Research

The response of Canada's clinical health research ecosystem to the COVID-19 pandemic

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Abstract

Background: The response of Canada's research community to the COVID-19 pandemic provides a unique opportunity to examine the country's clinical health research ecosystem. We sought to describe patterns of enrolment across Canadian Institutes of Health Research (CIHR)–funded studies on COVID-19.

Methods: We identified COVID-19 studies funded by the CIHR and that enrolled participants from Canadian acute care hospitals between January 2020 and April 2023. We collected information on study- and site-level variables from study leads, site investigators, and public domain sources. We described and evaluated factors associated with cumulative enrolment.

Results: We obtained information for 23 out of 26 (88%) eligible CIHR-funded studies (16 randomized controlled trials [RCTs] and 7 cohort studies). The 23 studies were managed by 12 Canadian and 3 international coordinating centres. Of 419 Canadian hospitals, 97 (23%) enrolled a total of 28 973 participants — 3876 in RCTs across 78 hospitals (median cumulative enrolment per hospital 30, interquartile range [IQR] 10–61), and 25 097 in cohort studies across 62 hospitals (median cumulative enrolment per hospital 158, IQR 6–348). Of 78 hospitals recruiting participants in RCTs, 13 (17%) enrolled 50% of all RCT participants, whereas 6 of 62 hospitals (9.7%) recruited 54% of participants in cohort studies.

Interpretation: A minority of Canadian hospitals enrolled the majority of participants in CIHR-funded studies on COVID-19. This analysis sheds light on the Canadian health research ecosystem and provides information for multiple key partners to consider ways to realize the full research potential of Canada's health systems.

Providing "best care at lower cost" is the goal of a learning health system.[1] Accomplishing this goal hinges on an efficient health research ecosystem, and a cohesive national research portfolio that is deliberately planned to address national health priorities, while also offering a fertile environment for discoveries.[1–3] Clinical studies that are well suited to inform clinical practices share key features. They address a health problem that is important and reflects patient priorities, follow a rigorous evidence synthesis that informs the need for new evidence, enrol a large number of participants, occur in settings where the interventions would be implemented, incorporate cost-effectiveness evaluations to inform system-level decisions, are feasible, and are founded on transparent and rigorous methods.[3] Most studies do not meet these criteria.[4–8] A country's ability to produce practice-changing evidence depends on the infrastructure and processes that allow researchers to identify and approach potential research participants, deliver the interventions under evaluation, and collect research data and biological specimens according to the protocol.[9]

One indicator of the success of clinical research is the enrolment of a sufficient number of people to represent the country's diversity, and to detect, or rule out, realistic clinical effects within a reasonable time frame.[6,10] The response of Canada's research

community to the COVID-19 pandemic provided a unique opportunity to examine clinical research output and the effect of national public investments intended to enhance research productivity. To effectively and efficiently roll out practice-changing clinical research, clinical programs need to work collaboratively with researchers. However, several barriers may impede the integration of studies into clinical care settings. Rates of recruitment into clinical studies can provide insight into issues that affect patient participation and can help improve accountability to research funding agencies. Such knowledge was critical during the global COVID-19 pandemic, when generating knowledge about new and existing therapeutics was essential to inform clinical care. Funding agencies such as the Canadian Institutes of Health Research (CIHR) need to make sure that every dollar spent will produce the highest-quality research output.[11,12] Ensuring that Canada has appropriate mechanisms of monitoring and accountability of major research programs is therefore important.

Our primary objective was to describe enrolment across CIHR-funded COVID-19 investigations that prospectively recruited patients in hospital during the pandemic. Secondary objectives were to describe the characteristics of included studies and participating hospitals, illustrate the network formed by coordinating centres and hospitals participating in included studies, and identify factors that were associated with enrolment.

Methods

Study design and setting

This system-level program evaluation was conducted by the Canadian Clinical Research Network (CCRN, https://www.ccrn-rrcc.ca/), a publicly funded organization established to document the conduct of clinical research across the country and to characterize the supporting research infrastructure within publicly funded Canadian acute care hospitals. This analysis covers the period of enrolment in included studies between January 2020 and April 2023. Data collection for this analysis occurred between Jan. 11, 2021, and Apr. 20, 2023. Study enrolment data were updated monthly and site-level data were updated annually.

