Characterizing the clinical and economic burden of COVID-19 among individuals with immunocompromising conditions in Ontario, Canada: A matched, population-based observational study

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Introduction

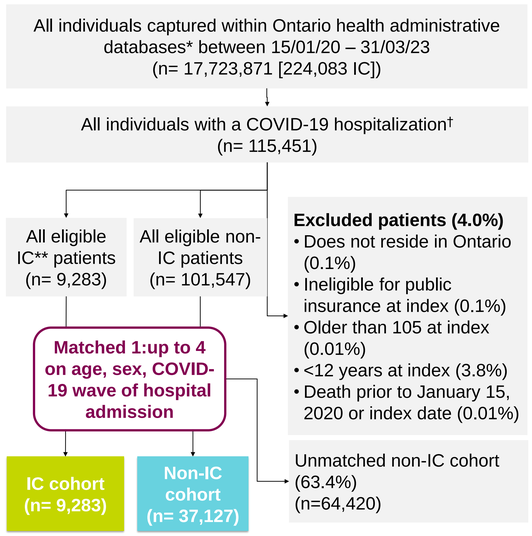
- COVID-19 continues to be associated with substantial burden, particularly among immunocompromised (IC) patients[1,2]
- IC individuals are more likely to experience suboptimal immune responses to vaccines, and thus experience more severe COVID-19 related outcomes

Objective

This study aimed to describe and compare the burden of illness, resource utilization, and healthcare costs during and following COVID-19 hospitalizations among IC and non-IC patients in Canada

Methods

Figure 1: Study cohort diagram



*Data housed and linked at ICES
†Only initial COVID-19 hospitalizations were considered for each patient
**IC status was determined at index hospitalization, using data prior to and including the index hospitalization, and included those with ≥1 of: solid organ or stem cell transplant; hematological malignancy; rheumatoid arthritis; multiple sclerosis; or primary immunodeficiency

Outcomes & Statistical Methods

- Clinical burden, healthcare resource use (HCRU), and costs were assessed during index COVID-19 hospitalization and post-discharge (within 30- and 180-day periods post discharge) and compared between IC and non-IC patients
  - Relative risks, relative rates and 95% confidence intervals (CIs) of clinical outcomes were estimated using log-binomial and modified Poisson regression
  - Relative and absolute mean (95% CI) differences in costs were estimated using gamma regression
  - Models were adjusted for neighborhood deprivation, long-term care residency, baseline comorbidities (i.e., Charlson comorbidity index [CCI], frailty), and COVID-19 vaccination status

Results

Cohort Characteristics

- 9,283 eligible IC patients hospitalized with COVID-19 (mean age 68.7 years; 52.1% female) were matched to 37,127 non-IC patients (Figure 1)
- In comparison to non-IC patients, IC patients were more likely to:
  - Have more comorbidities, according to hospitalization records from the past 2 years
  - Live in neighborhoods with lower degrees of material deprivation
  - Have a Hospital Frailty Risk Score[3] >15
  - Have received a complete COVID-19 vaccination regimen

Table 1: Baseline patient characteristics

Variable	IC (n=9,283)	Non-IC (n=37,127)
Age [mean(SD)]	68.7 (15.7)	68.7 (15.7)
Sex, F [n(%)]	4,834 (52.1)	19,335 (52.1)
COVID-19 wave of hospitalization [n(%)]		
Wave 1 (15/01/20-31/08/20)	329 (3.5)	1,314 (3.5)
Wave 2 (1/09/20-28/02/21)	814 (8.8)	3,254 (8.8)
Wave 3 (01/03/21-31/07/21)	847 (9.1)	3,388 (9.1)
Wave 4 (01/08/21-14/12/21)	293 (3.2)	1,172 (3.2)
Wave 5 (15/12/21-28/02/22)	1,942 (20.9)	7,767 (20.9)
Wave 6 (01/03/22-18/06/22)	1,527 (16.4)	6,108 (16.5)
Wave 7 (19/06/22-31/03/23)	3,531 (38.0)	14,124 (38.0)
CCI		
Unknown‡	4,112 (44.3)	22,000 (59.3)
Mean (SD)‡	2.5 (2.0)	2.1 (2.1)
Material deprivation quintile [n(%)]		
1 (least deprived)‡	1,581 (17.0)	5,530 (14.9)
5 (most deprived)‡	2,081 (22.4)	9,159 (24.7)
LTC resident [n(%)]‡	793 (8.5)	3,598 (9.7)
Frailty score > 15 [n(%)]‡	1,391 (15.0)	3,537 (9.5)
Vaccination status [n(%)]		
Unvaccinated	2,517 (27.1)	12,876 (34.7)
Partially vaccinated	428 (4.6)	1,643 (4.4)
Fully vaccinated*	6,338 (68.3)	22,608 (60.9)
Fully vaccinated + booster	4,715 (50.8)	15,302 (41.2)
IC conditions [n(%)]		
Rheumatoid arthritis	3,926 (42.3)	-
Haematological malignancy	2,435 (26.2)	-
Solid organ transplant	1,751 (18.9)	-
Multiple sclerosis	907 (9.8)	-
Primary immunodeficiency	461 (5.0)	-
Allogenic/autologous BMT	381 (4.1)	-

