

Post-acute health care burden after SARS-CoV-2 infection: a retrospective cohort study

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Abstract

Background: The post-acute burden of health care use after SARS-CoV-2 infection is unknown. We sought to quantify the post-acute burden of health care use after SARS-CoV-2 infection among community-dwelling adults in Ontario by comparing those with positive and negative polymerase chain reaction (PCR) test results for SARS-CoV-2 infection.

Methods: We conducted a retrospective cohort study involving community-dwelling adults in Ontario who had a PCR test between Jan. 1, 2020, and Mar. 31, 2021. Follow-up began 56 days after PCR testing. We matched people 1:1 on a comprehensive propensity score. We compared per-person-year rates for health care encounters at the

mean and 99th percentiles, and compared counts using negative binomial models, stratified by sex.

Results: Among 531 702 matched people, mean age was 44 (standard deviation [SD] 17) years and 51% were female. Females who tested positive for SARS-CoV-2 had a mean of 1.98 (95% CI 1.63 to 2.29) more health care encounters overall per-person-year than those who had a negative test result, with 0.31 (95% CI 0.05 to 0.56) more home care encounters to 0.81 (95% CI 0.69 to 0.93) more long-term care days. At the 99th percentile per-person-year, females who tested positive had 6.48 more days of hospital admission and 28.37 more home care encounters. Males who tested positive for SARS-CoV-2 had 0.66

(95% CI 0.34 to 0.99) more overall health care encounters per-person-year than those who tested negative, with 0.14 (95% CI 0.06 to 0.21) more outpatient encounters and 0.48 (95% CI 0.36 to 0.60) long-term care days, and 0.43 (95% CI -0.67 to -0.21) fewer home care encounters. At the 99th percentile, they had 8.69 more days in hospital per-person-year, with fewer home care (-27.31) and outpatient (-0.87) encounters.

Interpretation: We found significantly higher rates of health care use after a positive SARS-CoV-2 PCR test in an analysis that matched test-positive with test-negative people. Stakeholders can use these findings to prepare for health care demand associated with post-COVID-19 condition (long COVID).

The public health effects of the COVID-19 pandemic are difficult to overstate.¹ More than 600 million SARS-CoV-2 infections and 6.5 million deaths have been reported worldwide as of September 2022,² which are likely gross undercounts as many infections go undetected.³

Long-term morbidity can be caused by SARS-CoV-2 infection.⁴⁻⁹ In the first pandemic wave, as many as 27% of people admitted to hospital died or were readmitted within 60 days, and as many as 70% of people who were not admitted to hospital reported at least 1 symptom 4 months after infection.^{10,11} By the World Health Organization (WHO) definition, about 10%–20% of those infected acquire a post-COVID-19 condition (long COVID).^{12,13}

Analysis of 10 prospective surveys and the medical records of 1.1 million patients with COVID-19 diagnosis codes before the emergence of the Omicron variant showed similar find-

ings: 7.8%–17% had symptoms 12 weeks after self-reported COVID-19, with 1.2%–4.8% reporting debilitating symptoms.¹⁴ Estimates of long COVID vary by methodology (e.g., definitions of initial infection and timing of symptoms, timing of data collection), but risk is thought to be influenced by infection severity, type of variant, patient characteristics, vaccination¹⁵ and, potentially, previous infection.¹⁶ Because each new SARS-CoV-2 infection carries some risk of long COVID, everyone remains at risk for developing the condition.

Health care funders, policy-makers and clinicians need a clear understanding of the impact of long COVID on use of health care resources to allocate resources equitably now and plan for future needs.¹⁷ We sought to quantify the post-acute burden of health care use after SARS-CoV-2 infection among community-dwelling adults in Ontario.

Methods

Study design and data sources

We conducted a retrospective cohort study using ICES data.¹⁸ The data holdings at ICES are comparable to the Healthcare Cost and Utilization Project (HCUP) in the United States but are more inclusive, encompassing all care provided in hospitals or by physicians for the population of Ontario, with linked patient-level data (Appendix 1, Table E1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220728/tab-related-content). These data sets were linked using unique encoded identifiers and analyzed at ICES.

We constructed a retrospective cohort of community-dwelling adults (≥ 18 yr) who underwent polymerase chain reaction (PCR) testing for SARS-CoV-2 between Jan. 1, 2020, and Mar. 31, 2021, in Ontario. We linked PCR test results to health care encounters, including outpatient, hospital-based and home care visits, which are reimbursed by the publicly funded health care system of Ontario. Physician services are administered by the Ontario Health Insurance Plan, which reimburses physician services for the 14.8 million residents of Ontario. We also linked PCR test results to clinical characteristics, mortality and other information such as the domains of the Ontario Marginalization Index:¹⁹ residential instability, material deprivation, dependency and ethnic concentration. Variable definitions and descriptions of source data sets are listed in Appendix 1, Table E1 and Table E2, respectively. All PCR tests were performed within, and reimbursed by, the health care system of Ontario.

For people with at least 1 positive PCR test result, we selected the index date to be the date of the first positive test. For people with several PCR test results and no positive test results, the index date was the last test date. We excluded people who died within 8 weeks (56 d) of their index date, were residing in long-term care facilities on their index date or who lacked valid date-of-birth, sex or death information.

Exposure and outcomes

We categorized people according to results of SARS-CoV-2 PCR testing as either test negative or test positive. We excluded pending or indeterminate test results ($< 0.02\%$).