Data sources

We screened the CIHR Funding Decisions Database and included randomized controlled trials (RCTs) and prospective cohort studies exclusively enrolling patients admitted to hospital with COVID-19.[13] We contacted the lead investigators of the eligible studies directly and via research networks when studies were conducted under the auspices of specific networks (e.g., the Canadian Critical Care Trials Group, Canadian Venous Thromboembolism Research Network, Association of Medical Microbiology and Infectious Disease Canada, Sepsis Canada, Canadian Network of COVID-19 Clinical Trials Networks, Réseau Québécois COVID–pandémie), and site investigators participating in these studies to collect additional data. We adapted information from a published cross-sectional study of Canadian hospitals (e.g., hospital addresses) to identify and count all Canadian acute care hospitals.[14]

Data collection

Studies

We initially collected information on each study from trial registries, published protocols, and study websites. Subsequently, we interviewed the investigators to collect information that was not in the public domain (Appendix 1, Figure S1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.230760/tab-related-content). Investigators also shared prospective enrolment data detailing the number of participants recruited at each hospital at regular intervals (weekly or monthly, depending on the study team capacity) or in real time via automatic notifications from randomization systems. Because we did not collect patient identifiers, participants could be co-enrolled in more than 1 study. We treated domains within platform trials as stand-alone studies. When studies recruited participants in other countries using non-CIHR funds (e.g., A Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia [REMAP-CAP], Canadian Treatments for COVID-19 [CATCO], Short Period Incidence Study of Severe Acute Respiratory Infection [SPRINT-SARI]), we collected data only in Canada as this was what CIHR funding supported. In contrast, when CIHR funding was used to recruit patients in other countries (e.g., Antithrombotic Therapy to Ameliorate Complications of COVID-19 [ATTACC], Host Response Mediators in Coronavirus (COVID-19) Infection — Is There a Protective Effect of Losartan and Other ARBs on Outcomes of Coronavirus Infection? [ARBs CORONA], Awake Prone Position in Hypoxemic Patients With Coronavirus Disease 19 [COVI PRONE]), we collected data on recruitment from other countries as well. For each study, we characterized the following: funding source, coordinating centre (defined as organizations, typically housed within universities or research centres, that oversee the design and conduct of multicentre studies across sites), research question, and consent model (e.g., a priori, deferred). Study-specific information (i.e., characteristics and enrolment data) was validated by lead investigators, and we invited coordinating centres to review the information on a publicly available CCRN dashboard (https://www.ccrn-rrcc.ca/); we issued a revised report in December 2022. We also recorded all study-related publications, preprints, and citations until Oct. 31, 2023.

Participating hospitals

For each hospital, we collected number of funded beds (in acute wards and, where applicable, in intensive care units [ICUs]), population (adult, pediatric, or both), and academic status (as defined by local collaborators). After receiving their names and email addresses from principal investigators, we sent local investigators and research coordinators an email describing the project and inviting them to share more information on their local capacity for clinical research participation. Using piloted data collection forms, the CCRN team conducted structured interviews via various virtual meeting platforms (at the discretion of interviewees) with local investigators and research coordinators to collect information on academic status, number of research staff supporting clinical research, their experience with specific

aspects of clinical study conduct (e.g., deferred consent, co-enrolment of a patient into more than 1 study), hospital departments within which clinical research could be conducted during the pandemic (e.g., ICUs, acute wards, emergency departments), the availability of pharmacy staff and infrastructure for research, and capacity to enrol outside conventional working hours and on weekends (Appendix 1, Figure S1). When local investigators and research coordinators were unable to provide this information, other local partners were interviewed (e.g., hospital administrators). People who shared information on the research infrastructure of participating hospitals received a site report that allowed them to validate or correct information, or provide further details.

Analyses

Descriptive analyses

We report dichotomous variables as counts and percentages, and continuous variables as means (standard deviations) or medians (interquartile ranges [IQRs]), as appropriate. We ranked hospitals by their cumulative enrolment across RCTs and cohort studies, separately. To account for hospital size, we also produced rankings using cumulative enrolment per total number of hospital beds.

Modelling enrolment according to study and site characteristics

We investigated the relationship between study and site characteristics and enrolment in an exploratory fashion using hierarchical Bayesian Poisson regression.[15] To investigate both site and study characteristics, we included only study–site pairs where 1 or more patients were enrolled. Many sites did not activate any CIHR-funded studies on COVID-19, so those sites could not be included in an analysis that considered study–site pairs. Sites that did not activate at least 1 CIHR-funded COVID-19 study had extensive missing data, so further investigation of those sites is planned for future work when more complete data can be gathered. The outcome for this analysis was based on the number of patients enrolled in each study at each site. We accounted for the clustered nature of the data with random intercepts for both studies and sites. In a sensitivity analysis, we included study–site pairs that activated a CIHR-funded COVID-19 study but enrolled no patients to that study at that site. Further details about both analyses are available in Appendix 1, Figure S2.

