


## RESEARCH ARTICLE

# Examining mechanisms for gender differences in admission to intensive care units

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## Abstract

**Objective:** To evaluate whether the male predominance of older people admitted to intensive care units (ICUs) is due to gender differences in the presence of spouses, partners, or children; rates of gender-specific disease; or triage decisions made by health system personnel.

**Data Sources and Collection:** Three population-based datasets, 2004-2012, of Canadians  $\geq 65$  years: provincial health care data from Manitoba ( $n = 250\ 190$ ) and national data of nursing home residents ( $n = 133\ 982$ ) and community-based home-care recipients ( $n = 210\ 090$ ).

**Study Design:** Retrospective observational study, using multivariable Cox proportional hazards and logistic regression.

**Principal Findings:** Males predominated in ICU admissions: from Manitoba (hazard ratio [HR] = 1.87, 95% CI = 1.80-1.95), nursing homes (HR = 1.47, 1.35-1.60), and homecare (odds ratio = 1.14, 1.11-1.17). Adjustment for spouses, partners, and children did not attenuate this effect. The HR for gender was lower by 13.5 percent, relative, after excluding ICU care for cardiac causes. Male predominance was not present during a second ICU admission among survivors of a first ICU-containing hospitalization (HR = 1.07, 0.96-1.20).

**Conclusions:** In three older cohorts, the male predominance of ICU admission was not explained by gender differences in the presence of a spouse, partner, or children, or cardiac disease rates. The third finding suggests that triage bias is unlikely to be responsible for the male predominance.

## KEYWORDS

acute inpatient care, epidemiology, gender/sex differences in health and health care

## 1 | INTRODUCTION

Since the 1980 publication of the Black Report,<sup>1</sup> there has been a growing awareness of social inequalities in health and health care use. Although ethnicity, age, socioeconomic status (SES), and others factors associated with health inequality have been identified,<sup>2-4</sup> the

mechanisms by which these factors work remain unclear. One example is the reported gender-related difference in admission to intensive care units (ICUs). Despite the fact that women greatly outnumber men in older age-groups, substantially more older men than older women are admitted to ICUs.<sup>5-9</sup> This finding is present even after adjustment for differing rates of critical illness between older men and women.<sup>10</sup>

Various determinants of health ranging from social and economic to physical, biological, and individual behaviors could possibly contribute to this male predominance in ICU admissions (Appendix S1), of which three are explored. First, as women generally outlive men, toward the end of life older women have less close family social support due to higher rates of widowhood.<sup>11-13</sup> This loss of social support may mean that older women have less decisional support or advocacy for ICU admission when they are critically ill. And the absence of social support can decrease willingness to receive aggressive medical care.<sup>14-17</sup> Second, disorders that cause critical illness, prominently including cardiovascular diseases,<sup>18</sup> can present differently between genders,<sup>19</sup> which could lead to differing intensities of health care use. Third, women are reported to receive less aggressive medical care than men,<sup>20</sup> which could be due to gender-based decisions made by medical personnel whose decisions also regulate eligibility for ICU admission, or due to gender-related differences in patient preferences for aggressive care.

The goal of this study was to examine three potential underlying mechanisms that may explain gender-related disparities in ICU admission: (a) close family social support through the presence of a spouse, partner, or children; (b) rates of cardiac disease; and (c) gender-based triage decisions. Hypothesis 1 was that the male predominance in ICU admissions would be attenuated by accounting for the more common absence of a close family social support network among older women. Hypothesis 2, derived from evidence showing that age-specific rates of cardiac disease are 40-50 percent higher in older men than women,<sup>21</sup> was that the male predominance would be attenuated by excluding ICU admissions for major categories of cardiac-related critical illness. Hypothesis 3 was that a similar male predominance of ICU admissions would be present for subsequent ICU admissions among individuals who survived a prior ICU-containing hospitalization. This hypothesis is based on the presumption that gender-based triage decisions would be consistent across first and subsequent hospitalizations. The study received ethics approval from the institutional review boards at the Universities of Manitoba and British Columbia, and Sunnybrook Health Sciences Centre (Toronto).