Our outcomes were health care encounters, assessed by type and overall: days in hospital, outpatient encounters (in person, by phone and virtual), home care visits (e.g., wound care), emergency department visits and days in a long-term care facility. For patients admitted to hospital or long-term care, we considered each day an encounter (e.g., a 6-d hospital admission was considered 6 encounters). In the overall analysis, we gave each encounter equal weight, so that 1 outpatient encounter received the same weight as 1 day in hospital or in long-term care. Follow-up began 8 weeks or later (≥ 56 d) after the index PCR test date, which we chose based on the duration of typical SARS-CoV-2 infectivity and acute symptoms.^{1,20-22} Follow-up ended on Sept. 30, 2021, or death, whichever occurred first.

Matching

We matched people with a positive SARS-CoV-2 PCR test result to those with only negative PCR test results by sex, test date, public

health unit and a propensity score that comprised recent health care use, age, baseline sociodemographics and comorbidities, neighbourhood-level socioeconomic indices¹⁹ and vaccination status (Appendix 1, Table E2; morbidity measure, Johns Hopkins ACG System, Version 10).²³ We matched on the logit of the propensity score to perform one-to-one matching with a caliper width equal to 0.05 times the standard deviation (SD) of the logit of the propensity score.²⁴ We assessed balance after matching using standardized differences: we considered a standardized difference of less than 0.1 to indicate a good match.^{23,25}

Statistical analysis

We conducted analyses at the patient level using SAS version 9.4. We reported baseline characteristics as means with SDs, medians and interquartile ranges (IQRs) or frequencies, as appropriate.

We used 2 different methods for summarizing the outcome for each person. First, for a given outcome (e.g., outpatient encounters), we computed the per-person-year rate of the outcome by dividing the number of encounters by the number of days at risk and then multiplying by 365 for each person. This produced the rate of encounters per year of follow-up (i.e., for a person with 2 outpatient encounters over a 6-mo period, the rate was 4 encounters per-person-year). Owing to the skewed distribution of health care use (i.e., a few people use a large number of resources), this process was used to compare the absolute difference in the mean, as well as the 99th percentile, of outcomes between the 2 groups. In the matched cohort, we computed the mean and 99th percentile of the per-person-year rate for types of health care encounters and overall in each group, and then computed their absolute difference. We constructed confidence intervals (CIs) using 1000 bootstrap replicates.²⁶

Second, for a given type of health care encounter, we used the count of the number of encounters in negative binomial regression analyses. The time from the 8-week postinfection index date to the end of follow-up was the offset variable to denote each person's time at risk for an outcome. These analyses estimated the relative difference in the rate of an outcome between groups. Using the count of the type of health care encounter, we fit a negative binomial model in the matched sample to determine the rate ratio, which compares the relative difference in the rate of health care encounters between test-positive and test-negative people (the sole independent variable in the model). We estimated the models using generalized estimating equations to account for the matched nature of the sample.²⁷ This estimated the relative difference in the rate of health care use associated with test positivity. As the p value was less than 0.001 for a Z-test assessing the potential effect modification by sex,²⁸⁻³⁰ we stratified results by sex (nonstratified results are shown in Appendix 1).

We conducted 4 sensitivity analyses: follow-up that began after hospital discharge or 56 days, whichever occurred later, follow-up censored at entry into long-term care, follow-up censored at 6 months and all previous sensitivity analyses in a cohort also matched by hospital admission within 2 weeks after PCR testing. We also performed a final sensitivity analysis with matching by admission to an intensive care unit.

Ethics approval

This study was conducted at ICES, previously the Institute for Clinical Evaluative Sciences, an independent, nonprofit research institute that has legal status to collect and analyze health care and demographic data without consent for the purposes of health system evaluation and improvement. Therefore, no research ethics board approval is necessary.

Results

Between Jan. 1, 2020, and Mar. 31, 2021, more than 11 million SARS-CoV-2 PCR tests were completed for 3 777 451 unique adults in Ontario (Figure 1). Of the 3 631 040 people who were included in our study, 268 521 (7.4%) had a positive PCR test result for SARS-CoV-2, and mean follow-up was 240 (SD 88) days. Matching was successful for 99%; the matched cohort comprised 531 702 people. Demographics, clinical characteristics and standardized differences between test-positive and test-negative people for the matched and unmatched cohorts are reported in Table 1 and Appendix 1, Table E3, respectively. We found that sociodemographic and clinical characteristics were well balanced in the matched cohort. Compared with the unmatched cohort, the matched cohort was younger, had fewer females and people with lower incomes, was more urban and more ethnically diverse, a greater proportion underwent PCR testing during late 2020 or early 2021 and fewer were vaccinated (2% were vaccinated with at least 2 doses in the unmatched cohort, whereas only 0.5% were vaccinated in the matched cohorts).

In the matched cohort, mean age was 44 (SD 17) years, 51% were female and 0.6% had received 1 or more doses of SARS-CoV-2 vaccine. Six-month mortality was 0.5%, with no differences by PCR test result or sex.

Females

For the per-person-year rate of each type of health care encounter, we found that the absolute differences in mean person-year rates were significantly higher for test-positive females than for test-negative females for all encounter types, with the exception of emergency department visits (Table 2). The increase was greatest for long-term care days (0.81 d per-person-year), followed by outpatient encounters (0.49), days in hospital (0.36) and home care encounters (0.31). The absolute increase in total health care encounters at the mean was 2.0.

