (7.7)	1,053 (8.4)
CTAS 2 (Emergent)	1,000 (32.1)	5,786 (46.0)
CTAS 3 (Urgent)	1,527 (49.1)	5,086 (40.4)
CTAS 4 (Less Urgent)	295 (9.5)	572 (4.6)
CTAS 5 (Non Urgent)	40 (1.3)	59 (0.5)
Arrival Vital Signs, Mean (SD)		
Heart Rate, beats per min	91.2 (21.2)	95.5 (23.9)
Systolic BP, mm Hg	134.7 (25.1)	133.6 (27.9)
Oxygen saturation, (%)	96.6 (3.4)	95.7 (4.1)
Respiratory Rate, beats per min	18.6 (4.4)	21.2 (6.3)
Temperature, degrees Celsius	36.6 (0.6)	36.8 (0.9)
Comorbidities (%)		
Hypertension	951 (30.6)	5,321 (42.3)
Psychiatric Condition	728 (23.4)	2,134 (17.0)
Dyslipidemia	425 (13.6)	2,434 (19.4)
Diabetes	427 (13.7)	2,577 (20.5)
Chronic Neuro Disorder	322 (10.3)	1,406 (11.2)

Coronary Artery Disease	284 (9.1)	1,796 (14.3)
Rheumatologic Disorder	229 (7.4)	1,249 (9.9)
Dementia	199 (6.4)	696 (5.5)
Active Cancer	231 (7.4)	1,647 (12.9)
Chronic Kidney Disease	195 (6.3)	1,319 (10.5)
Chronic Lung Disease (not asthma)	199 (6.4)	1,691 (13.5)
Congestive Heart Failure	159 (5.1)	1,392 (11.1)
Asthma	125 (4.0)	712 (5.7)
Obesity	57 (1.8)	344 (2.7)
Symptoms (%)		
Cough	-	2,763 (22.0)
Dyspnea	-	4,757 (37.8)
Fever	-	2,531 (20.1)
General Weakness	-	3,183 (25.3)
Chest Pain	-	2,714 (21.6)
Diarrhea	-	1,339 (10.7)
Nausea/Vomiting	-	3,345 (26.6)
Headache	-	784 (6.2)
Chills	-	957 (7.6)
Myalgia	-	466 (3.7)
Sore Throat	-	374 (3.0)
Altered Consciousness	-	2,502 (19.9)
Dysgusea/Anosmia	-	41 (0.3)
ED Diagnosis (%)		
Respiratory Disease, not specified	8 (0.3)	118 (0.9)
COPD Exacerbation	11 (0.4)	648 (5.2)
Asthma Exacerbation	<5	97 (0.8)
Congestive Heart Failure	44 (1.4)	1,003 (8.0)
Shortness of Breath, NYD*	-	466 (3.6)
Cough, NYD*	-	63 (0.5)
Fever, NYD*	-	482 (3.8)
Outcome (%)		
Positive SARS-CoV-2 NAAT	13 (0.4)	109 (0.9)

*NYD denotes “not yet determined”

Table 2: Multivariate analysis of factors associated with positive SARS-CoV-2 nucleic tests (N=15,690)

	Univariate analysis odds ratio (95% CI)	Final model with fully adjusted odds ratio (95% CI)[1]	P-value
Sex			
Male	*Reference*	*Reference*	0.18
Female	0.84 (0.59 – 1.21)	0.78 (0.54 – 1.12)	
Age			
	1.00 (1.00 – 1.02)	1.00 (0.99 – 1.01)	0.27
7-day average incident COVID-19 cases			
0 – 1.99 daily cases per 100,000 population	*Reference*	*Reference*	< 0.001
2 to 7.99 daily cases per 100,000 population	1.42 (0.91 – 2.22)	1.47 (0.94 – 2.31)	
≥8 daily cases per 100,000 population	2.99 (1.95 – 4.59)	3.17 (2.05 – 4.89)	
COVID-19 compatible symptoms present			
No	*Reference*	*Reference*	0.08
Yes	2.08 (1.71 – 3.71)	1.65 (0.90 – 3.00)	
Self-reported fever, or temperature ≥ 37.5 °C			
No	*Reference*	*Reference*	< 0.001
Yes	2.72 (1.89 – 3.90)	2.53 (1.74 – 3.67)	
Diarrhea present			
No	*Reference*	*Reference*	0.11
Yes	1.74 (1.04 – 2.92)	1.57 (0.93 – 2.67)	
Healthcare worker			
No	*Reference*	*Reference*	0.06
Yes	5.62 (1.35 – 23.43)	4.67 (1.05 – 20.54)	
Household contact or caregiver			
No	*Reference*	*Reference*	< 0.001
Yes	9.48 (5.01 – 17.96)	7.74 (3.98 – 15.04)	
Institutional exposure			
No	*Reference*	*Reference*	< 0.001
Yes	3.46 (2.17 – 5.52)	3.39 (2.10 – 5.47)	
Dysgeusia or anosmia present			
No	*Reference*	-	
Yes	3.21 (0.43 – 23.52)	-	
Dyspnea present			
No	*Reference*	-	
Yes	1.16 (0.80 – 1.70)	-	
Nausea or vomiting present			
No	*Reference*	-	
Yes	0.81 (0.51 – 1.29)	-	

[1] Final model determined by including variables with a p-value of p<0.20 during the sex and age adjusted analysis, and using the Akaike Information Criterion (AIC) to determine additional variables to exclude from the final model. Variables adjusted for all other variables present in the final model

Figure 1: Patient Flow Diagram

Figure 2: 7-day working average of COVID-19 NAAT positivity over the study period across sites.

Figure 3: Diagnostic Yield by Presenting Symptoms

Figure 4: Diagnostic Yield by ED Diagnosis

ETHICAL APPROVAL STATEMENT

The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015).