## 2 | METHODS

Three cohorts of individuals who were  $\geq 65$  years of age, April 1, 2004, to March 31, 2012, were analyzed to address the stated hypotheses. One was a general population-based cohort from the province of Manitoba (GP), and the others were national population-based Canadian cohorts of individuals who received either home care (HC) or resided in a nursing home (NH) facility. The Manitoba cohort was capable of assessing all three hypotheses, including exploring the role of children on ICU admission. The NH and HC cohorts were included to determine whether the observed findings varied by health service sector. All analyses used multivariable regression to assess whether the effect of gender on admission to an ICU was modified by the factors evaluated in our hypotheses. Cases

with missing data elements were excluded from the analyses. All analyses were done using SAS versions 9.4 and Enterprise Guide 6.1 (SAS Institute Inc). *P*-values  $< .05$  were considered to be significant.

### 2.1 | GP Cohort

This cohort consisted of all Manitoba residents who were  $\geq 65$  years of age at any time during the study period. Using data from the Manitoba Centre for Health Policy,<sup>22</sup> this used the Research Registry File (RRF), which contains information about all Manitoba residents. Four additional linked databases used for this cohort were as follows: (a) the hospital Discharge Abstract Database (DAD); (b) the Long-term Care Database; (c) the Public Use Census Data; and (d) the Drug Program Information Database (DPIN).

The DAD contains administrative hospital discharge data in a format standardized throughout Canada.<sup>23,24</sup> It identifies diagnoses, procedures, the timing of hospital admission and discharge, hospital disposition, and accurately identifies the existence and timing of ICU admissions.<sup>25</sup> The RRF includes postal code of residence and identifies spouses and children, when people move in or out of province, and date of death. The Long-term Care Database identifies persons who live in nursing homes. Canadian Census Data identifies various area-level indicators of socioeconomic status (SES) by postal code.<sup>26</sup> The DPIN includes all outpatient pharmacy prescriptions filled in the province.

Marital status and children are identifiable in Manitoba because families share a registration number in the RRF, with a specific field identifying family relationships. Although spousal identification is voluntary, validation done using the 1996 National Population Health Survey as the reference standard showed a high degree of validity among people  $> 55$  years in identifying marital status.<sup>27</sup> Children who turned 18 years old before the database came into existence on April 1, 1970, could not be identified. Under the assumption that few parents were  $\leq 15$  years old at the birth of their children, we can identify children of people  $\geq 34$  years old in 1970, that is,  $\geq 68$  years old in 2004. As data on children are unavailable in the national data, analyses including variables about children were limited to this Manitoba GP cohort.

### 2.2 | National NH and HC cohorts

These data were obtained from the Canadian Institute for Health Information (CIHI) and were linked by CIHI with the full national DAD, which includes all of Canada's hospitals and ICUs, except in Quebec. The NH cohort was derived from the Continuing Care Reporting System, which contains information on individuals in residential, chronic, or complex care facilities in British Columbia, Manitoba, Newfoundland and Labrador, Nova Scotia, Ontario, and the Yukon Territories, comprising 59 percent of Canada's population.<sup>28</sup> The HC cohort was derived from the Home Care Reporting System, containing information on persons receiving publicly funded home care services in British Columbia, Ontario, and Yukon Territories, comprising 52 percent of Canada's population.<sup>29,30</sup>

For both the NH and HC cohorts, we used linked data elements from the Resident Assessment Instrument-Minimum Dataset 2.0 (RAI), which is mandated for NH and HC in the provinces and territories included in our analyses. The RAI includes standardized assessment of numerous domains<sup>31,32</sup> which have been used extensively for describing client outcomes and health service utilization patterns (Appendix S2).<sup>30</sup> Marital status is also identified in the RAI instruments. Within NHs, the RAI is administered upon admission, quarterly, after any significant change in health status, and at discharge including death. For people who receive HC, it is administered at the time of enrollment.

### 2.3 | Analyses to test impact of close family social support (hypothesis 1)

Cox proportional hazards and general estimating equation (GEE) logistic regression were applied to all three study cohorts, to test hypothesis 1, regarding the presence of a living spouse or partner, with the presence of children limited to the GP cohort.

