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REPORTS OF ORIGINAL INVESTIGATIONS

Avoidable intensive care unit resource use and costs of unvaccinated patients with COVID-19: a historical population-based cohort study

Utilisation et coûts évitables des ressources des unités de soins intensifs pour les patients non vaccinés atteints de COVID-19 : une étude de cohorte historique basée sur la population

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Abstract

Purpose *SARS-CoV-2 vaccines have been proven effective at preventing poor outcomes from COVID-19; however, voluntary vaccination rates have been suboptimal. We assessed the potential avoidable intensive care unit (ICU) resource use and associated costs had unvaccinated or partially vaccinated patients hospitalized with COVID-19 been fully vaccinated.*

Methods *We conducted a retrospective, population-based cohort study of persons aged 12 yr or greater in Alberta (2021 population ~ 4.4 million) admitted to any ICU with COVID-19 from 6 September 2021 to 4 January 2022. We used publicly available aggregate data on COVID-19 infections, vaccination status, and health services use. Intensive care unit admissions, bed-days, lengths of stay, and costs were estimated for patients with COVID-19 and stratified by vaccination status.*

Results *In total, 1,053 patients admitted to the ICU with COVID-19 were unvaccinated, 42 were partially vaccinated, and 173 were fully vaccinated (cumulative incidence 230.6, 30.8, and 5.5 patients/100,000 population, respectively). Cumulative incidence rate ratios of ICU admission were 42.2 (95% confidence interval [CI], 39.7 to 44.9) for unvaccinated patients and 5.6 (95% CI, 4.1 to*

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7.6) for partially vaccinated patients when compared with fully vaccinated patients. During the study period, 1,028 avoidable ICU admissions and 13,015 bed-days were recorded for unvaccinated patients and the total avoidable costs were CAD 61.3 million. The largest opportunity to avoid ICU bed-days and costs was in unvaccinated patients aged 50 to 69 yr.

Conclusions *Unvaccinated patients with COVID-19 had substantially greater rates of ICU admissions, ICU bed-days, and ICU-related costs than vaccinated patients did. This increased resource use would have been potentially avoidable had these unvaccinated patients been vaccinated against SARS-CoV-2.*

Résumé

Objectif *Les vaccins contre le SRAS-CoV-2 se sont avérés efficaces pour prévenir les devenirs défavorables associés à la COVID-19; toutefois, les taux de vaccination volontaire ont été sous-optimaux. Nous avons évalué l'utilisation potentiellement évitable des ressources des unités de soins intensifs (USI) et les coûts associés si les patients non vaccinés ou partiellement vaccinés qui ont dû être hospitalisés pour la COVID-19 avaient été complètement vaccinés.*

Méthode *Nous avons réalisé une étude de cohorte rétrospective basée sur la population de personnes âgées de 12 ans ou plus en Alberta (population de 2021 ~ 4,4 millions) admises dans une unité de soins intensifs et atteintes de COVID-19 du 6 septembre 2021 au 4 janvier 2022. Nous avons utilisé des données agrégées accessibles au public sur les infections à la COVID-19, le statut vaccinal et l'utilisation des services de santé. Les admissions aux soins intensifs, les journées-patients, les durées de séjour et les coûts ont été estimés pour les patients atteints de la COVID-19 et stratifiés selon le statut vaccinal.*

Résultats *Au total, 1053 patients admis à l'USI souffrant de la COVID-19 n'étaient pas vaccinés, 42 étaient partiellement vaccinés et 173 étaient complètement vaccinés (incidence cumulative 230,6, 30,8 et 5,5 patients / 100 000 habitants, respectivement). Les taux d'incidence cumulés des admissions aux soins intensifs étaient de 42,2 (intervalle de confiance [IC] à 95 %, 39,7 à 44,9) pour les patients non vaccinés et de 5,6 (IC 95 %, 4,1 à 7,6) pour les patients partiellement vaccinés par rapport aux patients entièrement vaccinés. Au cours de la période à l'étude, 1028 admissions évitables aux soins intensifs et 13 015 journées-patients ont été enregistrées pour les patients non vaccinés, et les coûts totaux évitables étaient de 61,3 millions de dollars canadiens. L'économie potentielle la plus importante en matière de journées-patients et de coûts en soins intensifs touchait les patients non vaccinés âgés de 50 à 69 ans.*

