THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2016, Vol. 71, No. S1, S54–S61
doi:10.1093/gerona/glv059

OXFORD

Special Article

The Impact of Multimorbidity and Coronary Disease Comorbidity on Physical Function in Women Aged 80 Years and Older: The Women's Health Initiative

Eileen Rillamas-Sun,[1] Andrea Z. LaCroix,[2] Christina L. Bell,[3] Kelli Ryckman,[4] Judith K. Ockene,[5] and Robert B. Wallace[4]

[1]Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington. [2]Department of Family and Preventive Medicine, University of California San Diego, La Jolla. [3]Department of Geriatric Medicine, University of Hawaii John A. Burns School of Medicine, Honolulu. [4]Department of Epidemiology, University of Iowa College of Public Health. [5]Division of Preventive and Behavioral Medicine, University of Massachusetts Medical School, Worcester.

Address correspondence to Eileen Rillamas-Sun, PhD, MPH, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. N., Seattle, WA 98109. Email: erillama@whi.org

Received September 23, 2014; Accepted April 8, 2015

Decision Editor: Sally A. Shumaker, PhD

Abstract

Background. A better understanding of medically centered outcomes, such as physical function, for older women with multiple chronic conditions is a national public health priority.

Methods. The prevalence of multimorbidity (defined as having 2 chronic conditions from a list of 12) and comorbidity with coronary disease (CHD) were calculated for 33,386 women who were enrolled in the Women's Health Initiative since 1993–1998 and were ≥80 years old by mid-September 2012. Associations between multimorbidity and CHD comorbidity on RAND-36 physical function scores were estimated using linear regression models.

Results. The prevalence of multimorbidity in this sample was 59%. Women with 0–1 chronic condition had a mean physical function score of 74 (95% confidence interval [CI]: 73, 74). Relative decrements in physical function scores were −8 (95% CI: −8, −7), −13 (95% CI: −14, −12) and −19 (95% CI: −20, −18) in women with 2, 3, and ≥4 chronic conditions, respectively. Women with CHD in combination with hip fractures or cognitive impairment had the largest adjusted decreases in physical function scores compared to the scores for women with CHD only. The impact of select characteristics on physical function scores between multimorbid and non-multimorbid women were similar; however, overall mean physical functions scores were lower for women with multmorbidity.

Conclusions. Multimorbidity profoundly impacted physical functioning in women aged more than 80 years. Modifiable risk factors, such as obesity and physical activity, were similar in older women regardless of multimorbidity status and provide targets for health interventions aimed at preventing loss of late-age physical functioning.

Key Words: Multimorbidities—Physical function—Cardiovascular

Alongside the expected population growth of older U.S. adults will be a concurrent rise in the prevalence of multimorbidity. Recent estimates indicate two-thirds of U.S. adults ≥65 years old and more than 80% of U.S. adults ≥85 years old are multimorbid, which is defined as concurrently having at least two chronic conditions (1,2). Persons with multimorbidity are more likely to have lower functional status and quality of life, incur more medical and long-term care services and costs, and experience an earlier death compared with persons without multimorbidity (3–5). Recognizing that multimorbidity is an important public health concern, the U.S. Department of Health and Human Services (HHS) proposed a strategic framework aimed at improving the health of those with multimorbidities (6,7). One specific goal of the framework emphasized the need to address research gaps,

including understanding disease patterning and disease pairs (ie, comorbidity) and determining the impacts of multimorbidity on various health outcomes, such as physical functioning and quality of life (6,7).

Commonly cited challenges of multimorbidity research are inconsistency in its definition, including heterogeneity in the conditions selected and in the diagnosis and collection of data across studies (1,8–10). These issues in multimorbidity measurement limit comparability across studies. A conceptual model and a standard definition that comprise 20 chronic conditions have been proposed by HHS; however, it was acknowledged that standard definitions might be easier to develop by population subgroups and are limited to a study's available data, research question, and outcomes (9). Indeed, 5 of the 20 conditions proposed by HHS could not be matched to claims from the Center for Medicare and Medicaid Services (CMS) analytic datasets (9). Additionally, in his review of multimorbidity in older adults, Salive (1) recommended that research include geriatric conditions, which historically have been excluded from lists.

Due to these issues, the prevalence of multimorbidity in older women is not well-described. A report using CMS claims data reported that 82% of women ≥85 years old had two or more chronic conditions among a list of 15 (1). Yet, a study of 1,099 Swedish adults aged 77–100 years, reported that 56% of the female participants had multimorbidity among a list of 30 conditions (11). Since women aged more than 80 years are a rapidly growing segment of the U.S. population, a better understanding of the conditions and disease patterns that afflict older women is essential to improve knowledge about the impacts on health outcomes, effective aging, and quality of life.