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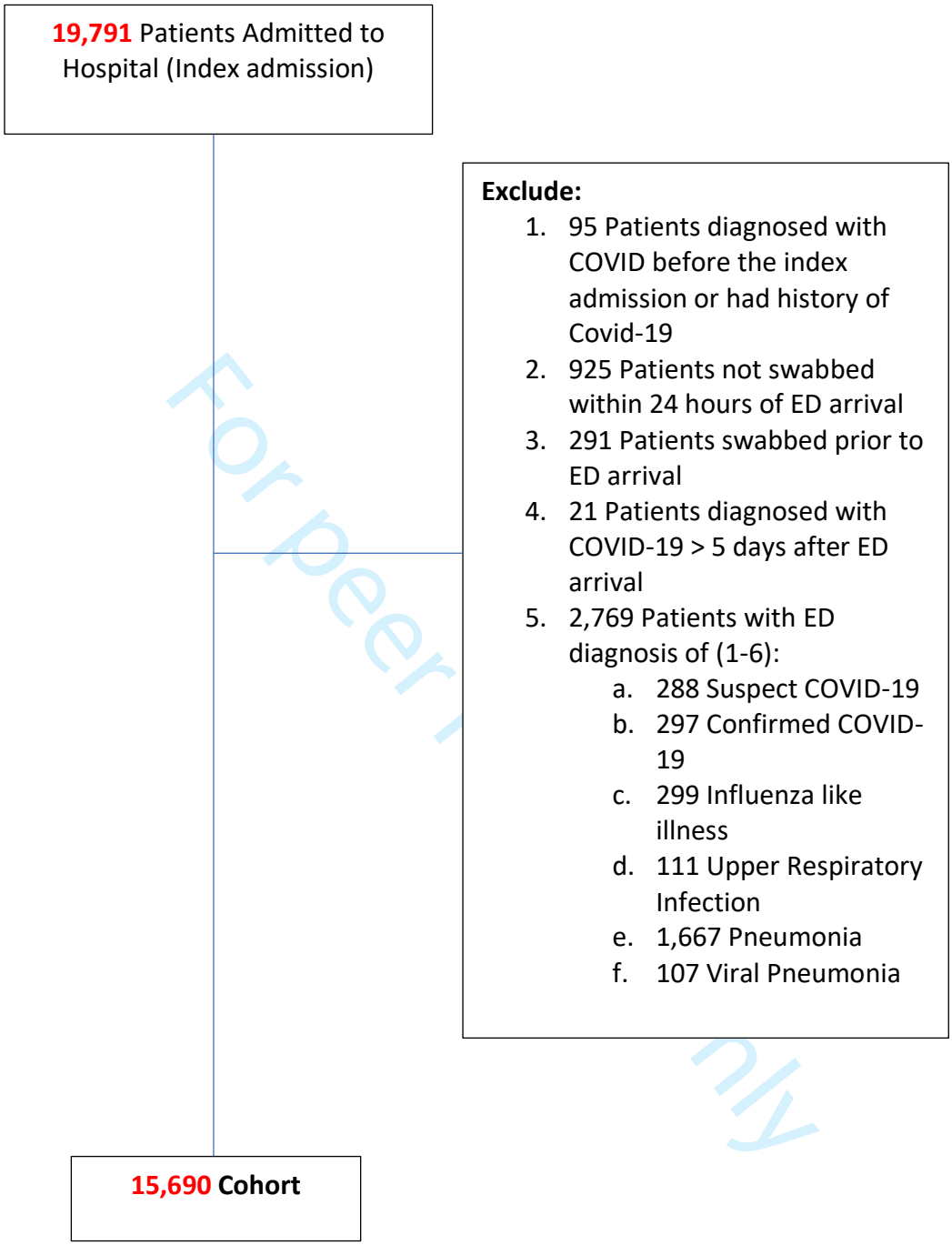
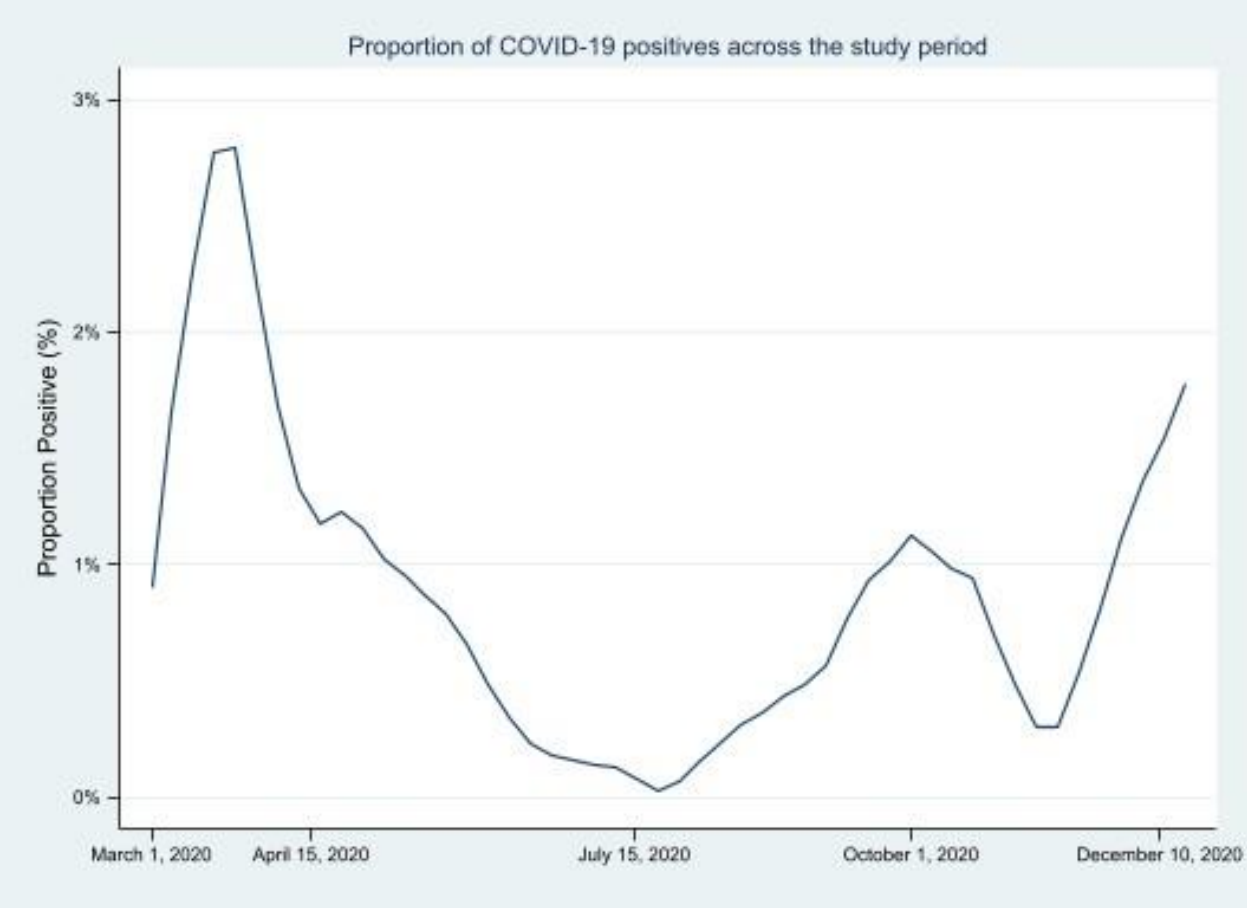
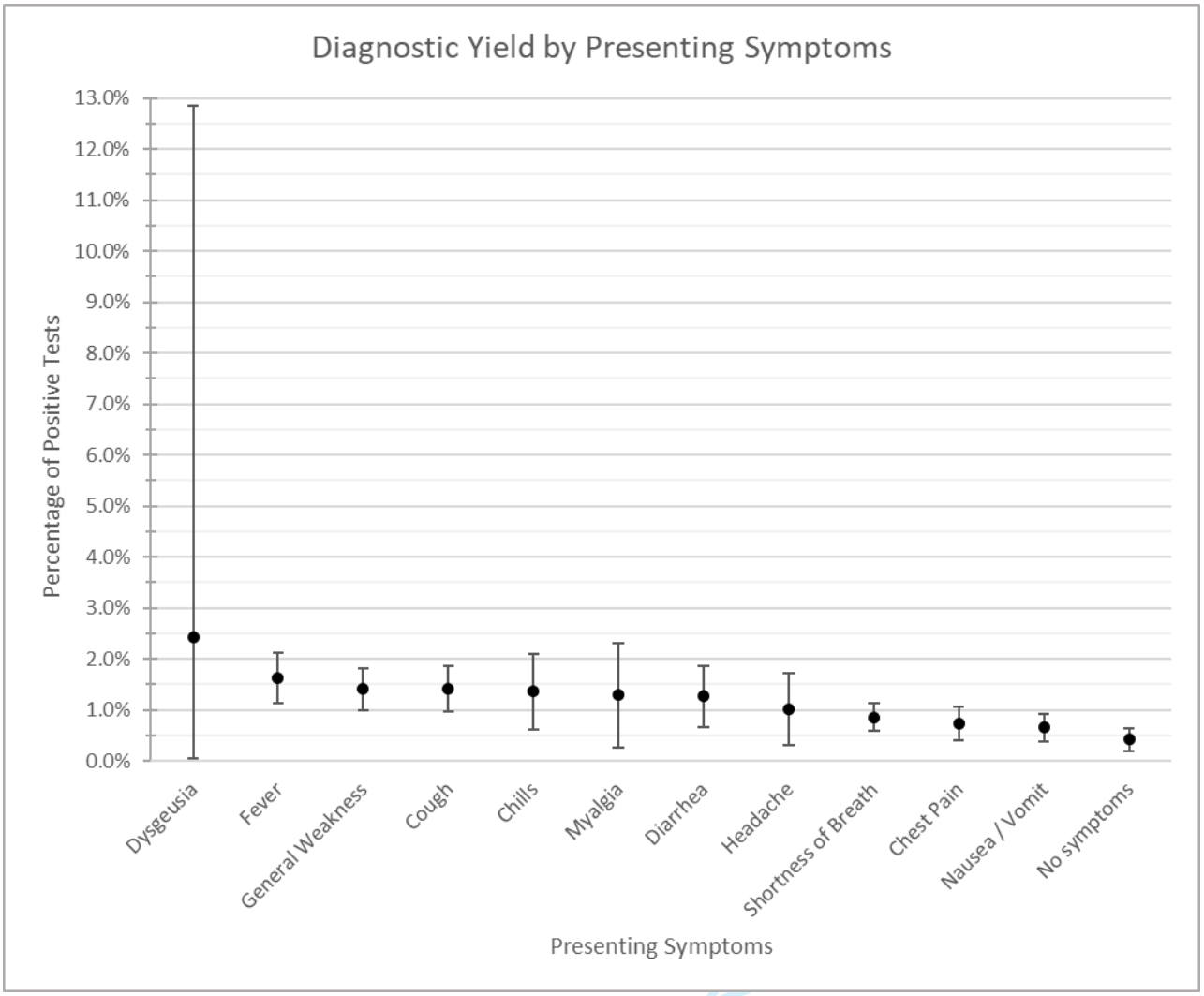
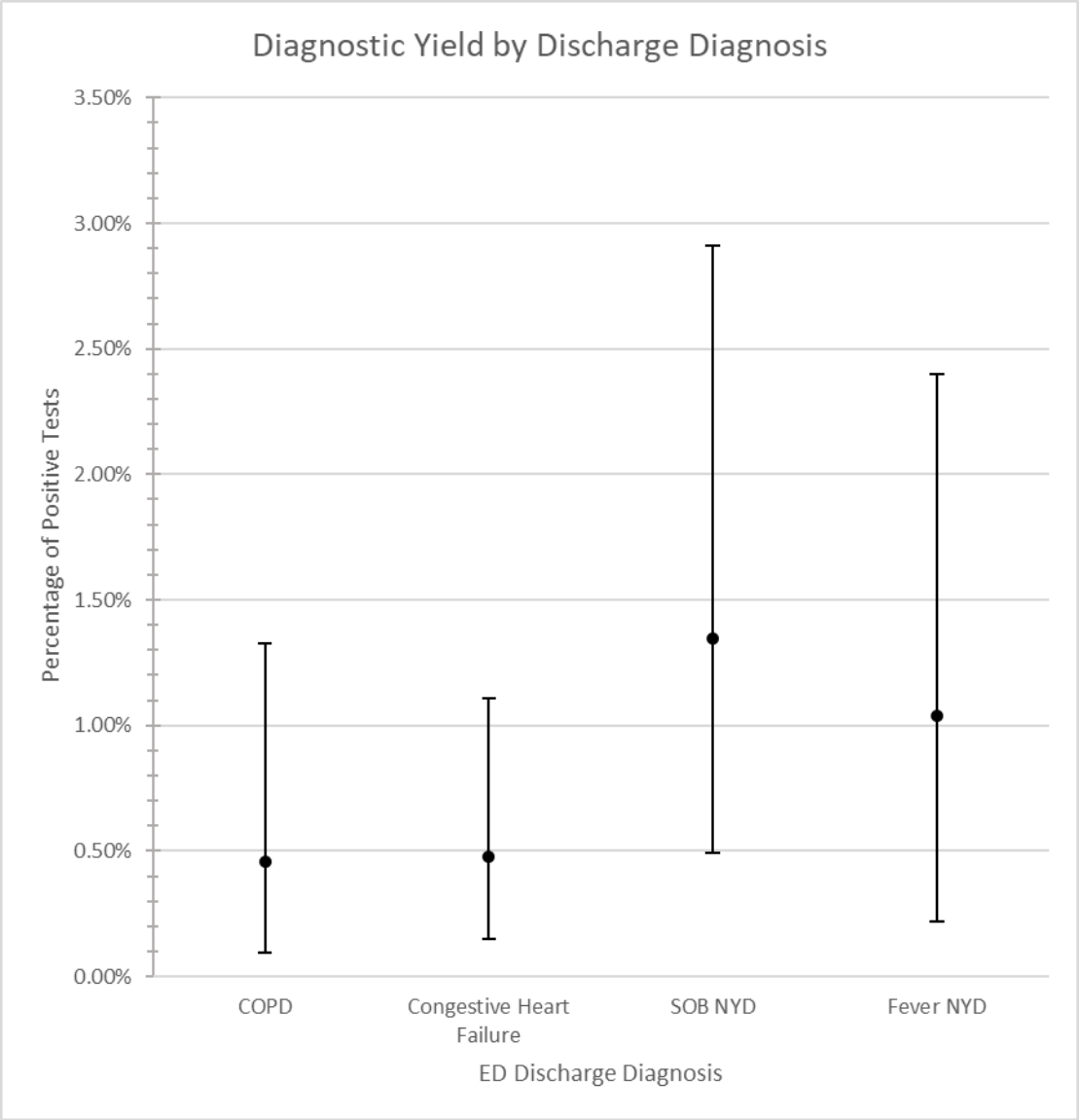


Figure 2: The 7-day working average of COVID-19 NAAT positivity among all eligible study patients over the study period across study sites.







*NYD denotes “not yet determined”

APPENDIX & SUPPLEMENT

Appendix A: List of hospital sites, with an inclusion start and end date for this study.

