

BACKGROUND & METHODS

- Assessing the impact of prior infection on the frequency and severity of COVID-19 is important.
- We asked: Was COVID-19 infection early in the pandemic associated with reduced severity of infection among patients with Omicron sub-lineages?
- Severity was measured in 3 ways: (1) An ordinal measure combining activities of daily living (ADL) and presence of fever; (2) if health care was required; and (3) illness duration.
- Outcomes were compared between two cohorts in Toronto, Canada: One with symptomatic COVID-19 between Mar & Sep 2020 (‘early COVID-19’) and another matched by age group, hospitalization status and COVID-19 testing date who did not test positive for SARS-CoV-2. Baseline then biweekly surveys were completed to identify SARS-CoV-2 infection episodes from Jan 2020 to Jan 2023.
- Multivariable binary and ordinal logistic regression models were used to assess the impact of early COVID-19 on severity of Omicron, adjusted for sociodemographic characteristics, comorbidities, COVID-19 vaccination status, and time from early COVID-19 to first Omicron infection.

RESULTS

Table 1: Characteristics and outcomes of cohort participants with Omicron infections.

Characteristic	Early COVID-19 (N=177)	No Early COVID-19 (N=84)	SMD§
Sex at birth, Female (N, %)	103 (58)	48 (57)	0.02
Age at the start of Omicron wave– (median, IQR)	49.0y (22)	52.0y (30)	-
Non-immunocompromising comorbidity (N, %)	47 (27)	34 (41)	0.30
Immunocompromised (N,%)	12 (6.8)	5 (6.0)	0.03
Timing of first Omicron infection:			
BA.1/2 (12-Dec-2021 to 03-June-2022)	79 (45)	39 (46)	0.03
BA.4/5 (04-June-2022 to 13-Nov-2022)	66 (37)	36 (43)	0.11
BA.5/BQ1.1/XBB (14-Nov-2022 to 24-April-2023)	32 (18)	9 (11)	0.21
Infection diagnosed by PCR (vs RAT) (N,%)	82 (46)	36 (43)	0.07
Neighbourhood income quintile (%):			
1 (lowest)	37 (21)	22 (26)	0.13
2	42 (24)	15 (18)	0.14
3	35 (20)	12 (14)	0.15
4	29 (16)	14 (17)	0.01
5 (highest)	34 (19)	21 (25)	0.14
Severity (fever/impact of illness on ADL)*†:			
1: No fever, able to do regular ADL	54 (31)	23 (27)	0.07
2: Febrile, but able to do regular ADL	31 (18)	13 (16)	0.05
3: No fever, not well enough to do regular ADL	32 (18)	15 (18)	0.01
4: Febrile and not well enough to do regular ADL	47 (27)	24 (29)	0.04
5: Bed bound or hospitalized	13 (7.3)	8 (9.5)	0.08
Healthcare required for infection*			
No	150 (85)	65 (77)	0.19
One or more visits	26 (15)	18 (21)	0.17
Time to full recovery (N,%)			
0 to 4 days	34 (19)	11 (13)	0.17
5 to 9 days	75 (42)	31 (37)	0.11
10 to 14 days	19 (11)	12 (14)	0.11
15 to 19 days	9 (5.1)	1 (1.2)	0.24
20+days	11 (6.2)	11 (13)	0.24
Time between early COVID-19 test and 1 st Omicron infection: (N,%)			
14 to 23 months	59 (33)	32 (38)	0.10
24 to 29 months	73 (41)	37 (44)	0.06
30 + months	45 (25)	15 (18)	0.18

* One participant was missing fever/ADL data, 2 were missing data on healthcare, 47 missing time to recovery data
† Severity assessed as a pooled outcome incorporating presence of fever and impact on ADL
§ SMD= Standardized mean difference, 0.10 or greater indicates a difference in proportion.

RESULTS

- 177 out of 261 participants with Omicron infection had early COVID-19 at a median of 26 months prior (IQR: 22 to 30 months).
- 118 (46%) Omicron infections occurred during the BA.1/2 period, 102 (39%) occurred during the BA.4/5 period, and 41 (16%) occurred during the BA.5/BQ1.1/XBB period.
- Those with early COVID-19 occurring over 24 months prior to their Omicron infection had lower odds of having severe Omicron-related illness as measured by impact on ADL and fever.
- Immunocompromise was associated with more severe illness based on all 3 outcomes while other non-immunocompromising comorbidities were associated with requiring healthcare, and longer illness duration (Figures 1, 2, and 3).
- 12 participants (median age 52 years, range 32-66) reported two Omicron infections during the study period. Characteristics and outcomes of these participants are reported in Table 2.