### 2.4 | Social support: GP Cohort

This analysis used Cox regression modeling of time from entering the cohort until admission to an ICU. Unadjusted Kaplan-Meier curves were also generated. Individuals entered the cohort, beginning their first study record, on either their 65th birthday or April 1, 2004 (whichever came first), being censored upon death, leaving the province, or at the end of the study period (March 31, 2012). Those who survived an ICU-containing hospitalization began a new study record on the day after ICU-containing hospital discharge. Because of the size of this dataset, we were unable to compute the shared frailty model of Cox regression to simultaneously evaluate all study records for each individual. Therefore, to avoid biasing toward younger age, we analyzed one randomly chosen study record for each person in the cohort.

For this cohort, we included admission into any of the 10 adult ICUs in the province's Winnipeg Regional Health Authority region. Only a single, nine-bed, mixed medical-surgical-cardiac ICU located in the southwestern portion of the province was excluded, because in a related analysis not reported here, we analyzed mortality rates using risk adjustment methodology derived from a clinical ICU database not available in that ICU. The 10 included ICUs comprised 93.7 percent of all ICU care provided in Manitoba.<sup>18</sup>

We developed three Cox models in which the parameter of interest was the hazard ratio (HR) for gender. Model A was adjusted only for age; model B adjusted for all covariates except marital status; and model C added marital status. The magnitude by which marital status confounded the relationship between gender and ICU admission was estimated as the percentage difference in HRs between models B and C. As recommended,<sup>33</sup> the importance of the percentage difference was evaluated through clinical judgment, with a 20 percent relative difference in hazard ratio deemed to be meaningful. Marital status and spousal residence were combined into the following

categories: married and spouse not in a nursing home, married and spouse in a nursing home, widowed, and not married due to reasons other than widowhood. Covariates were age, gender, calendar year, residence in a nursing home, SES, comorbid illnesses, prior medical resource use, previous ICU admission, and previous admission of a spouse (current or former) to an ICU.

Socioeconomic status was assessed as the SEFI-2 index, a multicomponent, area-level measure where higher values indicate lower SES.<sup>34</sup> Two measures of comorbid illness were the Charlson Comorbidity Index (CCI),<sup>35</sup> utilizing conditions identified from the DAD in the preceding 12 months,<sup>36</sup> and the number of prescription drug categories being used, as the fourth level of the Anatomical Therapeutic Chemical (ATC) classification system,<sup>37</sup> from the DPIN database. Prior medical resource use was the number of acute hospital days during the prior 5 years and number of outpatient physician visits during the prior 1 year. The Long-term Care Database identified nursing home residency. All variables except age and gender were included as time-dependent covariates. Standard errors were calculated using the Huber-White empiric sandwich estimator.<sup>38</sup> In a subset analysis, we included whether there were children of each gender living in Manitoba.

### 2.5 | Social support: NH cohort

In this cohort, we assessed nursing home residents who had at least one admission RAI assessment after 65 years of age within the study period. Using Cox regression, we assessed time from the first such RAI assessment to ICU admission, with censoring at death, transition to hospice care, transfer to a different nonacute care setting such as rehabilitative or complex continuing care, or the end of the study period. Modeling methods were similar to those in the GP cohort, again assessing one randomly chosen study record per individual to avoid possible age bias in the records. As a sensitivity analysis regarding the generalizability of Manitoba data, we repeated the fully adjusted model on the approximately 5 percent of the full NH cohort that were from Manitoba. Unadjusted Kaplan-Meier curves were also generated.

