CLINICAL INVESTIGATION

Multimorbidity Frameworks Impact Prevalence and Relationships with Patient-Important Outcomes

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OBJECTIVES: To explore how different frameworks and categories of chronic conditions impact multimorbidity (defined as two or more chronic conditions) prevalence estimates and associations with patient-important functional outcomes.

DESIGN: Baseline data from a population-based cohort study.

SETTING: National sample of Canadians.

PARTICIPANTS: A total of 51 338 community-living adults, aged 45 to 85 years.

MAIN OUTCOME MEASURES: Chronic conditions from three commonly recognized frameworks were categorized as: (1) diseases, (2) risk factors, or (3) symptoms. Estimates of multimorbidity prevalence were compared among frameworks by age and sex. Separate weighted logistic regression models were used to explore the impact of the different frameworks and categories of chronic conditions on odds ratios (ORs) for multimorbidity for four patient-important functional outcomes: disability, social participation restriction, and self-rated physical and mental health.

RESULTS: One framework included diseases and risk factors, and two frameworks included diseases, risk factors, and symptoms. The prevalence of multimorbidity differed among the frameworks, ranging from 33.5% to 60.6% having two or more chronic conditions. Including risk factors in frameworks increased prevalence estimates, while including symptoms increased prevalence estimates and associations with most patient-important outcomes. The two frameworks that included symptoms had the largest ORs for associations with disability, social participation restriction, and self-rated physical health but not self-rated mental health. Similar results were found when we compared ORs for patient-important outcome for multimorbidity based on three subframeworks: one including diseases only, one including diseases and risk factors, and one including diseases, risk factors, and symptoms.

CONCLUSIONS: Including risk factors appeared to increase only the prevalence of multimorbidity without significantly altering relationships to outcomes. The inclusion of symptoms increased prevalence and associations with patient-important outcomes. These findings underscore the importance of considering not only the number, but also the category, of conditions included in multimorbidity frameworks, as simply counting the number of diagnoses may reduce sensitivity to outcomes that are important to individuals. **J Am Geriatr Soc 00:1–9, 2019.**

Key words: aging; Canadian Longitudinal Study on Aging; functional disability; multimorbidity; self-rated health; social participation

Multimorbidity[1] is recognized as a risk factor for decreased quality of life,[2] increased functional disability,[3] and premature mortality.[4] Clinical guidelines tend to be disease specific,[5] and treatment regimens can become burdensome for people with multimorbidity.[6] As a result, care can become uncoordinated and fragmented, leading to higher costs,[7] polypharmacy, and adverse drug interactions.[8] Despite its importance, there are many methodological challenges to the study of multimorbidity. Currently, there is no universally accepted framework to define multimorbidity, and prevalence estimates range from 13.1% to 71.8% among population-based studies and from 3.5% to 98.5% in primary care–based studies.[9] Understanding the effect of different frameworks and

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definitions is important to accurately assess prevalence and adverse consequences of multimorbidity.

Willadsen et al recently distinguished three categories of conditions commonly included in multimorbidity frameworks: diseases, risk factors, and symptoms.[10] Risk factors, such as hypertension or dyslipidemia, are highly prevalent in the population but may have little impact on people's current functional status or quality of life. Symptoms, on the other hand, are associated with current illness burden and may be more highly associated with function in older adults.[11] Thus, defining multimorbidity as solely the presence of two or more chronic conditions is problematic, as it depends on the categories of conditions included in the framework.[9] This may partially explain why prevalence estimates differ so widely. Evidence to support effective clinical management must consider how the measurement of multimorbidity impacts not only prevalence, but also patient-important outcomes.[12] In this article, we explore how different disease frameworks, and their inclusion of diseases, risk factors, and symptoms, impact estimates of multimorbidity prevalence and associations between multimorbidity and patient-important outcomes.

METHODS

Study Design/Setting

The Canadian Longitudinal Study on Aging (CLSA) is one of the largest and most comprehensive research platforms examining health and aging.[13] CLSA participants are community-living women and men, aged 45 to 85 years, living in the 10 Canadian provinces at recruitment. All 51 338 participants provided a core set of information on demographics and measures of lifestyle/behavior, social, physical, psychological, and health status. This article uses baseline CLSA data collected between September 2011 and May 2015. Additional details are provided in Supplementary Text S1.

