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# Academic and Community ICUs Participating in a Critical Care Randomized Trial: A Comparison of Patient Characteristics and Trial Metrics

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**OBJECTIVES:** Clinical research in Canada is conducted primarily in "academic" hospitals, whereas most clinical care is provided in "community" hospitals. The objective of this nested observational study was to compare patient characteristics, outcomes, process-of-care variables, and trial metrics for patients enrolled in a large randomized controlled trial who were admitted to academic and community hospitals in Canada.

**DESIGN:** We conducted a preplanned observational study nested within the Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT, a randomized controlled trial comparing probiotics to placebo in mechanically ventilated patients) Research Program.

**SETTING:** ICUs.

**PATIENTS:** Mechanically ventilated patients.

**MEASUREMENTS:** We compared patient characteristics, interventions, outcomes, and trial metrics between patients enrolled in PROSPECT from academic and community hospitals.

**MAIN RESULTS:** Participating centers included 34 (82.9%) academic and seven (17.1%) community hospitals, which enrolled 2,203 (86.2%) and 352 (13.8%) patients, respectively. Compared with academic hospitals, patients enrolled in community hospitals were older (mean [SD] 62.7 yr [14.9 yr] vs 59.5 yr [16.4 yr]; $p = 0.044$), had longer ICU stays (median [interquartile range {IQR}], 13 d [8–23 d] vs 11 d [7–8 d]; $p = 0.012$) and higher mortality (percentage, [95% CI] in the ICU, 30.4% [25.8–35.4%]vs 20.5% [18.9–11.3%]; $p = 0.002$) and hospital (40.6% [35.6–45.8%] vs 26.1% [24.3–27.9%]; $p < 0.001$). Trial metrics, including informed consent rate (85.9% vs 76.3%; $p = 0.149$), mean (SD) monthly enrolment rate (2.1 [1.4] vs 1.1 [0.7]; $p = 0.119$), and protocol adherence (90.6% vs 91.6%; $p = 0.207$), were similar between community and academic ICUs.

**CONCLUSIONS:** Community hospitals can conduct high-quality research, with similar trial metrics to academic hospitals. Patient characteristics differed between community and academic hospitals, highlighting the need for broader engagement of community hospitals in clinical research to ensure generalizability of study results.

**KEY WORDS:** academic hospitals; community hospitals; critical care; intensive care; randomized controlled trials

Clinical research, including research in ICUs, has traditionally been conducted in university-affiliated or "academic" hospitals. However, the majority of Canadian patients receive their care in "community" hospitals, which historically have not participated in clinical research (1, 2). A lack of community hospital



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## KEY POINTS

**Question:** Did patient characteristics, interventions, clinical outcomes, and trial metrics differ between academic and community hospitals participating in a multicenter, randomized controlled trial of probiotics?

**Findings:** Patient characteristics, interventions, and clinical outcomes differed between academic and community hospitals. However, trial metrics, including consent rates, enrolment rates, and protocol adherence, were similar.

**Meaning:** Research conducted exclusively in academic hospitals may not reflect the clinical reality of community hospitals. There is a need for broader engagement of community hospitals in clinical research to ensure the generalizability of study results.

participation limits the pool of potential patients that can be recruited into clinical research studies. Furthermore, demographic variables and outcomes may differ between patients cared for in academic and community hospitals, thereby limiting the generalizability of research that is conducted exclusively in academic hospitals.

In Canada, there are 57 teaching or "academic" hospitals, which are affiliated with the 17 medical schools. These hospitals are typically located in major urban centers. All other hospitals are considered nonteaching or "community hospitals," and are typically located in suburban areas or smaller communities. The geographic differences between academic and community hospitals translate into important socioeconomic and cultural differences in patient populations that may impact social determinants of health. For instance, visible minorities and recent immigrants live disproportionately in suburban areas, which are served by community hospitals (3, 4). Although Canada has universal medical coverage, studies have shown that patients living in suburban and rural areas have less access to certain types of specialized care, such as cancer resection and stroke care, which may also impact health outcomes (5, 6). Finally, academic hospitals are teaching institutions staffed by medical trainees and educators. This may impact patterns of care, including adherence to guidelines and resource utilization.

