

Editor's key points

- > Determining the effect of multimorbidity on functional decline of older adults is important in planning both preventive care and health care resource needs. This study examined the effect of multimorbidity on functional status by analyzing secondary data from the Manitoba Study of Health and Aging, a population-based study conducted in Manitoba.
- In this study, those with multimorbidities were older, more likely to be women, had less education, had greater cognitive impairment, and had more depressive symptoms.
- ▶ This study found that multimorbidity predicts functional decline over a long time frame. Maintaining functional status is a central health goal for most older adults, and might be a more relevant clinical end point than death. A possible explanation is that functional decline is a mediator in the path from multimorbidity to death, with individuals passing through a period of functional decline before death.

Multimorbidity predicts functional decline in community-dwelling older adults

Prospective cohort study

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Abstract

Objective To determine if multimorbidity is associated with functional status, and to assess if multimorbidity predicts declining functional status over a 5-year time frame, after accounting for baseline functional status and other potential confounding factors.

Design Analysis of an existing population-based cohort study.

Setting Manitoba.

Participants Community-dwelling adults aged 65 and older.

Main outcome measures Age, sex, education, and the Mini-Mental State Examination (MMSE) and Center for Epidemiological Studies Depression Scale (CES-D) scores were recorded for each patient. Multimorbidity was measured using a simple tally of self-reported diseases. Function was measured using the Older Americans Resources and Services scale in 1991 to 1992 and again 5 years later. Good or excellent level of function was compared with level of disability (mild or moderate or higher). Cross-sectional and prospective analyses were conducted.

Results In a cross-sectional analysis, multimorbidity predicted disability. The unadjusted odds ratio (OR) (95% CI) for disability was 1.45 (1.39 to 1.52) for each additional chronic illness. In models adjusting for age, sex, education, and MMSE and CES-D scores, the adjusted OR (95% CI) was 1.35 (1.29 to 1.42) for each additional chronic illness. Multimorbidity also predicted disability 5 years later. The unadjusted OR (95% CI) was 1.31 (1.24 to 1.38). In models adjusting for age, sex, education, and MMSE and CES-D scores in addition to baseline functional status, the adjusted OR (95% CI) was 1.15 (1.09 to 1.24).

Conclusion Multimorbidity predicts disability in cross-sectional and prospective analyses.



La multimorbidité est un facteur de prédiction du déclin fonctionnel chez les aînés vivant dans la communauté

Étude prospective de cohortes

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Résumé

Objectif Déterminer si la multimorbidité est associée à l'état fonctionnel, et évaluer s'il s'agit d'un facteur de prédiction du déclin fonctionnel sur une période de 5 ans, après avoir tenu compte de l'état fonctionnel au point de départ et d'autres facteurs confusionnels possibles.

Conception L'analyse d'une étude existante de cohortes représentatives de la population.

Contexte Manitoba.

Participants Des adultes de 65 ans et plus vivant dans la communauté.

Principaux paramètres à l'étude Pour chaque patient, on a consigné l'âge, le genre, le niveau d'éducation ainsi que les résultats au mini-examen de l'état mental (MMSE) et selon l'échelle CES-D (Center for Epidemiological Studies Depression Scale). La multimorbidité était mesurée en se basant simplement sur la liste des maladies telle que fournie par les patients. L'échelle des Older Americans Resources and Services a servi à mesurer le fonctionnement de 1991 à 1992, puis à nouveau 5 ans plus tard. Le niveau de fonctionnement bon ou excellent était comparé au degré d'incapacité (faible, modéré ou plus élevé). Des analyses transversales et prospectives ont été effectuées.

Résultats Dans une analyse transversale, la multimorbidité permettait de prédire l'incapacité. Le rapport de cotes (RC) non corrigé (IC à 95%) pour l'incapacité était de 1,45 (1,39 à 1,52) pour chaque maladie chronique additionnelle. Dans les modèles corrigés en fonction de l'âge, du genre, du niveau d'éducation et des scores au MMSE et au CES-D, le RC corrigé (IC à 95%) était de 1,35 (1,29 à 1,42) pour chaque maladie chronique additionnelle. La multimorbidité permettait aussi de prédire l'incapacité 5 ans plus tard. Le RC non corrigé (IC à 95%) était de 1,31 (1,24 à 1,38). Dans les modèles corrigés en fonction de l'âge, du genre, du niveau d'éducation et des scores au MMSE et au CES-D, en plus de l'état fonctionnel au point de départ, le RC corrigé (IC à 95%) était de 1,15 (1,09 à 1,24).

