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Multi-morbidity and patient-reported functional limitations: a population-based cohort study

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Abstract

Background: Persons who accumulate chronic conditions at a rate faster than their peers may experience accelerated aging and poor health outcomes, including functional limitations.

Methods: Adults aged ≥40 years who resided in Olmsted County, Minnesota on 1 January 2006 were identified. The prevalence of 21 chronic conditions was ascertained, and age-specific quartiles of the number of chronic conditions was estimated within 4 age groups: 40–54, 55–64, 65–74, and ≥75 years. Difficulty with nine patient-reported functional limitations (including basic and instrumental activities of daily living and mobility activities) were ascertained through 31 October 2018. Cox regression was used to model associations of chronic condition quartiles with new-onset functional limitations considered separately. We estimated absolute risk differences and hazard ratios stratified by age group, and adjusted for sex, race, ethnicity, marital status, education, and the residual effect of age.

Results: Among 39,624 persons (44.5% men, 93.2% white), the most common reported new functional limitations were difficulty with climbing stairs, walking, and housekeeping. For all functional limitations, the absolute risk differences were largest among the oldest age group (≥75 years). Approximately twofold increased hazard ratios were observed among those in the highest vs. lowest quartile for the three oldest age groups, and approximately threefold or higher hazard ratios were observed for persons aged 40-54 years.

Conclusion: Persons with increased accumulation of chronic conditions experience increased risks of developing functional limitations compared to their peers. These findings underscore the importance of assessing health status and of employing interventions to prevent and effectively manage multi-morbidity at all ages.

Keywords

Multi-morbidity, chronic conditions, functional limitations, disability, activities of daily living, patient reported outcomes

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Introduction

It has been projected that 20% of the United States population will be aged 65 years and older by 2050.[1] This demographic aging of the population will result in an increasing number of persons affected by aging-related diseases. The prevalence of multi-morbidity (defined as the presence of 2 or more chronic conditions) and of functional limitations (defined as self-reported difficulty with 1 or more basic or instrumental activity of daily living - ADL) generally increase with age.[2–12] Multi-morbidity and functional limitations individually contribute to poor outcomes;[11,13–16] however, persons who have both multi-morbidity and functional limitations experience the poorest health care outcomes, including hospitalizations, death, and greater health care expenditures.[17,18] In addition, persons who accumulate chronic conditions at a faster rate than their peers of a similar age (those who may be experiencing accelerated aging) have greater mortality.[19]

It has been postulated that the aging process results in a chronic dysregulation of multiple organ systems, and in the accumulation of diseases as a result of loss of resilience and homeostasis.[20] This age-related multi-system loss of reserve and function manifests clinically as multi-morbidity, and affects health outcomes including hospitalizations, quality of life, disability, and death.[20] Population-based studies are needed to characterize outcomes in persons experiencing accelerated aging compared to same age peers. However, most studies utilizing administrative claims or electronic health records cannot study patient reported outcomes. The Rochester Epidemiology Project (REP) medical records-linkage system is a unique resource that includes both comprehensive electronic health record data and patient-reported information on functional limitation. Thus, we used the REP to study the associations of number of chronic conditions with development of new-onset functional limitations in a large geographically-defined population in Minnesota.

Methods

Study population

This study was conducted using the REP medical records-linkage system.[21–24] The REP captures all health care information from the few providers who deliver most of the health care to the residents of Olmsted County, Minnesota. Thus, the linkage of information from these health care providers captures virtually the entire health care experience of the Olmsted County population. For the current study, all adults aged ≥40 years who resided in Olmsted County on 1 January 2006 and who provided authorization to use their medical records for research (Minnesota Research Authorization; obtained from 97% of the REP population) were included (n = 55,736). This study was approved by the Mayo Clinic (IRB: 17-001538) and Olmsted Medical Center (IRB: 007-OMC-17) Institutional Review Boards. The study was considered minimal risk by both Institutional Review Boards; therefore, the requirement for informed consent was waived. Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to the Rochester Epidemiology Project at Mayo Clinic at info@rochesterproject.org.

Ascertainment of chronic conditions

We electronically searched the diagnostic indices of the REP to identify the International Classification of Diseases, Ninth Revision (ICD-9) codes associated with any health care visit (inpatient or outpatient) for a 5-year period from 1 January 2001 through 31 December 2005. The ICD-9 diagnostic codes were used to identify 20 chronic conditions defined by the United States Department of Health and Human Services for studies of multi-morbidity.[25,26] In addition, we added anxiety to the list because it is common in the United States population, resulting in a total of 21 chronic conditions. One diagnostic code assigned during either an inpatient or outpatient visit within the 5-year capture frame was used to define each of the chronic conditions.[27] The list of specific diagnostic codes used to define each of the chronic conditions has been reported elsewhere.[28] We counted the total number of chronic conditions (out of a total of 21 conditions) and estimated age-specific quartiles based on the distribution of number of conditions within each age group.