### 2.6 | Social support: HC cohort

In this cohort, we assessed HC clients who had at least one RAI assessment, followed by at least one acute hospitalization within the study period. Unlike for the other cohorts, here we required hospitalization because reference to hospitalization was the only way we had to establish vital status, as there is no national Canadian death index and the HC version of RAI does not identify deaths. Accordingly, this analysis assessed the presence of ICU admission during hospitalization. Individuals could have multiple study records if they survived an ICU stay and associated hospitalization and had a subsequent hospitalization. Accordingly, we analyzed ICU admission within hospitalizations including all study records for all individuals by use of general estimating equation (GEE) logistic regression, with an autoregressive correlation structure.<sup>39</sup>

Parameter	All	Males*	Females*
Baseline values			
# individuals (%)	250 190 (100)	112 409 (44.9)	137 781 (55.1)
# study records (range per individual)	262 656 (1-10)	119 670 (1-10)	142 986 (1-9)
Age (y), mean $\pm$ SD	72.0 $\pm$ 8.1	71.0 $\pm$ 7.4	72.9 $\pm$ 8.5
Charlson Comorbidity Score, n (%)			
0	146 382 (58.5)	64 336 (57.2)	82 046 (59.6)
1	39 269 (15.7)	16 333 (14.5)	22 936 (16.7)
2-3	29 577 (11.8)	13 830 (12.3)	15 747 (11.4)
$\geq 4$	34 962 (14.0)	17 910 (15.9)	17 052 (12.3)
Charlson Comorbidity Score, mean $\pm$ SD	1.0 $\pm$ 1.6	1.1 $\pm$ 1.7	0.95 $\pm$ 1.5
Hospital days in prior 5 y			
Percentage with zero hospital days	65.3	65.1	65.5
Outpatient physician visits in past 1 y, mean $\pm$ SD			
Percentage with zero physician visits	6.4	7.8	5.4
Number of classes of prescription drugs, mean $\pm$ SD			
Socio-Economic Factor Index (SEFI-2), mean $\pm$ SD (601 missing this data element; n = 249 589)	-0.056 $\pm$ 0.86	-0.078 $\pm$ 0.88	-0.037 $\pm$ 0.84
Prior ICU admission, n (%)			
Current or past spouse had been in an ICU previously, n (%)	18 777 (7.5)	5451 (4.9)	13 326 (9.7)
Lives in a nursing home, n (%)			
Marital situation, n (%)			
Married, spouse not in a nursing home	141 630 (56.6)	77 268 (68.7)	64 362 (46.7)
Married, spouse in a nursing home	1709 (0.7)	762 (0.7)	947 (0.7)
Widowed	41 977 (16.8)	9389 (8.4)	32 588 (23.7)
Not married due to reasons other than widowhood	64 874 (25.9)	24 990 (22.2)	39 884 (28.9)
Outcomes			
Follow-up time (y), mean $\pm$ SD	5.5 $\pm$ 3.1	5.3 $\pm$ 3.1	5.7 $\pm$ 3.1
Died during follow-up, n (%)			
At least one ICU-containing hospital admission during follow-up, n (%)	14 632 (5.8)	6201 (5.8)	8431 (6.1)

Abbreviation: ICU, intensive care unit.

\* $P < .001$  for all comparisons of males with females by Fisher's exact or chi-square test; SEFI-2 is a standardized measure with mean value of zero and 95% confidence interval of  $\pm 2$  and lower values indicating lower socioeconomic status.

**TABLE 1** Baseline data (at cohort entry) and outcomes for subjects in the Manitoba general population (GP) cohort

In both the NH and HC cohort analyses, most covariates were derived from their respective RAI instruments, which differed from each other somewhat due to differences between RAI versions used in the two care sectors. Covariates were age, gender, cohort entry year (epoch), marital status, bladder and bowel incontinence, Cognitive Performance Scale, Pain Scale, Depression Rating Scale, Activities of Daily Living Hierarchy Scale, Instrumental Activities of Daily Living Performance Scale, CHES (Changes in Health, End-Stage Disease, Signs, and Symptoms) scale, number of medications, use of psychiatric medications, falls, caregiver distress,

and the presence of directives to not resuscitate or not hospitalize (Appendix S3).<sup>31</sup> Additional covariates were obtained from the DAD (hospitalization and ICU admission during the preceding 1 year) and the 2006 Canadian Census (postal code-based, area-level SEFI-2 and household income quintile). To adjust for comorbidity in the NH cohort, we used the presence or absence of 48 specific medical conditions included in the RAI, restricted to those with a prevalence of  $\geq 0.2$  percent. For the HC cohort, we counted the number of comorbid conditions, as described by Elixhauser *et al*,<sup>40</sup> using the International Classification of Disease, Canadian