Conclusion La multimorbidité est un facteur de prédiction de l'incapacité dans des analyses transversales et prospectives.

Points de repère du rédacteur

- Il est important de déterminer les répercussions de la multimorbidité sur le déclin fonctionnel pour planifier à la fois les soins préventifs et les ressources nécessaires dans le secteur de la santé. Cette étude examinait les effets de la multimorbidité sur l'état fonctionnel en analysant les données secondaires de l'Étude sur la santé et le vieillissement au Manitoba, une étude sur la population effectuée dans cette province.
- Les sujets de cette étude ayant de multiples morbidités étaient typiquement plus âgés, le plus souvent de sexe féminin, avaient un niveau d'éducation moins élevé, présentaient une plus grande déficience cognitive, de même que plus de symptômes dépressifs.
- ▶ Cette étude a conclu que la multimorbidité est un facteur de prédiction d'un déclin fonctionnel sur une longue période de temps. Il est impératif de fixer comme objectif de santé le maintien de l'état fonctionnel pour la plupart des adultes plus âgés, et il pourrait s'agir d'un événement clinique cible plus pertinent que le décès. Ces constatations pourraient s'expliquer par le fait que le déclin fonctionnel est un médiateur dans le cheminement de la multimorbidité vers le décès, les personnes vivant une période de déclin fonctionnel avant de mourir.

iseases often co-occur (multimorbidity), and the cumulative disease burden might be more important than the effect of any one disease in particular.1 Multimorbidity has long been recognized2 yet remains understudied.3 In particular, the effect of multimorbidity on disability is not fully understood. There are cross-sectional studies that document a strong association between multimorbidity and functional status, but fewer prospective cohort studies exist. Ryan et al⁴ conducted a systematic review and noted many crosssectional studies; when pooled, there was a strong association between multimorbidity and poor functional status. However, they identified only 9 prospective studies.4 Most of these prospective studies showed an association between multimorbidity and functional decline. Since this systematic review was published, a further study conducted in primary care demonstrated no effect of multimorbidity on functional decline or the risk of hospitalization,5 but a secondary analysis of the Health and Retirement Study demonstrated a strong risk of functional decline in those with more chronic health problems.^{6,7}

Understanding the relationship between multimorbidity and functional status is important for several reasons. First, many older adults value maintaining functional status more than they value extending life.8,9 Second, functional status predicts adverse outcomes.10 Third, functional status predicts the use of health care resources.11-14 Determining the effect of multimorbidity on functional decline of older adults is therefore important in planning both preventive care and health care resource needs. We have previously investigated the effect of multimorbidity on mortality.15 We now report the effect of multimorbidity on functional status in cross-sectional and prospective analyses.

Specifically, our objective was to determine if multimorbidity is associated with functional status, and to assess if multimorbidity predicts declining functional status 5 years later, after accounting for baseline functional status and other potential confounding factors.

- Methods -

Population

We conducted analyses of the Manitoba Study of Health and Aging, a population-based study conducted in the Canadian province of Manitoba in conjunction with the Canadian Study of Health and Aging (CSHA).16 The sampling frame was from a list provided by Manitoba Health. Persons residing in institutions (nursing homes and chronic care hospitals) did not undergo the screening interview and were not included in these analyses. As health care coverage is universal, this is as complete a population registry as possible. Those with health care coverage from the federal government (active members of the Canadian Armed Forces, the Royal Canadian Mounted Police, and First Nations persons living on reserve) might

not have been included in the sampling frame. There was an oversampling of older age groups (older than 85 years) to ensure adequate representation of individuals with cognitive and functional impairment. Unlike the CSHA, sampling was not limited to those living within 50 km of a major city. Informed consent was obtained from participants or appropriate proxies. The sample was interviewed in 1991 to 1992 (this is referred to as time 1). Five years later (referred to as time 2), in 1996 to 1997, those who were still alive and living in the community were contacted and assessed with the same process and measures as in 1991 to 1992. The 5-year time frame was according to the CSHA protocol. We considered the end of the observation period at the time of the time 2 screening questionnaire and the categories of participant status then as mutually exclusive; however, some of the participants might have been in several categories (eg, entered nursing home and then died).