Conclusion *Les patients non vaccinés atteints de COVID-19 ont affiché des taux beaucoup plus élevés d'admissions à l'USI, de journées-patients à l'USI et de coûts liés à l'USI que les patients vaccinés. Cette utilisation accrue des ressources aurait été potentiellement évitable si ces patients non vaccinés avaient été vaccinés contre le SRAS-CoV-2.*

Keywords costs · COVID-19 · intensive care unit · prevention · vaccination

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Despite strong evidence that SARS-CoV-2 vaccines are highly effective at preventing severe COVID-19, hospitalizations (including intensive care unit [ICU] admissions), and deaths,[1] voluntary vaccination uptake has been slow despite availability and vaccination rates have been suboptimal across multiple jurisdictions, including the province of Alberta.

Successive waves of COVID-19 have threatened to overwhelm our healthcare system capacity. Health systems have responded by rapidly expanding and reorganizing acute care capacity, load-levelling, and transferring critically ill patients across jurisdictions, redeploying healthcare professionals after postponement or cancellation of nonemergent services including scheduled procedures and surgeries, and preparing standardized critical care triage protocols as a fallback if confronted with insufficient ICU capacity.[2,3] The need for recurring and sustained health system reorganization has generated

concern about substantial indirect harm to non-COVID-related population health during the COVID-19 pandemic.[4–6]

These concerns have magnified the dialogue about broad public health measures, including the use of mandatory vaccination policies in selected jurisdictions.[7] Mandatory vaccination has been a polarizing and contentious public health issue and has been variably implemented.[8] To deepen our understanding of this issue, we explored the potential avoidable ICU resource use and costs had unvaccinated patients hospitalized with COVID-19 been vaccinated.

Methods

We performed a historical, population-based cohort study of persons aged 12 yr or older in Alberta, Canada (2021 population, ~4.4 million) admitted to any ICU with COVID-19 from 6 September 2021 to 4 January 2022 (120-day study period). This period corresponded to the fourth (delta variant-of-concern) COVID-19 wave in Alberta. As of 6 September 2021, only 61.1% of the eligible population of Alberta had been fully vaccinated.[9]

We used publicly available age-stratified aggregate data on COVID-19 infections, vaccination status, and health service use provided by Alberta Health.[10] Because aggregate data were used, we were not able to confirm whether a given patient had been admitted to the ICU multiple times. Nevertheless, we believe that this was unlikely because a patient would only have been counted more than once if they developed a new COVID-19 infection and were re-hospitalized within the same 120-day study period.

SARS-CoV-2 vaccines were widely and freely available during this period. Vaccination status included fully vaccinated (receipt of $\geq$ 2 doses of a Health Canada [HC]-approved vaccine), partially vaccinated (receipt of 1 dose of a HC-approved vaccine), or unvaccinated.[11]

Data on ICU bed-days, lengths of stay, and costs were extracted from the Discharge Abstract Database for patients with COVID-19; values were estimated overall and stratified by age. Costs were based on the Canadian Institute for Health Information (CIHI) Case-Mix Group (CMG) Plus methodology[12] (see Electronic Supplementary Material [ESM] eTable 1).[13] As CMG costs are for the entire duration of hospitalization, we estimated ICU costs by comparing hospitalizations with and without ICU admission. We calculated the ICU length of stay in days by dividing the reported ICU hours by 24. We used the emergency International Classification of Disease 10 (ICD-10) code (U07.1), introduced on 1 April 2020, to identify hospitalizations for COVID-19. All cases of COVID-19 reported by Alberta Health were laboratory confirmed by HC-approved and validated SARS-CoV-2 polymerase chain reaction tests. Prior data showed that the ICD-10 code (U07.1) can identify patients hospitalized and admitted to ICU with COVID-19 with high sensitivity and a high positive predictive value in administrative data in Alberta.[14]