The Women's Health Initiative (WHI) study provides an opportunity to further the knowledge about multimorbidity in women aged 80 years and older. Drawing on the recommended definitions proposed by HHS (9) and by Salive (1), we examined multimorbidity using a list of 12 chronic conditions that are recognized to be highly prevalent and burdensome to older women. Furthermore, to address gaps in multimorbidity research (6), we described the association of multimorbidity and coronary disease (CHD) comorbidity (ie, CHD and its co-occurrence with one additional chronic condition) on late-age physical functioning. Although a variety of comorbidities can be considered, we focused specifically on co-occurrence with CHD because cardiovascular conditions are a primary outcome of interest for the WHI Program. We postulated that women with multimorbidity and CHD comorbidity would have lower physical functioning relative to women without multimorbidity. The findings from this article will improve understanding of multimorbidity in women aged 80 years and older and provide opportunities for targeted public health interventions aimed at improving or maintaining physical functioning in this population.

Methods

Study Population

The WHI Program is a collection of studies (four randomized clinical trials and an observational study) conducted among postmenopausal women, initially aged 50–79 years, who were recruited from 40 U.S. clinical centers between 1993 and 1998 (12,13). The initial phase of the WHI Clinical Trials and Observational Study provided data collection through 2005. The first WHI Extension Study was conducted between 2005 and 2010, and the second WHI Extension Study began in 2010 and will collect data through 2015. Study participants provided written informed consent at enrollment in the main study and at each study extension. The institutional review boards at all participating institutions approved all study protocols and materials. For this analysis, a subset of WHI women was selected if they met the following eligibility criteria: (a) consented to participate in the second WHI extension study; (b) were alive and at least 80 years of age by September 17, 2012, the date of the last medical history assessment; and (c) completed at least one physical functioning assessment after their 80th birthday.

Measures

Multimorbidity was defined as the presence of at least 2 chronic conditions among a list of 12 chronic conditions (Table 1). These conditions were selected in accordance with guidance from the literature (1,9) as well as based on their prevalence in older U.S. women, potential burden on physical functioning, and availability and reliability of diagnosis within the WHI data.

Both self-report and physician adjudication was used to identify the presence of these conditions in the WHI participants. Self-reported assessment was defined primarily as a positive response to the question, "Has a doctor told you that you have any of the following conditions or have you had any of the following procedures?" This assessment was broad and included data from the baseline visit when available. For a few conditions (osteoarthritis, depression, and chronic obstructive pulmonary disease [COPD]), no assessment was administered at baseline, so the presence of these conditions was determined during questions asked over the study follow-up. A participant needed only one positive response to this question at any time from baseline through follow-up to be regarded as having the condition. Throughout follow-up in the WHI study, incident CHD, cerebrovascular disease, cancer, and hip fracture were physician-adjudicated from medical records because they were primary outcomes of the main WHI Program. Thus, both prevalent and incident cases of these conditions were used to characterize their occurrence. In addition to self-reported diagnosis with Alzheimer's disease, cognitive impairment included a score of ≤88 on the last available modified mini-mental examination (14,15). Diabetes was characterized by self-report that included use of diabetic medications (16). Similarly, depression was classified by self-reported treatment for depression in the form of medications or therapy. Sensory impairment was defined as trouble with vision or hearing loss that was regarded as moderate or severe. Frequent fallers were women who self-reported falling at least two times in the past 12 months since the September 2012 outcome assessment. Urinary leakage was defined as reporting having ever leaked urine and feeling very or extremely bothered by it.

This was a cross-sectional study design because it analyzed the presence of multimorbidity as characterized in September 2012. The outcome was the last available physical function measurement that occurred after the participant's 80th birthday. We evaluated up to 19 years of available WHI data to cast a wide and conservative net and ensure we were sufficiently capturing the presence of the chronic conditions. To avoid misclassification bias, women with missing data and for whom the presence of any of the 12 chronic conditions could not be determined were classified as "undetermined." This prevented an inflation of women without multimorbidity. Multimorbidity was further categorized into five groups based on the number of conditions present: 0–1 (ie, not multimorbid), two, three, four or more, and undetermined.

We considered the inclusion of hypertension, hyperlipidemia, and obesity but elected not to add them to the list of 12 chronic conditions. Although these conditions are highly prevalent in older women, they are typically silent in their consequences until subsequent disease occurs. They are also major risk factors for many of the conditions on our list. Thus, we elected to define multimorbidity based on disease endpoints, geriatric impairments, and health burden. Accordingly, they were examined as risk factors by multimorbidity status and were adjusted for in the regression models.

To address research gaps about the prevalence and impacts of disease pairs, we evaluated the presence of comorbidity among women with CHD. We specifically focused on CHD because cardiovascular conditions are a major outcome of interest of the WHI Program. As described in Table 1, CHD was characterized as having at least one of the following: coronary artery bypass graft, coronary heart disease, congestive heart failure, clinical myocardial infarction, or percutaneous transluminal coronary angioplasty. These conditions were determined based on both self-report at baseline and physician-adjudication of medical records throughout study follow-up. The association of CHD comorbidity, defined as having CHD and one of the 11 other chronic conditions listed in Table 1, on physical function was examined. Women with CHD and ≥2 of the 11 other conditions listed were evaluated multiple times. For example, a woman with CHD, osteoarthritis, and sensory impairment was evaluated in two times in two separate models—the model for CHD with osteoarthritis and the model for CHD with sensory impairment.