The research was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Manitoba in Winnipeg and adhered to the Declaration of Helsinki.

Measures

Age, sex, and educational level (years of education) were self-reported. The Modified Mini-Mental State Examination¹⁷ was used as the screening test for cognitive impairment and dementia. The Modified Mini-Mental State Examination was conducted in a manner that allowed calculation of the MMSE score, 18 which is more widely used and thus reported here. We considered the MMSE score as a continuous factor. The Center for Epidemiologic Studies Depression Scale (CES-D)19 was used to measure depressive symptoms. This is a valid, reliable measure of depressive symptoms, which we also considered as a continuous factor.

Functional status was measured by asking participants about their ability to perform basic activities of daily living (ADLs) (eating, dressing, grooming, getting in and out of bed, taking a bath or shower, and using the bathroom), instrumental activities of daily living (using the telephone, getting to places farther than walking distance, going shopping, preparing meals, doing housework, taking medications, managing money), and ambulation. A disability was defined as needing help with, or an inability to perform, 1 or more of the activities listed. For ambulation, walking independently with a cane was not defined as a disability. These questions were derived from the ADL and instrumental activities of daily living portions of the Older Americans Resources and Services (OARS) Multidimensional Functional Assessment Questionnaire. 19-21 For the primary analysis, we considered the OARS score as a categorical variable using the methodology from the original OARS questionnaire to categorize subjects by function into the following groups: excellent or good function; mild disability; or moderate or severe disability.

Briefly, those with excellent or good functional status could perform all ADLs without assistance, and those with mild disability could perform all but 1 to 3 ADLs and could get through a single day without help. Those with moderate or severe disability needed regular assistance with at least 4 ADLs, and might have had difficulty getting through a single day unassisted. In logistic regression models, we considered excellent or good function versus the level of disability (mild disability or moderate or severe disability). As a sensitivity analysis, we considered the OARS score as a continuous variable; scores ranged from 0 to 28.22 A change of 3 or more points on this continuous score has been considered clinically relevant.23

In addition to these standardized measures, the participants in the Manitoba Study of Health and Aging were asked a series of questions about their health. The questions were introduced with the following sentence: "Now, I will read a list of health problems that people often have. For each problem that I read, please tell me if you have had it in the past year. You can just answer yes or no." The health conditions elicited were high blood pressure, heart and circulation problems, stroke or the effects of stroke, arthritis or rheumatism, Parkinson disease, other neurologic problems, eye trouble, ear trouble, dental problems, chest problems, stomach trouble, kidney trouble, loss of bladder control, loss of bowel control, diabetes, foot or ankle trouble, skin problems, fractures, cancer, and memory loss. Subsequently, participants were asked to report other health problems, and these were simply listed. We totaled the number of positive answers a participant gave, which produced a score from 0 to 36. The maximum score for any individual was 16. For baseline comparisons and for graphic representations, we categorized the score into the following: 0 health problems; 1 to 3 health problems; 4 to 6 health problems; and 7 or more health problems. For all other analyses, we considered the score as a continuous risk.

Analyses

We conducted cross-sectional and a prospective analyses. For the cross-sectional analysis (N=1751), we used the entire sample from time 1. For the prospective analysis (N=1028), we considered those who were alive and living in the community at time 2, who were able to be located, and who had complete data at time 2. For the baseline descriptive data, we considered a definition of multimorbidity as the presence of 3 or more chronic conditions.

Categorical variables were compared using χ^2 tests, and continuous variables were compared using Student t tests (assuming unequal variance) or ANOVA (analysis of variance). We then constructed logistic regression models with the outcome of the OARS score. We considered the OARS score as a dichotomous outcome, categorized as excellent or good function versus the level of disability (mild disability or moderate or severe disability). For the cross-sectional analysis, we determined the association

between multimorbidity and the OARS score at time 1, adjusting for age, sex, education, and the MMSE and CES-D scores. For the prospective analysis, our outcome variable was the time 2 OARS score. In these models, we included the time 1 factors, and also the baseline time 1 OARS score.