We estimated avoidable costs using the formula, CA = N x $(1 - R_2/R_1)$ x L x C, where CA is cost avoidance (Canadian dollars [CAD]), N is the number of unvaccinated or partially vaccinated patients, R_1 is the cumulative incidence of ICU admissions among unvaccinated or partially vaccinated patients, R_2 is the cumulative incidence of ICU admissions among fully vaccinated patients, L is the ICU length of stay, and C is the cost per ICU day. In the formula, avoidable admissions were N x $(1 - R_2/R_1)$ and avoidable bed-days were N x $(1 - R_2/R_1)$ x L.

This study was approved by the Research Ethics Board at the University of Alberta, Edmonton, Canada (File # Pro00116509; 22 December 2021). The need for written informed consent was waived.

Results

During the study period, 1,053 unvaccinated patients, 42 partially vaccinated patients, and 173 fully vaccinated patients were admitted to the ICU (cumulative incidences 230.6, 30.8, and 5.5 admissions/100,000 population, respectively) (Table 1; ESM eTable 2). The highest cumulative incidences of ICU admission for unvaccinated persons were in the age strata of 50–59, 60–69, and 70–79 yr (432.5, 968.6, and 1,631.9 admissions/100,000 populations, respectively).

The cumulative incidence rate ratios of ICU admission were 42.2 (95% CI, 39.7 to 44.9) for unvaccinated patients and 5.6 (95% CI, 4.1 to 7.6) for partially vaccinated patients, compared with fully vaccinated patients (Table 1). The highest cumulative incidence rate ratios for ICU admissions among unvaccinated relative to fully vaccinated persons were again in the age strata of 50–59, 60–69, and 70–79 yr (121.5, 82.9, and 78.6, respectively).

An estimated 1,028 ICU admissions and 13,015 ICU bed-days were recorded for unvaccinated persons. This represents 61.8% of the total non-pandemic baseline-funded ICU bed capacity in Alberta (n = 173 beds) being allocated to unvaccinated patients with COVID-19 during this 120-day period. For comparison, 35 potential avoidable ICU admissions and 437 ICU bed-days were recorded among partially vaccinated patients during the same period. The largest numbers of avoidable admissions

Table 1 Summary of age-stratified cumulative incidence, cumulative incidence rate ratio, ICU use, avoidable admissions, ICU services use, and ICU bed-day avoidance by vaccination status from 6 September 2021 to 4 January 2022

Age strata (yr)	Admissions (*n*)	Cumulative rate (*n*/100,000 population)	Cumulative rate ratio*	ICU stay (days) (mean [SD])	R_2/R_1	Avoidable admissions (*n*)	Avoidable ICU bed-days (days)	Cost per ICU day (CAD)	Avoidable ICU costs (CAD, millions)
Unvaccinated									
12–29	72	44.6	58.7	8.1 (9.1)	0.0170	7c.8	573.9	4,826.5	2.77
30–39	112	97.0	78.8	8.9 (8.5)	0.0127	110.6	989.7	4,976.0	4.92
40–49	159	213.5	61.0	11.9 (13.1)	0.0164	156.4	1,868.9	4,823.7	9.01
50–59	255	432.5	121.5	12.3 (11.8)	0.0082	252.9	3,113.2	4,501.3	14.01
60–69	258	968.6	82.9	14.9 (14.7)	0.0121	254.9	3,805.5	4,379.9	16.67
70–79	166	1,631.9	78.6	13.8 (13.0)	0.0127	163.9	2,255.1	4,593.1	10.36
80+	31	328.3	18.3	9.8 (9.6)	0.0548	29.3	285.7	4,936.0	1.41
Total	1,053	230.6	42.2	12.7 (12.8)	0.0237	1,028.1	13,015.4	4,712.4	61.33
Partially vaccinated									
12–29	3	5.6	7.3	8.1 (9.1)	0.1364	2.6	21.0	4,826.48	0.10
30–39	4	13.6	11.1	8.9 (8.5)	0.0904	3.6	32.6	4,975.95	0.16
40–49	7	36.9	10.5	11.9 (13.1)	0.0948	6.3	75.7	4,823.65	0.37
50–59	5	33.6	9.4	12.3 (11.8)	0.1060	4.5	55.0	4,501.32	0.25
60–69	13	117.1	10.0	14.9 (14.7)	0.0997	11.7	174.7	4,379.85	0.77
70–79	9	180.9	8.7	13.8 (13.0)	0.1148	8.0	109.6	4,593.12	0.50
80+	1	30.2	1.7	9.8 (9.6)	0.5958	0.4	3.9	4,936.04	0.02
Total	42	30.8	5.6	12.7 (12.8)	0.1774	34.5	437.4	4,712.38	2.06