Site Name	Province	Start Date	End Date
Vancouver General Hospital	British Columbia	1-Mar-2020	31-Aug-2020
Lions Gate Hospital	British Columbia	1-Mar-2020	29-Apr-2020
Saint Paul's Hospital	British Columbia	1-Mar-2020	23-May-2020
Mount Saint Joseph Hospital	British Columbia	1-Mar-2020	24-Mar-2020
Surrey Memorial Hospital	British Columbia	19-Mar-2020	30-Apr-2020
Royal Columbian Hospital	British Columbia	1-Mar-2020	31-May-2020
Abbotsford Regional Hospital	British Columbia	20-Apr-2020	15-Jul-2020
University of Alberta Hospital	Alberta	8-Apr-2020	7-May-2020
Foothills Medical Centre	Alberta	1-Mar-2020	7-Apr-2020
Rockyview General Hospital	Alberta	1-Mar-2020	7-Apr-2020
Peter Lougheed Centre	Alberta	1-Mar-2020	12-Dec-2020
South Health Campus	Alberta	1-Mar-2020	12-Dec-2020
St Paul's Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Royal University Hospital	Saskatchewan	17-Mar-2020	31-Oct-2020
Saskatoon City Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Sunnybrook Health Sciences Centre	Ontario	14-May-2020	31-Oct-2020
The Ottawa Hospital - Civic Campus	Ontario	14-May-2020	31-May-2020
Health Science North	Ontario	14-May-2020	29-Dec-2020
Toronto Western Hospital	Ontario	1-Sep-2020	31-Sep-2020
Hotel-Dieu de Lévis	Quebec	4-May-2020	18-May-2020
Jewish General Hospital	Quebec	1-Mar-2020	4-Jun-2020
Hôpital de l'Enfant-Jésus,CHU de Québec	Quebec	4-May-2020	23-Jul-2020
IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec	Quebec	4-May-2020	13-May-2020
Hôpital du Sacré-Coeur de Montreal	Quebec	4-May-2020	18-May-2020
Saint John Regional Hospital	New Brunswick	12-Mar-2020	12-Apr-2020
Halifax Infirmary	Nova Scotia	5-Apr-2020	15-Apr-2020
Dartmouth General Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Hants Community Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Cobequid Community Health Centre	Nova Scotia	5-Apr-2020	15-Apr-2020
Secondary Assessment Centers of Dartmouth General and Halifax Infirmary	Nova Scotia	26-Mar-2020	15-May-2020

Supplement Table 1. Network coordinating center staff at the University of British Columbia

Name	Roles	Contributions
Jeffrey Hau	Data manager	REDCap, data processing and analysis for manuscripts.
Vi Ho	National coordinator	Coordinate with provincial coordinators and training/onboarding of research assistants.
Serena Small	Research coordinator	Ethics & privacy reviews, data management plan, privacy impact assessment, and qualitative analyses
Amber Cragg	Research manager	Data and manuscript management
Wei Zhao	Data analyst	Data processing and analysis for manuscripts.
Vicky Wu	Data analyst	Data processing and analysis for manuscripts.
Elnaz Bodaghkhani	Research associate	Data and manuscript management

Supplement Table 2. Provincial Coordinators

Name	Province	Institutional affiliation	Contributions to CCEDRRN
Corinne DeMone	NS	Dalhousie University, Halifax, Nova Scotia	Research ethics board submission, manages research assistants, data cleaning and quality.
Jacqueline Fraser	NB	Dalhousie University, St. John New Brunswick	Site coordinator as well as research assistant.
Martyne Audet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis	Provincial research coordinator, translation of research material to French, ethics management.
Connie Taylor	ON	Queen's University, Kingston	Coordination of research assistants in Ontario, maintenance of REB applications for the province
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg	Lead RA for the province
Aimee Goss	SK	University of Saskatchewan, Saskatoon	Screens records in Saskatoon, data/extraction and entry, coordinates research assistants.
Hina Walia	AB	University of Calgary, Calgary	Provincial coordinator lead for Alberta, oversight of all Alberta sites.
Josie Kanu	BC	University of British Columbia, Vancouver	Provincial coordinator lead for BC, oversight of all BC sites.

Supplement Table 3. Institutional research assistant (RA) leads

Name	Province	Institutional affiliation(s)
Corinne DeMone	NS	Dartmouth General Hospital, Cobequid Community Health Centre, Hants Community Hospital Secondary Assessment Centers of the Dartmouth General Hospital, and Halifax Infirmary, Halifax
Jacqueline Fraser	NB	Saint John Regional Hospital, Saint John
Alexandra Nadeau	QC	CHU de Québec Université Laval, Quebec City
Audrey Nolet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis
Xiaoqing Xue	QC	Jewish General Hospital, Montréal
David Iannuzzi	QC	McGill University Health Center, Montréal
Chantal Lanthier	QC	Hôpital du Sacré-Cœur de Montréal, Montréal
Konika Nirmalanathan	ON	University Health Network, Toronto
Vlad Latiu	ON	Kingston General Hospital, Hotel Dieu Hospital, Kingston
Joanna Yeung	ON	Sunnybrook Health Sciences Center, Toronto
Natasha Clayton	ON	Hamilton General Hospital, Juravinski Hospital, Hamilton
Tom Chen	ON	London Health Sciences Centre, London
Jenna Nichols	ON	Health Sciences North, Sudbury
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg
Aimee Goss	SK	St. Paul's Hospital, Royal University Hospital, Saskatoon City Hospital, Saskatoon
Stacy Ruddell	AB	Foothills Medical Centre, Peter Lougheed Centre, Rockyview General Hospital, South Health Campus, Calgary
Natalie Runham	AB	University of Alberta Hospital, Edmonton
Karlin Su	AB	Royal Alexandra Hospital/Northeast Community Health Center, Edmonton
	BC	St. Paul's Hospital, Mount Saint Joseph, Vancouver
Bernice Huynh	BC	Abbotsford Regional Hospital and Cancer Center, Abbotsford
Amanda Swirhun	BC	Royal Columbian Hospital, New Westminster
Tracy Taylor	BC	Eagle Ridge Hospital and Health Care Centre, Port Moody
Mai Hayashi	BC	Royal Inland Hospital, Kamloops
Mackenzie Cheyne	BC	Kelowna General Hospital, Kelowna
Sarim Asim	BC	Surrey Memorial Hospital, Surrey
Katherine Lam	BC	Vancouver General Hospital, Vancouver
Kelsey Compagna	BC	Lions Gate Hospital, Vancouver

Supplement Table 4. Contributing Study Sites and Investigators

Lead Investigator	Contributing Site / Code	Member Investigators
Maritime		
Patrick Fok		
Nova Scotia		
Hana Wiemer	Halifax Infirmary/ 902	Patrick Fok
	Dartmouth General Hospital/ 903	Hana Wiemer
	Hants Community Hospital/ 904	Samuel Campbell
	Cobequid Community Health Centre/ 905	Kory Arsenault
	Secondary Assessment Centers of Dartmouth General and Halifax Infirmary/ 908	Tara Dahn
New Brunswick		
Kavish Chandra	Saint John Regional Hospital/ 901	Kavish Chandra
Quebec		
Patrick Archambault	Hotel-Dieu de Lévis/ 701	Patrick Archambault
	Jewish General Hospital/ 702	Joel Turner
	Centre Hospitalier de l'Université Laval (CHU de Québec)/ 703	Éric Mercier
	L'hôpital Royal Victoria - Royal Victoria Hospital/ 705	Greg Clark
	Hôpital de l'Enfant-Jésus,CHU de Québec/ 706	Éric Mercier
	Hôpital du Saint-Sacrement, CHU de Québec/ 707	Éric Mercier
	Hôpital Saint-François d'Assise, CHU de Québec/ 708	Éric Mercier
	Hôtel-Dieu de Québec,CHU de Québec/ 709	Éric Mercier
	IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec/ 710	Sébastien Robert
	Hôpital du Sacré-Coeur de Montreal/ 711	Raoul Daoust
Ontario		
Laurie Morrison & Steven Brooks	Sunnybrook/ 401	Ivy Cheng
	The Ottawa Hospital - Civic Campus/ 403	Jeffrey Perry
	The Ottawa Hospital - General Campus/ 404	Jeffrey Perry
	Kingston/Queens/ 406	Steven Brooks
	Hamilton General Hospital/ 407	Michelle Welsford
	Health Science North, Sudbury Ontario/ 408	Rob Ohle
	University Hospital – LHSC/ 409	Justin Yan
	North York General Hospital, Toronto/ 410	Rohit Mohindra
	Victoria Hospital – LHSC/ 412	Justin Yan
	Toronto Western Hospital/ 414	Megan Landes
Manitoba		
Tomislav Jelic	Health Sciences Centre/ 307	Tomislav Jelic
Saskatchewan		
Phil Davis	St Paul's Hospital, Saskatoon/ 303	Phil Davis
	Royal University, Saskatoon/ 304	Phil Davis

	Saskatoon City Hospital, Saskatoon/ 305	Phil Davis
Alberta		
Andrew McRae	University of Alberta Hospital, Edmonton/ 201	Brian Rowe
	Foothills, Calgary/ 202	Katie Lin
	Rockyview, Calgary/ 203	Andrew McRae
	Peter Lougheed Centre/ 204	Andrew McRae
	South Campus, Calgary/ 205	Stephanie VandenBerg
	Northeast Community Health Centre, Edmonton/ 206	Jake Hayward, Jaspreet Khangura
	Royal Alexandra Hospital, Edmonton/ 306	Jake Hayward, Jaspreet Khangura
British Columbia		
Corinne Hohl	Vancouver General Hospital/ 101	Daniel Ting
	Lions Gate Hospital/ 102	Maja Stachura
	Saint Paul's Hospital/ 103	Frank Scheuermeyer
	Mount St Joseph's/ 104	Frank Scheuermeyer
	Surrey Memorial Hospital/ 105	Balijeet Braar
	Royal Columbian Hospital/ 106	John Taylor
	Abbotsford Regional Hospital/ 107	Ian Martin
	Eagle Ridge Hospital/ 108	Sean Wormsbecker
	Royal Inland Hospital/ 112	Ian Martin
	Kelowna General / Hospital/ 115	Lee Graham

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2 (abstract)	"Cohort from the CCEDRRN registry"
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Included within the results and conclusions of the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	Relevant scientific literature has been cited and the rationale for the study is outlined.
Objectives	3	State specific objectives, including any prespecified hypotheses	5	"Our aim was to determine the diagnostic yield of screening patients admitted to hospital with a diagnosis unrelated to COVID-19 for SARS-CoV-2 in 2020, and identify risk factors for a positive test"
Methods				
Study design	4	Present key elements of study design early in the paper	5	The Study Design and Setting is outlined early in the Methods Section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Included in "Study Design and Setting" sub-section.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	Included in the "Study Patients" sub-section. Eligibility, sources and methods of selection are described.

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7	Variables are outlined in the "Data Collection" sub-section.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7	Data sources and methods of assessment are outlined in the "Study Design and Setting" and "Data Collection" sub-sections.
Bias	9	Describe any efforts to address potential sources of bias	6-7	Described within the "Study Patients" and the "Data Collection" sub-sections.
Study size	10	Explain how the study size was arrived at	6	Described within the "Study Patients" sub-section.