To choose predictors for this model, we generated a conceptual diagram of the relationship between measured variables and study enrolment at a particular site (Appendix 1, Figure S3). Study characteristics included study type (observational or interventional) and number of coordinating centres (≥ 1). Site characteristics included geographic region, number of active prospective CIHR-funded studies on COVID-19 at that site, number of hospital beds, university affiliation, and research infrastructure (availability of a research pharmacy, availability of research staff after hours, total full-time equivalents of research staff, previous experience with deferred consent, and previous experience with co-enrolment). We estimated the enrolment ratio corresponding to each independent variable introduced in the model (i.e., the relative change in enrolment attributed to each independent variable). We also estimated the median enrolment by site (or study), which describes the median relative change in enrolment when switching from a site (or study) with lower enrolment to a site (or study) with higher enrolment (i.e., the residual variation not explained by the model).[16] We did not test for interactions, given sample size limitations.

For descriptive analyses, we used complete case analysis. For the Bayesian hierarchical Poisson regression analysis and its sensitivity analysis, we addressed missing data through multiple imputation with chained equations using 10 imputed data sets.[17] We analyzed each data set separately and combined the posterior distributions to ensure that uncertainty owing to missingness was propagated through to the final results. Further details about missing data treatment are available in Appendix 1.

We coded the model in R using the brms package.[18,19] We used standard normal distributions as priors for the logarithm of the enrolment ratio (ER; weakly skeptical priors), and half-normal distributions with a standard deviation of 0.5 for the priors of the random intercept variance. The model was fit using 4 chains and 1000 post-warm-up iterations. We summarized posterior distributions with the mean and 95% credible interval (CrI).

Ethics approval

The study corresponds to a system-level program evaluation, which does not require ethics review under the Tri-Council Policy Statement 2, Articles 2.2–2.4.

Results

We received enrolment data for 23 out of 26 (88.5%) CIHR-funded clinical studies that exclusively enrolled patients admitted to hospital for COVID-19 (16 clinical trials and 7 cohort studies, shown in Appendix 1, Figure S1 and Tables S1 and Table S2). The lead investigators of 3 eligible RCTs did not respond (n = 2) or declined participation (n = 1).

We identified a total of 419 Canadian hospitals, distributed across 10 provinces and 3 territories (Figure 1; Table 1; and Appendix 1, Table S3), including 291 (69.5%) community hospitals, 65 (15.5%) university-affiliated, and 35 (8.4%) university hospitals (academic status was missing for 28 [6.7%] hospitals that did not enrol participants in included studies). We contacted all hospitals to seek information on their local capacity for research and received 205 responses (48.9%). Of the hospitals that enrolled at least 1 participant in at least 1 of the 23 CIHR-funded studies on COVID-19, 74 (76.3%) provided and validated the information on their local research infrastructure (Appendix 1, Figure S1).

Hospitals that recruited at least 1 patient to a study (n = 97, Table 1) employed a median of 3.5 full-time equivalent research staff (IQR 1.2–8.8) to enrol participants in a median of 2 (IQR 1–4) CIHR-funded studies. Research teams were composed of research coordinators (median 1.7 full-time equivalent, IQR 0.6–4.6), but some research teams also employed administrative assistants, students, or volunteers. Research teams at 33 hospitals (49.3%) were available outside conventional working hours