* Incidence rate ratio is the ratio of incidence of ICU admissions for unvaccinated or partially vaccinated patients with COVID-19 (per 100,000 population) divided by the incidence of ICU admission for fully vaccinated patients with COVID-19 (per 100,000 population)

ICU = intensive care unit; R_2/R_1 = ratio of the rate of ICU admissions among fully vaccinated to the rate of ICU admission for the unvaccinated or partially vaccinated patients

and ICU bed-days were in the age strata of 50–59 and 60–69 yr (Table 1; Figure 1).

The avoidable ICU costs for unvaccinated patients totalled CAD 61.3 million for the 120-day study period. This was 20.6% of the total annual provincial budget for ICU services, assuming a baseline of 173 funded ICU beds. The largest opportunity for ICU bed-day (53%) and cost avoidance (50%) were for unvaccinated patients in the age strata 50–59 and 60–69 yr (Figure 1).

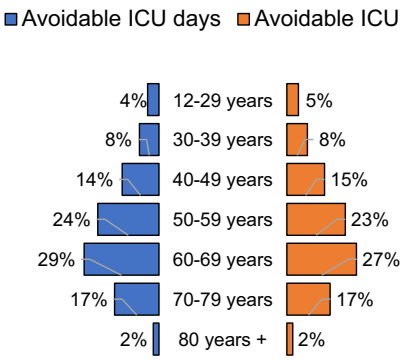

Figure 1 Age-stratified distribution of avoidable ICU bed-days and ICU costs for unvaccinated patients with COVID-19

Discussion

In a large province-wide health region with free universal access to SARS-CoV-2 vaccines, our population-based study reinforces how an unvaccinated population has a far greater likelihood of ICU admission and excess health resource use due to COVID-19 infection than a population vaccinated against COVID-19 with breakthrough infection.[15] We found that unvaccinated persons, particularly within the age strata of 50–79 yr, accounted for more than 1,000 potentially avoidable ICU admissions, 13,000 potentially avoidable ICU bed-days, and CAD 61 million in excess healthcare costs during only the four-month COVID-19 wave dominated by the delta variant-of-concern. Had this unvaccinated population been fully vaccinated, substantial excess health resource use and costs could have been avoided, and strain across the health

system could have been mitigated. Strain on the ICU and hospital capacity has been strongly associated with incremental and excess attributable mortality during the COVID-19 pandemic.[16,17] This has necessitated considerable reorganization of health services and reallocation of health resources during the delta variant-of-concern wave, such as redeployment of healthcare professionals, deferral of routine health services, and postponement of scheduled procedures and surgeries.