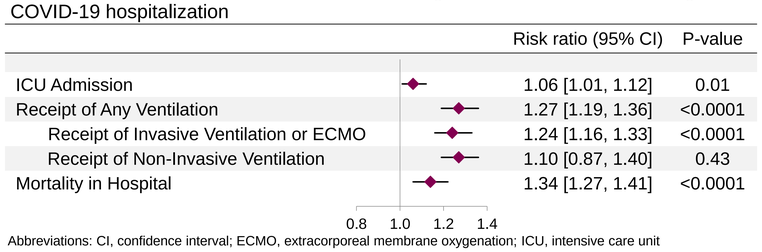
Abbreviations: BMT, bone marrow transplant; CCI, Charlson Comorbidity Index; IC, immunocompromised; LTC, long term care; non-IC, non-immunocompromised; SD, standard deviation.
*Defined as having received any of the following: 1) one dose of Janssen, or 2) two doses of a Health Canada authorized vaccine, or 3) one dose of a non-Health Canada authorized vaccine and one dose of a Health Canada authorized vaccine), or 4) three or more doses of a vaccine (Health Canada authorized or not). ‡p<0.05

References: 1. Public Health Agency of Canada (2022). Canadian COVID-19 vaccination coverage report. 2. Government of Canada (2023). COVID-19 Epidemiology update: Current situation. 3. Gilbert et al. (2018). *Lancet* 391(10132):1775:1782

Clinical outcomes during and post index hospitalization

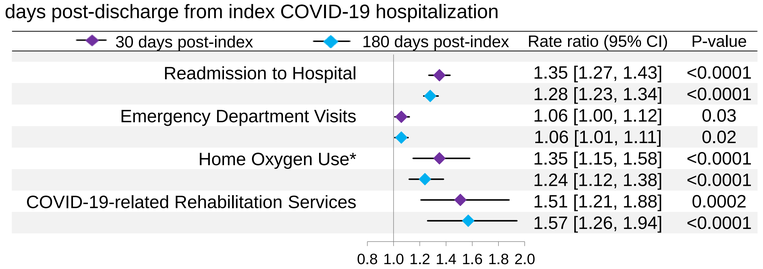
- In comparison to non-IC patients, IC patients were at significantly greater risk of the following, after adjusting for baseline patient characteristics (Figure 2):
  - ICU admission (**+6%**)
  - Receipt of any ventilation (**+27%**)
  - Receipt of invasive ventilation, including ECMO (**+24%**)
  - In-hospital mortality (**+34%**)
- Within 30-days post-discharge, IC patients experienced significantly greater adjusted rates of (Figure 4):
  - All-cause readmission to hospital (**+35%**)
  - Emergency department visits (**+6%**)
  - Home oxygen use (**+31%**)
  - COVID-19-related rehabilitation services (**+51%**)
- Within 180-days post-discharge, the rates of HCRU among IC patients remained significantly higher than HCRU rates among non-IC patients; the rate of hospital readmissions decreased slightly over time (Figure 3)

Figure 2: Relative risk of clinical outcomes among IC vs. non-IC patients during index COVID-19 hospitalization



Abbreviations: CI, confidence interval; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit

Figure 3: Relative rate of clinical outcomes among IC vs. non-IC patients 30- and 180-days post-discharge from index COVID-19 hospitalization