Variables

Chronic Conditions

For each chronic condition, participants were asked "Has a physician ever told you that you have ___?" Participants were asked to report only conditions that lasted, or were expected to last, at least 6 months and were diagnosed by a health professional. Self-report is commonly used in population-based studies to define multimorbidity.[9] Conditions were grouped into body systems using the Cumulative Illness Rating Scale[14] domains. Overweight was defined as a body mass index (BMI) of greater than 25 kg/m^2 and obesity as a BMI of greater than 30 kg/m^2 by self-reported or measured height and weight.

Multimorbidity Frameworks

We included three frameworks developed based on systematic reviews of the multimorbidity literature and proposed for use by clinicians and by researchers to improve comparability across multimorbidity studies (Table 1).[9,15,16] Diederichs et al suggested that a framework used to operationalize multimorbidity should include at least 11 conditions most often diagnosed in people aged 65 years or older.[15] Fortin et al originally suggested that including fewer than seven chronic conditions may underestimate multimorbidity prevalence, and that at least the 12 most prevalent conditions with a high impact in a given population should be included.[9] Subsequently, Fortin et al proposed a framework including 20 chronic conditions based on their relevance to primary care services, their impact on patients, and how often the conditions were included in other frameworks.[16] Henceforward, we refer to the prevalence-based framework as "Fortin-prevalence" and the 20-item framework as "Fortin-20."

In their systematic review, Willadsen et al[10] identified 10 diseases, 6 risk factors, and 10 symptoms that were commonly included in frameworks used to define multimorbidity. We used the proposed categorization of Willadsen et al[10] to classify each condition in the three frameworks as a "disease," "risk factor," or "symptom." The framework of Diederichs et al included diseases and risk factors, while the two Fortin frameworks included diseases, risk factors, and symptoms. While Willadsen et al[10] did not propose a specific framework for use by clinicians and researchers, they did highlight the importance of considering what category of chronic conditions is included in multimorbidity frameworks. Thus, we used the results of their review to create three additional subframeworks: one with diseases only (Willadsen-D), one including diseases and risk factors (Willadsen-DR), and one including diseases, risk factors, and symptoms (Willadsen-DRS). For conditions not included in the article by Willadsen et al,[10] the categorization was done by consensus between a geriatrician (C.P.) and family physician (D.M.). Willadsen et al considered a disease (or "illness") as being associated with a pathological process that the patient experiences in symptoms or functional limitation (eg, osteoarthritis). The authors considered a symptom as a functional effect that may be clearly linked to one or more disease processes (eg, breathlessness links to heart failure, chronic obstructive pulmonary disease, and ischemic heart disease) and a risk factor (eg, hypertension) as one that is measured and predicts development of later morbidity or mortality. Of the 11 conditions of Diederichs et al, the CLSA did not record heart arrhythmias. All of the Fortin-prevalence conditions were included in the CLSA, but the CLSA did not collect self-reported hyperlipidemia or chronic hepatitis from the Fortin-20 framework. The CLSA included all 10 of the diseases of Willadsen et al,[10] 5 of 6 risk factors (omitting hyperlipidemia), and 6 of the top 10 symptoms (omitting alcohol abuse, dizziness, tobacco abuse, and sleep disorders). The conditions included in each multimorbidity framework and in the systematic review of Willadsen et al[10] are in Table 1.

Patient-Important Outcomes

Functional Disability

Disability was measured using the Older Americans Resources and Services (OARS) Multidimensional Functional Assessment Questionnaire.[17] The OARS questionnaire contains 14 items related to functional disability in both basic activities of daily living (ADLs: eating, dressing, putting on clothes, walking, getting to bed, bathing, and toileting) and instrumental ADLs (IADLs: telephone use, travel, shopping, meal preparation, housework, taking own medicine, and handling personal finances). Functional disability was defined as needing help with, or inability to perform, one or more of the basic ADL or IADL activities.

Social Participation Restriction

After completing questions about participation in eight community-related activities, participants were asked whether they felt that they wanted to participate in more activities and, if so, what prevented them from doing so. Social participation restriction was operationalized as not participating as desired because of limitations due to health conditions.

Self-Rated Health

General physical and mental health was measured on a five-point scale, ranging from excellent to poor. The measures of self-rated health were dichotomized as poor or fair vs good to excellent.

Sociodemographic Factors

In the prevalence analysis, we explored the two sociodemographic factors most commonly associated with multimorbidity: age and sex.[18] Age was categorized into four groups: 45 to 54, 55 to 64, 65 to 74, and 75 to 85 years. Sex was categorized using self-reported sex. Other covariates included as potential confounders in regression analyses were: education (less than high school, high school, some postsecondary education, or postsecondary degree), race (white vs other), location (rural vs urban), and living alone (yes vs no).