Patient-reported activities of daily living

A questionnaire that was administered on at least a yearly basis to persons seen at one of the institutions participating in the REP (Mayo Clinic) included assessment of functional limitations. The questionnaire could have been completed by the patient or by a proxy, such as a family member, domestic partner, legal guardian, or other person. Functional limitations for a total of 9 activities (walking, climbing stairs, eating, dressing, toileting, bathing, housekeeping, transportation, and managing medications) were ascertained from a single question asking the person to select all of the activities with which they had difficulty performing on their own. These activities included basic ADLs, instrumental ADLs, and mobility activities. All questionnaires from 1 January 2001 through 31 December 2005 were used to identify functional limitations present at baseline (1 January 2006). If a person had more than one questionnaire during the 5-year capture frame, self-report

of a functional limitation on at least one of the questionnaires was considered as having a pre-existing functional limitation. Persons with a pre-existing functional limitation at baseline were excluded from the analysis related to that functional limitation because they were not considered to be at risk. In the subset of at-risk patients, all questionnaires from 1 January 2006 through 31 October 2018 were used to identify new-onset functional limitations. Persons were followed to the date of the last questionnaire completed.

Statistical analysis

A total of 12,853 persons in the cohort (23%) did not have baseline functional limitation information because they did not complete a questionnaire in the 5-year capture frame prior to baseline, and another 41 were missing baseline covariate information (either marital status or education). In addition, 3218 (6%) were missing follow-up functional limitation information because they did not complete any questionnaires during follow-up. The analysis excluded persons with missing baseline and follow-up information (complete case analysis), resulting in a total of 39,624 persons.

Characteristics of persons included and excluded from the analysis were compared using chi-square and Wilcoxon-Mann-Whitney tests. All other analyses were stratified by age group (ages 40–54, 55–64, 65–74, and ≥75 years). Descriptive characteristics were summarized by age group using number (%) for categorical variables and median (interquartile range; IQR) for continuous variables. Differences across age groups were tested using the Cochran-Armitage test for trend for categorical variables and Kruskal-Wallis test for continuous variables. The number of chronic conditions within each age group was categorized into quartiles, with quartile 1 serving as the reference group. Cox proportional hazards regression models were used to model the association of quartiles of chronic conditions with new-onset limitation for each of the 9 functional limitations, with time-to-event defined as the time to the questionnaire where a person first reported difficulty performing the activity on their own. If there was no report of difficulty performing the functional limitation, persons were censored at the date of the last questionnaire completed. We report both the absolute risk differences and hazard ratios (with corresponding 95% confidence intervals) to aid in interpretation of the results. The absolute risk differences represent the absolute difference between the risk of developing a functional limitation for each quartile versus quartile 1 at a specific time point during follow-up and were calculated based on the methods of Austin.[29] Briefly, for a given duration of follow-up, the predicted probability of the event occurring is computed assuming each subject is in quartile 1 for the number of chronic conditions, and the mean probability is calculated. Similarly, the predicted probability of the event occurring is computed assuming each subject is in quartile j for the number of chronic conditions, where $j = 2, 3, 4$, and the mean probabilities are calculated. The difference between the mean assuming all subjects are in quartile j minus the mean assuming all subjects are in quartile 1 is the absolute risk difference for quartile j compared to quartile 1. By contrast, the hazard ratios represent the ratio of the risk of developing a functional limitation for each quartile compared to quartile 1 at any point in time. Because hazard ratios are relative measures of risk, a similar hazard ratio may be observed for a small difference in absolute risks when the absolute risks are low and for a large difference in absolute risks when the absolute risks are high. Therefore, absolute risk differences aid in understanding the impact of a study finding. The absolute risk differences and hazard ratios were adjusted for sex, race (White, Black, Asian, other, unknown), ethnicity (Hispanic, non-Hispanic), marital status (married/committed relationship, not married/committed relationship), and education (less than high school, high school/some college, 4-year college degree/post-graduate studies). In addition, because we stratified our analyses by large age groupings (ages 40–54, 55–64, 65–74, and ≥75 years), we included continuous age in our model to adjust for any residual confounding by age. The absolute risk differences and hazard ratios were presented graphically. Statistical significance of the hazard ratios was determined after adjustment for multiple comparisons using the false discovery rate (9 comparisons).[30] Graphical and numerical methods were used to assess the proportional hazards assumption for all models, and they were found not to be violated.[31] Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC), and R version 3.6.2.