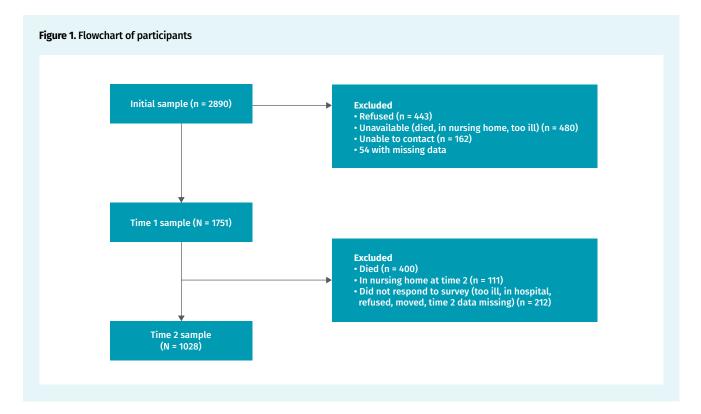
The analysis of functional change over 2 time points is complicated, particularly when there are competing outcomes (ie, death). We therefore conducted sensitivity analyses. First, we treated the OARS as a continuous score at time 1 and time 2. For the cross-sectional analysis, we constructed linear regression models including age, sex, education, and the MMSE and CES-D scores. For the prospective analysis, our outcome variable was the time 2 OARS score. In these models, we included the time 1 factors, and also the baseline time 1 OARS score. Second, we considered multiple outcomes. The loss to follow-up was not random, but strongly related to time 1 multimorbidity. To account for this, we constructed a multinomial logistic regression model with the time 2 outcomes of death, nursing home residence, functional decline, and no functional decline. Here, we considered a decline of 3 or more points on the OARS scale as clinically relevant.23

– Results –

There were 1751 participants in the cross-sectional analysis and 1028 in the prospective analysis. Figure 1 presents a participant flowchart. Those with multimorbidities were older, more likely to be women, and had less education; they also had lower MMSE scores and more depressive symptoms (Table 1).

At both time 1 and time 2, there was a relationship between multimorbidity and OARS score (Tables 2 and 3). In the time 1 analysis, multimorbidity was associated with poor functional status (Table 2). Lower functional status was also associated with being older and being a woman, as well as having greater cognitive impairment and more depressive symptoms. In the time 2 analysis, multimorbidity also predicted a lower functional status (Table 3). Older age, lower baseline functional status, and a lower MMSE score at time 1 also predicted worse functional status at time 2.

This association between multimorbidity and functional impairment was noted whether we considered the OARS scale as a categorical variable or as a continuous score (Figure 2). Multimorbidity predicted the OARS score at time 1 and time 2 in linear regression models considering age, sex, education, and MMSE and CES-D scores (data available upon request). When considering multiple outcomes, multimorbidity was a strong predictor of death, living in a nursing home, and functional decline (Figure 3). In this study, 44.6% of those with multimorbidity at time 1 had data missing at time 2 versus 33.3% of those without multimorbidity. This effect was mostly due to higher rates of death and nursing home residence at time 2 in those with



	CROSS SECTIONAL ANALYSES			PROSPECTIVE ANALYSES		
CHARACTERISTICS	NO MULTIMORBIDITY (N 514)	MULTIMORBIDITY (N 1237)	TOTAL SAMPLE (N 1751)	NO MULTIMORBIDITY (N 343)	MULTIMORBIDITY (N 685)	TOTAL SAMPLE (N 1028)
Mean age, y	75.2*	78.5*	77.5	74.5*	76.5*	75.8
Female sex, %	52.5*	61.0*	58.5	53.1*	63.9*	60.3
Mean education, y	9.9*	9.1*	9.3	10.3*	9.6*	9.8
Mean MMSE score	27.0*	25.9*	26.2	27.6*	26.9*	27.1
Mean CES-D score	4.1*	9.1*	7.6	3.8*	8.0*	6.6
Functional status, %						
• Excellent or good	86.0*	52.1*	62.1	90.1*	64.1*	73.0
• Mild impairment	9.9*	32.3*	25.7	7.9*	28.3*	21.5
 Moderate or severe impairment 	4.1*	15.6*	12.2	1.5*	7.6*	5.5

CES-D-Center for Epidemiologic Studies Depression Scale, MMSE-Mini-Mental State Examination. *Denotes significance (P<.05).

multimorbidities (Figure 3). In an unadjusted multinomial model, multimorbidity predicted all of these outcomes. After accounting for baseline functional status, multimorbidity predicted functional decline, but not nursing home residence or death (Table 4). The results for mortality in these multinomial models were very similar to the results of Cox regression models for mortality, which we have previously reported¹⁵: multimorbidity predicted death in models that did not adjust for functional status, cognition, or depressive symptoms. Once these were included in the model, the effect of multimorbidity was attenuated.