Recently, the Canadian Critical Care Trials Group and its affiliated investigators have encouraged greater community ICU participation in clinical research studies. One such study was the Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT), a randomized controlled trial that compared probiotics to placebo, showing no effect on preventing ventilator-associated pneumonia (VAP) (7). PROSPECT enrolled patients at 41 Canadian hospitals, of which 34 were academic and seven were community hospitals. The objective of this nested observational study was to compare the patients enrolled in PROSPECT from community and academic hospitals with respect to patient demographics, interventions, and outcomes, and to compare trial metrics, including consent rate, enrolment rate, coenrolment rate, protocol adherence, and adverse events, between community and academic sites.

## MATERIALS AND METHODS

This is a preplanned observational study nested within the PROSPECT Research Program (7). In PROSPECT, mechanically ventilated patients 18 years old and older were randomized to receive either $1 \times 10^{10}$ colony forming units of *Lactobacillus rhamnosus* GG or an identical placebo, twice daily. The primary outcome was VAP. Secondary outcomes were ICU-acquired infections (including *Clostridioides difficile*), diarrhea (including antibiotic-associated diarrhea), antimicrobial use, ICU and hospital length of stay, and mortality. Trial participation was open to all interested centers.

All Canadian PROSPECT sites were included in this substudy. Community and academic hospital status was determined according to the Canadian Institute for Health Information classification, which differentiates Canadian hospitals by "teaching status" (8). In Canada, there are 17 medical schools, which are affiliated with 57 "teaching" or academic hospitals. For the purposes of this study, "teaching" hospitals were considered "academic," while "nonteaching" hospitals were considered "community."

Study outcomes included patient demographics, interventions, and outcomes as well as trial metrics, including consent rate, enrolment rate, coenrolment rate, protocol adherence, and adverse events. Protocol adherence was defined by the percentage of patients who either: 1) received study product or 2) had a legitimate reason not to receive study product on greater than or equal to 90% of ICU days. A protocol deviation was defined as:

1) a patient received at least one dose of wrong study product, 2) at least one dose was not staggered by 4 hours for *Lactobacillus*-sensitive oral antibiotic, and 3) at least one dose of open-label probiotic was administered.

### Statistical Analysis

Data are reported as mean (SD) or median (interquartile range [IQR]) for continuous variables or number of patients (percentage) for categorical variables. Community and academic hospitals were compared using mixed models, which included hospital as a random effect. Continuous variables were analyzed using linear mixed models. Continuous variables that were not normally distributed were log-transformed. Binary variables were analyzed using logistic mixed models. All statistical tests were two-tailed, and statistical significance was defined as $p < 0.05$. Statistical sample size calculation was not performed a priori, and sample size was equal to the total number of patients enrolled at Canadian sites in PROSPECT. Post hoc subgroup analysis comparing community and academic hospital patients with respect to the effect of probiotics on the primary outcome of VAP was performed using time-to-event analysis. Cox regression was performed adjusting for medical/surgical/trauma diagnosis and with hospital entered as a random effect. Data analysis was performed using the SAS software, Version 9.4 (SAS Institute, Cary, NC).

### Ethical Considerations

PROSPECT trial was approved by the Hamilton Integrated Research Ethics Board (15-322). Initial approval date was on July 13, 2015. Informed consent was obtained from all participants. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as most recently amended.

## RESULTS

### Site Characteristics

The PROSPECT trial enrolled patients at 41 sites across Canada, including 34 academic hospitals (82.9%) and seven community hospitals (17.1%). Canadian patient enrollment totaled 2,555 patients, of whom 2,203 (86.2%) were enrolled in academic ICUs and 352 (13.8%) in community ICUs (9). Site characteristics are found in **Table 1** and **Appendix 1** (http://links.lww.com/CCX/B86). Mean enrollment at academic