Statistical Analysis

Multimorbidity was operationalized using three frameworks: (Diederichs, Fortin-prevalence, and Fortin-20). We also used the most commonly reported diseases, risk factors, and symptoms, identified by Willadsen et al,[10] to explore the different categories of conditions included in multimorbidity frameworks (three subframeworks: Willadsen-D, Willadsen-DR, and Willadsen-DRS). Descriptive and regression analyses used the most commonly used multimorbidity definition of two or more chronic condictions.[9] Multimorbidity prevalence was estimated using the three frameworks. Weighted logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals for multimorbidity for four outcomes:

Table 1. Diseases, Risk Factors, and Symptoms Included in Each Multimorbidity Framework

		Framework			
Disease system	**CLSA Chronic Conditions**	**Diederichs**	**Fortin-Prevalence**	**Fortin-20**	**Willadsen**
Musculoskeletal	Osteoarthritis	D	D	D[a]	D
	Rheumatoid arthritis				
	Osteoporosis		R	R	R
Respiratory	Asthma		D	D[a]	D
	COPD	D			D
Cardiac	Heart disease (including CHF)	D	D	D	D
	Angina	D		D[a]	D[a]
	Myocardial infarction	D			
Vascular	Peripheral vascular disease				
	Hypertension	R	R	R	R
Endocrine-metabolic	Diabetes	D	D	D	D
	Hypothyroidism/hyperthyroidism		D	D	
Neurological	Stroke or CVA	D		D[a]	D
	Transient ischemic attack				
	Migraine headaches		S		S
Gastrointestinal tract (upper and lower)	Intestinal or stomach ulcer			D	
	Bowel disorder		S	S	S[a]
	Bowel incontinence				
Genitourinary	Urinary incontinence			S	S
Ophthalmologic	Cataracts, glaucoma, or macular degeneration		D		
Psychiatric	Mood disorder (depression)[b]	D	D	D[a]	D
	Anxiety disorder[c]				
	Alzheimer disease/dementia			D	
Renal	Kidney disease			D	D
Cancer	Cancer	D	D	D	D
Other risk factors/symptoms	Overweight				R[d]
	Obesity			R	
	Back problems			S	S
	Visual impairment				S
	Hearing impairment				S

Abbreviations: CHF, congestive heart failure; CLSA, Canadian Longitudinal Study on Aging; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; D, diseases; R, risk factors; S, symptoms.

[a]Merged cells indicate that chronic conditions were combined in the framework (eg, osteoarthritis or rheumatoid arthritis).

[b]Mood disorders include depression, bipolar disorder, mania, and dysthymia.

[c]Anxiety disorders include phobias, obsessive-compulsive disorder, and panic disorder.

[d]Willadsen reported both overweight and obese as commonly used risk factors. Because obese is a subcategory of overweight, we combined them into one risk factor (overweight or obese).

disability, social participation restriction, and self-rated physical and mental health. For the regression analyses, multimorbidity was defined using each of the three frameworks and the Willadsen subframeworks. All regression models used analytic weights[19] and were adjusted for age, sex, education, race, location, and living alone. Since more than half of the people with a multimorbidity are younger than 65 years,[20] we included all participants aged 45 to 85 years to examine age- and sex-stratified prevalence analyses. Because our outcomes, especially disability, are more common in older adults, and to align our analyses with age groups most often included in multimorbidity interventions,[21] we restricted our regression analyses to people aged 65 years and older, with the results for other age groups (45-85 and 75-85 years) included in supplemental figures. All analyses were conducted using SAS, version 9.4.[22]

RESULTS

Participants

Table 2 displays the characteristics of the CLSA population (unweighted) by age group (younger than 65 years and 65 years and older) and sex. Conditions are grouped by type of condition (disease, risk factor, or symptom) and ranked according to the overall prevalence in the CLSA sample. The weighted results, reflecting the target population in Canada, were similar and are included in Supplementary

Table 2. Characteristics of 51 338 Participants of the Canadian Longitudinal Study on Aging