At the 99th percentile of the per-person-year rate of each type of health care encounter (Appendix 1, Figure E1), test-positive females had an additional 28.37 more home care encounters per-person-year than their matched test-negative counterparts and had 6.48 additional days in hospital, with no significant difference in outpatient encounters, emergency department visits or long-term care days. The 99th percentile of total health care encounters was 56.7 higher in test-positive than in test-negative females.

In the negative binomial model using the count outcome summary, for test-positive versus test-negative females, we found that the rate ratio of the rate of long-term care days was

2.51 (95% CI 2.18 to 2.91), 1.48 (95% CI 1.37 to 1.58) for days in hospital, 1.07 (95% CI 1.01 to 1.13) for home care encounters and 1.06 (95% CI 1.05 to 1.07) for outpatient encounters. The rate of emergency department visits was not statistically different. For total health care encounters, the rate ratio was 1.14 (95% CI 1.11 to 1.16; Table 3).

Males

For the per-person-year rate of each type of health care encounter, the absolute differences in the mean per-person-year rate of health care use were significantly higher for test-positive than for test-negative males for all encounter types, with the exception of home care visits, which were lower (-0.43), and emergency department visits, which were not different (Table 2). We found that the increase was greatest for long-term care (0.48 d per-person-year), followed by days in hospital (0.47) and outpatient encounters (0.14). The absolute increase in total health care encounters at the mean was 0.66.

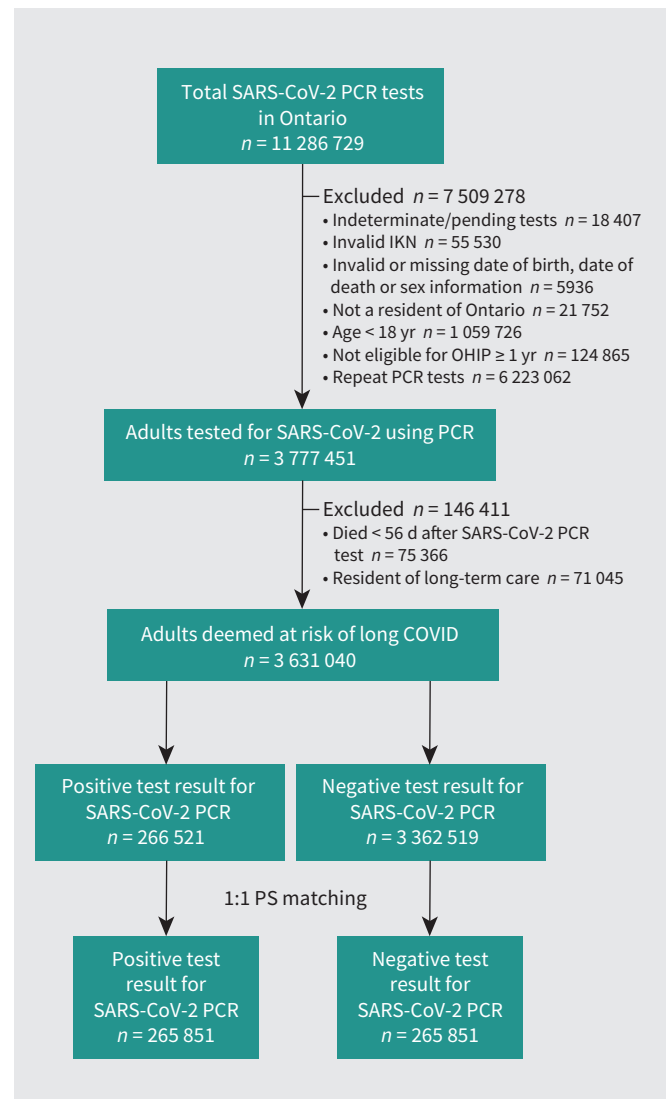


Figure 1: Flow chart of cohort construction. Note: IKN = ICES Key Number, OHIP = Ontario Health Insurance Plan, PCR = polymerase chain reaction, PS = propensity score.

Table 1 (part 1 of 2): Baseline demographic and clinical characteristics of the matched cohort*