**TABLE 1.**
**Summary of Site Characteristics of Participating Academic and Community Hospitals by Provinces**

| Province | Type of Center | *N* | Census Subdivision Population < 400,000, *n* (%) | Located in Distant Suburb Zone, *n* (%) | Antibiotic Stewardship Program | | |
|---|---|---|---|---|---|---|---|
| | | | | | Mean ICU Beds, *n* (SD) | Mean Total Enrolment per Sites (SD) | ASP Program (*n*) |
| British Columbia | Community | 0 | -- | -- | -- | -- | -- |
| | Academic | 4 | 2 (50.0) | 2 (50.0) | 22.3 (8.0) | 35.5 (21.7) | 3 |
| Alberta | Community | 0 | -- | -- | -- | -- | -- |
| | Academic | 4 | 0 (0.0) | 0 (0.0) | 27.3 (4.1) | 16.8 (8.2) | 3 |
| Manitoba | Community | 0 | -- | -- | -- | -- | -- |
| | Academic | 2 | 0 (0.0) | 0 (0.0) | 20.0 (9.9) | 7.0 (5.7) | 2 |
| Ontario | Community | 6 | 4 (66.7) | 2 (33.3) | 18.8 (3.7) | 52.6 (44.4) | 6 |
| | Academic | 13 | 1 (7.7) | 1 (7.7) | 25.6 (5.3) | 103.0 (63.3) | 11 |
| Quebec | Community | 1 | 1 (100.0) | 1 (100.0) | 18 (N/A) | 37 (N/A | 1 |
| | Academic | 10 | 1 (10.0) | 1 (10.0) | 34.6 (16.2) | 60.7 (45.5) | 5 |
| Nova Scotia | Community | 0 | -- | -- | -- | -- | -- |
| | Academic | 1 | 0 (0.0) | 0 (0.0) | 21 (N/A) | 36 (N/A) | 1 |

sites was 57 (SD = 65) and at community sites was 50 (SD = 41).

## Patient Characteristics

Patients enrolled in community ICUs were older than those in academic ICUs (mean [SD], 62.7 yr [14.9 yr] vs 59.5 yr [16.4 yr]; $p = 0.044$), but the proportion of females was similar (40.6% vs 40.2%, respectively; $p = 0.925$) (**Table 2**). Admitting diagnostic categories are found in **Appendix 2** (http://links.lww.com/CCX/B86). Illness severity at enrollment was similar between community and academic ICUs (Acute Physiology and Chronic Health Evaluation II score, 22.1 [8.6] vs 21.9 [7.7]; $p = 0.957$); however, patients in community hospitals were more likely to have a medical admission diagnosis (92.3% vs 74.0%; $p = 0.007$) rather than a surgical or trauma diagnosis (Table 2).

## Interventions: Life Supports and Medical Therapies

The proportion of patients receiving inotropes or vasopressors (59.1% vs 60.8%; $p = 0.402$) and renal replacement therapy (7.4% vs 8.3%; $p = 0.712$) at study enrollment was similar between community and academic ICUs (**Table 3**). However, the duration of mechanical ventilation was longer in community ICUs (median [IQR], 8 d [4–16 d] vs 7 d [3–12 d]); $p = 0.037$) (Table 3).

Antimicrobial use data were collected for 2,283 patients, totaling 31,059 patient days. Days of therapy per 1,000 patient-days, defined as daily dose per 1,000 patient-days and antimicrobial-free days per 1,000 patient-days, were similar between community and academic ICUs (**Table 4**). During the trial, antimicrobial stewardship programs were in place in seven of seven (100%) community ICUs and in 25 of 34 (73.5%) academic ICUs (Table 1).

## Clinical Outcomes

The median duration of ICU stay was longer for patients enrolled in community ICUs (13 d [8–23 d]) compared with academic ICUs (11 d [7–18 d]); $p = 0.012$, whereas the median duration of hospital stay was similar. However, mortality was significantly higher in community hospitals, both in the ICU (30.4% [25.8–35.4%] vs 20.5% [18.9–11.3%]; $p = 0.002$) and in hospital (40.6% [35.6–45.8%] vs 26.1% [24.3–27.9%]; $p < 0.001$) (**Table 5**). The incidence of VAP and *C. difficile* infection was similar between community and academic ICUs (Table 5).