	Aged <65 y		Aged ≥65 y	
Characteristics	**Males**	**Females**	**Males**	**Females**
Total population	14 441 (48.4)	15 406 (51.6)	10 742 (50.0)	10 749 (50.0)
Age, mean (SD), y	55.6 (5.5)	55.4 (5.4)	73.4 (5.7)	73.3 (5.8)
Diseases				
Eye disease (cataracts, glaucoma, or macular degeneration)	1569 (11.0)	2073 (13.6)	5389 (51.1)	6577 (62.2)
Osteoarthritis	2226 (15.6)	3646 (24.0)	2994 (28.3)	4713 (44.6)
Diabetes	2224 (15.4)	2002 (13.0)	2666 (24.9)	1971 (18.4)
Mood disorder (depression)[a]	2043 (14.2)	3545 (23.1)	978 (9.1)	1684 (15.7)
Hypothyroidism/hyperthyroidism	716 (5.0)	2726 (17.8)	974 (9.2)	2769 (26.3)
Asthma	1632 (11.3)	2354 (15.3)	941 (8.8)	1404 (13.1)
Heart disease (including CHF)	1128 (7.8)	656 (4.3)	2461 (23.1)	1449 (13.6)
Cancer	713 (4.9)	1069 (6.9)	1940 (18.1)	1591 (14.8)
Anxiety[b]	1051 (7.3)	1756 (11.4)	458 (4.3)	892 (8.3)
Intestinal or stomach ulcer	933 (6.5)	994 (6.5)	1014 (9.5)	971 (9.1)
Peripheral vascular disease	576 (4.0)	716 (4.7)	902 (8.4)	971 (9.1)
COPD	623 (4.3)	788 (5.1)	819 (7.7)	931 (8.7)
Myocardial infarction	639 (4.4)	223 (1.4)	1395 (13.1)	521 (4.9)
Angina	439 (3.0)	255 (1.7)	1114 (10.4)	665 (6.2)
Rheumatoid arthritis	419 (2.9)	580 (3.8)	409 (3.9)	650 (6.1)
Transient ischemic attack	229 (1.6)	219 (1.4)	661 (6.2)	604 (5.7)
Kidney disease	310 (2.2)	274 (1.8)	465 (4.3)	411 (3.8)
Stroke or CVA	163 (1.1)	140 (0.9)	381 (3.6)	228 (2.1)
Alzheimer disease/dementia	18 (0.1)	16 (0.1)	50 (0.5)	27 (0.3)
Risk Factors				
Hypertension	4425 (30.7)	3660 (23.8)	5413 (50.7)	5365 (50.3)
Obesity	4241 (29.5)	4292 (28.0)	2546 (23.8)	2859 (26.8)
Osteoporosis	235 (1.6)	1348 (8.8)	451 (4.2)	2664 (25.1)
Symptoms				
Back problems	3886 (27.0)	3850 (25.0)	2883 (26.9)	2969 (27.7)
Migraine headaches	1184 (8.2)	3247 (21.1)	584 (5.5)	1758 (16.4)
Bowel disorder	862 (6.0)	1791 (11.7)	662 (6.2)	1461 (13.7)
Urinary incontinence	329 (2.3)	1438 (9.3)	934 (8.7)	1687 (15.8)
Bowel incontinence	163 (1.1)	294 (1.9)	219 (2.0)	398 (3.7)
ADL/IADL disability[c]	593 (4.1)	1477 (9.6)	1075 (10.0)	2324 (21.7)
Social participation restriction[d]	868 (6.0)	1194 (7.8)	771 (7.2)	1044 (9.7)
Poor or Fair Self-Rated Health[e]				
Physical	1565 (10.8)	1606 (10.4)	1249 (11.6)	1220 (11.4)
Mental	892 (6.2)	1027 (6.7)	401 (3.7)	459 (4.3)

Data are given as number (percentage) of each group, unless otherwise indicated.

Abbreviations: ADL, activity of daily living; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; IADL, instrumental ADL.

[a]Mood disorders include depression, bipolar disorder, mania, and dysthymia.

[b]Anxiety disorders include phobias, obsessive-compulsive disorder, and panic disorder.

[c]ADL/IADL disability indicates needing help with, or inability to perform, one or more of the basic ADL or IADL activities.

[d]Social participation restriction indicates not participating socially as one desired because of limitations due to health conditions.

[e]Self-rated physical and mental health indicates responding poor or fair on a five-point scale, ranging from excellent to poor.

Table S1. The most common disease for men (15.6% in those younger than 65 years; 28.3% in those 65 years and older) and women (24.0% in those younger than 65 years; 44.6% in those 65 years and older) was osteoarthritis. Hypertension was the most common risk factor in those 65 years and older (50.7% men; 50.3% women) and for younger men (29.5%), but obesity (28.0%) was the most common risk factor in women. The most common symptom was "back problems" for men (27.0% in those younger than 65 years; 28.3% in those 65 years and older) and women (25.0% in those younger than 65 years; 27.7% in those 65 years and older).