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8	Included within the "Data Collection" and "Data Analysis" sub-sections.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8	Descriptive statistics, sub-group analyses, and regression models were used. Confounding was addressed via multivariable regression.
		(*b*) Describe any methods used to examine subgroups and interactions	8	Sub-group analyses were planned for patients presenting with and without COVID compatible symptoms.
		(*c*) Explain how missing data were addressed	6-7	"Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study" "We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing)"
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7-8	Loss to follow-up was not an issue. Study enrolled consecutive patients who met the inclusion/exclusion criteria and data collected through chart review.
		(*e*) Describe any sensitivity analyses	N/A	Not performed.
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically

				suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients."
		(b) Give reasons for non-participation at each stage	N/A	Study was based on chart review.
		(c) Consider use of a flow diagram	Figure 1	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9	Paragraph 2 of the results includes the descriptive summaries.
		(b) Indicate number of participants with missing data for each variable of interest	N/A	See methods.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020".
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8	"During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites."
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A	
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9	Descriptive results and comparative findings are described in the latter 2 paragraphs of the "Results"
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9	Follows the sentence "We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1)."
Discussion				
Key results	18	Summarise key results with reference to study objectives	9-10	The study objective is recalled and situated within the context of the results.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11	"A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield."
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	Key references are recalled, and the study results are situated with these references.
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11	"While our study is based on a Canadian population without international sites, we believe our

				findings are likely generalizable given the wide geographic spread of our study sites."
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11	Included under "Funding" Section.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

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Diagnostic Yield of Screening for SARS-CoV-2 among Patients Admitted to Hospital for Alternate Diagnoses: An Observational Cohort Study

Phil Davis[1], Rhonda J. Rosychuk[2], Jeffrey P Hau[3,14], Ivy Cheng[4,5], Andrew D. McRae[6], Raoul Daoust[7], Eddy Lang[8], Joel Turner[9], Jaspreet Khangura[10], Patrick T. Fok[11], Maja Stachura[12], Baljeet Brar[13], and Corinne Hohl[14] **on behalf of the CCEDRRN investigators, and for the Network of Canadian Emergency Researchers and the Canadian Critical Care Trials Group**

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Keywords: screening, COVID-19, coronavirus disease, health services utilization, diagnostic testing, pandemic

Abstract:

Objectives: To determine the diagnostic yield of screening patients for SARS-CoV-2 who were admitted with a diagnosis unrelated to COVID-19, and identify risk factors for positive tests.

Design: Cohort from the Canadian COVID-19 Emergency Department Rapid Response Network (CCEDRRN) registry

Setting: 30 acute care hospitals across Canada

Participants: Patients hospitalized for non-COVID-19 related diagnoses who were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 1, and December 29, 2020

Main outcome: Positive nucleic acid amplification test (NAAT) for SARS-CoV-2

Outcome measure: Diagnostic yield

Results: We enrolled 15,690 consecutive eligible adults who were admitted to hospital without clinically suspected COVID-19. Among these patients, 122 tested positive for COVID-19, resulting in a diagnostic yield of 0.8% (95% CI 0.64% – 0.92%). Factors associated with a positive test included presence of a fever, being a healthcare worker, having a positive household contact or institutional exposure, and living in an area with higher 7-day average incident COVID-19 cases.

Conclusions: Universal screening of hospitalized patients for COVID-19 across two pandemic waves had a low diagnostic yield and should be informed by individual-level risk assessment in addition to regional COVID-19 prevalence.

Trial registration: NCT04702945

Strengths and Limitations

- Pan-Canadian study including over 40 academic, non-academic, rural, and urban hospitals.
- Inclusion of patient partners, as well as public engagement, who assisted in the development and presentation of this manuscript.
- Inclusion of pertinent clinical variables, as well as relevant demographic and community level variables.
- Exclusion of non-NAAT tests due to their infrequent use in the Canadian context.

INTRODUCTION

Healthcare institutions initiated widespread testing of admitted patients for coronavirus disease 2019 (COVID-19) in the spring of 2020 (1). Patients without any reported symptoms of COVID-19 were routinely tested even in jurisdictions where COVID-19 rates were low in order to identify asymptomatic carriers and prevent hospital outbreaks (2). Some jurisdictions have continued this practice without robust evidence to support this practice. An Alberta study of 3,375 patients admitted to hospital for alternate diagnoses during the first wave of the pandemic when COVID-19 prevalence was very low found that none of the patients tested positive (3). In contrast, other studies from times and regions with higher COVID-19 prevalence reported positive tests in between 2.6 and 15.5% of otherwise asymptomatic patients (4–8).

Universal testing has several potential downsides if diagnostic yield is low. First, it may worsen Emergency Department (ED) crowding, as admitted patients with pending COVID-19 tests are boarded in EDs until their test results are reported. While ED volumes were lower than usual in the early pandemic such that EDs could absorb this delay, high patient volumes have since returned, exacerbating the impact of this practice on hospital crowding (9). This in turn increases patient morbidity and mortality (10). In addition, diagnostic workups and therapeutic interventions may be delayed until COVID-19 test results are back, as it takes longer to move patients on isolation precautions through the system. This can further exacerbate patient outcomes and hospital crowding. Thirdly, diagnostic testing capacity may be limited, potentially delaying processing of tests for symptomatic patients. In addition, the use of Personal Protective Equipment (PPE) may be increased as institutions have placed patients with pending COVID-19 tests under isolation precautions. The use of PPE during resuscitation has been associated with worse patient outcomes (11). Lastly, there is also an opportunity cost for hospitals as money spent on universal testing could be allocated to other areas. These unintended consequences of liberal testing policies need to be weighed carefully against the anticipated diagnostic yield and potential benefits.

As for any diagnostic test, rational COVID-19 testing guidelines should be informed by the level of risk of the patient, such that testing is reduced in situations when risk is low, and more widespread when risk is high. Based on expert opinion, the Infectious Diseases Society of America (IDSA) recommended a testing strategy based on the prevalence of the disease in the community (12). They recommended universal testing of asymptomatic hospitalized patients in times and places of high disease prevalence defined as ≥10% or ≥10,000 active cases per 100,000 population and did not recommend universal testing in times and places of low prevalence, defined as under 2% prevalence of disease, or less than 2,000 active cases per 100,000. Most jurisdictions never met the proposed screening threshold as public health measures were enacted to reduce disease prevalence to avoid overwhelming hospital capacity. The IDSA was unable to provide further guidance due to lack of available evidence. Our aim was to determine the diagnostic yield of screening patients for SARS-CoV-2 who had been admitted with a diagnosis unrelated to COVID-19 and identify risk factors for positive tests.

METHODS

Study Design and Setting

The Canadian COVID ED Rapid Response Network (CCEDRRN, pronounced 'sedrin') is a pan Canadian population-based registry that has enrolled consecutive eligible patients presenting with suspected or confirmed COVID–19 from EDs across Canada starting on March 1, 2020. The study population, data collection, data quality assurance, management and governance structure are described in the network's methods paper (13). The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015). Thirty CCEDRRN sites in 7 provinces contributed data to this study (Appendix A). Data are available upon reasonable request and can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Patient and Public Involvement

CCEDRRN has an active patient engagement committee with patient partners who have lived experience with COVID-19 from geographically representative areas of Canada. Patient partners provided input into the development of this research question and study protocol and the final manuscript.

Study Patients

Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study. Data from sites and periods that did not meet this quality threshold were excluded. We included consecutive eligible patients who were admitted to hospital and swabbed for SARS-CoV-2 using a nucleic acid amplification test (NAAT) within 24 hours of ED arrival. We enrolled patients between March 1, 2020 and December 29, 2020. To identify a population of admitted patients in whom COVID-19 disease was not suspected, we excluded patients with ED diagnoses that would have been clinically suspicious for COVID-19. These included all patients with ED diagnoses of suspected or confirmed COVID-19, influenza-like-illness (ILI), upper respiratory infections, and pneumonia or viral pneumonia for which testing would have been indicated based on clinical suspicion. We excluded patients who were discharged directly from the ED, diagnosed with COVID-19 before ED arrival (based on a NAAT done in the community), those whose first swab occurred more than 24 hours after their arrival, and repeat admissions. We also excluded patients in whom initial SARS-CoV-2 testing was negative and repeat testing became positive more than 5 days after arrival, as these patients could have contracted nosocomial COVID.

Data Collection

Trained research assistants collected data retrospectively from electronic and/or paper-based medical records into a central, web-based REDCap database (Vanderbilt University; Nashville, TN, USA). Research assistants captured demographics, infection risk, ED vital signs, presenting symptoms, comorbid conditions and the results of COVID-19 tests. The coordinating centre implemented regular

data quality checks, including logic checks in REDCap as well as site-level record verifications for nonsensical or outlying values.

In addition to these clinical variables, we calculated the seven-day moving average incident COVID-19 case count for the health region of each participating site using publicly available epidemiological data (14). For each calendar day within each health region represented in the study, we calculated the average daily incident rate of new infections per 100,000 population over the preceding seven days. This seven-day moving average incidence was assigned to each patient based on the date of their index emergency department encounter and the health region of their postal code of residence. We allocated patients with no fixed address to the health region of the hospital in which they were tested. We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing), COVID-19 case data were not publicly available for the early pandemic. The seven-day moving average incident COVID-19 case count was categorized as 0 – 1.99 per 100,000 population, 2 – 7.99 per 100,000 population, and ≥8 per 100,000 population based on the relationship between incidence and COVID-19 positive results in a previous analysis (15).

Outcome:

The primary outcome was a positive NAAT for SARS-CoV-2 in patients admitted with non-COVID-related diagnoses.

Data Analysis:

We divided the cohort into two groups, those without symptoms of COVID-19 and those with symptoms compatible with COVID-19 that were attributed to an alternate diagnosis (i.e., CHF, COPD, Asthma, etc.). We considered cough, dyspnea, fever, general weakness, chest pain, diarrhea, nausea and vomiting, headache, chills, myalgia, sore throat, altered level of consciousness, and dysgeusia/anosmia to be COVID-19-compatible symptoms. We used descriptive statistics to describe the population. We

calculated the diagnostic yield by dividing the number of positive NAATs over the total number of NAATs performed. We calculated 7-day average of NAAT positivity over the study period by dividing the number of positive NAATs over all tests performed and averaging over a 7-day period. We calculated the exact binomial proportion 95% confidence intervals (95% CI) for all proportions and used the modified Clopper-Pearson interval for small samples. We completed a planned subgroup analyses for patients presenting with and without COVID compatible symptoms to determine associated factors for a positive test. The initial multivariable logistic regression model to identify factors associated with a positive NAAT considered candidate variables with a p-value cut-off point of 0.20 based on the Wald test from univariable analyses. From the full model, a step-down procedure reduced the model to key predictors based on Akaike's information criterion (AIC) scores (e.g., chose the model with the smallest AIC score). Candidate variables included seven-day moving average incident COVID-19 case count category, patient age, gender, infection risk, and presenting symptoms. We limited the number of predictor variables in the model to one variable for every 10 outcomes in our data to avoid overfitting. Statistical analysis was preformed using Stata (Version 16.1, StataCorp, College Station, Texas).