With respect to the primary outcome of the PROSPECT trial, a post hoc subgroup analysis by hospital status showed no difference in the treatment

**TABLE 2.**
**Comparison of Baseline Patient Characteristics Between Community and Academic ICUs**

| Baseline Patient Characteristics | Community, *n* = 352 | Academic, *n* = 2,203 | Total, *n* = 2,555 | *p* Adjusted for Center |
|---|---|---|---|---|
| Age, yr, mean (SD) | 62.7 (14.9) | 59.5 (16.4) | 59.9 (16.2) | 0.044 |
| Acute Physiology and Chronic Health Evaluation II, mean (SD) | 22.1 (8.6) | 21.9 (7.7) | 22.0 (7.8) | 0.957 |
| Clinical Frailty Score[a] | | | | |
| Mean (SD) | 3.7 (1.6) | 3.3 (1.6) | 3.4 (1.6) | 0.230 |
| ≥5, *n* (%) | 96(27.6) | 350(19.9) | 446 (21.2) | |
| Females, *n* (%) | 143 (40.6) | 886 (40.2) | 1029 (40.3) | 0.925 |
| Type of patient, number (%)[b] | | | | |
| Medical | 325 (92.3) | 1,631 (74.0) | 1,956 (76.6) | 0.007 |
| Surgical | 26 (7.4) | 242 (11.0) | 268 (10.5) | 0.223 |
| Trauma | 1 (0.3) | 330 (15.0) | 331 (13.0) | 0.017 |
| Days from hospital admission to ICU admission, median (interquartile range) | 0 (0–1) | 0 (0–1) | 0 (0–1) | 0.425[c] |

[a]Total *n* = 2,103, community sites *n* = 348 and academic sites *n* = 1,755.
[b]*p* values correspond to medical vs not medical, surgical vs not surgical, and trauma vs not trauma.
[c]Using Poisson regression.

**TABLE 3.**
**Comparison of Interventions Between Community and Academic ICUs**

| Interventions | Community, *n* = 352 | Academic, *n* = 2,203 | Total, *n* = 2,555 | *p* Adjusted for Center |
|---|---|---|---|---|
| On study day 1 | | | | |
| Invasive mechanical ventilation, *n* (%)[#] | 352 (100.0) | 2,203 (100.0) | 2,555 (100.0) | - |
| Inotropes or vasopressors, *n* (%) | 208 (59.1) | 1340 (60.8) | 1548 (60.6) | 0.402 |
| Dialysis/renal replacement, *n* (%) | 26 (7.4) | 183 (8.3) | 209 (8.2) | 0.712 |
| At any time during study enrollment | | | | |
| Dialysis/renal replacement, *n* (%) | 60 (17.0) | 306 (13.9) | 366 (14.3) | 0.178 |
| Duration of mechanical ventilation in days | | | | |
| Median (Q1–Q3) | 8 (4–16) | 7 (3–12) | 7 (4–13) | 0.037[†] |
| Total range | 1–60 | 1–60 | 1–60 | |

[#]Invasive mechanical ventilation is an inclusion criteria.
[†]Using the log-transformed variable.

**TABLE 4.**
**Comparison of Antimicrobial Metrics Between Community and Academic ICUs**

| Antimicrobial Metrics | Community, *n* = 352 | Academic, *n* = 1,931 | Total, *n* = 2,283 | *p* Adjusted for Center |
|---|---|---|---|---|
| Antibiotics, antifungals, and antivirals | | | | |
| Days of therapy per 1,000 patient-days in ICU | 1,280.6 | 1,287.1 | 1,285.9 | 0.326[a] |
| Antimicrobial-free days per 1,000 patient-days in ICU | 290.4 | 288.2 | 288.6 | 0.994[a] |
| Defined daily dose per 1,000 patient-days in ICU | 1,668.4 | 1,806.3 | 1,780.5 | 0.333[a] |

[a]Using the square root transformed variable.

effect of probiotics on VAP between academic and community ICUs (test for interaction *p* value 0.0.575; **Appendix 3**, http://links.lww.com/CCX/B86).