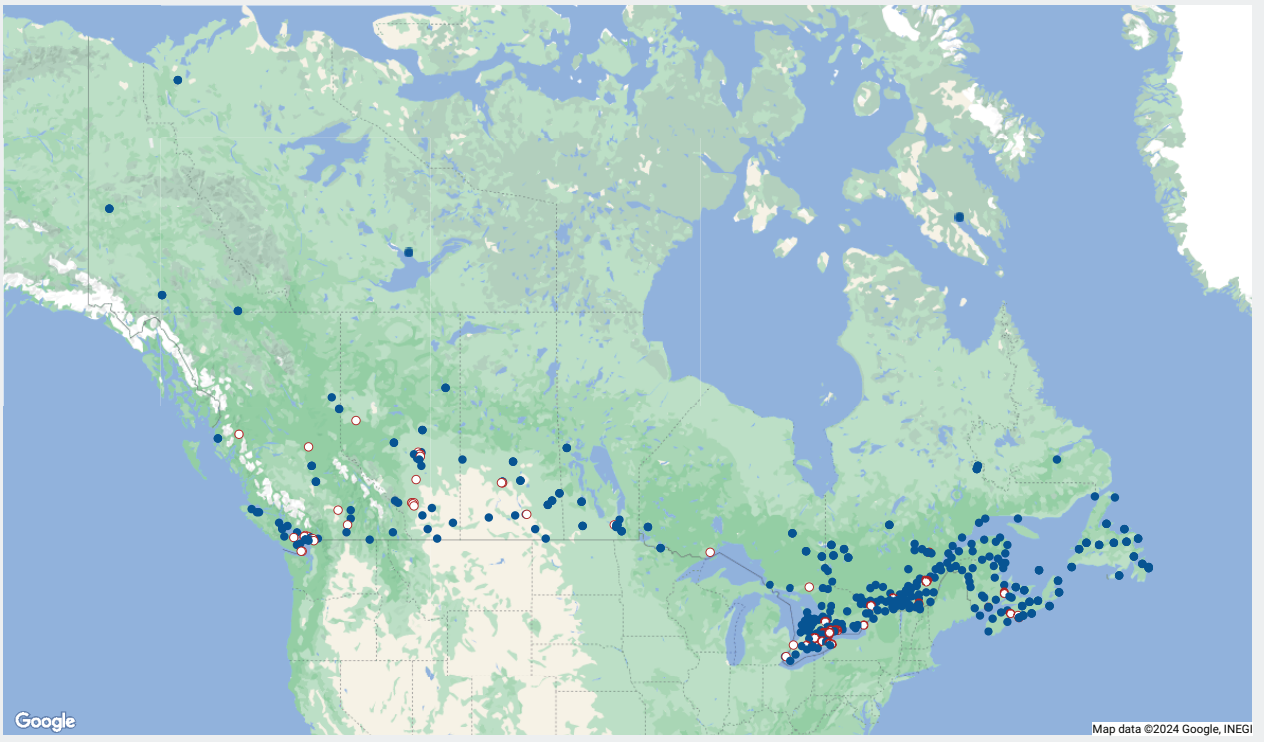

Figure 1: Geographical distribution of Canadian hospitals. Blue dots represent hospitals that did not recruit participants in any of the studies included in this analysis. Red circles represent hospitals that enrolled at least 1 participant in at least 1 study included in this analysis.

and on weekends, and reported experience with co-enrolment of patients in multiple studies at 56 (82.4%) hospitals, and with deferred consent at 53 (77.9%) hospitals. A research pharmacy service was available at 65 (95.6%) hospitals.

During the period covered by this analysis, 97 recruiting hospitals enrolled a total of 28 973 participants in CIHR-funded COVID-19 research: 3876 in RCTs across 78 hospitals (median cumulative enrolment per hospital 30, IQR 10–61) and 25 097 in cohort studies across 62 hospitals (median cumulative enrolment per hospital 158, IQR 46–348). For 4 RCTs (ARBs CORONA [unpublished], ATTACC,[20,21] Convalescent Plasma for Hospitalized Adults with Acute COVID-19 Respiratory Illness [CONCOR],[22] and COVI-Prone[23]), CIHR funds supported enrolment of participants from international sites (median proportion of international enrolment 59%, IQR 48%–66%).

The percentage of hospitals recruiting in CIHR-funded studies on COVID-19 varied across provinces (Table 1). Of 78 hospitals recruiting participants in RCTs, 13 (17%) recruited 50% of all RCT participants (Figure 2), whereas 6 of 62 hospitals (9.7%) recruited 54% of participants in cohort studies (Appendix 1, Figure S4).

The 23 studies were managed by 12 Canadian and 3 international coordinating centres. Thirteen studies were managed by 2 or more coordinating centres (12 RCTs, 1 cohort).

As of Oct. 31, 2023, the main results of 12 of the 16 RCTs[20–28] (75%) and 4 of the 7 cohort studies[29–33] (57.1%) had been published. References and citation metrics appear in Appendix 1, Table S4.