RESULTS

We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients. During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites. The 7-day average diagnostic test positivity varied between 0 and 2.9% across sites during the study period (Figure 2).

We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1). Most patients arrived from home and were full code. The most common comorbidities were hypertension, diabetes and mental health illness.

Of 3,113 patients admitted without COVID-19 compatible symptoms, 13 (0.4%, 95% CI 0.19% – 0.64%) tested positive for COVID-19. Of the 12,570 with COVID-19-compatible symptoms, 109 patients (0.9%, 95% CI 0.70% – 1.03%) tested positive for COVID-19. Among the 122 individuals who tested positive for COVID-19, 33 (27.0%, 95% CI 19.0% - 35.0%) were from a geographic region that had a moving average daily incident rate of ≥8 infections per 100,000 population. The diagnostic yield of testing among patients with COVID-19 compatible symptoms admitted for alternative diagnoses did not vary substantially by presenting symptom (Figure 3) or ED diagnosis (Figure 4).

When examining the association between patient factors and screening positive self-reported fever, being a healthcare worker, having a positive household contact or institutional exposure, and being from an area where the seven-day moving average incident COVID-19 case count was ≥8 per 100,000 population were associate with a greater risk of testing positive (Table 2). The most important risk factor was reporting a household contact or being the caregiver of a known COVID-19 case.

DISCUSSION

Our aim was to evaluate the diagnostic yield of screening non-COVID-19 admissions for SARS-CoV-2 across Canada in 2020 and identify patient-level risk factors for positive tests. The diagnostic yield of screening patients with non-COVID-19 related ED diagnoses who were admitted to hospital was low overall, and extremely low in patients without COVID compatible symptoms. The most important patient factors associated with a positive test were having a positive household contact, being a healthcare worker, or having had an institutional exposure to COVID-19. Those factors were more important than a high (≥8 daily cases per 100,000 population) 7-day moving average incident COVID-19 case count.

Our study has several strengths. We used data from a large pan-Canadian registry that enrolls from large geographically and culturally diverse areas and is one of the largest registries in the world. CCEDRRN's patient enrolment and data verification protocols are rigorous, ensuring consecutive eligible patients and high-quality clinical data (13). We have previously demonstrated the inter-rater reliability for our data collection methods, including for symptoms (13).

Prior studies have examined the diagnostic yield of universal screening in single centers with varied diagnostic yield estimates between 0 and 15.5% (3–8). Many of these were case series with limited methods from the early pandemic. There is one known multi-center study which examines the benefit of universal screening for elective and emergent surgical admissions at 14 centers in the Netherlands (1). Like our study, the authors found that the overall COVID-19 NAAT positivity varied with community prevalence. Our finding that positive SARS-CoV-2 tests were associated with self-reported or measured fever is in keeping with a prior Cochrane systematic review that noted considerable variability in COVID-19 associated symptoms (16).

Our study is interesting in the context of current IDSA recommendations which were based on expert opinion and of "very low certainty" (12). The IDSA panel recommended avoiding universal screening for COVID-19 in times and areas of low COVID prevalence, defined as a disease prevalence of under 2% , or fewer than 2,000 active cases per 100,000 population, a threshold so high that it was never met at any of our study sites, even though multiple sites were in COVID-19 hotspots in 2020 (12). The IDSA threshold would have equated to over 6 million cases of active COVID-19 infection in the United States at any given time, which would have vastly overwhelmed hospital capacity, and thus represents an untenable threshold for hospitals. It is therefore not surprising that the prevalence of COVID-19 during the study period was far below the IDSA recommended threshold for initiating screening. While the number needed to screen to identify one positive case among admitted patients in our study was between 110 and 250 among unvaccinated patients, we propose that new screening thresholds need to be adopted which would ideally be based on readily available measures of local incident cases or test positivity.

A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield. Additionally, our study was performed before the newer COVID-19 variants, such as Omicron, circulated widely. However, our methods are easily replicated, and we intend to repeat our study in a recent dataset reflective of new COVID-19 variants. While our study is based on a Canadian population without international sites, we believe our findings are generalizable given their wide geographic spread, and the cultural and racial diversity of our patient population. Finally, as data becomes available on the fourth wave of the pandemic, a future study should examine the impact of widespread vaccination on the yield of screening. As a larger proportion of the population is protected from severe disease and death through vaccination, decision makers should carefully consider the low diagnostic yield of a universal testing strategy going forward.

ACKNOWLEDGEMENTS

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Thank you to all of our patient partners who shared their lived experiences and perspectives to ensure that the knowledge we co-create addresses the concerns of patients and the public. Creating the largest network of collaboration across Canadian Emergency Departments would not have been feasible without the tireless efforts of Emergency Department Chiefs, and research coordinators and research assistants at participating sites. Finally, our most humble and sincere gratitude to our colleagues in medicine, nursing,

and the allied health professions who have been on the front lines of this pandemic from day one staffing our ambulances, Emergency Departments, hospitals and ICUs bravely facing the risks of COVID-19 to look after our fellow citizens and after one another. We dedicate this network to you.

COMPETING INTERESTS

None identified.

FUNDING

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AUTHOR CONTRIBUTION STATEMENT

All authors conceived and planned the study together, and iteratively refined the study objectives and analytic plan. PH, RJR, ADM, EL and CMH obtained funding for the study. PD, IC, ADM, RD, JT, JK, PRF, MS and BB supervised data collection. JPH analyzed the data under the supervision of RJR. All authors interpreted the analysis. PD drafted the manuscript. All authors were actively involved in reporting out work by revising the manuscript for content. All authors take responsibility for the manuscript as a whole.

DATA SHARING

Data are available upon reasonable request. They can be shared after approval by the Executive Committee through a process outlined on our website (https://www.ccedrrn.com/).

Table 1: Baseline Characteristics of admitted patients without clinical suspicion of COVID-19 (N=15,690)

	Patients without COVID-19 symptoms (N=3,113)	Patients with COVID-19 compatible symptoms attributed to an alternate diagnosis (N=12,570)
Demographics		
Age (mean, SD)	57.6 (22.6)	64.6 (20.4)
Female (%)	1,418 (45.6)	5,924 (47.1)
Pregnant (%)	18 (0.6)	45 (0.4)
Tobacco use (%)	491 (15.8)	1,656 (13.2)
Illicit substance use (%)	421 (13.5)	967 (7.7)
Arrival by Ambulance (%)	1,724 (55.4)	7,189 (57.2)
Arrival From (%)		
Home	2,552 (82.0)	10,943 (87.0)
Long-term care or rehab facility	217 (7.0)	832 (6.6)
Unstable housing*	190 (6.1)	414 (3.3)
Corrections	7 (0.2)	14 (0.1)
Interfacility transfer	121 (3.9)	262 (2.1)
Risk for Infection (%)		
Travel	32 (1.0)	134 (1.1)
Institutional (LTC/prison)	231 (7.4)	721 (5.7)
Household contact	28 (0.9)	144 (1.1)
Occupational	10 (0.3)	38 (0.3)
Unknown	1,502 (48.2)	5,377 (42.8)
Pre-ED Goals of Care (%)		
Full code	2,946 (94.6)	11,259 (89.5)
Intermediate GOC	18 (0.6)	173 (1.4)
Do not resuscitate	149 (4.8)	1,142 (9.1)
Acuity		
CTAS 1 (Resuscitation)	241 (7.7)	1,053 (8.4)
CTAS 2 (Emergent)	1,000 (32.1)	5,786 (46.0)
CTAS 3 (Urgent)	1,527 (49.1)	5,086 (40.4)
CTAS 4 (Less Urgent)	295 (9.5)	572 (4.6)
CTAS 5 (Non Urgent)	40 (1.3)	59 (0.5)
Arrival Vital Signs, Mean (SD)		
Heart Rate, beats per min	91.2 (21.2)	95.5 (23.9)
Systolic BP, mm Hg	134.7 (25.1)	133.6 (27.9)
Oxygen saturation, (%)	96.6 (3.4)	95.7 (4.1)
Respiratory Rate, beats per min	18.6 (4.4)	21.2 (6.3)
Temperature, degrees Celsius	36.6 (0.6)	36.8 (0.9)
Comorbidities (%)		
Hypertension	951 (30.6)	5,321 (42.3)
Psychiatric Condition	728 (23.4)	2,134 (17.0)
Dyslipidemia	425 (13.6)	2,434 (19.4)
Diabetes	427 (13.7)	2,577 (20.5)
Chronic Neuro Disorder	322 (10.3)	1,406 (11.2)

Coronary Artery Disease	284 (9.1)	1,796 (14.3)
Rheumatologic Disorder	229 (7.4)	1,249 (9.9)
Dementia	199 (6.4)	696 (5.5)
Active Cancer	231 (7.4)	1,647 (12.9)
Chronic Kidney Disease	195 (6.3)	1,319 (10.5)
Chronic Lung Disease (not asthma)	199 (6.4)	1,691 (13.5)
Congestive Heart Failure	159 (5.1)	1,392 (11.1)
Asthma	125 (4.0)	712 (5.7)
Obesity	57 (1.8)	344 (2.7)
Symptoms (%)		
Cough	-	2,763 (22.0)
Dyspnea	-	4,757 (37.8)
Fever	-	2,531 (20.1)
General Weakness	-	3,183 (25.3)
Chest Pain	-	2,714 (21.6)
Diarrhea	-	1,339 (10.7)
Nausea/Vomiting	-	3,345 (26.6)
Headache	-	784 (6.2)
Chills	-	957 (7.6)
Myalgia	-	466 (3.7)
Sore Throat	-	374 (3.0)
Altered Consciousness	-	2,502 (19.9)
Dysgusea/Anosmia	-	41 (0.3)
ED Diagnosis (%)		
Respiratory Disease, not specified	8 (0.3)	118 (0.9)
COPD Exacerbation	11 (0.4)	648 (5.2)
Asthma Exacerbation	<5	97 (0.8)
Congestive Heart Failure	44 (1.4)	1,003 (8.0)
Shortness of Breath, NYD*	-	466 (3.6)
Cough, NYD*	-	63 (0.5)
Fever, NYD*	-	482 (3.8)
Outcome (%)		
Positive SARS-CoV-2 NAAT	13 (0.4)	109 (0.9)

*NYD denotes “not yet determined”

Table 2: Multivariate analysis of factors associated with positive SARS-CoV-2 nucleic tests (N=15,690)