The main outcome was physical functioning, measured using a subscale of the RAND 36-Item Health Survey (17). The subscale includes 10 questions that asked the respondent to report on a 3-point scale whether their health limits their ability to perform specific activities (18). Scores from the 3-point scale are rescaled and averaged. A higher score (range: 0–100) is suggestive of better physical functioning. Physical function was evaluated numerous times throughout the WHI study, but the most recent score collected after the participant's 80th birthday was used as the outcome for this analysis.

Age at the time the last physical function measurement was calculated from date of birth. All women were at least 80 years old. Race/ethnicity and highest level of education was self-reported at the WHI baseline visit. Physical activity was characterized in metabolic equivalents (METs) per week, calculated from participant's responses to questions about duration and frequency of exercise at baseline (19). Smoking status (never, past, and current) was self-reported from the most current follow-up questionnaires. Body mass index (BMI) was calculated from the participant's most current clinically collected height and weight measures and categorized into four groups using the standard World Health Organization cut-points (20). Hypertension and hyperlipidemia was characterized from current self-reported use of medications used to manage those conditions.

Statistical Analysis

Overall prevalence for each chronic condition was estimated. Then, among those with the condition, the distribution of women with the condition only, the condition plus exactly one of the remaining 11 conditions, or the condition plus two or more of the remaining 11 conditions was reported. Distributions by total number of chronic conditions (0–1, 2, 3, and 4 or more) and for comorbidity with CHD were calculated. Percent distributions of the sample characteristics stratified by the total number of chronic conditions were described.

Linear regression models were used to estimate the association of multimorbidity and CHD comorbidity on physical function score. The number of chronic conditions present was regressed on physical function score using women with 0–1 condition (not multimorbid) as the reference group (intercept). To interpret, the intercept represented the mean physical function score for women with 0–1 condition. Subsequently, the β-coefficients associated with the multimorbidity categories estimated the mean difference in physical function score relative to women with 0–1 condition. Similarly, 11 separate linear regression models were applied for each CHD comorbidity, using women with CHD only as the reference group (intercept). Thus, for these models, the β-coefficient represented the mean difference in physical function score associated with having CHD plus the other condition, relative to having only CHD. Statistical significance was reported using 95% confidence intervals [CIs]. As appropriate for linear regression modeling, CIs that did not include zero were regarded as statistically significant at $\alpha = 0.05$. Crude and adjusted models were reported. Adjusted models included age, race/ethnicity, highest education level, baseline physical activity, current smoking status, BMI, and presence of hypertension and/or hyperlipidemia.

Table 1. List of 12 Chronic Conditions Used to Characterize Multimorbidity in a Sample of ≥80-Year Old Women From the Women's Health Initiative Study

Chronic Condition	Definition/Characterization
1.Coronary disease	One or more of the following: coronary artery bypass graft, coronary heart disease, congestive heart failure, clinical myocardial infarction, or percutaneous transluminal coronary angioplasty.
2.Stroke	One or more of the following: carotid artery disease, stroke, transient ischemic attack
3.Cancer	Any cancer, excluding nonmelanoma skin cancer
4.Diabetes (16)	Self-reported physician-diagnosis of diabetes plus treatment (pills, insulin) for diabetes
5.Hip fracture	Broken hip
6.Osteoarthritis	Self-reported physician-diagnosis
7.Depression	Self-reported treatment (pills or therapy) for depression
8.Chronic obstructive pulmonary disease	Self-reported physician-diagnosis
9.Cognitive impairment	Self-reported physician diagnosis with dementia or Alzheimer's disease or having a last measured 3MSE score of ≤88 (14,15)
10.Sensory impairment	Self-reported trouble with vision or hearing loss that was moderate or severe
11.Frequent faller	Self-reported ≥2 falls in the 12 months prior to September 2012
12.Urinary incontinence	Self-reported urinary leakage that is very or extremely bothersome

Mean differences in physical function score for selected characteristics by multimorbid status was also estimated using linear regression models. We executed separate regression models for those with and without multimorbidity. In these models, the mean physical function score for women who had characteristics from all reference groups was estimated. Thus, the β-coefficients estimated the mean difference in physical function score for each characteristic relative to the referent characteristic. Similarly, 95% CIs that did not include zero were regarded as statistically significant. All analyses were completed using SAS statistical software v9.3 (SAS Institute, Inc., NC).

Results

About 91% of the 33,386 WHI women aged 80 years and older had at least 1 of the 12 selected chronic conditions (Table 2). The most prevalent conditions were osteoarthritis (61%) and history of cancer (25%), while the least common were COPD (5%), prior hip fracture (6%), and prior stroke (8.5%). The prevalence of the other conditions ranged between 9% and 18%. In general, about a quarter of the women had exactly two conditions, while about 54%–78% of women had more than two chronic conditions from the list (Table 2). Having more than two chronic conditions was least common for women with osteoarthritis and most common for women with depression, COPD, or cognitive impairment. The presence of the select chronic conditions could not be determined for 20% of women because of missing data.

Women with the highest burden of multiple chronic conditions were more likely to be older, less educated, current or past smokers, physically inactive, obese, and have high blood pressure and/or high cholesterol (Table 3). Among women with four or more chronic conditions, 30% were obese compared with 18% in the group with 0–1 chronic condition. There was no apparent association between race/ethnicity and number of chronic conditions. Women whose multimorbidity status could not be determined were most similar to women who had two chronic conditions.