Site-level enrolment in a given study varied according to both study and site characteristics (Table 2 and Figure 3). Higher enrolment was associated with studies managed by a single, as opposed to more than 1, coordinating centre (posterior mean ER 2.70, 95% credible interval [CrI] 1.12–6.51), and observational as opposed to interventional studies (ER 4.67, 95% CrI 1.79–11.71). Among site characteristics, an increase in number of hospital beds was possibly associated with higher enrolment (per additional 100 beds, ER 1.09, 95% CrI 0.95–1.26; 88.5% probability of ER > 1). Variation across provinces was similar, with wide credible intervals. No research infrastructure characteristics were associated with enrolment but the model showed significant unexplained variability at both study level (median ER 2.61, 95% CrI 2.30–3.01) and site level (median ER 2.47, 95% CrI 2.30–2.67) (i.e., the median change in enrolment rate between 2 studies, after accounting for all other variables included in the analysis, was a factor of 2.61; the median enrolment rate change between 2 otherwise identical sites enrolling to the same study, after accounting for all other variables included in the analysis, was a factor of 2.47). In both cases, the difference in ER by study or site was much larger than the difference by many of the other model parameters, such as research infrastructure or geographic variables. We did not find evidence for collinearity in the posterior distribution of model parameters (Appendix 1, Figure S5). Results were similar in a sensitivity analysis including study–site pairs without patient enrolment (Appendix 1, Figure S2).

Table 1: Acute care hospitals in Canada (*n* = 419) and participant enrolment in a CIHR-funded clinical study on COVID-19 (randomized controlled trials or cohort studies)*

Characteristic	Hospitals in Canada that enrolled at least 1 participant *n* = 97	Hospitals in Canada that enrolled no participants *n* = 322
No. of hospitals		
University	25	10
University-affiliated	39	26
Community	33	258
NA	0	28
No. of beds		
Median (IQR)	422 (280–521)	76 (35–166)
NA	1	75
Total	40 975	28 012
Research staff participating in CIHR-funded studies on COVID-19 (FTE)		
Median (IQR)	1.25 (0.0–5.5)	0 (0–0)
NA	27	182
Research team available outside working hours	Yes = 33, No = 34, NA = 30	Yes = 22, No = 122, NA = 178
Local experience with deferred consent	Yes = 53, No = 15, NA = 29	Yes = 29, No = 117, NA = 176
Local experience with co-enrolment	Yes = 56, No = 12, NA = 29	Yes = 30, No = 114, NA = 178
Research pharmacy	Yes = 65, No = 3, NA = 29	Yes = 32, No = 114, NA = 176

Province	Enrolled at least 1 participant *n* = 97	Enrolled no participants *n* = 322	Percentage of hospitals participating in studies at the provincial level	Provincial distribution of hospitals participating in studies *n* = 97
Alberta	13	17	43.3	13.4
British Columbia	13	31	29.5	13.4
Manitoba	3	11	2.1	3.1
New Brunswick	2	20	9.1	2.1
Newfoundland and Labrador	2	18	10	2.1
Nova Scotia	1	19	5	1
Ontario	43	75	36.4	44.3
Quebec	18	109	14.2	18.5
Saskatchewan	2	14	12.5	2.1

Note: CIHR = Canadian Institutes of Health Research, FTE = full-time equivalent, IQR = interquartile range, NA = not available.
*The full list of hospitals is available in Appendix 1, Table S3 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.230760/tab-related-content).

Interpretation

We found that CIHR funded 26 clinical studies that exclusively enrolled patients admitted to hospital for COVID-19 over a 3-year period. Those studies recruited participants in 97 of the 419 Canadian acute care hospitals, but most of the recruitment occurred in 20 sites. Given the scope of this study (i.e., COVID-19 pandemic), the top-enrolling sites arguably constitute the research-ready Canadian hospitals capable of rapidly contributing to the acquisition of data in response to a pandemic.[34,35] Our findings indicate that it is feasible to monitor the conduct of health research occurring within Canada's health systems and may provide valuable information on Canada's health research ecosystem as a whole. Our study underscores the value of prospectively monitoring the contributions of health care institutions to the national research endeavour. In other countries, prospective monitoring is promoted in an attempt to optimize research productivity, efficiency, and representativeness.[36–40] In the United Kingdom, government initiatives to support and incentivize the integration of clinical research within the health system also enable monitoring of prioritized studies and their impact on the UK health system.[41] For example, 13% of all UK patients admitted to hospital with COVID-19 in the first months of the pandemic participated in the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial,[42] and about 20% of patients treated in