### Adverse Events and Serious Adverse Events

Adverse events were uncommon in PROSPECT, and no difference was noted between community and academic ICUs (Table 5). Serious adverse events related to isolation of *L. rhamnosus* GG from a sterile site (or as the predominant organism in a nonsterile site) were found in 0 instances in community ICUs and in two instances (0.1% patients) in academic ICUs (Table 5).

### Trial Metrics

The informed consent rate was similar between community ICUs (85.9%) and academic ICUs (76.3%) ($p = 0.149$) (**Table 6**). The mean [SD] monthly enrolment rate for this trial (enrolments per month indexed to a 15-bed ICU) was similar in community ICUs (2.1 [1.4]) and academic ICUs (1.1 [0.7]) ($p = 0.119$). The percentage of patients coenrolled in other studies was similar between (8.0% in community ICUs vs 23.1% in academic ICUs; $p = 0.061$) (Table 6).

Protocol adherence was similar between community and academic ICUs (90.6% vs 91.6%; $p = 0.207$), and there was no difference in the percentage of patients without protocol violations (318 [90.3%] vs 2,052 [93.1%]; $p = 0.232$) (Table 6).

### Interpretation

In this large, multicenter, randomized controlled trial of probiotics versus placebo for mechanically ventilated patients, we identified key differences between

## TABLE 5.
### Comparison of Clinical Outcomes of Community and Academic ICUs

| Clinical Outcomes | Community, *n* = 352 | Academic, *n* = 2,203 | Total, *n* = 2,555 | *p* Adjusted for Center |
|---|---|---|---|---|
| Incident of ventilator-associated pneumonia, *n* (%) | 83 (23.6) | 474 (21.5) | 557 (21.8) | 0.882 |
| Incident of *Clostridioides difficile* infection, number of patients (%) | 4 (1.1) | 51 (2.3) | 55 (2.2) | 0.231 |
| Duration of ICU stay in days | | | | |
| Median (Q1–Q3) | 13 (8–23) | 11 (7–18) | 12 (7–19) | 0.012[a] |
| Total range | 2–447 | 1–346 | 1–447 | |
| Duration of hospital stay in days | | | | |
| Median (Q1–Q3) | 22 (12–42.5) | 22 (13–40) | 22 (13–40) | 0.726[a] |
| Total range | 3–630 | 1–493 | 1–630 | |
| Death in ICU, *n* (%), 95% CI | 107 (30.4), 25.8–35.4 | 452 (20.5), 18.9–22.3 | 559 (21.9) | 0.002 |
| Death in hospital, *n* (%), 95% CI | 143 (40.6), 35.6–45.8 | 574 (26.1), 24.3–27.9 | 717 (28.1) | <0.001 |
| AEs, *n* (%) | 2 (0.6) | 12 (0.5) | 14 (0.5) | 0.835 |
| SAEs, *n* (%) | 0 (0.0) | 2 (0.1) | 2 (0.1) | - |
| AE/SAE, *n* (%) | 2 (0.6) | 14 (0.6) | 16 (0.6) | 0.957 |

AE = adverse event, SAE = serious adverse events.
[a]Using the log-transformed variable.

## TABLE 6.
### Comparisons of Trial Metrics Between Community and Academic ICUs

| Trial Metrics | Community, *n* = 352 | Academic, *n* = 2203 | Total, *n* = 2555 | *p* Adjusted for Center |
|---|---|---|---|---|
| Total approached for consent, *n* | 410 | 2,888 | 3,298 | |
| Informed consent obtained, *n* | 352 | 2203 | 2,555 | |
| Consent rate (%) | 85.9 | 76.3 | 77.5 | 0.149 |
| Monthly enrollment per 15-bed ICU, mean (SD) | 2.1 (1.4) | 1.1 (0.7) | 1.3 (0.9) | 0.119[a] |
| Coenrolled, *n* (%) | 28 (8.0) | 508 (23.1) | 536 (21.0) | 0.061 |
| **Protocol adherence** | | | | |
| Either a) received study product or b) had a legitimate reason not to receive study product on ≥90% of ICU days, *n* (%) | 319 (90.6) | 2,019 (91.6) | 2,338 (91.5) | 0.207 |
| Received at least one dose of study product, *n* (%) | 348 (98.9) | 2,187 (99.3) | 2,535 (99.2) | 0.422 |
| No protocol violation[b], *n* (%) | 318 (90.3) | 2,052 (93.1) | 2,370 (92.8) | 0.232 |