**TABLE 2** Association of male gender with ICU admission for in all three cohorts

Model	Covariates in the model <sup>†</sup>	Manitoba general population (GP) cohort HR, (95% CI)	National nursing home (NH) cohort HR, (95% CI)	National homecare (HC) cohort HR, (95% CI)
A	Age only	1.87 (1.80, 1.95)*	1.47 (1.35, 1.60)*	1.14 (1.11, 1.17)*
B	All except for marital status	1.71 (1.64, 1.78)*	1.35 (1.23, 1.49)*	1.10 (1.07, 1.13)*
C	All including marital status	1.78 (1.70, 1.86)*	1.35 (1.22, 1.49)*	1.07 (1.04, 1.10)*
	% difference, that is, (C-B)/B	+4.1%	0%	-2.7%

Abbreviations: CI, confidence interval; HR, hazard ratio.

\* $P < .001$ .

<sup>†</sup>See Appendices S7 (GP cohort) and 6 (NH and HC cohorts) for full lists of covariates.

version 10 (ICD-10-CA) diagnostic codes recorded for the index hospitalization and other hospitalizations within 1 year preceding it.<sup>35,41</sup> In the NH cohort, we imputed certain RAI-derived variables (Appendix S4), but excluded records with other missing variables.

## 2.7 | Analyses to test impact of cardiac disease (hypothesis 2) and triage bias (hypothesis 3)

As the GP cohort was the only one that was general population-based, we chose to evaluate these hypotheses only in that cohort, not in the NH and HC cohorts, which comprised specialty health service sectors. Both hypotheses were tested using the same Cox regression methods outlined earlier for hypothesis 1. We tested hypothesis 2 by excluding as outcomes ICU admissions for patients whose hospitalizations included acute myocardial infarction or cardiac surgery, as identified by standard coding used in the DAD (Appendix S5). Comparison was made between the HR for gender in this model versus the model that included all ICU admissions. We tested hypothesis 3 by comparing the gender effect for first study records for the whole GP cohort with that in second study records among individuals who survived a first ICU-containing hospitalization.

## 3 | RESULTS

### 3.1 | Hypothesis 1: Effect of spouse, partner, and children on male predominance

The GP cohort included 250 190 individuals and a total of 262 656 records (Table 1). We excluded from analysis 769 (0.3 percent) individuals with missing data elements. Among the remaining 249 421 individuals, the unadjusted Kaplan-Meier curve (Appendix S6) demonstrates the male predominance of ICU admission. In the Cox model, the male predominance was indicated by a HR of 1.87 (95% CI 1.80-1.95) when adjusted only for age (Table 2). There was no reduction of the male predominance by marital status (change in HR of + 4.1 percent, Table 2). Being unmarried was associated with a higher hazard for ICU admission (Appendix S3) regardless of whether it was via widowhood (HR = 1.16) or otherwise (HR = 1.18). The finding that ICU admission was strongly associated with prior

ICU admission is not new.<sup>7,42</sup> In the subset analysis that included children (N = 117 385; 2805 ICU admissions), binary variables for the presence of any children living in Manitoba did not alter the male predominance of ICU admission (HR = 1.81, 95% CI 1.67-1.96), nor were those covariates significantly associated with ICU admission (HR = 1.03,  $P = .41$  for sons; HR = 1.03,  $P = .54$  for daughters).

The national NH cohort included 133 982 individuals (Table 3, Appendix S7), of which 82 were excluded because their gender was missing. Among the single, randomly chosen study records for each individual, 183 people (0.14 percent) had missing data elements. Among the remaining 133 799 people, the unadjusted Kaplan-Meier curve (Appendix S6) demonstrates the male predominance of ICU admission. In the Cox model, the male predominance was indicated by a HR of 1.47 (95% CI 1.35-1.60) when adjusted only for age (Table 2). There was no reduction of the male predominance by marital status (change in HR = 0 percent, Table 2). Marital status was not significantly associated with ICU admission (Appendix S6). The HR for the fully adjusted model limited to Manitoba residents (1.58; 95% CI 0.85, 2.94) was compatible with that of the full NH cohort (1.35, 95% CI 1.22, 1.49).