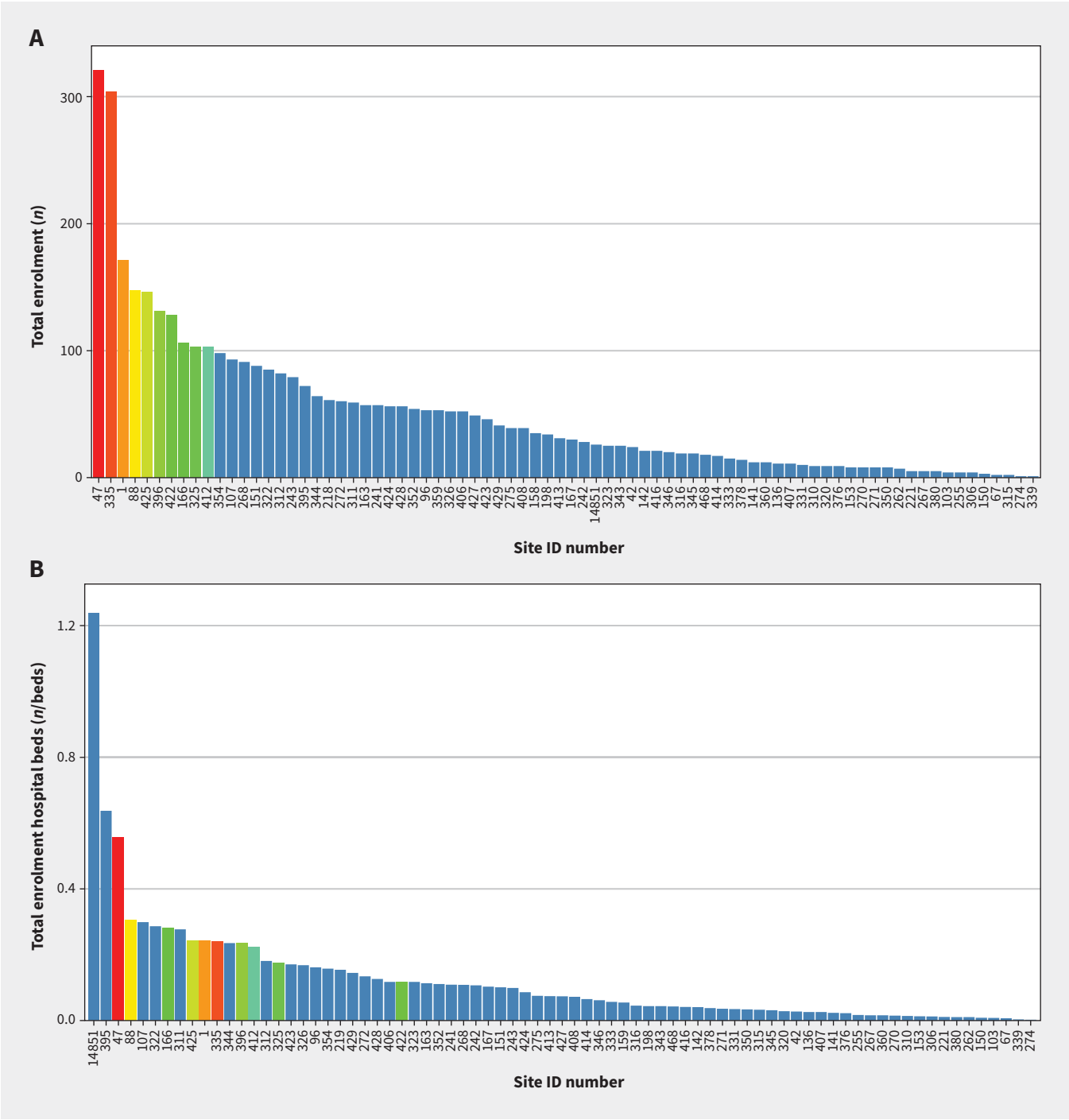

Figure 2: Hospitals ranked by (A) cumulative enrolment in randomized controlled trials (RCTs) and (B) cumulative enrolment in RCTs per number of hospital beds. Each bar represents a site that enrolled at least 1 participant in 1 of the Canadian Institutes of Health Research–funded RCTs that evaluated therapies for COVID-19. In panel A, the Y axis corresponds to the cumulative enrolment at sites ranked from left (highest) to right (lowest). The top 10 enrolling sites are tagged by a different colour to enable their identification in panel B, where site ranking is a function of cumulative enrolment by total number of hospital beds.

ICUs were enrolled in REMAP-CAP.[43] In Australia, reports on research conducted during the pandemic suggested that a failure to monitor and regulate research in real time led to the multiplication of overlapping and underpowered studies.[44] In Canada, more work is needed to ascertain the total burden of disease, which would provide a better measure of research efficiency.