Multimorbidity Prevalence

The magnitude of prevalence estimates and relationship with sex differed by framework (Figure 1A). Diederichs' framework resulted in the lowest prevalence estimates and did not differ by sex, whereas the Fortin-prevalence and Fortin-20 frameworks estimated higher prevalence overall and higher prevalence for women than men. The addition of nondisease conditions increased the prevalence substantially (Figure 1B). The addition of three risk factors (Willadsen-DR) was associated with an average absolute increase in prevalence of 33.4% for males and 32.3% for females and, in most cases, doubled to tripled the prevalence estimates. The addition of three risk factors and six symptoms (Willadsen-DRS) resulted in an average absolute increase of 43.4% for males and 76.0% for females. Adding the nine additional conditions was associated with prevalence estimates two to five times higher. Other definitions of multimorbidity were explored in Supplementary Figure S1 and Supplementary Figure S2.

Relationship with Patient-Important Outcomes

The magnitude of effect differed among the multimorbidity frameworks (Figures 2 and 3), but the framework including the largest number of symptoms, Fortin-20, consistently had the largest ORs with patient-important outcomes. Compared to the Willadsen-D framework, for example, the ORs for the Willadsen-DRS framework were higher: 49.1% for disability, 27.4% for social participation restriction, and 41.8% for self-rated physical health. Despite the increase in the number of conditions, adding risk factors to the framework resulted in, at most, marginally higher ORs for any patient-important outcomes. For example, compared to the Willadsen-D framework, the ORs for Willadsen-DR ranged from 8.7% higher to 7.8% lower. The patterns were generally similar when the analysis included all participants aged 45 to 85 years (Supplementary Figure S3 and Supplementary Figure S4) and when restricting the analysis to participants aged 75 to 85 years (Supplementary Figure S5 and Supplementary Figure S6), but the width of the confidence intervals reflected the increase or decrease in sample size.

DISCUSSION

Including risk factors in frameworks used to define multimorbidity increases the prevalence of multimorbidity but has