In our study sample, 47% of women had two or more chronic conditions and 33% had 0–1 condition (Table 4). When women with missing data were excluded from the denominator, the prevalence of multimorbidity was 59%. The unadjusted (crude) mean physical functioning score was 65.9 (95% CI: 65.4, 66.4) among women with 0–1 chronic condition (Table 4), and levels declined precipitously in women with higher numbers of chronic conditions. After adjusting for characteristics highly associated with multimorbidity, the mean physical functioning score was 73.7 (95% CI: 72.9, 74.4) for women with 0–1 chronic condition, and the decrements in physical function score associated with having higher numbers of chronic conditions ranged from −7.6 (95% CI: −8.4, −6.8) in women with two conditions to −19.4 (95% CI: −20.4, −18.3) in women with four or more conditions.

Examination of CHD comorbidity indicated that osteoarthritis co-occurred most frequently (62%), followed by history of cancer (26%), diabetes (23%), and falling at least twice in the past year (21%; Table 4). Prior hip fracture and COPD were least likely to co-occur with CHD (7% and 8%, respectively). Eight percent of women had CHD only, and these women were found to have an adjusted mean physical functioning score of 65.4 (95% CI: 61.8, 68.9; Table 4). The largest average decrements in physical functioning for morbidity in combination with CHD were hip fracture (−22.4; 95% CI: −26.4, −18.3), cognitive impairment (−20.0; 95% CI: −23.7, −16.2), COPD (−19.0; 95% CI: −22.8, −15.2), and falling two or more times in the past year (−19.0; 95% CI: −22.1, −15.8). For all other chronic conditions, average decrements in physical function score ranged from −12.8 to −18.1.

Among women with 0–1 chronic condition, the mean physical functioning score (ie, for those with characteristics from all reference groups) was 74.4 (95% CI: 73.1, 75.7; Table 5). In contrast, women with two or more chronic conditions had a mean physical functioning score of 62.9 (95% CI: 61.4, 64.3). In general, risk factors affecting physical function scores were quite similar in women with and without multiple chronic conditions. Focusing specifically on the multimorbid group, women aged 90 years and older had an

Table 2. Prevalence and Multimorbidity Distribution of Select Chronic Conditions in 33,386 Women Aged 80 Years and Older

Chronic Condition		Has Condition and		
	Overall Prevalence	No Other Condition Listed	Exactly 1 Other Condition Listed	>1 Other Condition Listed
		n (%)		
Coronary disease	5,219 (15.8)	412 (7.9)	1,026 (19.7)	3,781 (72.5)
Stroke	2,812 (8.5)	206 (7.3)	524 (18.6)	2,082 (74.0)
Cancer, excluding nonmelanoma skin cancer	8,160 (24.6)	1,040 (12.8)	2,117 (25.9)	5,003 (61.3)
Diabetes	5,390 (16.2)	418 (7.8)	1,167 (21.7)	3,805 (70.6)
Hip fracture	1,835 (6.4)	164 (8.9)	441 (24.0)	1,230 (67.0)
Osteoarthritis	20,224 (60.6)	4,114 (20.3)	5,194 (25.7)	10,916 (54.0)
Depression	3,443 (10.3)	157 (4.6)	592 (17.2)	2,694 (78.3)
Chronic obstructive pulmonary disease	1,731 (5.2)	89 (5.1)	292 (16.9)	1,350 (78.0)
Cognitive impairment	3,465 (10.4)	161 (4.7)	602 (17.4)	2,702 (78.0)
Sensory impairment	5,295 (16.1)	383 (7.2)	1,155 (21.8)	3,757 (71.0)
Fell ≥2 in past 12 months	5,808 (17.6)	408 (7.0)	1,173 (20.2)	4,227 (72.8)
Urinary incontinence	2,862 (8.9)	211 (7.4)	565 (19.7)	2,086 (72.9)
Had none of above conditions	3,266 (9.8)	N/A	N/A	N/A
Undetermined	6,700 (20.1)	N/A	N/A	N/A

Note: N/A = not applicable.

Table 3. Characteristics of Sample by Number of Chronic Conditions (n = 33,386)