[a]Center is the unit of analysis for month enrollment; therefore, a *t* test was performed without adjustment for center.
[b]No protocol violation refers to patients who experienced none of the following: 1) received dose(s) of wrong study product, 2) received dose(s) not staggered by 4 hr when concurrently receiving a *Lactobacillus*-sensitive oral antibiotic, and 3) received dose(s) of open label probiotic.

patients enrolled in academic and community ICUs that may affect the generalizability of results when trials were enrolled exclusively in academic hospitals. Patients recruited from community ICUs were, on average, older and more likely to have a medical admission diagnosis. Severity of illness and frequency of life support interventions (vasopressor and renal replacement therapy) were similar; however, the duration of mechanical ventilation, duration of ICU stay, and ICU and hospital mortality were higher among patients enrolled in community ICUs.

These findings have important implications for clinical trials as differences in patient characteristics, and outcomes may affect the efficacy of trial interventions. To ensure that trial results are generalizable, it is essential that enrolled populations resemble as closely as possible the eventual treatment population, by involving as broad a range of practice settings as possible. Depending on the characteristics of the patients and interventions being evaluated, investigators may want to consider subgroup analyses to explore the risk-benefit ratio of tested interventions in academic and community ICU populations.

The mortality difference observed between academic and community hospital patients in the present study is likely multifactorial. All of the community hospital ICUs that participated in PROSPECT were designated level 3 ICUs, caring for mechanically ventilated patients and run by specialist intensivists. Adjudicated rates of VAP and *C. difficile* infection were similar between academic and community ICUs, two important quality of care markers. However, there may have been differences in care processes between community and academic hospitals that were not adequately captured in this dataset. In addition, there may have been demographic differences between patients in academic and community hospitals that impact health outcomes but that were not captured in this study, including race, ethnicity, and socioeconomic status. For example, visible minority and recent immigrant populations are concentrated in suburban areas in Canada, which are primarily served by community hospitals (3, 4). This is not the first study to report a mortality difference between patients in community and academic hospitals in Canada. A recent study of out-of-hospital cardiac arrest patients reported higher mortality among patients admitted to non-teaching (community) hospitals relative to teaching (academic) hospitals (10). Mortality differences between teaching, minor-teaching and non-teaching hospitals have also been reported in the United States (11) as have mortality differences between hospitals that participate in research and those that do not, even when adjusted for teaching status (12, 13). Further studies will be required to elucidate the reasons for these important outcome differences, which may be complex.

Another key finding of this study was that trial metrics, including informed consent rate and enrollment rate, were similar between community ICUs and academic ICUs. Successful completion of randomized controlled trials depends upon efficiently screening patients and obtaining informed consent. Although community ICUs typically have less research experience than academic ICUs, their research teams were able to achieve similar recruitment rates. The high consent rate also indicates that patients in community ICUs were open to participating in clinical research. Recruitment in community ICUs may also be facilitated by the presence of fewer competing studies, leading to a more focused approach to a consent encounter.

Protocol adherence in PROSPECT was similar between community and academic centers. Protocol nonadherence can increase the risk of bias as well as diminish the feasibility of clinical trials (14, 15). The high level of protocol adherence confirms that community ICU participation is feasible and can augment recruitment without compromising trial quality. Furthermore, we found no difference in the rate of adverse events and serious adverse events between community and academic ICUs, which were very low overall.