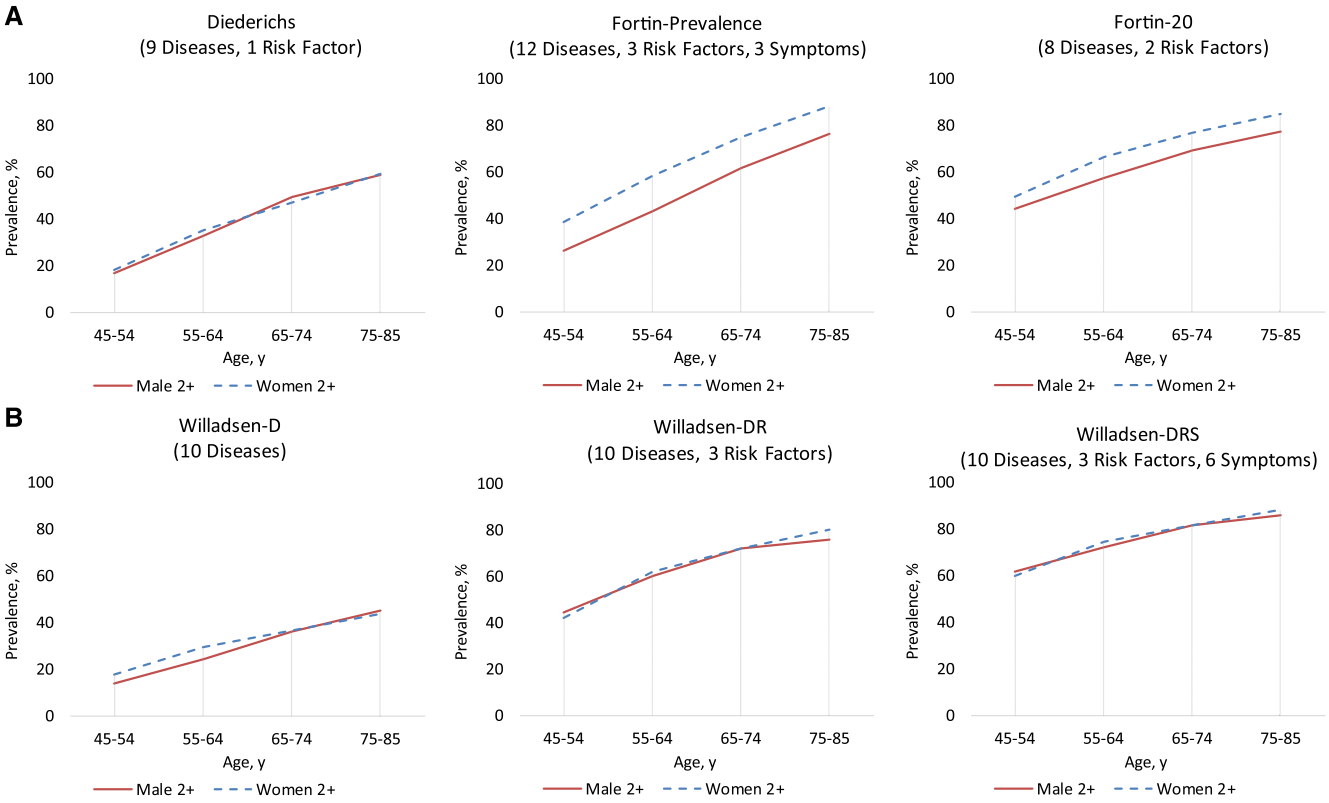

Figure 1. Multimorbidity prevalence (two or more chronic conditions) by sex and age group. Prevalence estimates are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20; A) and the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]; B). The number of diseases, risk factors, and symptoms is indicated below each named framework or subframework.

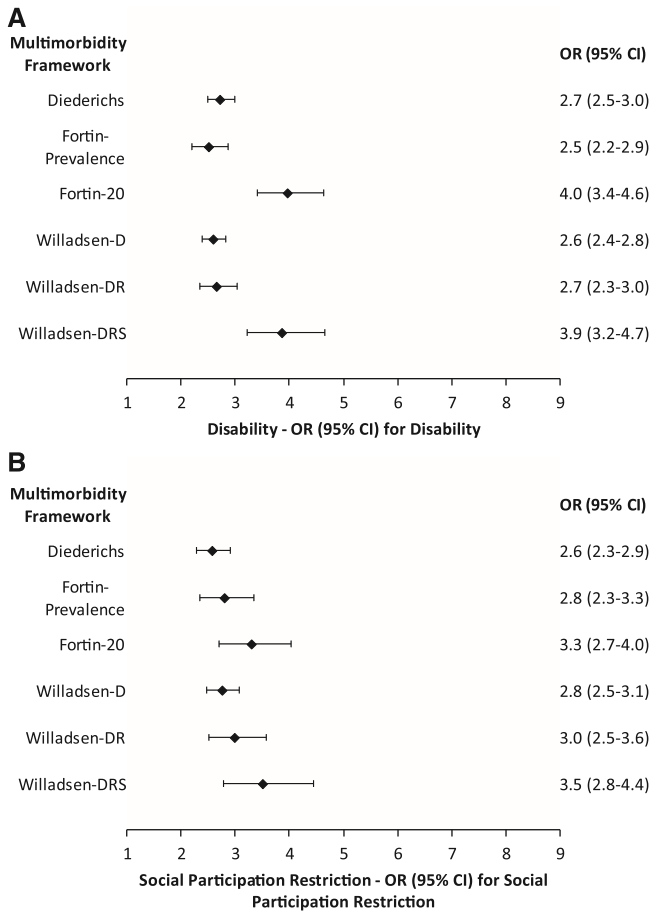

Figure 2. Multivariable association between multimorbidity (two or more chronic conditions) and odds of disability (A) and social participation restriction (B) in participants aged 65 to 85 years. Odds ratio (OR) estimates and 95% confidence intervals (CIs) are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]). All models are adjusted for age, sex, education, race, location, and living alone.