The national HC cohort included 210 090 people (Appendix S7). Of these, 13 821 (6.6 percent) had missing data elements, mainly income. Among the remaining 196 269 individuals, the male predominance of ICU admission was indicated by an odds ratio (OR) of 1.14 (95% CI 1.11-1.17) when adjusted only for age (Table 2). After adding marital status to the regression model, the OR for the gender effect was slightly reduced, by 2.7 percent. In contrast to findings in the Manitoba cohort, being unmarried was associated with lower odds of ICU admission in comparison with married individuals (Appendix S7).

### 3.2 | Hypothesis 2: Effect of excluding cardiac ICU admissions on male predominance (Manitoba cohort)

Excluding as outcomes ICU admissions during hospitalization for cardiac surgery and/or acute myocardial infarction, the HR for male sex in the fully adjusted model was 1.54 (95% CI 1.44-1.65,  $P < .0001$ , Appendix S8), a value of 13.5 percent lower than the value of 1.78 (95% CI 1.70-1.86) in the fully adjusted base model (Table 2, Model C).

**TABLE 3** Selected baseline variables (at cohort entry) and outcomes for the national cohorts

Variable	Nursing home (NH) cohort			Homecare (HC) cohort		
	All	Men <sup>a,*</sup>	Women <sup>a,*</sup>	All	Men <sup>†</sup>	Women <sup>†</sup>
Baseline values						
# individuals, n (%)	133 982 (100)	47 762 (35.7)	86 138 (64.3)	210 090 (100)	80 314 (38.2)	129 776 (61.8)
Age (y), mean ± SD	84 ± 8	82 ± 8	85 ± 7	82 ± 8	81 ± 8	83 ± 8
Marital status, %						
Married	32.5	53.8	20.9	38.7	60.7	25.2
Widowed/divorced/separated	58.4	36.1	70.7	55.5	32.8	69.5
Never married	5.8	6.9	5.1	4.3	4.8	4.0
Other/missing (excluded from models)	3.3	3.2	3.3	1.5	1.7	1.3
Bladder incontinence, %	49.8	49.0	50.3	43.9	38.7	47.2
Bowel incontinence, %	34.2	37.9	32.2	16.9	18.1	16.3
Cognitive Performance Scale	2 (1.3)	2 (1.3)	2 (1.3)	1 (0.2)	1 (0.2)	1 (0.2)
Pain Scale	1 (0.2)	0 (0.1)	1 (0.2)	2 (0.2)	1 (0.2)	2 (0.2)
Depression Rating Scale	1 (0.2)	0 (0.2)	1 (0.2)	0 (0.2)	0 (0.1)	0 (0.2)
ADL Hierarchy Scale	3 (2.5)	3 (2.5)	3 (2.5)	0 (0.2)	0 (0.2)	0 (0.1)
IADL Difficulty Scale				5 (3.5)	5 (4.5)	4 (2.5)
CHESS score	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)
# of medications	10 (7.13)	10 (7.13)	10 (7.13)	9 (6.9)	8 (5.9)	9 (6.9)
Psychiatric medication in past wk, %	61.8	61.8	61.7	43.4	39.0	46.0
Any falls in past 30 d, %	24.1	24.9	23.6			
# of falls in past 90 d				0 (0.1)	0 (0.1)	0 (0.1)
Primary caregiver distress: (%)						
No caregiver				2.3	2.7	2.1
No challenges				77.1	71.9	80.2
Distressed				12.2	14.8	10.6
Feels unable to continue				8.4	10.6	7.1
Do not resuscitate directive, %	59.6	58.2	60.4	NA		
Do not hospitalize directive, %	10.8	10.1	11.1	NA		
Hospitalized during prior 1 y, %	71.8	74.8	70.2	33.5	39.4	29.8
ICU admission within the prior year, %	8.3	10.6	7.0	6.9	9.0	5.6
Follow-up time (d), mean ± SD	338 ± 384	311 ± 367	352 ± 393	358 ± 384	338 ± 351	370 ± 370
Outcomes						
Died during follow-up, n (%)	47 513 (35.5)	19 664 (41.2)	27 819 (32.3)	53 255 (25.4)	24 434 (30.4)	28 821 (22.2)*
Admitted at least once to an ICU during follow-up, n (%)	3344 (2.5%)	1527 (3.2)	1817 (2.1)	26 826 (12.8)	11 605 (14.4)	15 221 (11.7)*

Abbreviations: ADL, activities of daily living; IADL, instrumental activities of daily living.