	Univariate analysis odds ratio (95% CI)	Final model with fully adjusted odds ratio (95% CI)[1]	P-value
Sex			
Male	*Reference*	*Reference*	0.18
Female	0.84 (0.59 – 1.21)	0.78 (0.54 – 1.12)	
Age			
	1.00 (1.00 – 1.02)	1.00 (0.99 – 1.01)	0.27
7-day average incident COVID-19 cases			
0 – 1.99 daily cases per 100,000 population	*Reference*	*Reference*	< 0.001
2 to 7.99 daily cases per 100,000 population	1.42 (0.91 – 2.22)	1.47 (0.94 – 2.31)	
≥8 daily cases per 100,000 population	2.99 (1.95 – 4.59)	3.17 (2.05 – 4.89)	
COVID-19 compatible symptoms present			
No	*Reference*	*Reference*	0.08
Yes	2.08 (1.71 – 3.71)	1.65 (0.90 – 3.00)	
Self-reported fever, or temperature ≥ 37.5 °C			
No	*Reference*	*Reference*	< 0.001
Yes	2.72 (1.89 – 3.90)	2.53 (1.74 – 3.67)	
Diarrhea present			
No	*Reference*	*Reference*	0.11
Yes	1.74 (1.04 – 2.92)	1.57 (0.93 – 2.67)	
Healthcare worker			
No	*Reference*	*Reference*	0.06
Yes	5.62 (1.35 – 23.43)	4.67 (1.05 – 20.54)	
Household contact or caregiver			
No	*Reference*	*Reference*	< 0.001
Yes	9.48 (5.01 – 17.96)	7.74 (3.98 – 15.04)	
Institutional exposure			
No	*Reference*	*Reference*	< 0.001
Yes	3.46 (2.17 – 5.52)	3.39 (2.10 – 5.47)	
Dysgeusia or anosmia present			
No	*Reference*	-	
Yes	3.21 (0.43 – 23.52)	-	
Dyspnea present			
No	*Reference*	-	
Yes	1.16 (0.80 – 1.70)	-	
Nausea or vomiting present			
No	*Reference*	-	
Yes	0.81 (0.51 – 1.29)	-	

[1] Final model determined by including variables with a p-value of p<0.20 from univariable analyses, and using the Akaike Information Criterion (AIC) to determine additional variables to exclude from the final model. Variables adjusted for all other variables present in the final model.

Figure 1: Patient Flow Diagram

Figure 2: 7-day working average of COVID-19 NAAT positivity over the study period across sites.

Figure 3: Diagnostic Yield by Presenting Symptoms

Figure 4: Diagnostic Yield by ED Diagnosis

ETHICAL APPROVAL STATEMENT

The research ethics boards of all participating institutions approved this study with a waiver of informed consent for data collection and linkage (UBC REB: H20-01015).

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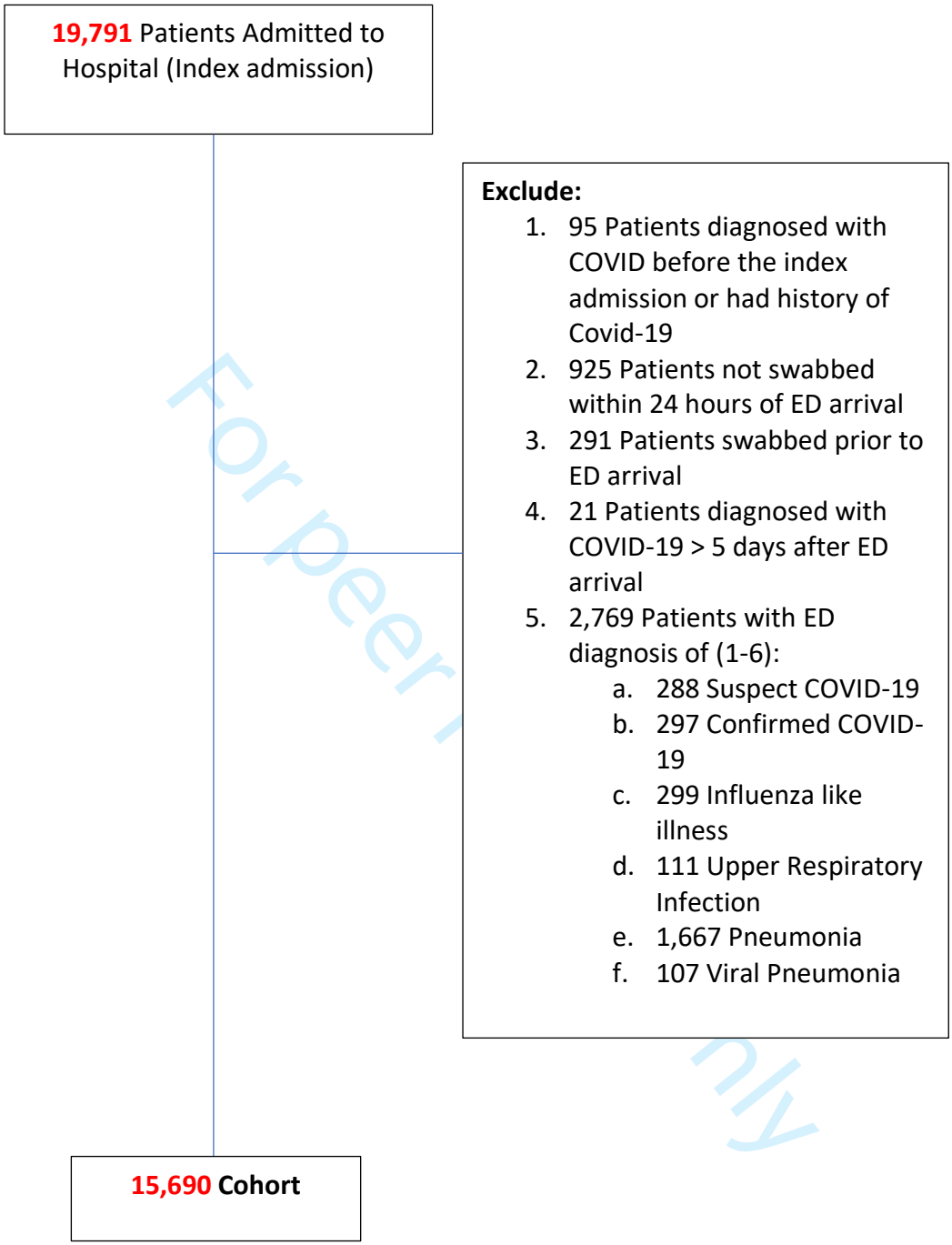
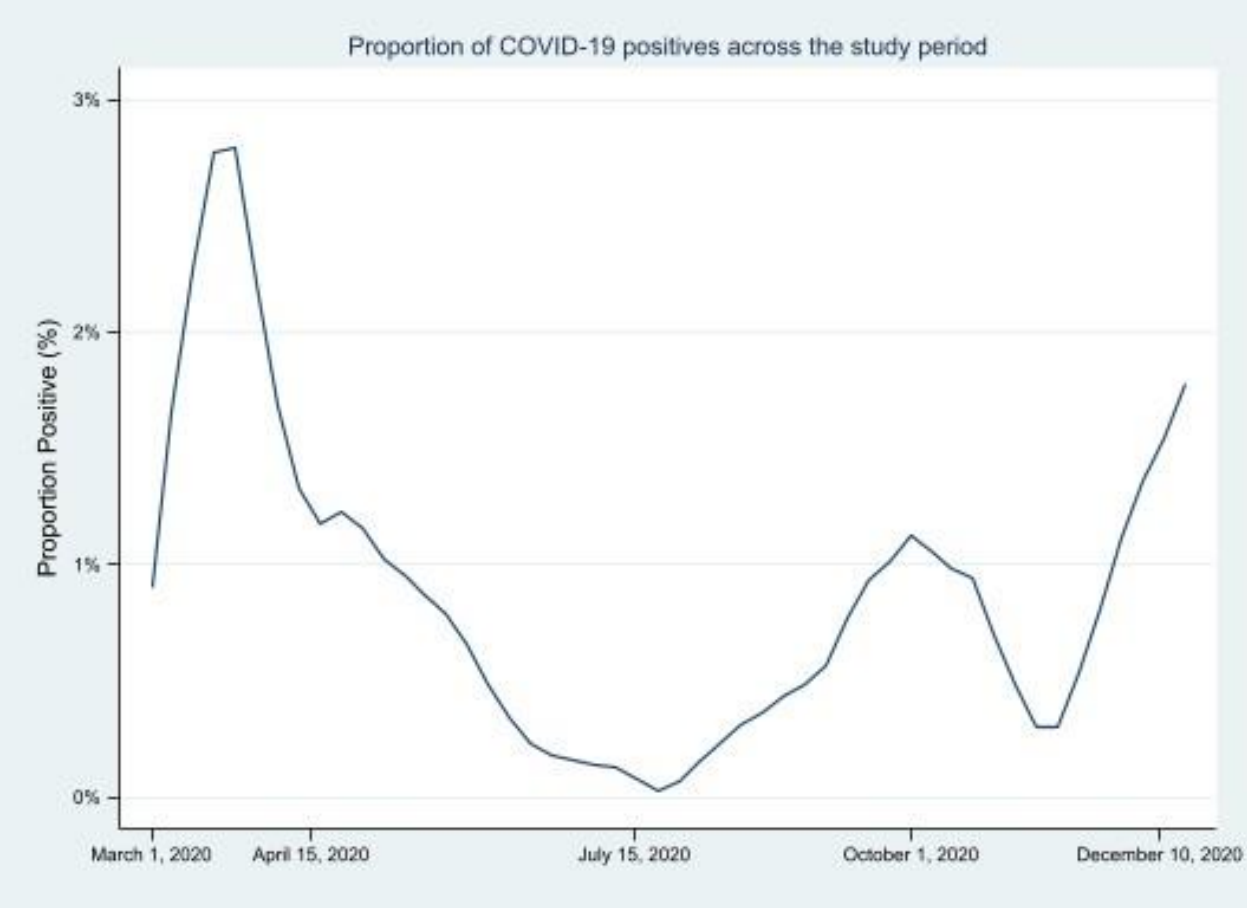
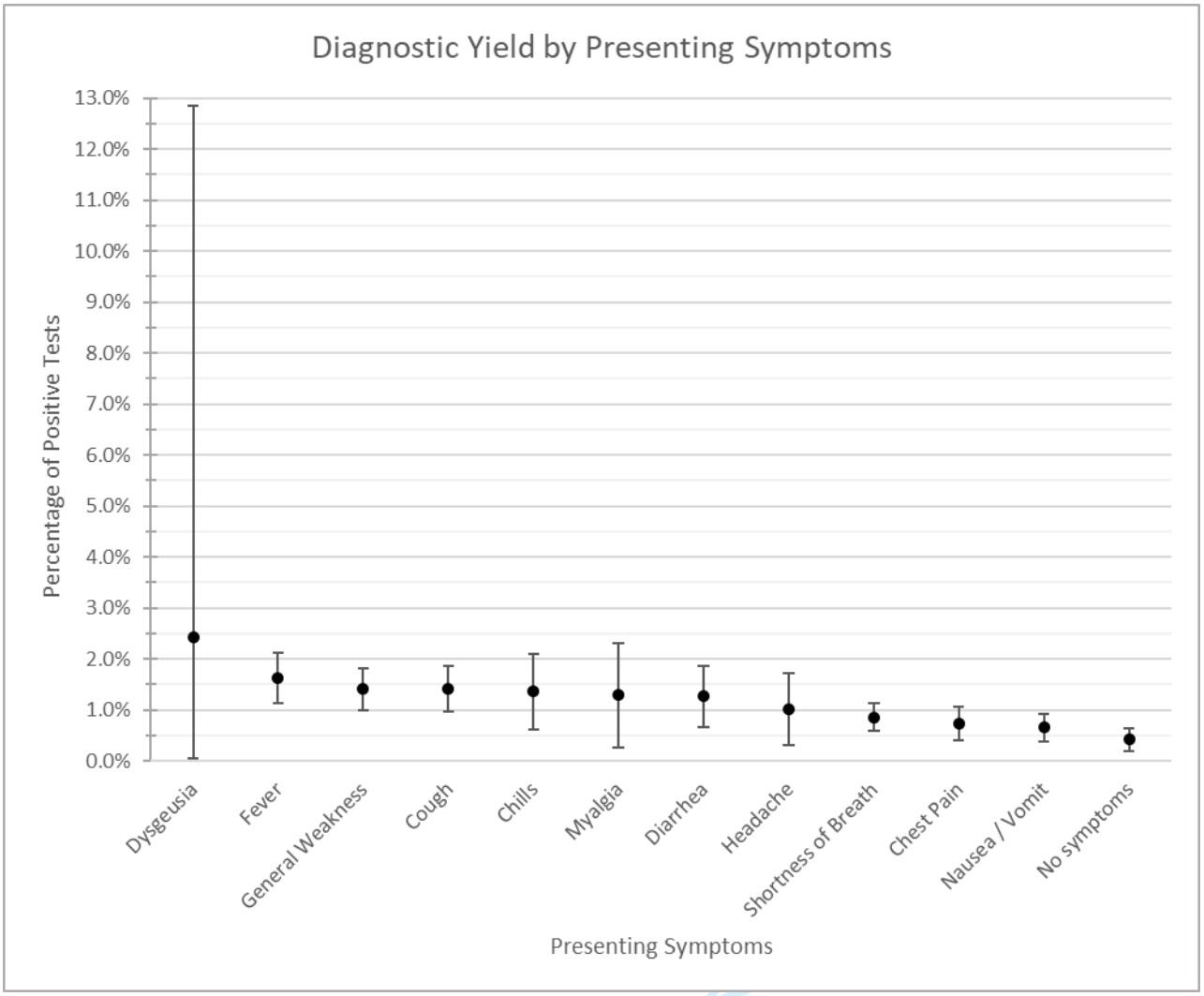
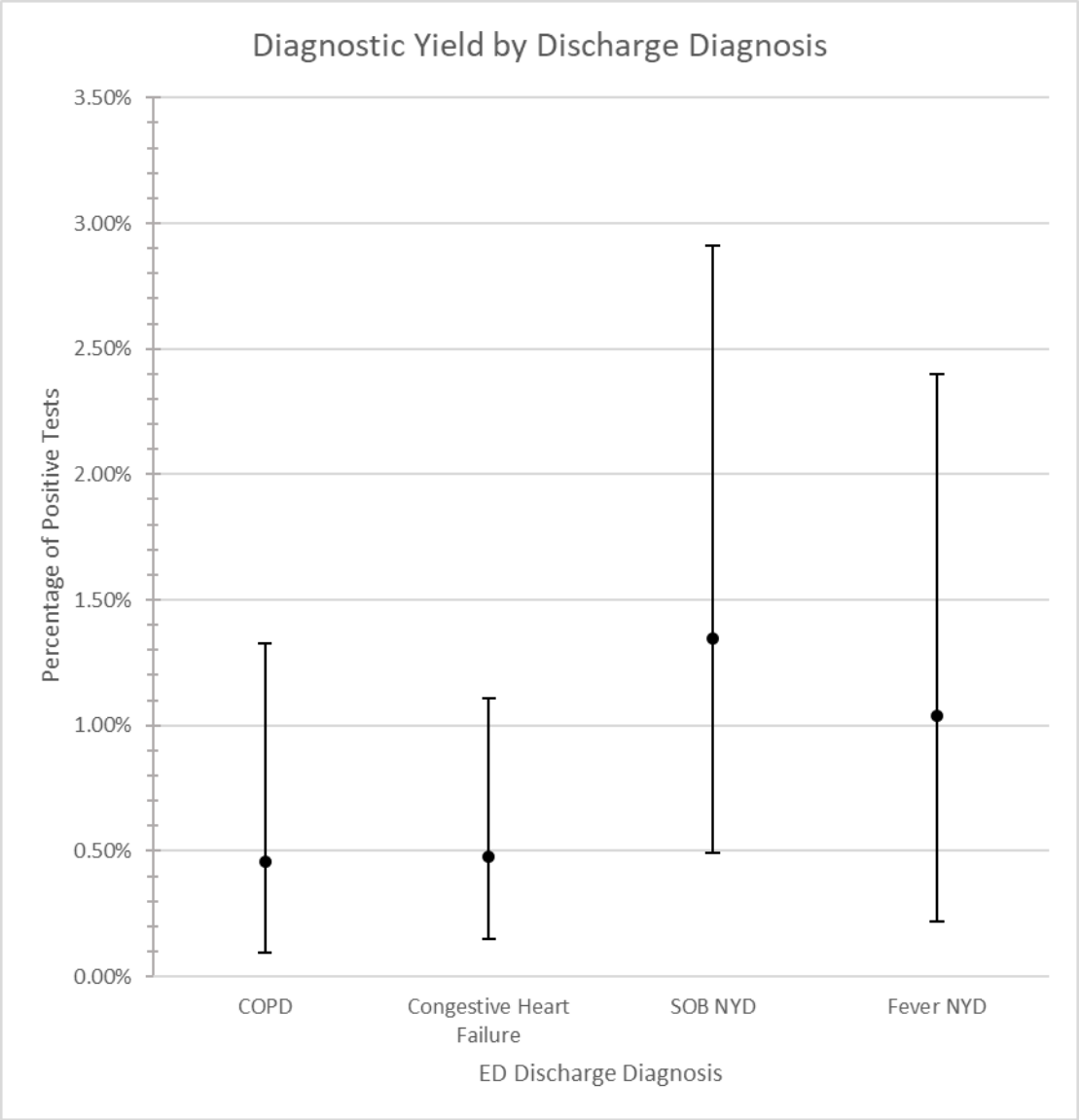