Characteristic	No. (%) of people†			Standardized difference
	Negative SARS-CoV-2 PCR test result n = 265 851	Positive SARS-CoV-2 PCR test result n = 265 851	Total n = 531 702	
Age, yr; mean ± SD	44.1 ± 17.2	44.1 ± 17.2	44.1 ± 17.2	0
Sex, female	135 983 (51.2)	135 983 (51.2)	271 966 (51.2)	0
Admitted to hospital within 2 wk of PCR test	16 680 (6.3)	14 674 (5.5)	31 354 (5.9)	0.03
Pandemic quarter				0
2020 (Q1)	3480 (1.3)	3346 (1.3)	6826 (1.3)	
2020 (Q2)	20 673 (7.8)	20 812 (7.8)	41 485 (7.8)	0
2020 (Q3)	14 697 (5.5)	14 668 (5.5)	29 365 (5.5)	0
2020 (Q4)	102 873 (38.7)	103 641 (39.0)	206 514 (38.8)	0.01
2021 (Q1)	124 128 (46.7)	123 384 (46.4)	247 512 (46.6)	0.01
Income quintile				
1 (lowest)	66 292 (24.9)	65 582 (24.7)	131 874 (24.8)	0.01
2	57 777 (21.7)	57 876 (21.8)	115 653 (21.8)	0
3	56 708 (21.3)	57 033 (21.5)	113 741 (21.4)	0
4	47 048 (17.6)	47 244 (17.8)	94 083 (17.7)	0
5 (highest)	38 235 (14.4)	38 116 (14.3)	76 351 (14.4)	0
Residential instability quintile				
1 (least)	71 764 (27.0)	72 177 (27.1)	143 941 (27.1)	0
2	44 694 (16.8)	44 501 (16.7)	89 195 (16.8)	0
3	40 777 (15.3)	40 686 (15.3)	81 463 (15.3)	0
4	43 699 (16.4)	43 572 (16.4)	87 271 (16.4)	0
5 (most)	64 917 (24.4)	64 915 (24.4)	129 832 (24.4)	0
Material deprivation quintile				
1 (least)	44 442 (16.7)	45 028 (16.9)	89 470 (16.8)	0.01
2	47 378 (17.8)	47 567 (17.9)	94 945 (17.9)	0
3	52 453 (19.7)	52 416 (19.7)	104 869 (19.7)	0
4	55 586 (20.9)	55 490 (20.9)	111 076 (20.9)	0
5 (highest)	65 992 (24.8)	65 350 (24.6)	130 702 (24.7)	0.01
Dependency quintile				
1 (lowest)	91 105 (34.3)	91 742 (34.5)	182 847 (34.4)	0.01
2	59 590 (22.4)	59 819 (22.5)	119 409 (22.5)	0
3	44 091 (16.6)	44 138 (16.6)	88 229 (16.6)	0
4	37 751 (14.2)	37 430 (14.1)	75 181 (14.1)	0
5 (highest)	33 314 (12.5)	32 722 (12.3)	66 036 (12.4)	0.01
Ethnic concentration quintile				
1 (lowest)	17 730 (6.7)	17 192 (6.5)	34 922 (6.6)	0.01
2	24 934 (9.4)	24 829 (9.3)	49 763 (9.4)	0
3	34 470 (13.0)	35 072 (13.2)	69 542 (13.1)	0.01
4	55 727 (21.0)	56 985 (21.4)	112 712 (21.2)	0.01
5 (highest)	132 990 (50.0)	131 773 (49.6)	264 763 (49.8)	0.01
Rural	9617 (3.6)	9558 (3.6)	19 175 (3.6)	0
Received 2 vaccine doses	292 (0.1)	292 (0.1)	584 (0.1)	0
Received 1 vaccine dose	1314 (0.5)	1314 (0.5)	2628 (0.5)	0
Aggregated Diagnosis Group				
Mean ± SD	5.59 ± 3.69	5.58 ± 3.68	5.58 ± 3.68	0
Median (IQR)	5 (3–8)	5 (3–8)	5 (3–8)	0

Table 1 (part 2 of 2): Baseline demographic and clinical characteristics of the matched cohort*

Characteristic	No. (%) of people†			Standardized difference
	Negative SARS-CoV-2 PCR test result n = 265 851	Positive SARS-CoV-2 PCR test result n = 265 851	Total n = 531 702	
Hospital Frailty Risk Score				
Mean ± SD	2.3 ± 4.8	2.4 ± 5.0	2.3 ± 4.9	0.01
Median (IQR)	0 (0–2)	0 (0–2)	0 (0–2)	0.02
Hospital admissions in previous year				
Mean ± SD	0.08 ± 0.4	0.07 ± 0.4	0.07 ± 0.4	0.02
Median (IQR)	0	0	0	0.03
Days in hospital in previous year				
Mean ± SD	0.8 ± 6.6	0.8 ± 7.8	0.8 ± 7.2	0
Median (IQR)	0	0	0	0.06
Outpatient encounters in previous year				
Mean ± SD	6.3 ± 7.9	6.3 ± 7.9	6.3 ± 7.9	0
Median (IQR)	4 (1–9)	4 (1–9)	4 (1–9)	0
Home care visits in previous year				
Mean ± SD	2.9 ± 25.7	2.9 ± 25.9	2.9 ± 25.8	0
Median (IQR)	0	0	0	0.02
Visits to the ED in previous year				
Mean ± SD	0.4 ± 1.1	0.4 ± 1.4	0.4 ± 1.3	0
Median (IQR)	0	0	0	0.01
Surgery in previous 6 wk	2278 (0.9)	2161 (0.8)	4439 (0.8)	0
Johns Hopkins Frailty Index	7665 (2.9)	7606 (2.9)	15 271 (2.9)	0
Flu vaccine within previous year	65 608 (24.7)	65 921 (24.8)	131 529 (24.7)	0
Pregnant at index date	2363 (0.9)	1844 (0.7)	4207 (0.8)	0.02
Hypertension	60 595 (22.8)	60 933 (22.9)	120 496 (22.7)	0
Diabetes	36 626 (13.8)	37 169 (14.0)	73 795 (13.9)	0.01
Emphysema	4312 (1.6)	4046 (1.5)	8358 (1.6)	0.01
Heart failure	4949 (1.9)	4883 (1.8)	9832 (1.8)	0
Dementia	3142 (1.2)	3174 (1.2)	6316 (1.2)	0
Asthma	28 220 (10.6)	27 949 (10.5)	56 169 (10.5)	0
Cancer	5003 (1.9)	4723 (1.8)	9726 (1.8)	0.01
Ischemic stroke	2529 (1.0)	2503 (0.9)	5032 (0.9)	0
Hemorrhagic stroke	229 (0.1)	218 (0.1)	447 (0.1)	0
Valvular disease	272 (0.1)	231 (0.1)	503 (0.1)	0.01
Atrial fibrillation	4863 (1.8)	4803 (1.8)	9666 (1.8)	0
Myocardial infarction	1736 (0.7)	1753 (0.7)	3489 (0.7)	0
Percutaneous coronary intervention	2235 (0.9)	2183 (0.8)	4418 (0.8)	0
Coronary artery bypass	635 (0.2)	638 (0.2)	1273 (0.2)	0
Ischemic heart disease	9805 (3.7)	9693 (3.6)	19 498 (3.7)	0
Major bleeding	2154 (0.8)	2093 (0.8)	4247 (0.8)	0
Renal disease	2811 (1.0)	2705 (1.0)	5516 (1.0)	0
Pneumonia	19 702 (7.4)	19 783 (7.4)	39 458 (7.4)	0
Alcohol use disorder	1622 (0.6)	1527(0.6)	3149 (0.6)	0
Venous thromboembolism	24 065 (9.1)	23 738 (8.9)	47 801 (9.0)	0
Mental health hospital admission	4336 (1.7)	4271 (1.6)	8607 (1.6)	0
Mental health emergency visit	11 323 (4.3)	11 074 (4.2)	22 397 (4.2)	0
Mental health clinic visit	48 699 (18.3)	47 018 (18.1)	96 717 (18.2)	0.01