<sup>a</sup>Sum of males and females in NH cohort excludes 82 individuals for whom gender was missing from the data.

\* $P < .001$  comparing males vs females for all comparisons in NH cohort except for ADL Hierarchy Scale ( $P = .10$ ) and use of psychiatric medication ( $P = .77$ ).

<sup>†</sup> $P < .001$  comparing men vs women for all comparisons in HC cohort; Values are median (interquartile range), unless indicated otherwise. See Appendices S2 and S6 for more details on variables.

### 3.3 | Hypothesis 3: Gender predominance of second ICU admissions (Manitoba cohort)

Among the 11 150 individuals who survived a first ICU-containing hospitalization, the male predominance for ICU admission

was statistically eliminated when considering a subsequent second ICU admission (HR = 1.07, 95% CI 0.96-1.20; Appendix S8). This was 41.2 percent lower than the HR for male gender in a model of the first record for every individual (HR = 1.82; 95% CI 1.76-1.89).



## 4 | DISCUSSION

In three separate large cohorts of older adults who were followed forward in time, we have confirmed prior findings of a marked predominance of males in admission to ICUs. This imbalance exists even though women outnumber men in these older age-groups.<sup>43</sup>

While there were significantly more men than women admitted to ICUs in all three cohorts (Table 2, model A), the model-based numerical excess was largest in the GP cohort and smallest in the HC cohort. There are multiple likely contributors to this difference. First, the cohorts are very different from one another. As a population-based general population cohort, the Manitoba cohort is comprised of predominantly independent, community-living, reasonably healthy people (59 percent have a CCI of zero), while those in nursing homes and receiving homecare would clearly be quite different. The fact that over half of Canadian nursing home residents have dementia<sup>44</sup> alone provides sufficient reason to expect differences in care decisions in that cohort. Second, unlike the hazard ratios from survival analysis calculated for the GP and NH cohorts to follow people from their usual place of residence to ICU, the HC analysis calculated odds ratios from logistic regression to assess whether people admitted to hospital were admitted to ICU. So, not only are the questions being assessed slightly different, but there is no direct comparability between hazard ratios and odds ratios. What is most notable is not the numerical differences shown in Table 2, but rather that the male predominance exists in all three cohorts.

One possible mechanism for men outnumbering women in ICUs relates to fewer older women having intact close family social networks (spouses, partners, or children), due to being older and having higher rates of widowhood toward the end of life. As such, older men are more likely to have such a recognized advocate when decisions about invasive or aggressive medical care are needed. However, our findings do not support this mechanism, as the status of this type of network did not attenuate the gender imbalance. It remains possible that broader social networks may differ between genders and account for the gender disparity in ICU admission.

Another possible mechanism explaining the imbalance is that men may experience higher rates or severity of critical illness than women and therefore be more likely to be admitted to ICUs. Indeed, men suffer higher rates of all three most common types of critical illness: cardiovascular,<sup>21</sup> respiratory,<sup>45</sup> and trauma,<sup>46</sup> with the first of these being responsible for half or more of all ICU care in our Manitoba cohort.<sup>18</sup> However, when we excluded ICU admissions related to acute myocardial infarction and cardiac surgery from that cohort, the male gender imbalance was only mildly attenuated. Although our adjustment here for cardiac causes is an incomplete assessment of this mechanism, using the same cohort we previously showed that the male predominance persists in this older age-group after accounting for gender-specific, population-based rates of all critical illness.<sup>10</sup> And other studies have reported that the average severity of illness among male ICU patients is no higher<sup>5</sup> or lower<sup>18</sup> than that of female ICU patients.