Results

Persons excluded from the cohort due to missing baseline information (23%) or follow-up information (6%) were more likely to be male, non-White, Hispanic, and were younger than persons included in our cohort (Table 1). In addition, persons excluded because of missing baseline information (the majority missing functional limitation information) had fewer chronic conditions than those included in our cohort (median number of chronic conditions of 1 vs. 2, respectively).

Among the 39,624 persons in our cohort, 44.5% were men, and the majority were White (93.2%), non-Hispanic (97.2%), and under 65 years of age (46.8% aged 40–54 years, 22.5% aged 55–64 years; Table 1). The median (interquartile range; IQR) number of chronic conditions at baseline increased with advancing age from 1 (0–3) in those aged 40–54 years to 5 (3–7) in those aged 75 years

Table 1. Comparison of characteristics among persons included and excluded from the study.

	Included	Excluded		
	(*N* = 39,624) *N* (%)	Missing baseline information[†] (*N* = 12,894) *N* (%)	Missing follow-up functional limitations (*N* = 3,218) *N* (%)	*p*-value*
Sex				<.01
Male	17,616 (44.5)	6755 (52.4)	1573 (48.9)	
Female	22,008 (55.5)	6139 (47.6)	1645 (51.1)	
Age group, years				<.01
40–54	18,526 (46.8)	8158 (63.3)	1696 (52.7)	
55–64	8925 (22.5)	2687 (20.8)	553 (18.2)	
65–74	6149 (15.5)	1212 (9.4)	263 (8.2)	
≥75	6024 (15.2)	837 (6.5)	706 (21.9)	
Race				<.01
White	36,938 (93.2)	11,325 (87.8)	2638 (82.0)	
Black	687 (1.7)	385 (3.0)	164 (5.1)	
Asian	1100 (2.8)	444 (3.4)	116 (3.6)	
Other	684 (1.7)	570 (4.4)	107 (3.3)	
Unknown	215 (0.5)	170 (1.3)	193 (6.0)	
Ethnicity				<.01
Hispanic	1126 (2.8)	543 (4.2)	93 (2.9)	
Non-Hispanic	38,498 (97.2)	12,351 (95.8)	3125 (97.1)	
Number of chronic conditions, median (IQR)	2 (1,4)	1 (0,2)	2 (1,4)	<.01
Number of visit days[‡], median (IQR)	41 (24,70)	13 (5,25)	28 (14,57)	<.01

Values are presented as number (%) or median (interquartile range - IQR).
*Differences between those with and without baseline information on functional limitations were tested using the chi-square test for categorical variables and Wilcoxon-Mann-Whitney test for continuous variables.
[†]*N* = 12,853 missing baseline functional limitations; *N* = 41 missing marital status or education.
[‡]Number of days with at least one diagnosis in the 5-year capture frame prior to baseline (1 January 2001 to 31 December 2005).

and older (Table 2). The age-specific quartiles were: ages 40–54 years (0, 1, 2, and ≥3 chronic conditions), ages 55–64 years (0–1, 2, 3, and ≥4 chronic conditions), ages 65–74 years (0–2, 3, 4–5, and ≥6 chronic conditions), and ages ≥75 years (0–3, 4, 5–6, and ≥7 chronic conditions). The median (IQR) number of questionnaires completed prior to baseline was 3 (2–5) with a range of 1-15. The median (IQR) time from the most recently completed questionnaire prior to baseline to the baseline date was 0.74 (0.34–1.4) years. Difficulty with walking, climbing stairs, and housekeeping were the most common functional limitations at baseline, reported by more than 20% of persons aged 75 years of age or older. The sample sizes for each functional limitation differed and are presented in Table S1.