	Number of Chronic Conditions				
	0–1	2	3	4 or More	Undetermined
N (%)	11,029 (33.0)	7,424 (22.2)	4,570 (13.7)	3,663 (11.0)	6,700 (20.1)
Current age, *n* (%)					
80–84 years	7,187 (65.2)	4,334 (58.4)	2,601 (56.9)	1,863 (50.7)	3,930 (58.7)
85–89 years	3,152 (28.6)	2,462 (33.2)	1,519 (33.2)	1,325 (36.2)	2,176 (32.5)
90 years or more	690 (6.3)	628 (8.5)	450 (9.9)	475 (13.0)	594 (8.9)
Race/ethnicity, *n* (%)					
White	9,992 (91.7)	6,714 (91.3)	4,136 (91.9)	3,346 (92.7)	6,109 (92.2)
Black/African-American	481 (4.4)	341 (4.6)	198 (4.4)	151 (4.2)	313 (4.7)
Hispanic/Latina	150 (1.4)	124 (1.7)	85 (1.9)	62 (1.7)	113 (1.7)
Asian/Pacific-Islander	250 (2.3)	161 (2.2)	61 (1.4)	36 (1.0)	81 (1.2)
American Indian/Alaskan native	20 (0.2)	11 (0.2)	21 (0.5)	13 (0.4)	12 (0.2)
Some college or higher, *n* (%)	7,843 (71.5)	5,039 (68.2)	3,028 (66.7)	2,367 (65.0)	4,737 (71.0)
Smoking status, *n* (%)					
Never	6,267 (57.1)	4,100 (55.5)	2,438 (53.7)	1,852 (50.9)	3,557 (53.7)
Past	4,583 (41.8)	3,220 (43.6)	2,053 (45.2)	1,719 (47.3)	2,981 (45.0)
Current	124 (1.1)	72 (1.0)	52 (1.1)	66 (1.8)	91 (1.4)
Total MET-h/wk, mean (*SD*)	14.7 (14.1)	13.5 (13.6)	13.1 (13.4)	12.3 (13.3)	14.2 (13.9)
Body mass index categories, *n* (%)					
Underweight	222 (2.0)	155 (2.1)	82 (1.8)	60 (1.6)	142 (2.1)
Normal	4,977 (45.1)	2,934 (39.5)	1,739 (38.1)	1,225 (33.4)	2,681 (40.0)
Overweight	3,836 (34.8)	2,701 (36.4)	1,626 (35.6)	1,295 (35.4)	2,445 (36.5)
Obese	1,994 (18.1)	1,634 (22.0)	1,123 (24.6)	1,083 (29.6)	1,432 (21.4)
High blood pressure and/or cholesterol, *n* (%)	7,899 (71.6)	5,718 (77.0)	3,695 (80.9)	3,176 (86.7)	5,163 (77.1)

Note: MET = metabolic equivalent.

Table 4. Mean Difference in Physical Function Score by Number of Chronic Conditions and Comorbidity With Coronary Disease[a]

	N (%)	Crude Model	Adjusted Model[b]
		Mean Difference (95% Cl)	Mean Difference (95% Cl)
0–1 Conditions (reference)	11,029 (33.0)	65.9 (65.4, 66.4)	73.7 (72.9, 74.4)
Number of conditions (multimorbid):			
2	7,424 (22.2)	−9.9 (−10.7, −9.0)	−7.6 (−8.4, −6.8)
3	4,570 (13.7)	−16.2 (−17.3, −15.2)	−13.1 (−14.0, −12.2)
4 or more	3,663 (11.0)	−25.1 (−26.3, −24.0)	−19.4 (−20.4, −18.3)
Undetermined	6,700 (20.1)	−9.1 (−10.0, −8.2)	−8.0 (−8.9, −7.1)
Coronary disease only (reference)	412 (7.9)	59.1 (56.3, 61.8)	65.4 (61.8, 68.9)
Has coronary disease and:			
Stroke	814 (15.6)	−19.2 (−22.7, −15.7)	−17.5 (−20.8, −14.2)
Cancer, excluding nonmelanoma skin cancer	1,341 (25.7)	−14.2 (−17.4, −11.0)	−12.8 (−15.8, −9.7)
Diabetes	1,193 (22.9)	−20.0 (−23.3, −16.8)	−16.8 (−20.0, −13.7)
Hip fracture	357 (6.8)	−24.7 (−29.0, −20.5)	−22.4 (−26.4, −18.3)
Osteoarthritis	3,221 (61.7)	−15.1 (−18.1, −12.2)	−13.4 (−16.2, −10.6)
Depression	640 (12.3)	−20.1 (−23.8, −16.3)	−18.1 (−21.6, −14.5)
Chronic obstructive pulmonary disease	408 (7.8)	−20.2 (−24.2, −16.2)	−19.0 (−22.8, −15.2)
Cognitive impairment	658 (12.6)	−21.8 (−25.7, −17.9)	−20.0 (−23.7, −16.2)
Sensory impairment	967 (18.5)	−17.7 (−21.1, −14.3)	−15.0 (−18.2, −11.8)
Fell ≥2 in past 12 months	1,096 (21.0)	−21.1 (−24.4, −17.8)	−19.0 (−22.1, −15.8)
Urinary incontinence	544 (10.4)	−17.1 (−20.9, −13.2)	−13.8 (−17.5, −10.2)

Notes: CI = confidence interval.

[a]Mean difference in physical function score relative to the reference group.