Note: ED = emergency department, IQR = interquartile range, Q = quartile, PCR = polymerase chain reaction, SD = standard deviation.
 *Detailed variable definitions are provided in Appendix 1, Table E1 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220728/tab-related-content).
 †Unless specified otherwise.

Table 2: Absolute differences in per-person-year rates of health care encounters 56 days or more after a positive compared with negative polymerase chain reaction test result for SARS-CoV-2, stratified by sex*

Type of health care encounter	Rate of health care use, per-person-year	
	Rate difference at mean (95% CI)	Rate difference at 99th percentile* (95% CI)
Females, n = 271 966		
Days in hospital	0.36 (0.29 to 0.43)	6.48 (5.00 to 7.97)
Outpatient encounters	0.49 (0.41 to 0.58)	0.38 (-0.68 to 1.32)
Home care encounters	0.31 (0.05 to 0.56)	28.37 (2.61 to 46.54)
Emergency department visits	0 (-0.01 to 0.02)	-0.07 (-0.17 to 0.05)
Long-term care days	0.81 (0.69 to 0.93)	0
Total health care encounters	1.98 (1.63 to 2.29)	56.60 (41.69 to 72.71)
Males, n = 259 736		
Days in hospital	0.47 (0.38 to 0.57)	8.69 (6.12 to 11.10)
Outpatient encounters	0.14 (0.06 to 0.21)	-0.87 (-2.06 to -0.18)
Homecare encounters	-0.43 (-0.67 to -0.21)	-27.31 (-40.53 to -13.22)
Emergency department visits	0.01 (0 to 0.02)	0.12 (-0.03 to 0.24)
Long-term care days	0.48 (0.36 to 0.60)	0
Total health care encounters	0.66 (0.34 to 0.99)	39.27 (17.25 to 65.21)

Note: CI = confidence interval.
*All comparisons are for test-positive versus test-negative people after matching. Mean total health care use may differ from summary of component use owing to rounding errors. 99th percentiles of health care use are not additive.

At the 99th percentile of the per-person-year rate of each type of health care encounter (Appendix 1, Figure E1), we determined that test-positive males had an additional 8.69 days in hospital per-person-year than their matched test-negative counterparts, whereas the decrease in home care visits was even greater at the 99th percentile (-27.31). There was no difference in emergency department visits or days in long-term care. The 99th percentile of total health care encounters was 39.27 higher for test-positive than for test-negative males.

In the negative binomial model using the count outcome summary, for test-positive males, we found that the patterns of relative increases in rates of health care use were similar to females (Table 3), with the exception of home care encounters, which were lower for test-positive males (rate ratio 0.89, 95% CI 0.83 to 0.95), despite similar mortality between sexes.

We report the absolute differences in per-person-year rates of health care use and rate ratios not stratified by sex in Appendix 1, Table E4.

Results of sensitivity analyses did not show much difference from the main results (Appendix 1, Table E5 and Table E6).

Interpretation

In our population-wide study of people in Ontario who underwent publicly funded SARS-CoV-2 PCR tests, we found that mean days in hospital per-person-year increased 47% and 53%, respectively, 8 weeks or more after infection for test-positive females and males, after we accounted for sociodemographic factors, comorbidities and pandemic wave. Mean days in long-

Table 3: Rate ratios for health care encounters 56 days or more after a polymerase chain reaction test for SARS-CoV-2 infection, stratified by sex*

Health care use	Rate ratio (95% CI)
Females	
Days in hospital	1.48 (1.37 to 1.58)
Outpatient clinic encounters	1.06 (1.05 to 1.07)
Homecare encounters	1.07 (1.01 to 1.13)
Emergency department visits	1.02 (1.00 to 1.05)
Long-term care days	2.51 (2.18 to 2.91)
Total health care encounters	1.14 (1.11 to 1.16)
Males	
Days in hospital	1.53 (1.41 to 1.09)
Outpatient clinic encounters	1.03 (1.01 to 1.04)
Homecare encounters	0.89 (0.83 to 0.95)
Emergency department visits	1.04 (1.01 to 1.07)
Long-term care days	1.92 (1.64 to 2.25)
Total health care encounters	1.06 (1.03 to 1.09)