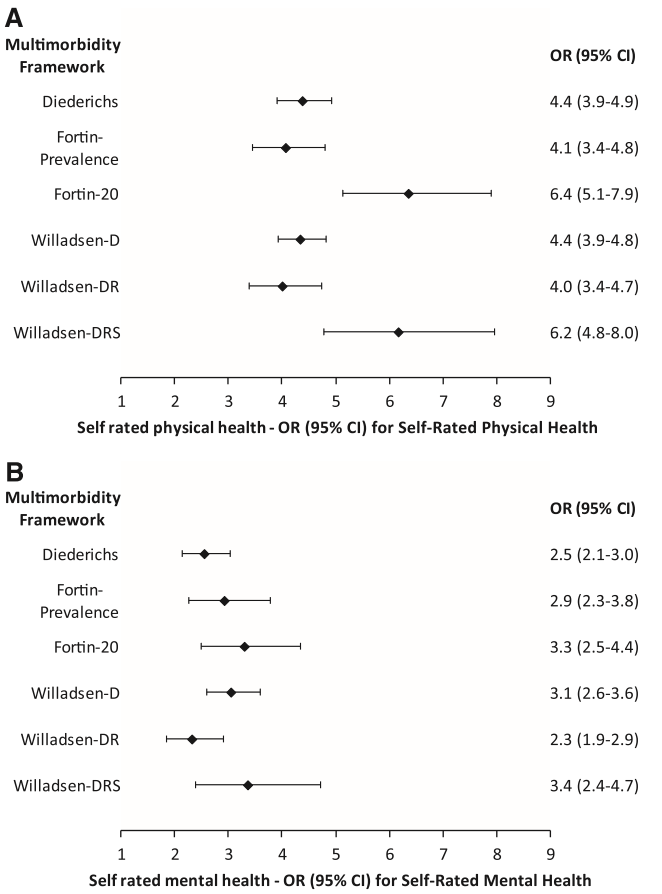

Figure 3. Multivariable association between multimorbidity (two or more chronic conditions) and odds of self-rated physical health (A) and self-rated mental health (B) in participants aged 65 to 85 years. Odds ratio (OR) estimates and 95% confidence intervals (CIs) are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]). All models are adjusted for age, sex, education, race, location, and living alone.

little impact on patient-important outcomes. Symptoms, on the other hand, are related to prevalence, sex differences, and, most important, patient-important outcomes, which likely diminish quality of life and increase health services use.[23]

Several factors influence prevalence estimates among studies of multimorbidity, including differing geographic settings, recruitment methods, and data collection methods, and the operational definition of multimorbidity.[9,18,24–27] In this study, we found that including risk factors has the largest impact on prevalence estimates. Compared to most diseases and symptoms, risk factors are generally based on objective, rather than subjective, measures; are easy to quantify; and are often collected as part of routine examinations (eg, blood pressure and BMI). In their review of 115 articles with multimorbidity definitions, Willadsen et al indicated that 98 (85%) of chronic condition frameworks included risk factors.[10] Risk factors common in the population, like hypertension, do not have a large contemporaneous impact on patients' functional status or quality of life.[28] This poses two possible issues when studying multimorbidity. The first may be "double counting" when including physiological measures that are risk factors for later diseases (eg, hyperlipidemia and hypertension for coronary artery disease).[10] The second is that risk factors frequently fail to influence current symptom burden (morbidity).

Recently, Xu et al[27] identified five systematic reviews that examined correlates associated with multimorbidity. Of these reviews, three identified female sex as a factor associated with increased multimorbidity, but most of the included studies did not adjust for other factors, such as age. We found that the impact of sex depends on the multimorbidity framework used. It is possible that frameworks including risk factors and symptoms may show a greater difference in prevalence between women and men than those including diseases only. Willadsen et al[10] identified hypertension and osteoporosis as the most common risk factors, and they identified back pain, visual impairment, and urinary incontinence as the most common symptoms, included in multimorbidity frameworks. In our population, the largest sex differences among risk factors was for osteoporosis; and among symptoms, urinary

incontinence (both more common in women). Our results indicate that sex differences in multimorbidity prevalence may not be a general finding but rather may depend on the specific chronic conditions included in each framework.

While it is not surprising that the inclusion of symptoms influences patient-important outcomes,[11] the strength of this association is notable. Several systematic reviews have found an association among multimorbidity and disability, quality of life, and social participation restrictions.[18,29,30] Nutzel et al examined factors associated with self-rated health in multimorbidity patients aged 65 to 85 years[31] and concluded that symptoms and consequences of disease, such as pain, were more strongly associated with self-rated health than the diseases themselves. Perruccio et al investigated the interrelationships among the different health domains of multimorbidity and self-rated health.[32] Although "medical comorbidity" explained the most variance in self-rated health (11.7%), other domains explained 27.3% of the variance, with the largest contributions coming from geriatric problems (eg, vision, hearing and memory problems, and incontinence). In our study, the definitions including symptoms had larger ORs, indicating that symptoms may have an important role beyond medical comorbidity.

The only patient-important outcome that appeared less affected by the content of the framework was self-rated mental health. None of the studies examining self-rated health in patients with multimorbidity examined physical and mental health separately. We found that, in contrast to self-rated physical health and healthy aging, there was little difference in the magnitude of association with self-rated mental health among the different frameworks. This may be because the constituent conditions contain relatively few mental health conditions (except for depression),[15] despite their importance in terms of burden[33] and relationship with socioeconomic status.[20] Further work in this area is needed.