Vaccines are highly cost-effective population health interventions because of their proven capacity to reduce avoidable deaths, defer healthcare costs, and prevent long-term disability attributable to communicable diseases.[18,19] Similar data on the broad patient, health system, and society benefits of vaccination against SARS-CoV-2 from varying jurisdictions have now been shown.[18,20,21] In a modelling study of the Italian population, widespread vaccination was predicted to effectively reduce hospitalizations by 74.9% (2,379,144 hospitalizations avoided) and ICU admissions by 71.3% (259,224 ICU admissions avoided), and over EUR 2.9 billion (CAD 3.95 billion) in avoided healthcare costs in 2021.[21] In an economic modelling study in the USA, widespread SARS-CoV-2 vaccination was estimated to generate USD 5 trillion (CAD 6.1 trillion) in societal economic benefits. These benefits were attributed largely to avoided SARS-CoV-2 infections (with reduced hospitalizations and rehospitalizations), reduced medical conditions exacerbated by the pandemic (e.g., mental health impairment and depression), more lives saved from fewer COVID-19 infections, and the earlier lifting of public health restrictions with more rapid resumption of normal economic activity and gains to the USA's gross domestic product.[18] The societal benefits extend well beyond COVID-19-specific infections and attributable deaths. A substantial increase in excess deaths was observed in the USA during the early phases of the pandemic when vaccines were not available, with a large proportion attributed to causes other than COVID-19, such as heart disease, diabetes, and nonrespiratory related disease.[5,6,22] This excess mortality may be related to delayed or impeded access to acute care and strained health systems.[17]

This study has limitations. First, we used aggregate data on vaccination status and lengths of stay that were age adjusted only and do not account for comorbidity and acuity. Second, estimated bed-days and costs per ICU bed-day were aggregated for the total and age-stratified patients with COVID-19 and were not specifically stratified by vaccination status. Further, these estimates represent the ICU only and do not capture total hospitalization. Nevertheless, the data used to derive estimates were real-world, population level and included vaccination status and health services use. Lastly, these data were derived in Alberta and may have limited generalizability to other health jurisdictions. Nevertheless, similar resource and cost avoidance would be likely under comparable conditions.

In conclusion, our findings have important implications for discourse on the relative balance of increasingly stringent public health protection (restrictions), including mandatory vaccination policies, and the sustainability and function of health system infrastructure and capacity during the ongoing COVID-19 pandemic.[23]

Author contributions *Sean M. Bagshaw* and *Thanh X. Nguyen* contributed to study conception and design, data analysis, and drafting of the manuscript. *Sean M. Bagshaw*, *Annalise Abbott*, *Sanjay Beesoon*, *Braden Manns, Tracy Wasylak*, *Danny J. Zuege*, and *Thanh X. Nguyen* contributed to the acquisition, analysis, and interpretation of data. *Sean M. Bagshaw*, *Danny J. Zuege*, *Tracy Wasylak*, *Braden Manns* and *Thanh X. Nguyen* contributed to administrative, technical, and material support. All authors contributed to the critical revision of the manuscript for important intellectual content.

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References

1. *Rotshild V, Hirsh-Raccah B, Miskin I, Muszkat M, Matok I.* Comparing the clinical efficacy of COVID-19 vaccines: a systematic review and network meta-analysis. Sci Rep 2021; 11: 22777. https://doi.org/10.1038/s41598-021-02321-z
2. *Bagshaw SM, Zuege DJ, Stelfox HT, et al.* Association between pandemic coronavirus disease 2019 public health measures and reduction in critical care utilization across ICUs in Alberta, Canada. Crit Care Med 2022; 50: 353–62. https://doi.org/10.1097/ccm.0000000000005275
3. *Kerlin MP, Costa DK, Davis BS, Admon AJ, Vranas KC, Kahn JM.* Actions taken by US hospitals to prepare for increased demand for intensive care during the first wave of COVID-19: a national survey. Chest 2021; 160: 519–28. https://doi.org/10.1016/j.chest.2021.03.005
4. *Baldi E, Sechi GM, Mare C, et al.* COVID-19 kills at home: the close relationship between the epidemic and the increase of out-of-hospital cardiac arrests. Eur Heart J 2020; 41: 3045–54. https://doi.org/10.1093/eurheartj/ehaa508
5. *Bhambhvani HP, Rodrigues AJ, Yu JS, Carr JB 2nd, Gephart MH.* Hospital volumes of 5 medical emergencies in the COVID-19 pandemic in 2 US medical centers. JAMA Intern Med 2020; 181: 272–74. https://doi.org/10.1001/jamainternmed.2020.3982
6. *Kansagra AP, Goyal MS, Hamilton S, Albers GW.* Collateral effect of Covid-19 on stroke evaluation in the United States.