Note: CI = confidence interval.
*We computed point estimate and CIs using negative binomial regression models after accounting for matching.

term care also increased for both test-positive females and males, whereas home care visits increased for females but decreased for males. However, comparison of mean rates does

not tell the entire story of how SARS-CoV-2 influences post-acute health care use because the greatest increase in health care use occurred among 1% or less of people infected (relative to test negative, top 1% of users of health care resources). Although most of the people with SARS-CoV-2 infection had little-to-no change in health care use, a small but important subset of people experienced large increases in their rate of health care use: at the 99th percentile, test-positive females had about 7 additional days in hospital per-person-year and test-positive males had about 9 more days in hospital than their test-negative counterparts at the 99th percentile. These findings indicate that a subset of people experience substantial burden of morbidity well after a SARS-CoV-2 infection.

Given the number of recent infections, our findings portend substantial health care use by people in Canada.³¹ An estimated 45% of Canadians had SARS-CoV-2 infection in early 2022.³² In the next year alone, 1% of these people with recent infections will likely be admitted to hospital about 1 week longer than similar people without infection, consuming 6.6% of pre-pandemic hospital bed-days, when almost 20% of hospitals already averaged more than 100% annual occupancy rates.³³ A family physician who had 20 outpatient encounters per day before the COVID-19 pandemic and who had half of their patients recently infected would have to accommodate an additional 100 clinical encounters per year to meet a 5% mean increase in outpatient encounters, along with the associated time and resources for communication, documentation and staffing. Such increases in health care use will occur in the context of greater need for long-term care (further compounding pressure for hospital beds), as well as substantial care backlogs, critical staffing shortages and a shrinking health care workforce.³⁴⁻⁴¹ Although most people with SARS-CoV-2 infection will not need more health care, they will be competing for scarce health care resources with the subset of people whose use increases considerably. Such increased demand will require substantial population-level restructuring and investment of resources.

A study from Korea found that in the 6–12 months after SARS-CoV-2 infection, 16.4% of those admitted to hospital continued to report malaise compared with 10.9% of those who were not admitted to hospital,⁴² and 5% reported receiving treatment for symptoms a median of 454 days after COVID-19 diagnosis, although no people with asymptomatic infection reported symptoms at 12 months.⁴³ Increased outpatient clinic visits after hospital admission for COVID-19 and increased risk of myocardial infarction and stroke have been identified using health care data from the US Department of Veterans Affairs.^{44,45} Although numerous studies have addressed the nature and prevalence of long COVID symptoms after varying severities of acute infection,⁴⁶⁻⁵⁰ to the best of our knowledge, no other studies have assessed system-wide health care use after acute infection.

Our findings add to what is known about the differential effects of SARS-CoV-2 by sex.^{28,51-57} Health care use was greater for females than males and increased more across the distribution of health care use and types of encounters. In contrast, additional health care use for males was highly concentrated among a small subset and home care decreased, which suggests that

males may have received unpaid care from family that might have been provided by other means before the COVID-19 pandemic.

Limitations

Health care burden may have been underestimated, as health care encounters decreased during the initial phases of the COVID-19 pandemic owing to public health interventions and changes in patient behaviours.^{33,58-60} No generally accepted method exists for weighing severity of different types of health care encounters,^{61,62} although our findings were robust in sensitivity analyses with secondary definitions of health care burden. Our findings may not generalize to populations with substantial barriers to testing, and we were unable to determine whether indication for testing or employment (e.g., health care worker) may modify associations between SARS-CoV-2 infection and type of health care use after acute infection. To address potential changes in testing indications and capacity over time, we hard matched on test date and included it in the propensity score. During the study period, publicly funded testing was widely available for both symptomatic and asymptomatic people, which reduced the risk of selection bias. Our matched cohort ended March 2021, when 4.2% of the population of Ontario had received 1 or more doses of SARS-CoV-2 vaccine, and publicly available outpatient PCR testing ended in December 2021. Reasons why people sought medical care are not known. Finally, our results may not generalize to other variants or immunity levels of individuals and populations.⁶³⁻⁶⁵ However, our findings may provide guidance in the conditions of emerging variants, waning immunity and removal of public health interventions.⁶³

Conclusion

The burden of health care use after a positive SARS-CoV-2 PCR test is substantial and has important health policy implications. Although better understanding is needed regarding the causes for and specific areas of increased post-acute health care use after SARS-CoV-2 infection, as well as the impact of novel variants and treatments, stakeholders may use these findings to prepare for health care demand caused by long COVID.

References

1. Soriano JB, Murthy S, Marshall JC, et al. WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis* 2022;22:e102-7.
2. WHO coronavirus disease (COVID-19) dashboard. Geneva: World Health Organization. Available: <https://covid19.who.int> (accessed 2022 Sept. 19).
3. Fuhrmann J, Barbarossa MV. The significance of case detection ratios for predictions on the outcome of an epidemic: a message from mathematical modelers. *Arch Public Health* 2020;78:63.
4. Greenhalgh T, Knight M, A'Court C, et al. Management of post-acute COVID-19 in primary care. *BMJ* 2020;370:m3026.
5. Xiao AT, Tong YX, Zhang S. False negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: rather than recurrence. *J Med Virol* 2020;92:1755-6.
6. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 2020;5:434-5.