This research draws on a large-scale, national, population-based study that used standardized protocol to collect data. The breadth of data collected allows for comparison across a number of patient-important outcomes that are not usually available in other routinely collected data sources. The CLSA sample size also allows the simultaneous exploration of both age and sex effects on measures of multimorbidity. Our study also has some limitations. First is the issue of the accuracy of self-reported medical conditions. Although diagnoses were not confirmed, self-reported diagnoses of prevalent conditions have been shown to be valid and reliable in epidemiologic research.[34] Furthermore, while CLSA collected information on over 30 chronic conditions, three conditions from the proposed frameworks were omitted: heart arrhythmias in the Diederichs' framework and hyperlipidemia and hepatitis in the Fortin-20 framework. The inclusion of these three conditions would not likely influence our results. There is also subjectivity in categorizing diseases, risk factors, and symptoms. We used the systematic review of Willadsen et al[10] to categorize chronic conditions from each framework, while a geriatrician (C.P.) and a family physician (D.M.) categorized chronic conditions not included in their systematic review. We focused on three frameworks for defining multimorbidity, and our finding may not be generalizable to all multimorbidity frameworks. Future work could involve simulating frameworks from pools of diseases, risk factors, and symptoms to better understand the impact of categories of conditions more generally. Finally, there are many potentially important outcomes that were beyond the scope of this article (eg, healthcare cost, hospitalization, polypharmacy, and death), and the same frameworks that are less strongly related to function may be more strongly related to other outcomes.

Clinical and Public Health Importance

It is unlikely that there will be an ideal measure of multimorbidity for use in all situations and all data sources. Diagnosis counts may be of interest to healthcare practitioners and planners, but the impact on an individual's ability to function and participate in society is surely one of the most important impacts of multimorbidity. When one illness complicates another or when the treatment of one condition conflicts with the treatment of another, only two conditions are necessary to cause serious clinical dilemmas. On the other hand, multiple asymptomatic conditions may cause no distress to an individual, nor interfere with function, quality of life, or ability to participate in society, even though their eventual impact may be grave. The inclusion of risk factors may be appropriate if taking a public health perspective on multimorbidity (eg, to help identify preventative interventions on modifiable risk factors for future conditions). To make multimorbidity research more patient centered, the definition should embody "morbidity" as ill health appreciated by the individual. In such situations when one is interested in the effect on functional status or participation, a framework including symptoms but without risk factors may be more appropriate. Different frameworks, however, may be better suited to the other outcomes of interest.[35,36] Thus, the framework one uses will depend on his/her specific goal and purpose.[37]

There is a trend to broaden the definition of multimorbidity. Le Reste et al have suggested that biopsychosocial factors also be included.[38]This may reflect the clinical reality of influences on, and management of, complex patients with multimorbidity, but will substantially impact prevalence estimates. In clinical trials, health services, and policy interventions targeting multimorbidity, the addition of symptoms may increase the power to detect, intervene, or assess effects on patient-important outcomes, such as disability and perceived health. Regardless of the context, it is important that definitions of morbidity for clinical, policy, and health service interventions are aligned with patient-important outcomes.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Supplementary Text S1. Provides additional information about the Canadian Longitudinal Study on Aging (CLSA) method.

Supplementary Table S1. Characteristics of Canadians using weighted data from participants of the Canadian Longitudinal Study on Aging.

Supplementary Figure S1. Weighted prevalence of Canadians with two, three, four, five, and six or more chronic conditions using the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]).

Supplementary Figure S2. Multimorbidity prevalence (two or more and three or more chronic conditions) by sex and age group. Prevalence estimates are presented for three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20; A) and the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]; B).

Supplementary Figure S3. Multivariable association between multimorbidity (two or more chronic conditions) and odds of disability (A) and social participation restriction (B) in participants aged 45 to 85 years. Odds ratio estimates and 95% confidence intervals are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]).

Supplementary Figure S4. Multivariable association between multimorbidity (two or more chronic conditions) and odds of self-rated physical health (A) and self-rated mental health (B) in participants aged 45 to 85 years. Odds ratio estimates and 95% confidence intervals are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]).

Supplementary Figure S5. Multivariable association between multimorbidity (two or more chronic conditions) and odds of disability (A) and social participation restriction (B) in participants aged 75 to 85 years. Odds ratio estimates and 95% confidence intervals are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]).

Supplementary Figure S6. Multivariable association between multimorbidity (two or more chronic conditions) and odds of self-rated physical health (A) and self-rated mental health (B) in participants aged 75 to 85 years. Odds ratio estimates and 95% confidence intervals are presented for the three multimorbidity frameworks (Diederichs, Fortin-prevalence, and Fortin-20) and for the three Willadsen subframeworks (including diseases only [Willadsen-D], diseases and risk factors [Willadsen-DR], and diseases, risk factors, and symptoms [Willadsen-DRS]).