Figure 2: The 7-day working average of COVID-19 NAAT positivity among all eligible study patients over the study period across study sites.







*NYD denotes “not yet determined”

APPENDIX & SUPPLEMENT

Appendix A: List of hospital sites, with an inclusion start and end date for this study.

Site Name	Province	Start Date	End Date
Vancouver General Hospital	British Columbia	1-Mar-2020	31-Aug-2020
Lions Gate Hospital	British Columbia	1-Mar-2020	29-Apr-2020
Saint Paul's Hospital	British Columbia	1-Mar-2020	23-May-2020
Mount Saint Joseph Hospital	British Columbia	1-Mar-2020	24-Mar-2020
Surrey Memorial Hospital	British Columbia	19-Mar-2020	30-Apr-2020
Royal Columbian Hospital	British Columbia	1-Mar-2020	31-May-2020
Abbotsford Regional Hospital	British Columbia	20-Apr-2020	15-Jul-2020
University of Alberta Hospital	Alberta	8-Apr-2020	7-May-2020
Foothills Medical Centre	Alberta	1-Mar-2020	7-Apr-2020
Rockyview General Hospital	Alberta	1-Mar-2020	7-Apr-2020
Peter Lougheed Centre	Alberta	1-Mar-2020	12-Dec-2020
South Health Campus	Alberta	1-Mar-2020	12-Dec-2020
St Paul's Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Royal University Hospital	Saskatchewan	17-Mar-2020	31-Oct-2020
Saskatoon City Hospital	Saskatchewan	17-Mar-2020	30-Apr-2020
Sunnybrook Health Sciences Centre	Ontario	14-May-2020	31-Oct-2020
The Ottawa Hospital - Civic Campus	Ontario	14-May-2020	31-May-2020
Health Science North	Ontario	14-May-2020	29-Dec-2020
Toronto Western Hospital	Ontario	1-Sep-2020	31-Sep-2020
Hotel-Dieu de Lévis	Quebec	4-May-2020	18-May-2020
Jewish General Hospital	Quebec	1-Mar-2020	4-Jun-2020
Hôpital de l'Enfant-Jésus,CHU de Québec	Quebec	4-May-2020	23-Jul-2020
IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec	Quebec	4-May-2020	13-May-2020
Hôpital du Sacré-Coeur de Montreal	Quebec	4-May-2020	18-May-2020
Saint John Regional Hospital	New Brunswick	12-Mar-2020	12-Apr-2020
Halifax Infirmary	Nova Scotia	5-Apr-2020	15-Apr-2020
Dartmouth General Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Hants Community Hospital	Nova Scotia	5-Apr-2020	15-Apr-2020
Cobequid Community Health Centre	Nova Scotia	5-Apr-2020	15-Apr-2020
Secondary Assessment Centers of Dartmouth General and Halifax Infirmary	Nova Scotia	26-Mar-2020	15-May-2020

Supplement Table 1. Network coordinating center staff at the University of British Columbia

Name	Roles	Contributions
Jeffrey Hau	Data manager	REDCap, data processing and analysis for manuscripts.
Vi Ho	National coordinator	Coordinate with provincial coordinators and training/onboarding of research assistants.
Serena Small	Research coordinator	Ethics & privacy reviews, data management plan, privacy impact assessment, and qualitative analyses
Amber Cragg	Research manager	Data and manuscript management
Wei Zhao	Data analyst	Data processing and analysis for manuscripts.
Vicky Wu	Data analyst	Data processing and analysis for manuscripts.
Elnaz Bodaghkhani	Research associate	Data and manuscript management

Supplement Table 2. Provincial Coordinators

Name	Province	Institutional affiliation	Contributions to CCEDRRN
Corinne DeMone	NS	Dalhousie University, Halifax, Nova Scotia	Research ethics board submission, manages research assistants, data cleaning and quality.
Jacqueline Fraser	NB	Dalhousie University, St. John New Brunswick	Site coordinator as well as research assistant.
Martyne Audet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis	Provincial research coordinator, translation of research material to French, ethics management.
Connie Taylor	ON	Queen's University, Kingston	Coordination of research assistants in Ontario, maintenance of REB applications for the province
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg	Lead RA for the province
Aimee Goss	SK	University of Saskatchewan, Saskatoon	Screens records in Saskatoon, data/extraction and entry, coordinates research assistants.
Hina Walia	AB	University of Calgary, Calgary	Provincial coordinator lead for Alberta, oversight of all Alberta sites.
Josie Kanu	BC	University of British Columbia, Vancouver	Provincial coordinator lead for BC, oversight of all BC sites.