7. Raj SR, Arnold AC, Barboi A, et al.; American Autonomic Society. Long-COVID postural tachycardia syndrome: an American Autonomic Society statement. *Clin Auton Res* 2021;31:365-8.
8. Tabacof L, Tosto-Mancuso J, Wood J, et al. Post-acute COVID-19 syndrome negatively impacts physical function, cognitive function, health-related quality of life, and participation. *Am J Phys Med Rehabil* 2022;101:48-52.
9. Choi B, Choudhary MC, Regan J, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. *N Engl J Med* 2020;383:2291-3.
10. Donnelly JP, Wang XQ, Iwashyna TJ, et al. Readmission and death after initial hospital discharge among patients with COVID-19 in a large multihospital system. *JAMA* 2021;325:304-6.
11. Dennis A, Wamil M, Alberts J, et al.; COVERSCAN study investigators. Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study. *BMJ Open* 2021;11:e048391.
12. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. WHO reference number: WHO/2019-nCoV/Post_COVID-19_condition/Clinical_case_definition/2021.1. Geneva: World Health Organization (WHO); 2021. Available: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1 (accessed 2022 Sept. 20).
13. Coronavirus disease (COVID-19): post COVID-19 condition [news release]. Geneva: World Health Organization; 2021 Dec. 16. Available: [https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-\(covid-19\)-post-covid-19-condition](https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-post-covid-19-condition) (accessed 2022 Sept. 20).
14. Thompson EJ, Williams DM, Walker AJ, et al. Long Covid burden and risk factors in 10 UK longitudinal studies and electronic health records. *Nat Commun* 2022;13:3528.
15. Al-Aly Z, Bowe B, Xie Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 2022;28:1461-7.
16. Sotoodeh Ghorbani S, Taherpour N, Bayat S, et al. Epidemiologic characteristics of cases with reinfection, recurrence, and hospital readmission due to COVID-19: a systematic review and meta-analysis. *J Med Virol* 2022;94:44-53.
17. Ramchand R, Harrell MC, Berglass N, et al. *Veterans and COVID-19: projecting the economic, social, and mental health needs of America's veterans*. New York: Bob Woodruff Foundation; 2020. Available: https://bobwoodrufffoundation.org/wp-content/uploads/2021/09/BWF_WhitePaper-COVID19-5.0-Final.pdf (accessed 2020 May 26).
18. Schull MJ, Azimae M, Marra M, et al. ICES: data, discovery, better health. *Int J Popul Data Sci* 2020;4:1135.
19. Matheson FI, Dunn JR, Smith KL, et al. Development of the Canadian Marginalization Index: a new tool for the study of inequality. *Can J Public Health* 2012;103 (Suppl 2):S12-6.
20. Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, et al. Defining post-Covid symptoms (post-acute Covid, long Covid, persistent post-Covid): an integrative classification. *Int J Environ Res Public Health* 2021;18:2621.
21. Akbarialiabad H, Taghbir MH, Abdollahi A, et al. Long COVID, a comprehensive systematic scoping review. *Infection* 2021;49:1163-86.
22. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. *Nat Med* 2021;27:601-15.
23. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res* 2011;46:399-424.
24. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat* 2011;10:150-61.
25. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009;28:3083-107.
26. Austin PC, Small DS. The use of bootstrapping when using propensity-score matching without replacement: a simulation study. *Stat Med* 2014;33:4306-19.
27. Austin PC. Type I error rates, coverage of confidence intervals, and variance estimation in propensity-score matched analyses. *Int J Biostat* 2009;5:13.
28. Tharakan T, Khoo CC, Giwerzman A, et al. Are sex disparities in COVID-19 a predictable outcome of failing men's health provision? *Nat Rev Urol* 2022;19:47-63.
29. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, et al. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ* 2020;11:29.
30. Bienvenu LA, Noonan J, Wang X, et al. Higher mortality of COVID-19 in males: sex differences in immune response and cardiovascular comorbidities. *Cardiovasc Res* 2020;116:2197-206.
31. Khan JR, Awan N, Islam MM, et al. Healthcare capacity, health expenditure, and civil society as predictors of COVID-19 case fatalities: a global analysis. *Front Public Health* 2020;8:347.
32. Seroprevalence against SARS-CoV-2 due to infection in Canada: results from the Government of Canada's COVID-19 Immunity Task Force and other partners' funded studies through to May 31, 2022. Montréal: COVID-19 Immunity Task Force; 2022. Available: https://www.covid19immunitytaskforce.ca/wp-content/uploads/2022/07/CITF_Bespoke-report_Omicron-tsunami_2022_FINAL_ENG.pdf (accessed 2022 Aug. 29).
33. *Ontario health sector: a preliminary review of the impact of the COVID-19 outbreak on hospital capacity*. Toronto: Financial Accountability Office of Ontario; 2020. Available: <https://www.fao-on.org/web/default/files/publications/FA2008HospitalCapacity/2020HospitalCapacity-EN.pdf> (accessed 2022 Aug. 29).
34. *Ministry of Health: spending plan review*. Toronto: Financial Accountability Office of Ontario; 2021. Available: <https://www.fao-on.org/en/Blog/Publications/2021-health-estimates> (accessed 2022 Mar. 4).
35. *The impact of COVID-19 on long-term care in Canada: focus on the first 6 months*. Ottawa: Canadian Institute for Health Information; 2021.
36. Barrett KA, VandeVyvere C, Haque N, et al. Ontario COVID-19 Science Advisory Table. Critical care capacity during the COVID-19 pandemic. Version 1.0 Ontario COVID-19 Science Advisory Table. Available: <https://covid19-sciencetable.ca/sciencebrief/critical-care-capacity-during-the-covid-19-pandemic/> (accessed 2022 Sept. 26).
37. Brophy JT, Keith MM, Hurley M, et al. Sacrificed: Ontario healthcare workers in the time of COVID-19. *New Solut* 2021;30:267-81.
38. Cantor J, Whaley C, Simon K, et al. US health care workforce changes during the first and second years of the COVID-19 pandemic. *JAMA Health Forum* 2022;3:e215217.
39. Wilensky GR. The COVID-19 pandemic and the US health care workforce. *JAMA Health Forum* 2022;3:e220001.
40. Wang J, Vahid S, Eberg M, et al. Clearing the surgical backlog caused by COVID-19 in Ontario: a time series modelling study. *CMAJ* 2020;192:E1347-56.
41. Salenger R, Etchill EW, Ad N, et al. The surge after the surge: cardiac surgery post-COVID-19. *Ann Thorac Surg* 2020;110:2020-5.
42. Vedel Sørensen AI, Spiliopoulos L, Bager P, et al. Post-acute symptoms, new onset diagnoses and health problems 6 to 12 months after SARS-CoV-2 infection: a nationwide questionnaire study in the adult Danish population [preprint]. *medRxiv* 2022 Feb. 28. doi: 10.1101/2022.02.27.22271328.
43. Kim Y, Bitna-Ha, Kim S-W, et al. Post-acute COVID-19 syndrome in patients after 12 months from COVID-19 infection in Korea. *BMC Infect Dis* 2022;22:93.
44. Xie Y, Xu E, Bowe B, et al. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022;28:583-90.
45. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. *Nature* 2021;594:259-64.
46. Doikov I, Hallqvist J, Gilmour KC, et al. 'The long tail of COVID-19': the detection of a prolonged inflammatory response after a SARS-CoV-2 infection in asymptomatic and mildly affected patients. *F1000Res* 2020;9:1349.
47. Fan BE, Umaphathi T, Chua K, et al. Delayed catastrophic thrombotic events in young and asymptomatic post COVID-19 patients. *J Thromb Thrombolysis* 2021;51:971-7.
48. Yomogida K, Zhu S, Rubino F, et al. Post-acute sequelae of SARS-CoV-2 infection among adults aged \geq 18 years: Long Beach, California, April 1–December 10, 2020. *MMWR Morb Mortal Wkly Rep* 2021;70:1274-7.
49. Azzolini E, Levi R, Sarti R, et al. Association between BNT162b2 vaccination and long COVID after infections not requiring hospitalization in health care workers. *JAMA* 2022;328:676-8.
50. Ayoubkhani D, Bermingham C, Pouwels KB, et al. Trajectory of long covid symptoms after COVID-19 vaccination: community based cohort study. *BMJ* 2022;377:e069676.
51. Takahashi T, Ellingson MK, Wong P, et al. Sex differences in immune responses that underlie COVID-19 disease outcomes. *Nature* 2020;588:315-20.
52. Förster C, Colombo MG, Wetzel A-J, et al. Persisting symptoms after COVID-19: prevalence and risk factors in a population-based cohort. *Dtsch Arztebl Int* 2022;119:167-74.
53. Kashif A, Chaudhry M, Fayyaz T, et al. Follow-up of COVID-19 recovered patients with mild disease. *Sci Rep* 2021;11:13414.