Figure 1: Adjusted ordinal regression model results for the association between early COVID-19 infection and impact of activities of daily living (ADL) and fever, for 1st Omicron infection

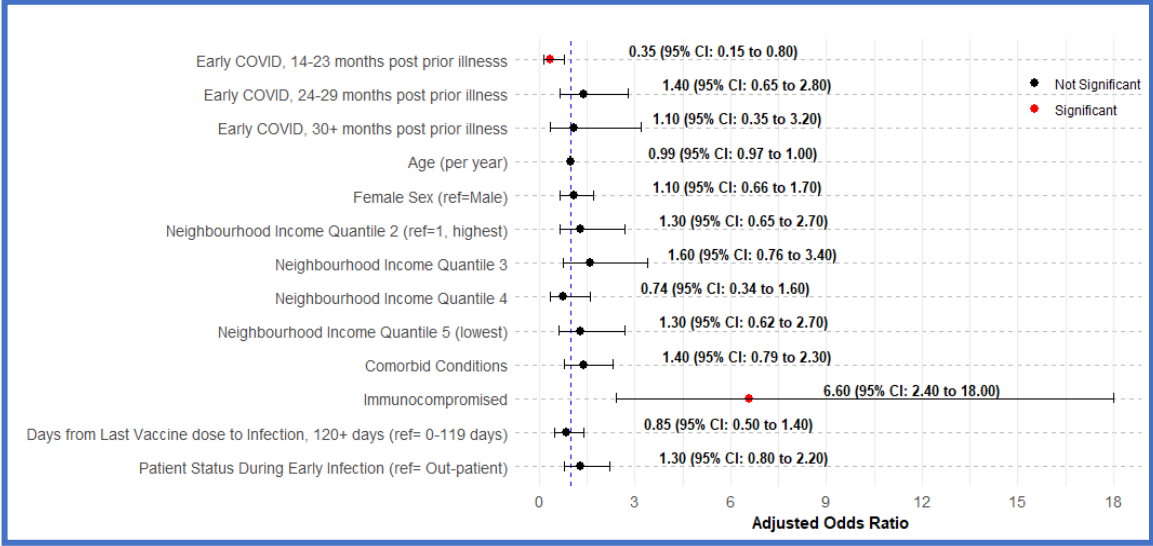
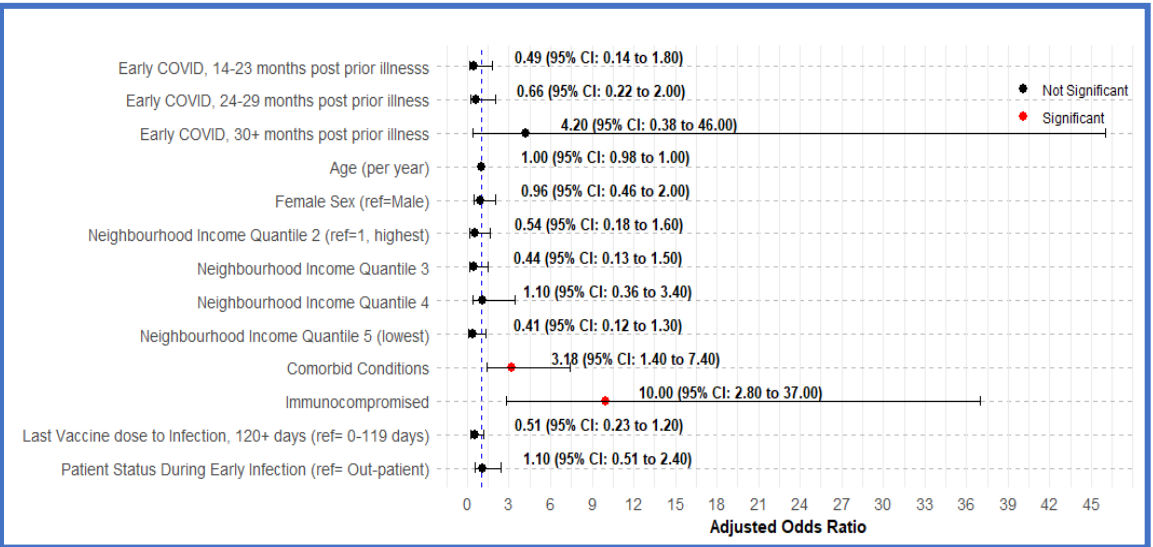