[b]Adjusted for age, race/ethnicity, education, smoking status, body mass index, physical activity, hypertension, and hypercholesterolemia.

average physical functioning score that was 18.1 (95% CI: −19.6, −16.5) points lower than women 80–84 years old. Women from race/ethnicity groups other than white had physical function values that were 3.0–5.5 points higher than white women, with Hispanic/Latina women exhibiting the highest advantage (6; 95% CI: 2, 9). Physical activity was associated with higher physical function levels (0.31, 95% CI: 0.27, 0.34) for every additional MET-hour/week increase. Overweight and obese women had scores that were 7 (95% CI: −8, −5) and 17 (95% CI: −18, −16) points lower, respectively, compared to normal weight women. Current smoking behavior was

Table 5. Adjusted Mean Difference in Physical Function Score Associated With Select Characteristics by Multimorbidity Status[a]

	Has 0–1 Condition	Has ≥2 Conditions
	Mean Difference (95% Cl)	Mean Difference (95% Cl)
Intercept (β_0)[b]	74.4 (73.1, 75.7)	62.9 (61.4, 64.3)
Current age		
80–84 years	Reference	Reference
85–89 years	−7.6 (−8.6, −6.5)	−8.4 (−9.4, −7.4)
90 years or more	−19.0 (−21.0, −17.0)	−18.1 (−19.6, −16.5)
Race/ethnicity		
White	Reference	Reference
Black/African-American	+0.6 (−1.8, 3.0)	+3.6 (1.2, 5.9)
Hispanic/Latina	+0.7 (−3.4, 4.8)	+5.5 (1.9, 9.1)
Asian/Pacific-Islander	+1.5 (−1.6, 4.6)	+3.5 (−0.1, 7.0)
American Indian/Alaskan native	+2.0 (−9.5, 13.6)	+3.0 (−5.4, 11.3)
Highest education at baseline		
Some college or higher	Reference	Reference
No college or less	−1.0 (−2.0, 0.04)	−1.4 (−2.4, −0.4)
Smoking status		
Never	Reference	Reference
Past	−1.8 (−2.7, −0.8)	−1.4 (−2.3, −0.4)
Current	−1.4 (−6.3, 3.4)	−6.1 (−10.4, −1.8)
Physical activity[c]		
Per 1 MET-h/wk increase	+0.29 (0.25, 0.32)	+0.31 (0.27, 0.34)
Body mass index categories		
Normal	Reference	Reference
Underweight	−1.1 (−4.5, 2.3)	−3.8 (−7.2, −0.4)
Overweight	−7.1 (−8.1, −6.0)	−6.5 (−7.5, −5.4)
Obese	−18.1 (−19.4, −16.7)	−17.1 (−18.3, −15.9)
High blood pressure and/or cholesterol		
No	Reference	Reference
Yes	−3.9 (−5.0, −2.9)	−5.0 (−6.2, −3.9)

Notes: CI = confidence interval; MET = metabolic equivalent.
[a]Adjusted for all other factors listed.
[b]Mean physical function score of women inclusive of all reference groups.
[c]Centered at mean value of 13.8 MET-h/wk.

associated with physical functioning scores that were 6 (95% CI: −10, −2) points lower than never smokers.

Discussion

In this study of WHI women aged 80 years and older, multimorbidity was associated with poorer physical functioning. We found an inverse relationship between the number of chronic conditions present and physical function score. Moreover, women with CHD in combination with another chronic condition had lower physical functioning compared with women with CHD alone. Decrements in physical function by select demographic or health characteristics were similar for women with and without multimorbidity, but overall mean physical function levels were lower for multimorbid women.

Despite the heterogeneity in the conditions used to define multimorbidity, the observation that having more chronic conditions was associated with lower functioning had been consistently reported in previous studies of older adults (21–24). Marengoni and colleagues (21) reported that older adults with ≥4 conditions had the highest prevalence of activity of daily living (ADL) disability. Older adults with ≥3 conditions at the Longitudinal Aging Study Amsterdam baseline visit had a 4-fold risk of decline in physical function 3 years later (24). Our study provides further credence about the long-term impacts of multimorbidity on physical functioning.

The strategic framework developed by HHS identified the need for more research about chronic disease dyads and triads as a goal to increase our knowledge about multiple chronic conditions (6). To address this research gap, we examined CHD comorbidity and its impact on physical function. Although rankings were influenced by the overall prevalence of conditions in the study population, osteoarthritis, a history of cancer, and type-2 diabetes were most likely to co-occur with CHD among women at least 80 years of age in our sample. However, compared to women with CHD alone, the largest decrements in physical function score were seen among the CHD pairings least prevalent in our population—specifically, hip fractures and COPD. Large deficits in physical functioning also were observed among women with CHD and either cognitive impairment, falls in the past year, or depression. This suggests that the pairing of CHD with certain disabling morbidities that almost always limit activities results in the biggest negative impact on physical function in women aged 80 years and older. This finding is in concert with older Swedish adults from the Kungsholmen Project, which identified that disease pairings between dementia, cardiovascular disease, hip fracture, and depression had the highest frequencies of ADL disability (21).

A number of studies have examined the relationship between disease dyads and functional status (3,21,24–26). However, many of these studies examined associations only among the most prevalent dyads. Had we utilized that approach, we would not have identified

women with CHD in combination with hip fracture or COPD as groups that might be most vulnerable to poorer physical functioning since these combinations were not highly prevalent in our population. Furthermore, many studies used those with neither disease as the referent group, so specificity about who to target for public health interventions might be diminished.