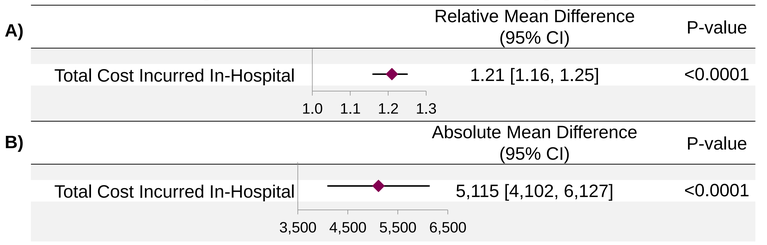


Abbreviations: CI, confidence interval; COVID-19, coronavirus-19. *only a risk ratio was calculated for home oxygen use due to this being a binary measure.

Costs during and post index hospitalization

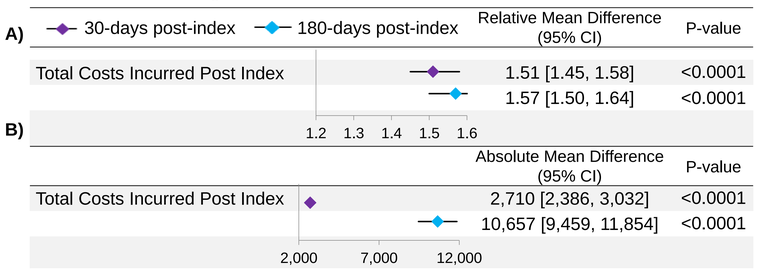
- The mean (SD) cost of an index COVID-19 hospitalization was $25,496 ($42,520) for an IC patient and $21,983 ($38,504) for a non-IC patient.
- Total costs incurred during index COVID-19 hospitalization were **21% higher** in the IC cohort relative to the non-IC cohort, after adjusting for patient characteristics (Figure 4A)
  - The absolute mean difference in cost per IC versus non-IC patient per index COVID-19 hospitalization was **$5,115** (Figure 4B)
- Total adjusted costs incurred 30- and 180-days post-discharge were **51% and 57% higher** in the IC cohort versus the non-IC cohort, respectively, after adjusting for patient characteristics (Figure 5A)
  - The absolute mean difference in HCRU costs per IC versus non-IC patient were $2,719 30-days post-discharge, and $10,657 180-days post-discharge (Figure 5B)

Figure 4: A) Relative mean difference and **B)** absolute mean differences in total costs incurred during index COVID-19 hospitalization among IC vs. non-IC patients



Abbreviations: CI, confidence interval

Figure 5: A) Relative mean difference and **B)** absolute mean difference in total costs incurred 30- and 180-days post-discharge from index COVID-19 hospitalization among IC vs. non-IC patients



Abbreviations: CI, confidence interval

Discussion

- Between January 2020 and March 2023, 9,283 patients with IC were hospitalized with COVID-19 from a total of 224,083 patients with IC in Ontario.
  - Although the IC subgroup represented 1% of the total population, they accounted for approximately 10% of all COVID-19 hospitalizations
  - IC patients experienced significantly greater clinical burden during hospitalization, associated with greater healthcare resource use and costs
  - Each IC patient incurred $5K more per hospitalization, $2.7K more 30-days post-discharge, and $10.7K more 180-days post-discharge compared to a non-IC patient with similar baseline risk factors (e.g., age, sex, vaccination status, SARS-CoV-2 strains circulating at time of admission)
- **Strengths:** This study used population-based data capturing all COVID-19 hospitalizations from a population of >17 million residents in Canada
- **Limitations:** Unmeasured confounding between IC and non-IC cohorts remain; given the lack of complete prescription data for younger patients and lack of in-hospital prescription data in the databases used, the use of additional prophylactic treatments for COVID-19 (e.g., remdesivir) were not adjusted for. IC patients may have been more likely to receive these treatments, which may lead to underestimation of risk of outcomes among the IC cohort.

Conclusions

- IC patients experienced more severe COVID-19 outcomes in hospital and post-discharge in comparison to non-IC patients, resulting in greater costs associated with the care of IC patients in hospital and post-discharge
- COVID-19 mitigating policies and prophylactic treatments are needed to continue to protect IC populations

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