A third possible mechanism explored was the role of triage bias in favor of older males, that is, that older women have less access to ICU treatment due to triage decisions made by medical personnel. Research has shown that women often have less access to medical treatments.<sup>47</sup> Also, gender bias does exist in some triage decisions, having been demonstrated for trauma care<sup>48</sup> and knee replacement surgery.<sup>49</sup> However, the role of triage is the most difficult mechanism to evaluate using administrative data because such decisions commonly have a strong subjective element. Since our GP cohort were older people living in their usual places of residence, several different triage decisions made at multiple points in their illness trajectory could influence whether they were admitted to an ICU. For example, ICU admission of a nursing home resident could involve serial triage choices by a physician in the nursing home, an emergency department physician, and an ICU physician. We assumed that triage effects would manifest similarly for all ICU admissions, including potential repeat admissions. Under that presumption, our finding that a strong male predominance in first ICU admissions disappears among those who have survived a prior ICU-containing hospitalization appears inconsistent with the presence of strong triage bias in favor of men. The alternative is that the string of triage decisions—almost certainly made by different individuals for a given patient's successive ICU admissions during different hospitalizations—is gender-based for those who have not been in an ICU before, but gender-neutral for those who have been. This does not seem plausible.

We recognize that our interpretation of these findings is not definitive, but merely inconsistent with a triage bias explanation for the generally observed male predominance of ICU admissions, *under the assumption that its effects would manifest similarly for all ICU admissions*. What we can say is that if gender-based triage bias for ICU admission exists, it is not consistent and seems to be overridden by other dynamics. But it is difficult to imagine a practical and direct way to assess this potentially important mechanism. Choice-supportive bias makes self-report of triage personnel rationale unreliable.<sup>50</sup> While seemingly attractive, direct evaluation of triage decisions is fraught with its own problems. First, it will be impractical or at best extremely difficult to assess the entire sequence of triage decisions that often occur for an individual to get into an ICU, and these would all be prone to Hawthorne effect biases. Perhaps the sole convincing way to assess ICU-related triage decisions is akin to the experiment done by Borkhoff *et al*,<sup>49</sup> who sent standardized patients of each sex to outpatient orthopedic clinics for evaluation. In that study, in a blinded fashion, each orthopedic practice received one male and one female standardized patient who were coached to describe identical symptomatology and came to the appointments with identical knee MRIs. The difference in sex-based bias in outpatient physician referral for surgery could thus be clearly evaluated. But given the nature of critical illnesses, and the immediacy of ICU care, it seems impractical to do a similar experiment for ICU triage decisions.

Given our findings, in light of our schema for ICU admission (Appendix S1), alternative explanations for the male predominance in ICU admission include differences by gender in: (a) access to

health care and (b) patient preferences. While both are plausible, our findings lead us to hypothesize that the ICU gender imbalance is due, at least in part, to older women (or their surrogates), being *in general*, less willing to accept aggressive care as provided in ICUs. This is consistent with a survey of elderly outpatients in which older women less frequently stated that they would want life-supporting medical therapies.<sup>51</sup> If true, it would be expected that ICU survivors of both genders represent a select subgroup of older people who are equally accepting of such aggressive care, which should result in the gender neutrality we observed for second ICU admissions in this subgroup.

The study has some notable strengths. It is the first study that we are aware of to evaluate the possible role of multiple mechanisms in explaining the gender imbalance in ICU admissions. Our use of provincial- and national-level population datasets to study ICU admissions across geographic regions ensures that our findings do not simply reflect local practice. Also, our analyses adjusted for a large variety of potentially confounding covariates often related to health inequalities, such as patient demographics, income, clinical diagnosis, comorbidity, and functional and cognitive health, many of which were significantly associated with ICU admission (Appendices S3 and S6). The main limitation of our study is that administrative data alone do not allow one to directly assess the role of personal patient preferences, various social networks, and triage decisions in ICU admission.

In summary, using three cohorts of older men and women, the male predominance of ICU admission does not appear to be readily explained by gender differences in the presence or absence of a spouse, partner, or children; differential rates of cardiovascular disease; nor clearly by triage bias. Further research is needed to directly explore the role of personal patient preferences on ICU admissions.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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