Our findings appeared to be aligned with the existing literature despite methodological differences among the studies. Cardiovascular disease with depression or with dementia was associated with a 14.5-fold and a nearly 40-fold odds, respectively, of ADL disability relative to older adults without these disease combinations (21). Likewise, the odds of functional dependence in older adults from Spain who had both cardiovascular and bone disease was 1.9 relative to those without these diseases (26). Although Fried and colleagues (25) examined cognitive dysfunction and hip fracture within their definition of multimorbidity, these conditions were not examined among their disease pairs because they were not highly prevalent in their study population.

We also examined whether participants' demographic and health characteristics impacted physical function differently for multimorbid compared to non-multimorbid women. In general, we observed no differences by age, education, physical activity levels, BMI, or presence of hypertension or hyperlipidemia. In other words, using age as an example, being older was associated with similar decreases in physical function score for both multimorbid and non-multimorbid women. Interestingly, we found that Black/African American and Latina women had a 3.6 and 5.5 higher physical function score, respectively, relative to whites, but only if they were multimorbid. Most previous studies on multimorbidity and physical function have not been ethnically diverse. It would be worthwhile to determine if similar patterns in physical function score by race/ethncity and multimorbidity are seen in other studies. Despite this, we noted that the average physical function scores collected after women turned 80 years old were 11.5 points lower for women with multimorbidity. Thus, although most characteristics affect physical function similarly by multimorbidity status, overall functioning remains lower for those who were multimorbid.

Almost two-thirds of the WHI women in our study had at least 2 of 12 chronic conditions, while 10% had none of the selected conditions. Multimorbidity was most common in women with depression, COPD or cognitive impairment. Women with multimorbidity were older, less likely to have attended college, and at baseline were more physically active, more likely to be past or current smokers, obese, and have high blood pressure or high cholesterol. The prevalence of multimorbidity was similar compared with other studies of older adults, ranging from 55% to 82% (1,21,25,26). Differences in the selection of conditions and methods used to define multimorbidity limit comparability of prevalence rates across studies.

Our characterization of multimorbidity as the presence of at least two chronic conditions is a widely accepted and commonly used definition in multimorbidity research (27). Again, the conditions chosen and how they were assessed or diagnosed varied across studies, which hinder comparability (1,8–10,27). To address this challenge, a HHS working group compiled a list of 20 conditions, selected based on chronicity, prevalence, and opportunity for public health or clinical impact, as a framework for standardizing a multimorbidity definition (9). Despite this, differences in study populations, design, and research objectives, and in available data deter from use of a uniform definition. Furthermore, selecting conditions tailored to the burden and prevalence of the population group of interest might have greater public health impact and importance. Indeed, a recent review noted that geriatric conditions, including incontinence and falls, have been excluded in multimorbidity research of older adults (1). Therefore, the choice of our conditions was guided both by the published literature, but also by our research question and the data available in WHI. Of the 12 conditions, 9 are represented in the list compiled from the HHS working group. The three conditions not represented were sensory impairment, falls, and urinary incontinence—geriatric conditions that were more relevant to our study population.

Strengths of this study include the very large study population of women aged 80 and older, perhaps the largest group of very old women ever studied in the United States. About 8% of these women were from minority race/ethnicity groups allowing us to examine physical function scores in these understudied subgroups of very old women. Participation in the WHI Program since enrollment in 1993–1998 allowed us to characterize many of the recommended chronic conditions for studying multimorbidity including some that most studies have excluded, such as falls and urinary incontinence. Since we used all available information prior to the reference date in September 2012, including physician-adjudication data when available, we believe we adequately identified those with the conditions and that misclassification was low.

We were unable to classify morbidity in one-fifth of the study population due to missing data. However, we included this subgroup in our analysis, and their characteristics were more similar to multimorbid women with exactly two conditions. Therefore, we are less concerned that our results were underestimated as a consequence of excluding women whose missing data was due to higher multimorbidity. In addition, we did not have health information on WHI women who did not consent to the extended follow-up phases of WHI (reference paper by Espeland in this supplement). It is possible that we underestimated multimorbidity in the WHI cohort who originally enrolled and survived to age 80 years, due to selective attrition among women with a greater illness burden. Thus, the multimorbidity prevalence estimates we reported in this study population should be regarded as conservative. Our list of chronic conditions did not include all 20 chronic conditions recommended by the HHS strategic framework; however, many conditions excluded, such as autism, HIV, and substance abuse disorders, are arguably less relevant for older populations. Finally, we recognize that our list of conditions was not exhaustive and excluded other diseases that are highly debilitating and likely to have a strong impact on physical functioning; however, this is a limitation for all studies examining multimorbidity.

Nonetheless, these data illustrate the major impact of multimorbidity on physical function among women aged 80 years and older. Multimorbid women are in the majority of this age group, which is a fast growing segment of the U.S. population. Several modifiable risk factors, including obesity, physical activity, smoking, and blood pressure and cholesterol control, appeared to influence physical function in these women to a similar extent as their counterparts without multimorbidity. This emphasizes the need to include multimorbid women in interventions designed to preserve physical function and provides opportunities for targeted health interventions. In addition, more research about these relationships might improve our knowledge about disease pathology and impacts on physical functioning. Finally, our results showed that especially vulnerable women included those with depression, COPD, and cognitive impairment, all conditions that can result in severe deconditioning and social isolation, which impact physical function. Moreover, women with at least four chronic condition and those with CHD in combination with hip fracture, cognitive

impairment, COPD, and frequent falling were more susceptible to lower physical functioning. These findings help to identify women at higher risk of poor physical function and provide an opportunity to tailor clinical and public health approaches that prevent loss of or maintain higher functioning in these women.