Figure 2: Adjusted binary logistic regression model results for the association between early COVID-19 infection and healthcare required for 1st Omicron infection



RESULTS

Figure 3: Adjusted ordinal regression model results for the association between early COVID-19 infection and duration of illness, for first Omicron infection

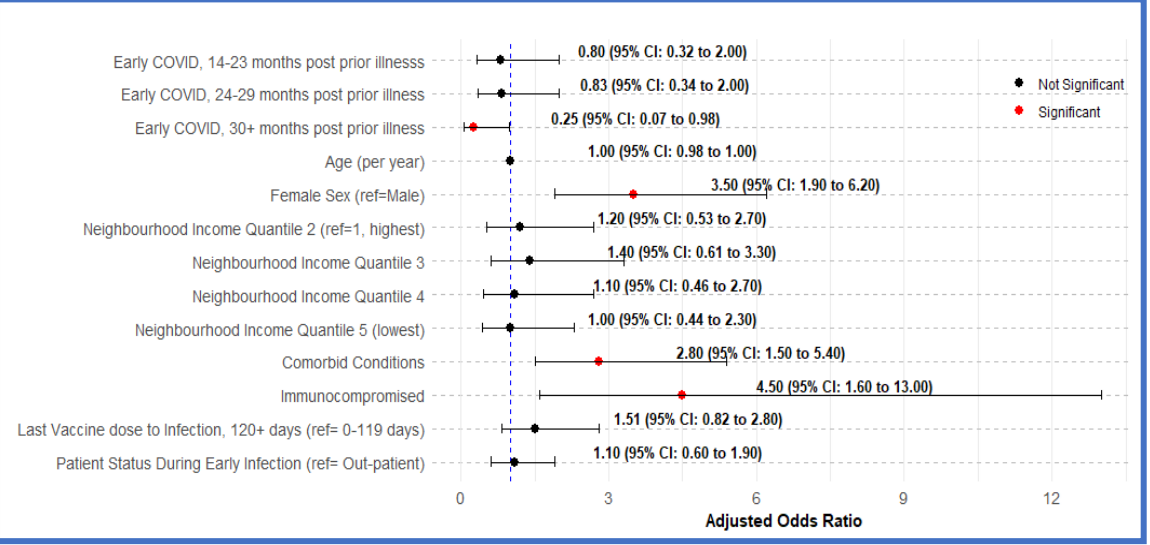


Table 2: Characteristics of participants and infections for participants with more than one Omicron infection (n=12)

Characteristic	Early COVID-19 (n=5)	No Early COVID-19 (n=7)
Sex (male)	1 (20%)	3 (43%)
Age, years (median, range)	51 (32-66)	53 (30-66)
Any comorbidity	2 (40%)	6 (86%)
Immunocompromised	0	1 (14%)
First Omicron infection:		
BA.1/2	3	5
BA.4/5	2	2
Number of COVID-19 vaccine doses before first Omicron infection		
Two doses	1	1
Three doses	3	6
Four doses	1	NA
Second Omicron infection period		
BA.4/5	1	1
BQ.1.1/XXB	4	6
Total number of COVID-19 vaccine doses		
Two doses	1	1
Three doses	2	2
Four doses	2	3
Five doses	NA	1
Outcomes:		
Fever/ADL score (mean, SD)	First: 2 (0.9); Second: 2 (1.3)	First: 3 (0.9); Second: 1 (1.4)
Healthcare required (Y/N)	First: 0; Second: 0	First: 2; Second: 2
Duration of illness, days (mean, range)	First: 7.5 (4-26); Second: 5 (1-7)	First: 4.5 (2-30); Second: 8 (5-9)

CONCLUSIONS

- Developing COVID-19 early in the pandemic was associated with reduced severity of first Omicron infection if it occurred less than 24 months later.
- Immunocompromise and the presence of other underlying comorbidities were associated with increased severity. Women reported longer duration of illness.
- Future studies will be needed to assess the changing severity of COVID-19 over time.