We used the term "ecosystem" because we consider that researchers, coordinating centres, and hospitals coexist in an environment with limited resources. Like species within an ecosystem, some nodes within this network collaborate synergistically — some compete; some thrive, others do not. If this work expanded to include all research conducted across Canadian

publicly funded health systems, it could provide a national benchmark for capacity-building and potentially inform strategies to optimize collaboration between the large number of health institutions, research sponsors, and coordinating centres that constitute the pillars of the Canadian clinical research ecosystem. In this regard, research funders, health system administrators, health policy and systems experts, and other partners could contemplate a number of complementary strategies, such as increasing the number of participating sites, implementing interventions designed to maximize enrolment at sites that are already research active, or regulating and limiting the inflow of studies competing for the same patient population. The effectiveness of these strategies may depend on the context (e.g., health crises), and the scientific area (e.g., primary care v. specialized care in hospitals), but monitoring the productivity and impact of the research endeavour would allow stakeholders to evaluate and manage their investments in research.

Limitations

We focused on CIHR-funded studies that prospectively enrolled patients admitted to hospital with COVID-19, and therefore our findings may not accurately represent the productivity of Canada's entire clinical health research ecosystem. In addition, without a comprehensive and publicly available repository of studies on COVID-19 conducted across Canada's health systems, CIHR's publicly available Funding Decisions Database proved the only reliable source of a traceable COVID-19 research portfolio, which limits our ability to draw conclusions regarding Canada's contribution to COVID-19 research that was not funded by CIHR. We also chose CIHR for this inaugural analysis because, as a steward of Canada's investments in health research, it may be more sensitive and receptive than other funders when it comes to matters of research value and accountability.[11,12] We focused on prospective studies because they provide a better measure of research integration within health systems than retrospective studies, which are often feasible through data linkage even in the absence of a clinical research workforce within hospitals. The fact that research teams associated with 3 CIHR-funded studies on COVID-19 did not contribute data means that we have underestimated the productivity of the Canadian health research ecosystem. We did not evaluate whether study participants accurately represented the target population of patients in Canada hospitalized for COVID-19 because this would require granular primary individual patient data that were not collected for this analysis. We also did not ascertain to what degree individual studies answered their primary research questions because this would entail a subjective assessment of the study results and their precision, ideally in the context of the existing body of literature, which was beyond the scope of our work.

We also acknowledge limitations regarding the hospital component of this analysis. Most Canadian hospitals that did not participate in CIHR-funded COVID-19 studies did not respond to our request for more information on their research infrastructure, which limited our ability to compare the characteristics of hospitals as a function of their participation in

Table 2: Unadjusted results by study and site characteristics*

Characteristic	Median enrolment (IQR)
No. of coordinating centres	
1	24 (7–67)
2	17 (5–66)
3	5 (2–16)
Study type	
Interventional	10 (3–24)
Observational	72 (13–262)
Site type	
University	16 (4–49)
University-affiliated	14 (5–46)
Community	18 (5–48)
Total FTEs	
< 4 FTEs	13 (4–54)
≥ 4 FTEs	16 (3–52)
Missing	20 (8–30)
Coordinator available after hours	
No	12 (3–43)
Yes	20 (4–57)
Missing	17 (7–33)
Experience with co-enrolment	
No	7 (4–48)
Yes	16 (4–48)
Experience with deferred consent	
No	8 (4–46)
Yes	16 (4–54)
Missing	16 (7–31)
No. of beds	
< 300	10 (4–25)
300–499	16 (4–73)
≥ 500	16 (5–48)
Missing	26 (15–36)
Research pharmacy available	
No	6 (3–14)
Yes	16 (4–53)
Missing	18 (7–31)
Region	
Ontario	14 (5–52)
Alberta	27 (10–45)
Atlantic	24 (5–33)
British Columbia	16 (4–168)
Manitoba	13 (2–26)
Quebec	14 (4–35)
Saskatchewan	5 (3–16)

Note: FTE = full-time equivalent, IQR = interquartile range, total FTEs = the total full-time equivalents of research staff working at that institution.
*This table shows the median enrolment (IQR in parentheses) for study–site pairs grouped according to study or site characteristics.

Predictor	Enrolment ratios (95% CrI)
Unexplained variability	
Median enrolment ratio* by site	2.66 (2.46–2.90)
Median enrolment ratio* by study	2.71 (2.37–3.14)
Hospital size	
No. of beds, 100s	1.09 (0.95–1.26)
> 5 active studies	1.89 (1.08–3.29)
Site research infrastructure	
Co-enrolment experience	0.79 (0.27–2.29)
Deferred consent experience	0.94 (0.47–1.86)
Coordinator available	0.98 (0.55–1.80)
Total FTEs	0.98 (0.94–1.03)
Research pharmacy	0.99 (0.30–3.31)
Site affiliation	
University hospital	Ref.
University-affiliated hospital	1.44 (0.68–3.09)
Community hospital	1.57 (0.78–3.02)
Region of site	
Alberta	0.85 (0.44–1.64)
BC	0.93 (0.41–2.13)
Ontario	Ref.
Atlantic	1.04 (0.29–3.18)
Manitoba	1.10 (0.36–3.33)
Saskatchewan	1.20 (0.33–4.04)
Quebec	1.54 (0.80–2.91)
Study characteristics	
1 v. ≥ 2 coordinating centres	2.70 (1.12–6.51)
Observational v. interventional	4.67 (1.79–11.71)