N Engl J Med 2020; 383: 400–1. https://doi.org/10.1056/nejmc2014816
7. *Emanuel EJ, Skorton DJ*. Mandating COVID-19 vaccination for health care workers. Ann Intern Med 2021; 174: 1308–10. https://doi.org/10.7326/m21-3150
8. *Hagan K, Forman R, Mossialos E, Ndebele P, Hyder AA, Nasir K*. COVID-19 vaccine mandate for healthcare workers in the United States: a social justice policy. Expert Rev Vaccines 2021: 21: 37–45. https://doi.org/10.1080/14760584.2022.1999811
9. *Government of Alberta*. COVID-19 Alberta statistics: vaccinations. Available from URL: https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#vaccinations (accessed May 2022).
10. *Government of Alberta*. COVID-19 Alberta statistics: vaccine outcomes. Available from URL: https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#vaccine-outcomes (accessed May 2022).
11. *Government of Canada.* Approved COVID-19 vaccines. Available from URL: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html (accessed May 2022).
12. *Canadian Institute for Health Information*. CMG+. Available from URL: www.cihi.ca/en/cmg (accessed May 2022).
13. *Canadian Institute for Health Information*. Canadian coding standards for version 2022 ICD-10-CA and CCI — addendum: pandemics and epidemics (COVID-19), 2022. Available from URL: https://secure.cihi.ca/free_products/COVID-19_Addendum_Pandemics_Epidemics-en.pdf (accessed July 2022).
14. *Wu G, D'Souza AG, Quan H, et al.* Validity of ICD-10 codes for COVID-19 patients with hospital admissions or ED visits in Canada: a retrospective cohort study. BMJ Open 2022; 12: e057838. https://doi.org/10.1136/bmjopen-2021-057838
15. *Bahl A, Johnson S, Maine G, et al*. Vaccination reduces need for emergency care in breakthrough COVID-19 infections: a multicenter cohort study. Lancet Reg Health Am 2021; 4: 100065. https://doi.org/10.1016/j.lana.2021.100065
16. *Bravata DM, Perkins AJ, Myers LJ, et al*. Association of intensive care unit patient load and demand with mortality rates in US Department of Veterans Affairs hospitals during the COVID-19 pandemic. JAMA Netw Open 2021; 4: e2034266. https://doi.org/10.1001/jamanetworkopen.2020.34266
17. *French G, Hulse M, Nguyen D, et al*. Impact of hospital strain on excess deaths during the COVID-19 pandemic - United States, July 2020-July 2021. MMWR Morb Mortal Wkly Rep 2021; 70: 1613–16. https://doi.org/10.15585/mmwr.mm7046a5
18. *Kirson N, Swallow E, Lu J, et al*. The societal economic value of COVID-19 vaccines in the United States. J Med Econ 2022; 25: 119–28. https://doi.org/10.1080/13696998.2022.2026118
19. *VoICE*. Key concept: vaccines are among the most cost-effective health interventions available. Johns Hopkins Bloomberg School of Public Health. Available from URL: https://immunizationevidence.org/key-concepts/vaccines-are-among-the-most-cost-effective-health-interventions-available/ (accessed May 2022).
20. *López F, Català M, Prats C, et al*. A cost-benefit analysis of COVID-19 vaccination in Catalonia. Vaccines (Basel) 2021; 10: 59. https://doi.org/10.3390/vaccines10010059
21. *Marcellusi A, Fabiano G, Sciattella P, Andreoni M, Mennini FS*. The impact of COVID-19 vaccination on the Italian healthcare system: a scenario analysis. Clin Drug Investig 2022; 42: 237–42. https://doi.org/10.1007/s40261-022-01127-9
22. *Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L*. Excess deaths from COVID-19 and other causes, March-April 2020. JAMA 2020; 324: 510–13. https://doi.org/10.1001/jama.2020.11787
23. *Cukier A*. Fracturing political commitment to implement vaccine mandates. CMAJ 2021; 193: E1819. https://doi.org/10.1503/cmaj.1095975