54. Bliddal S, Banasik K, Pedersen OB, et al. Acute and persistent symptoms in non-hospitalized PCR-confirmed COVID-19 patients. *Sci Rep* 2021;11:13153.
55. Augustin M, Schommers P, Stecher M, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. *Lancet Reg Health Eur* 2021;6:100122.
56. Stavem K, Ghanima W, Olsen MK, et al. Persistent symptoms 1.5–6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study. *Thorax* 2021;76:405-7.
57. Wynberg E, van Willigen HDG, Dijkstra M, et al.; RECOVERED Study Group. Evolution of COVID-19 symptoms during the first 12 months after illness onset. *Clin Infect Dis* 2022;75:e482-90.
58. Howarth A, Munro M, Theodorou A, et al. Trends in healthcare utilisation during COVID-19: a longitudinal study from the UK. *BMJ Open* 2021;11:e048151.
59. Moynihan R, Sanders S, Michaleff ZA, et al. Impact of COVID-19 pandemic on utilisation of healthcare services: a systematic review. *BMJ Open* 2021;11:e045343.
60. Mehrotra A, Bhatia RS, Snoswell CL. Paying for telemedicine after the pandemic. *JAMA* 2021;325:431-2.
61. Guilcher SJT, Bronskill SE, Guan J, et al. Who are the high-cost users? A method for person-centred attribution of health care spending. *PLoS One* 2016;11:e0149179.
62. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188:182-8.
63. Liu L, Iketani S, Guo Y, et al. Striking antibody evasion manifested by the Omicron variant of SARS-CoV-2. *Nature* 2022;602:676-81.
64. Antonelli M, Penfold RS, Merino J, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. *Lancet Infect Dis* 2022;22:43-55.
65. Tsuchida T, Hirose M, Inoue Y, et al. Relationship between changes in symptoms and antibody titers after a single vaccination in patients with Long COVID. *J Med Virol* 2022;94:3416-20.

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