— Discussion —

We found that multimorbidity predicts functional decline over a long time frame. Multimorbidity has previously been shown to predict death in this 15 and other data sets.24 This effect might be confounded or mediated by disability. There has been less evidence that multimorbidity predicts functional decline. Maintaining functional status is a central health goal for most older adults, and might be a more relevant clinical end point than death. Our results build on previous analyses of this data set, in

Table 2. Logistic regression models for the outcome of the OARS score at time 1; the ORs and 95% CIs for the unadjusted and adjusted models are presented: With each additional chronic condition, the odds of disability at time 1 increased.

CHARACTERISTICS	UNADJUSTED OR (95% CI)	ADJUSTED OR (95% CI)	ADJUSTED OR FROM FULL MODEL (95% CI)
Age (per y)		1.11 (1.09 to 1.13)	1.09 (1.07 to 1.11)
Sex (reference = men)		1.97 (1.55 to 2.51)	2.16 (1.68 to 2.78)
Education (per y)		0.99 (0.95 to 1.02)	1.04 (1.00 to 1.08)
MMSE score (per point)			0.90 (0.85 to 0.94)
CES-D score (per point)			1.05 (1.03 to 1.06)
Multimorbidity (per condition)	1.45 (1.39 to 1.52)	1.42 (1.35 to 1.48)	1.35 (1.29 to 1.42)

CES-D—Center for Epidemiologic Studies Depression Scale, MMSE—Mini-Mental State Examination, OARS—Older Americans Resources and Services, OR-odds ratio.

Table 3. Logistic regression models for the outcome of the OARS score at time 2; the ORs and 95% CIs are presented for the unadjusted and adjusted models: With each additional chronic condition, the odds of disability at time 2 increased.

CHARACTERISTICS	UNADJUSTED OR (95% CI)	ADJUSTED OR (95% CI)	ADJUSTED OR (95% CI)	ADJUSTED OR FROM FULL MODEL (95% CI)
Age (per y)		1.13 (1.10 to 1.16)	1.12 (1.09 to 1.15)	1.12 (1.09 to 1.15)
Sex (reference = men)		1.43 (1.07 to 1.91)	1.53 (1.14 to 2.06)	1.13 (0.82 to 1.54)
Education (per y)		0.99 (0.95 to 1.03)	1.02 (0.98 to 1.07)	1.02 (0.97 to 1.07)
MMSE (per point)			0.90 (0.84 to 0.96)	0.91 (0.85 to 0.98)
CES-D (per point)			1.02 (1.00 to 1.05)	1.01 (0.99 to 1.04)
OARS score at time 1 (reference=no disability)				7.04 (4.64 to 10.71)
Multimorbidity (per condition)	1.31 (1.24 to 1.38)	1.28 (1.21 to 1.35)	1.25 (1.17 to 1.32)	1.15 (1.09 to 1.24)

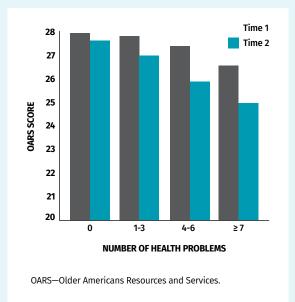
CES-D—Center for Epidemiologic Studies Depression Scale, MMSE—Mini-Mental State Examination, OARS—Older Americans Resources and Services, OR-odds ratio.

which multimorbidity predicts death in models that did not consider functional status. The most likely explanation is that functional decline is a mediator in the path from multimorbidity to death, with individuals passing through a period of functional decline before death.