The median (IQR) follow-up time to the date of last questionnaire completed was 10.8 (7.5–11.7) years. Table S1 contains the median follow-up time for each functional limitation outcome. The median (IQR) number of questionnaires completed during follow-up was 7 (4–10). The most common reported new functional limitations were related to mobility, climbing stairs and walking (Table S1). In addition, difficulty with housekeeping was the most common reported instrumental ADL. An increasing risk of development of a functional limitation was observed across quartiles of chronic conditions (Figure 1; Table 3). The largest absolute risk differences were observed for walking, climbing stairs, and housekeeping. The lowest absolute risk differences were observed for the basic ADL of eating. The absolute risk differences were higher for persons in the oldest age group. For persons aged 75 years of age and older, the absolute risk differences at 10 years for quartile 4 vs. quartile 1 were 20% or higher for all functional limitations except for eating (absolute risk difference, 12%). For the hazard ratios, similar patterns were observed for each of the 9 functional limitations. An approximately twofold increased risk was observed among persons in the highest quartile compared to the lowest quartile for each of the age groups except for the youngest age group. Persons aged 40–54 years generally

Table 2. Demographic characteristics, functional limitations, and chronic conditions at baseline by age group (*N* = 39,624).

	Age group				
	40–54 (*N* = 18,526) *N* (%)	55–64 (*N* = 8925) *N* (%)	65–74 (*N* = 6149) *N* (%)	≥75 (*N* = 6024) *N* (%)	P-trend*
Demographics					
Sex					<.01
Male	8171 (44.1)	4134 (46.3)	2909 (47.3)	2402 (39.0)	
Female	10,355 (55.9)	4791 (53.7)	3240 (52.7)	3622 (60.1)	
Race					<.01
White	16,925 (91.4)	8339 (93.4)	5841 (95.0)	5833 (96.8)	
Black	440 (2.4)	132 (1.5)	75 (1.2)	40 (0.7)	
Asian	601 (3.2)	261 (2.9)	148 (2.4)	90 (1.5)	
Other	426 (2.3)	139 (1.6)	70 (1.1)	49 (0.8)	
Unknown	134 (0.7)	54 (0.6)	15 (0.2)	12 (0.2)	
Ethnicity					<.01
Hispanic	698 (3.8)	260 (2.9)	118 (1.9)	50 (0.8)	
Non-Hispanic	17,828 (96.2)	8665 (97.1)	6031 (98.1)	5974 (99.2)	
Marital status					<.01
Married/committed relationship	13,953 (75.3)	6,606 (74.0)	4203 (68.4)	2566 (42.6)	
Not married/committed relationship	4573 (24.7)	2319 (26.0)	1946 (31.6)	3458 (57.4)	
Education					<.01
<High school	349 (1.9)	251 (2.8)	370 (6.0)	887 (14.7)	
High school/some college	8791 (47.5)	4617 (51.7)	3700 (60.2)	3373 (56.0)	
4-year college degree/ post graduate studies	9386 (50.7)	4057 (45.5)	2079 (33.8)	1764 (29.3)	
Functional limitations†					
Walking	809 (4.4)	602 (6.7)	689 (11.2)	1,489 (24.7)	<.01
Climbing stairs	993 (5.4)	863 (9.7)	895 (14.6)	1877 (31.2)	<.01
Eating	206 (1.1)	145 (1.6)	127 (2.1)	295 (4.9)	<.01
Dressing	407 (2.2)	270 (3.0)	246 (4.0)	542 (9.0)	<.01
Toileting	219 (1.2)	148 (1.7)	149 (2.4)	330 (5.5)	<.01
Bathing	338 (1.8)	250 (2.8)	250 (4.1)	705 (11.7)	<.01
Housekeeping	802 (4.3)	539 (6.0)	505 (8.2)	1227 (20.4)	<.01
Transportation	458 (2.5)	286 (3.2)	288 (4.7)	1025 (17.0)	<.01
Managing medications	291 (1.6)	190 (2.1)	182 (3.0)	638 (10.6)	<.01
Number of limitations, median (IQR)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,2)	<.01
Chronic conditions					
Hypertension	3845 (20.8)	3934 (44.1)	3887 (63.2)	4711 (78.2)	<.01
Hyperlipidemia	5623 (30.4)	4813 (53.9)	4337 (70.5)	4036 (67.0)	<.01
Diabetes	1774 (9.6)	1684 (18.9)	1762 (28.7)	1773 (29.4)	<.01
Cardiac arrhythmias	2273 (12.3)	1829 (20.5)	2002 (32.6)	3042 (50.5)	<.01
Coronary artery disease	980 (5.3)	1396 (15.6)	1715 (27.9)	2563 (42.5)	<.01
Congestive heart failure	141 (0.8)	235 (2.6)	328 (5.3)	1034 (17.2)	<.01
Stroke	314 (1.7)	370 (4.1)	640 (10.4)	1144 (19.0)	<.01
Arthritis	3087 (16.7)	2976 (33.3)	2680 (43.6)	3240 (53.8)	<.01
Osteoporosis	317 (1.7)	557 (6.2)	859 (14.0)	1573 (26.1)	<.01
Cancer	1956 (10.6)	1647 (18.5)	1921 (31.2)	2610 (43.3)	<.01
Chronic kidney disease	457 (2.5)	444 (5.0)	546 (8.9)	1018 (16.9)	<.01