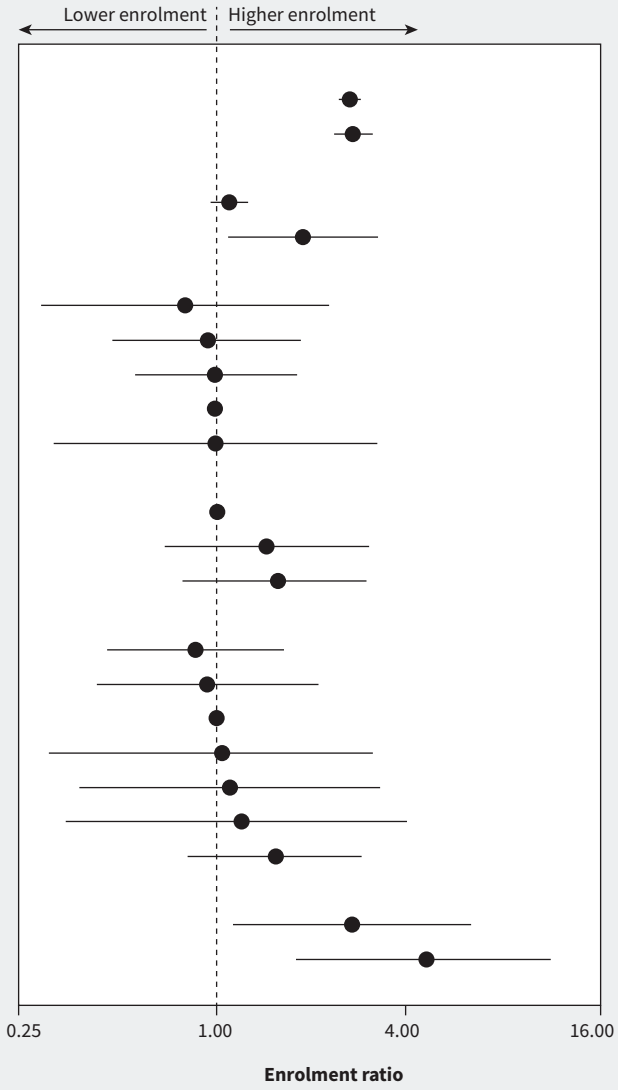

Figure 3: Forest plot of exploratory modelling of enrolment according to study and site characteristics. *Median enrolment ratio by site (or study) describes the median relative change in enrolment when switching from a site (or study) with lower enrolment to a site (or study) with higher enrolment. It captures the residual variation not explained by the model. Note: CrI = credible interval, FTE = full-time equivalent, Ref. = reference. See Related Content tab for accessible version.

research. Because research-active hospitals were larger, focusing on the number of enrolling hospitals rather than the number of beds accounted for by enrolling versus nonenrolling hospitals may overestimate the untapped research potential. Model precision is contingent on the number of actively enrolling hospitals. The current model, based on information collected from 97 enrolling hospitals, yielded credible intervals that are wide, indicating low precision. Future iterations of this work beyond COVID-19 may yield more precise estimates. The description of site-level research infrastructure relied on concepts that remain ill defined (e.g., academic status) and dynamic (e.g., fluxes in the research workforce). Accordingly, characterization of the site-level research infrastructure should be considered a best estimate at 1 time point. In addition, research infrastructure is often specific to units and wards rather than hospitals. As such, the data reported herein should be interpreted as a description of the research infrastructure mobilized during a brief period for participation in CIHR-funded studies on COVID-19. We treated domains within platform trials as stand-alone studies and reported the enrolment of research participants rather than individual patients. In both instances, this overestimated the number of individuals enrolled in studies, because without individual patient data, we could not identify individuals enrolled in multiple studies. However, because our focus was on the ecosystem's ability to answer research questions, the number of participants was an appropriate unit of analysis and study results generally ignore co-enrolment.

Conclusion

This study describes the contribution made by Canada's clinical research ecosystem to CIHR-funded studies on COVID-19 during the pandemic and provides information for multiple key partners to consider ways to realize the full research potential of Canada's health system.

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