Supplement Table 3. Institutional research assistant (RA) leads

Name	Province	Institutional affiliation(s)
Corinne DeMone	NS	Dartmouth General Hospital, Cobequid Community Health Centre, Hants Community Hospital Secondary Assessment Centers of the Dartmouth General Hospital, and Halifax Infirmary, Halifax
Jacqueline Fraser	NB	Saint John Regional Hospital, Saint John
Alexandra Nadeau	QC	CHU de Québec Université Laval, Quebec City
Audrey Nolet	QC	Centre intégré de santé et de services sociaux de Chaudière-Appalaches (Hôtel-Dieu de Lévis site), Lévis
Xiaoqing Xue	QC	Jewish General Hospital, Montréal
David Iannuzzi	QC	McGill University Health Center, Montréal
Chantal Lanthier	QC	Hôpital du Sacré-Cœur de Montréal, Montréal
Konika Nirmalanathan	ON	University Health Network, Toronto
Vlad Latiu	ON	Kingston General Hospital, Hotel Dieu Hospital, Kingston
Joanna Yeung	ON	Sunnybrook Health Sciences Center, Toronto
Natasha Clayton	ON	Hamilton General Hospital, Juravinski Hospital, Hamilton
Tom Chen	ON	London Health Sciences Centre, London
Jenna Nichols	ON	Health Sciences North, Sudbury
Kate Mackenzie	MB	Health Sciences Centre, Winnipeg
Aimee Goss	SK	St. Paul's Hospital, Royal University Hospital, Saskatoon City Hospital, Saskatoon
Stacy Ruddell	AB	Foothills Medical Centre, Peter Lougheed Centre, Rockyview General Hospital, South Health Campus, Calgary
Natalie Runham	AB	University of Alberta Hospital, Edmonton
Karlin Su	AB	Royal Alexandra Hospital/Northeast Community Health Center, Edmonton
	BC	St. Paul's Hospital, Mount Saint Joseph, Vancouver
Bernice Huynh	BC	Abbotsford Regional Hospital and Cancer Center, Abbotsford
Amanda Swirhun	BC	Royal Columbian Hospital, New Westminster
Tracy Taylor	BC	Eagle Ridge Hospital and Health Care Centre, Port Moody
Mai Hayashi	BC	Royal Inland Hospital, Kamloops
Mackenzie Cheyne	BC	Kelowna General Hospital, Kelowna
Sarim Asim	BC	Surrey Memorial Hospital, Surrey
Katherine Lam	BC	Vancouver General Hospital, Vancouver
Kelsey Compagna	BC	Lions Gate Hospital, Vancouver

Supplement Table 4. Contributing Study Sites and Investigators

Lead Investigator	Contributing Site / Code	Member Investigators
Maritime		
Patrick Fok		
Nova Scotia		
Hana Wiemer	Halifax Infirmary/ 902	Patrick Fok
	Dartmouth General Hospital/ 903	Hana Wiemer
	Hants Community Hospital/ 904	Samuel Campbell
	Cobequid Community Health Centre/ 905	Kory Arsenault
	Secondary Assessment Centers of Dartmouth General and Halifax Infirmary/ 908	Tara Dahn
New Brunswick		
Kavish Chandra	Saint John Regional Hospital/ 901	Kavish Chandra
Quebec		
Patrick Archambault	Hotel-Dieu de Lévis/ 701	Patrick Archambault
	Jewish General Hospital/ 702	Joel Turner
	Centre Hospitalier de l'Université Laval (CHU de Québec)/ 703	Éric Mercier
	L'hôpital Royal Victoria - Royal Victoria Hospital/ 705	Greg Clark
	Hôpital de l'Enfant-Jésus,CHU de Québec/ 706	Éric Mercier
	Hôpital du Saint-Sacrement, CHU de Québec/ 707	Éric Mercier
	Hôpital Saint-François d'Assise, CHU de Québec/ 708	Éric Mercier
	Hôtel-Dieu de Québec,CHU de Québec/ 709	Éric Mercier
	IUCPQ: Institut universitaire de cardiologie et de pneumologie de Québec/ 710	Sébastien Robert
	Hôpital du Sacré-Coeur de Montreal/ 711	Raoul Daoust
Ontario		
Laurie Morrison & Steven Brooks	Sunnybrook/ 401	Ivy Cheng
	The Ottawa Hospital - Civic Campus/ 403	Jeffrey Perry
	The Ottawa Hospital - General Campus/ 404	Jeffrey Perry
	Kingston/Queens/ 406	Steven Brooks
	Hamilton General Hospital/ 407	Michelle Welsford
	Health Science North, Sudbury Ontario/ 408	Rob Ohle
	University Hospital – LHSC/ 409	Justin Yan
	North York General Hospital, Toronto/ 410	Rohit Mohindra
	Victoria Hospital – LHSC/ 412	Justin Yan
	Toronto Western Hospital/ 414	Megan Landes
Manitoba		
Tomislav Jelic	Health Sciences Centre/ 307	Tomislav Jelic
Saskatchewan		
Phil Davis	St Paul's Hospital, Saskatoon/ 303	Phil Davis
	Royal University, Saskatoon/ 304	Phil Davis

	Saskatoon City Hospital, Saskatoon/ 305	Phil Davis
Alberta		
Andrew McRae	University of Alberta Hospital, Edmonton/ 201	Brian Rowe
	Foothills, Calgary/ 202	Katie Lin
	Rockyview, Calgary/ 203	Andrew McRae
	Peter Lougheed Centre/ 204	Andrew McRae
	South Campus, Calgary/ 205	Stephanie VandenBerg
	Northeast Community Health Centre, Edmonton/ 206	Jake Hayward, Jaspreet Khangura
	Royal Alexandra Hospital, Edmonton/ 306	Jake Hayward, Jaspreet Khangura
British Columbia		
Corinne Hohl	Vancouver General Hospital/ 101	Daniel Ting
	Lions Gate Hospital/ 102	Maja Stachura
	Saint Paul's Hospital/ 103	Frank Scheuermeyer
	Mount St Joseph's/ 104	Frank Scheuermeyer
	Surrey Memorial Hospital/ 105	Balijeet Braar
	Royal Columbian Hospital/ 106	John Taylor
	Abbotsford Regional Hospital/ 107	Ian Martin
	Eagle Ridge Hospital/ 108	Sean Wormsbecker
	Royal Inland Hospital/ 112	Ian Martin
	Kelowna General / Hospital/ 115	Lee Graham

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2 (abstract)	"Cohort from the CCEDRRN registry"
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Included within the results and conclusions of the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	Relevant scientific literature has been cited and the rationale for the study is outlined.
Objectives	3	State specific objectives, including any prespecified hypotheses	5	"Our aim was to determine the diagnostic yield of screening patients admitted to hospital with a diagnosis unrelated to COVID-19 for SARS-CoV-2 in 2020, and identify risk factors for a positive test"
Methods				
Study design	4	Present key elements of study design early in the paper	5	The Study Design and Setting is outlined early in the Methods Section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Included in "Study Design and Setting" sub-section.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	Included in the "Study Patients" sub-section. Eligibility, sources and methods of selection are described.

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7	Variables are outlined in the "Data Collection" sub-section.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7	Data sources and methods of assessment are outlined in the "Study Design and Setting" and "Data Collection" sub-sections.
Bias	9	Describe any efforts to address potential sources of bias	6-7	Described within the "Study Patients" and the "Data Collection" sub-sections.
Study size	10	Explain how the study size was arrived at	6	Described within the "Study Patients" sub-section.

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8	Included within the "Data Collection" and "Data Analysis" sub-sections.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8	Descriptive statistics, sub-group analyses, and regression models were used. Confounding was addressed via multivariable regression.
		(*b*) Describe any methods used to examine subgroups and interactions	8	Sub-group analyses were planned for patients presenting with and without COVID compatible symptoms.
		(*c*) Explain how missing data were addressed	6-7	"Participating sites needed to demonstrate ≥99% compliance in enrolling consecutive eligible patients for their data to be included in this study" "We imputed values for the first five weeks of the pandemic by modeling the reported COVID-19 cases that had accumulated in every health region over time using linear interpolation (0.1% missing)"
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7-8	Loss to follow-up was not an issue. Study enrolled consecutive patients who met the inclusion/exclusion criteria and data collected through chart review.
		(*e*) Describe any sensitivity analyses	N/A	Not performed.
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020 (Figure 1). We excluded 4,101 patients, of which 2,769 had ED diagnoses that were clinically

				suspicious for COVID-19 and warranted SARS-CoV-2 testing on clinical grounds. The final cohort contained 15,690 patients."
		(b) Give reasons for non-participation at each stage	N/A	Study was based on chart review.
		(c) Consider use of a flow diagram	Figure 1	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9	Paragraph 2 of the results includes the descriptive summaries.
		(b) Indicate number of participants with missing data for each variable of interest	N/A	See methods.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8	"We identified 19,791 patients admitted to hospital who presented to a participating ED between March 1, 2020, and December 29, 2020".
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8	"During the study period Canada experienced two pandemic waves with the local 7-day average incident case count ranging from between 0 and 42.6 cases per 100,000 population across sites."
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A	
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9	Descriptive results and comparative findings are described in the latter 2 paragraphs of the "Results"
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9	Follows the sentence "We divided the cohort into two groups, those without any COVID-19 compatible symptoms, and those with COVID-19 compatible symptoms that were attributed to an alternate diagnosis in the ED (Table 1)."
Discussion				
Key results	18	Summarise key results with reference to study objectives	9-10	The study objective is recalled and situated within the context of the results.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11	"A limitation of our study is that we only considered NAATs and did not consider the diagnostic yield of antigen-based COVID-19 tests, as they were not widespread in Canada in 2020 (16). We were unable to examine the sensitivity and specificity of the SARS-CoV-2 NAATs as we were unable to define false positive tests, so it is possible that some of the positive test results we encountered are false positives, leading to an overestimation of diagnostic yield."
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	Key references are recalled, and the study results are situated with these references.
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11	"While our study is based on a Canadian population without international sites, we believe our

				findings are likely generalizable given the wide geographic spread of our study sites."
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11	Included under "Funding" Section.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.