The strengths of this study include its preplanned design and large sample size. Data on patient demographics, life supports, and treatments were collected prospectively, as were trial metrics and adverse events. Our analysis is limited by the nested observational design and the potential for ecological fallacy—that is, although differences between patients enrolled in community versus academic ICUs may reflect differences in populations, they could also reflect differences in patient selection for study enrollment in these centers. Moreover, since the number of community ICUs in PROSPECT was relatively small and there was a lack of rural hospital involvement, the results may not be generalizable to all Canadian community ICUs.

Engaging community ICUs in clinical research has the potential to increase study recruitment and improve the generalizability of study results. The Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial in the United Kingdom is an example of what can be achieved with broad engagement of community hospitals in research. RECOVERY harnessed the infrastructure of the National Institute of Health Research Clinical Research Network to recruit 11,000 patients from 176 hospital trusts in just 3 months, resulting in immediate worldwide practice-change for COVID-19 (16). The engagement of so many community hospitals accelerated recruitment and ensured that the study findings were applicable to a broad range of clinical settings. Our results show that community ICUs can conduct high-quality clinical research with excellent recruitment rates and protocol adherence. The differences observed in patient characteristics and outcomes between community and academic ICUs highlight the need for broader engagement of Canadian community ICUs in clinical research to ensure efficient study completion and generalizability of study results.

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## REFERENCES

1. Dimond EP, St. Germain D, Nacpil LM, et al: Creating a "culture of research" in a community hospital: Strategies and tools from the National Cancer Institute Community Cancer Centers Program. *Clin Trials* 2015; 12:246–56
2. DiDiodato G, DiDiodato JA, McKee AS: The research activities of Ontario's large community acute care hospitals: A scoping review. *BMC Health Serv Res* 2017; 17:566
3. Carmen T: Visible Minorities Now the Majority in 5 B.C. Cities. CIBC News. 2017. https://www.cbc.ca/news/canada/british-columbia/visible-minorities-now-the-majority-in-5-b-c-cities-1.4375858. Accessed September 20, 2022
4. Ontario Go: 2016 Census Highlights 2016. Available at: https://www.ontario.ca/document/2016-census-highlights#. Accessed September 20, 2022
5. Walker BB, Schuurman N, Wen CK, et al: Cancer resection rates, socioeconomic deprivation, and geographical access to surgery among urban, suburban, and rural populations across Canada. *PLoS One* 2020; 15:e0240444
6. Kapral MK, Hall R, Gozdyra P, et al: Geographic access to stroke care services in rural communities in Ontario, Canada. *Can J Neurol Sci* 2020; 47:301–308
7. Johnstone J, Meade M, Lauzier F, et al; Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT) Investigators and the Canadian Critical Care Trials Group: Effect of probiotics on incident ventilator-associated pneumonia in critically ill patients: A randomized clinical trial. *JAMA* 2021; 326:1024–1033
8. Canadian Institute for Health Information: *Hospital Beds Staffed and in Operation, 2020–2021*. Canadian Institute for Health Information, Ottawa, ON, 2022
9. Canadian Institute for Health Information: *Hospital Beds Staffed and in Operation, 2018–2019*. Canadian Institute for Health Information, Ottawa, ON, 2020
10. Czarnecki A, Qiu F, Koh M, et al: Association between hospital teaching status and outcomes after out-of-hospital cardiac arrest. *Circ Cardiovasc Qual Outcomes* 2019; 12:e005349
11. Burke LG, Frakt AB, Khullar D, et al: Association between teaching status and mortality in US hospitals. *JAMA* 2017; 317:2105–2113
12. Majumdar SR, Roe MT, Peterson ED, et al: Better outcomes for patients treated at hospitals that participate in clinical trials. *Arch Intern Med* 2008; 168:657–662
13. Shahian DM, McCloskey D, Liu X, et al: The association of hospital research publications and clinical quality. *Health Services Res* 2022; 57:587–597
14. Dodd S, White IR, Williamson P: Nonadherence to treatment protocol in published randomised controlled trials: A review. *Trials* 2012; 13:84
15. Haynes RB, Dantes R: Patient compliance and the conduct and interpretation of therapeutic trials. *Control Clin Trials* 1987; 8:12–19
16. RECOVERY Collaborative Group: Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med* 2020; 384:693–704