Strengths and limitations

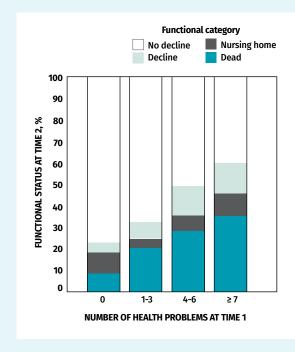
There are strengths and limitations to our approach. First, the data set is old, and the results might not apply fully to today's older population. Second, the choice of multimorbidity measure is difficult. We chose to simply total the number of chronic health problems and concerns into an index, and treated all diseases as equal contributors to disability. This is an oversimplification of the complex interaction between diseases to cause disability, 25,26 yet even this simple approach demonstrates the importance of cumulative disease burden. A further limitation is that the duration of disease is not known from the survey. There is evidence that the duration of time spent with disease predicts mortality, and the same might be true for disability. Because we do not have data on the duration of disease, we are unable to study it.27 We also do not have complete data on other potential confounding factors; social isolation, homelessness, and health behaviour patterns might moderate or

Figure 2. The association between the number of health problems and the OARS score at time 1 (N = 1751) and time 2 (N = 1028): Multimorbidity was associated with functional impairment in both cross-sectional and prospective analyses. Time 1 28



confound observations that we noted, but we were unable to account for these. We also did not consider if a participant's disease or concern resolved. A final limitation might be the result of nonresponse. Those with higher levels of multimorbidity were more likely to have a nonresponse at time 2. However, this would likely bias our findings toward finding no association between multimorbidity and functional decline, as the key reasons for nonresponse at time 2 was death and institutionalization, both of which were associated with higher levels of multimorbidity (Figure 3). When we consider the risk of multiple outcomes in multinomial logistic regression models, the association between time 1 multimorbidity and functional decline persisted.

Figure 3. The number of health problems at time 1 predicts functional decline, nursing home residence, and death 5 years later



The strength of our approach is the valid, reliable measures of functional status, cognition, and depressive symptoms gathered in a representative population of older adults.

Future research

Further research into nonmortality end points is needed. There might be aggressive interventions that extend life by a small amount at the expense of worsening functional status and quality of life.28 This might be particularly relevant for those older adults with multimorbidities. Understanding the effect of these treatments on functional decline is therefore important. Understanding the values that people attach to competing outcomes is also important.

Conclusion

Clinicians should be aware that there is a cumulative effect of health issues on the risk of disability over time. It is important to consider all other conditions in the care of a person with multiple health problems, rather than dealing exclusively with a failure in a single organ system. Clinicians should also be aware of changes in functional status in those with multiple chronic illnesses. At a policy level, our findings are also important. Comprehensive geriatric assessment has been shown to reduce functional decline, hospitalization, and nursing home use.29-32 However, these assessments target older adults with frailty or overt disability. Other models of care have been described for individuals with a single organ disease. 33-35 The ideal model of care for the much larger number of persons with multimorbidities who are functionally intact is less clear. In studying these models, functional status should be a measured outcome in addition to mortality. As these models are adopted into clinical care, attention to the effect of multimorbidity will also be an important consideration.

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Table 4. Results of multinomial logistic regression models: The effect of multimorbidity on multiple outcomes: Death, nursing home residence at time 2, and a functional decline of ≥3 points on the OARS scale, compared with a reference group of those who were alive in the community with a decline of <3 points on the OARS scale.

	EFFECT OF MULTIMORBIDITY ON			
LOGISTIC REGRESSION MODEL	FUNCTIONAL DECLINE, OR (95% CI)	NURSING HOME, OR (95% CI)	DEATH, OR (95% CI)	
Unadjusted	1.16 (1.10 to 1.24)	1.18 (1.11 to 1.27)	1.18 (1.13 to 1.23)	
Adjusted for age, sex, and education	1.14 (1.08 to 1.22)	1.10 (1.02 to 1.19)	1.14 (1.09 to 1.20)	
Plus MMSE and CES-D scores	1.16 (1.09 to 1.24)	1.06 (0.98 to 1.15)	1.10 (1.05 to 1.16)	
Plus baseline OARS points	1.14 (1.07 to 1.22)	1.01 (0.93 to 1.11)	1.06 (1.00 to 1.11)	

CES-D—Center for Epidemiologic Studies Depression Scale, MMSE—Mini-Mental State Examination, OARS—Older Americans Resources and Services, OR-odds ratio.

Contributors

Drs St John and Tyas were investigators in the Manitoba Study of Health and Aging. Dr St John conducted the data analysis and interpretation. Drs Tate and Griffith provided comments on the analyses and the manuscript. All authors contributed to the concept and design of the study and preparing the manuscript for submission.

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