Funding

The WHI program is funded by the National Heart, Lung, and Blood Institute at the National Institutes of Health, U.S. Department of Health and Human Services (HHSN268201100046C, HHSN 268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C).

Acknowledgments

The authors gratefully acknowledge the dedicated efforts of the WHI participants and of key WHI investigators and staff at the clinical centers and the Clinical Coordinating Center. A full listing of the WHI investigators can be found at: https://cleo.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf

References

1. Salive ME. Multimorbidity in older adults. *Epidemiol Rev*. 2013;35:75–83. doi:10.1093/epirev/mxs009
2. Ward BW, Schiller JS. Prevalence of multiple chronic conditions among US adults: estimates from the National Health Interview Survey, 2010. *Prev Chronic Dis*. 2013;10:E65. doi:10.5888/pcd10.120203
3. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. *J Clin Epidemiol*. 2001;54:661–674.
4. Koller D, Schön G, Schäfer I, Glaeske G, van den Bussche H, Hansen H. Multimorbidity and long-term care dependency—a five-year follow-up. *BMC Geriatr*. 2014;14:70. doi:10.1186/1471-2318-14-70
5. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med*. 2002;162:2269–2276.
6. Parekh AK, Goodman RA, Gordon C, Koh HK. Managing multiple chronic conditions: a strategic framework for improving health outcomes and quality of life. *Public Health Rep*. 2011;126(4):460–471.
7. Parekh AK, Kronick R, Tavenner M. Optimizing health for persons with multiple chronic conditions. *JAMA*. 2014;312:1199–1200. doi:10.1001/jama.2014.10181
8. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med*. 2012;10:142–151. doi:10.1370/afm.1337
9. Goodman RA, Posner SF, Huang ES, Parekh AK, Koh HK. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis*. 2013;10:E66. doi:10.5888/pcd10.120239
10. Schram MT, Frijters D, van de Lisdonk EH, et al. Setting and registry characteristics affect the prevalence and nature of multimorbidity in the elderly. *J Clin Epidemiol*. 2008;61(11):1104–1112. doi:10.1016/j.jclinepi.2007.11.021
11. Marengoni A, Winblad B, Karp A, Fratiglioni L. Prevalence of chronic diseases and multimorbidity among the elderly population in Sweden. *Am J Public Health*. 2008;98:1198–1200. doi:10.2105/AJPH.2007.121137
12. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. *Control Clin Trials*. 1998;19(1):61–109.
13. Anderson GL, Manson J, Wallace R, et al. Implementation of the Women's Health Initiative study design. *Ann Epidemiol*. 2003;13(9 suppl):S5–17.
14. Espeland MA, Rapp SR, Robertson J, et al. Benchmarks for designing two-stage studies using modified mini-mental state examinations: experience from the Women's Health Initiative Memory Study. *Clin Trials*. 2006;3(2):99–106.
15. Teng EL, Chui HC. The modified mini-mental state (3MS) examination. *J Clin Psychiatry*. 1987;48:314–318.
16. Margolis KL, Lihong Q, Brzyski R, et al. Validity of diabetes self-reports in the Women's Health Initiative: comparison with medication inventories and fasting glucose measurements. *Clin Trials*. 2008;5(3):240–247. doi:10.1177/1740774508091749
17. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473–483.
18. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. *Health Econ*. 1993;2:217–227.
19. Ainsworth BE, Haskell WL, Leon AS, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc*. 1993;25(1):71–80.
20. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. National Institutes of Health. *Obes Res*. 1998;6(suppl 2):51S–209S.
21. Marengoni A, Angleman S, Fratiglioni L. Prevalence of disability according to multimorbidity and disease clustering: a population-based study. 2011 2011;1(1):8.
22. Bayliss EA, Bayliss MS, Ware JE Jr, Steiner JF. Predicting declines in physical function in persons with multiple chronic medical conditions: what we can learn from the medical problem list. *Health Qual Life Outcomes*. 2004;2:47.
23. Kadam UT, Croft PR. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. *Fam Pract* 2007;24(5):412–419.
24. Kriegsman DM, Deeg DJ, Stalman WA. Comorbidity of somatic chronic diseases and decline in physical functioning: the Longitudinal Aging Study Amsterdam. *J Clin Epidemiol*. 2004;57:55–65.
25. Fried LP, Bandeen-Roche K, Kasper JD, Guralnik JM. Association of comorbidity with disability in older women: the Women's Health and Aging Study. *J Clin Epidemiol*. 1999;52:27–37.
26. Marventano S, Ayala A, Gonzalez N, Rodriguez-Blazquez C, Garcia-Gutierrez S, Forjaz MJ. Multimorbidity and functional status in community-dwelling older adults. *Eur J Intern Med*. 2014;25(7):610–616. doi:10.1016/j.ejim.2014.06.018
27. Schellevis FG. Epidemiology of multiple chronic conditions: an international perspective. 2013;3(2):5.