(continued)

Table 2. (continued)

	Age group				
	40–54 (*N* = 18,526) *N* (%)	55–64 (*N* = 8925) *N* (%)	65–74 (*N* = 6149) *N* (%)	≥75 (*N* = 6024) *N* (%)	P-trend*
Hepatitis	387 (2.1)	148 (1.7)	98 (1.6)	61 (1.0)	<.01
Asthma	1,716 (9.3)	787 (8.8)	518 (8.4)	545 (9.0)	.22
Chronic obstructive pulmonary disease	1599 (8.6)	1107 (12.4)	994 (16.2)	1368 (22.7)	<.01
Autism	1 (0)	0	0	0	.77
HIV	31 (0.2)	7 (0.1)	2 (0)	0	<.01
Dementia	224 (1.2)	144 (1.6)	203 (3.3)	702 (11.7)	<.01
Anxiety	2338 (12.6)	932 (10.4)	522 (8.5)	584 (9.7)	<.01
Depression	4059 (21.9)	1789 (20.1)	857 (13.9)	1116 (18.5)	<.01
Schizophrenia	213 (1.1)	123 (1.4)	104 (1.7)	297 (4.9)	<.01
Substance abuse disorders	992 (5.4)	337 (3.8)	180 (2.9)	137 (2.3)	<.01
Number of chronic conditions, median (IQR)	1 (0,3)	3 (1,4)	4 (2,5)	5 (3,7)	<.01

Values are presented as number (%) or median (interquartile range - IQR).
*Differences across age groups were tested using the Cochran-Armitage test for trend for categorical variables and Kruskal-Wallis test for continuous variables.
†A single question included a list of all the functional limitations and was phrased, 'Fill in the circle to the left of each activity which you have difficulty performing on your own.'

experienced more than a threefold increased risk of developing new-onset functional limitations.

Discussion

Major findings

In this large population-based cohort including more than 39,000 persons, we observed an increasing risk of 9 new-onset functional limitations (including basic ADLs, instrumental ADLs, and mobility) with increasing number of chronic conditions at baseline. The most common new-onset functional limitations were related to mobility (difficulty climbing stairs and walking). We used age-specific quartiles based on the number of chronic conditions to characterize multi-morbidity as opposed to the same cut-point across all age groups. It has been suggested that the number of chronic conditions as compared to same age peers may be used as a marker for accelerated aging.[20] Using age-specific cut-points, the absolute risk differences for all functional limitations were largest among the oldest age group (persons aged ≥75 years). However, the hazard ratios increased consistently across chronic condition quartiles for the 3 oldest age groups, and were higher in the youngest age group (persons aged 40–54 years).

Comparison with previous studies

Cross-sectional studies utilizing the National Health and Nutrition Examination Survey (NHANES) showed an increased risk of functional limitations with increasing number of chronic conditions in adults aged 50–64 years and ≥65 years.[9,32] However, because these studies were cross-sectional, it was not possible to examine the association between multi-morbidity with development of new-onset (incident) functional limitations. Longitudinal studies in Sweden have reported that persons with higher number of chronic conditions experienced increasing risks of functional limitations. In persons aged 77–100 years from the Kungsholmen Project, the number of chronic conditions incrementally increased the risk of functional decline.[33] Furthermore, in a random sample of persons aged ≥60 years from the Swedish National study on Aging and Care in Kungsholmen, persons who accumulated chronic diseases at a faster rate over time had higher risks of developing basic and instrumental ADL impairment.[34] However, the maximum follow-up of these studies was shorter (3 and 6 years, respectively) compared to our study which had a median follow-up of over 10 years. In addition, we included adults aged ≥40 years at baseline, and used age-specific quartiles to allow for better comparison of health outcomes across peers of the same age. We observed that persons aged 75 years of age and older had the highest absolute risk differences for all functional limitations, whereas the youngest persons aged 40–54 years of age had the highest hazard ratios. The hazard ratios for the oldest 3 age groups were consistent, with approximately twofold increased risk of developing a new functional limitation among persons in the highest quartile compared to the lowest quartile.

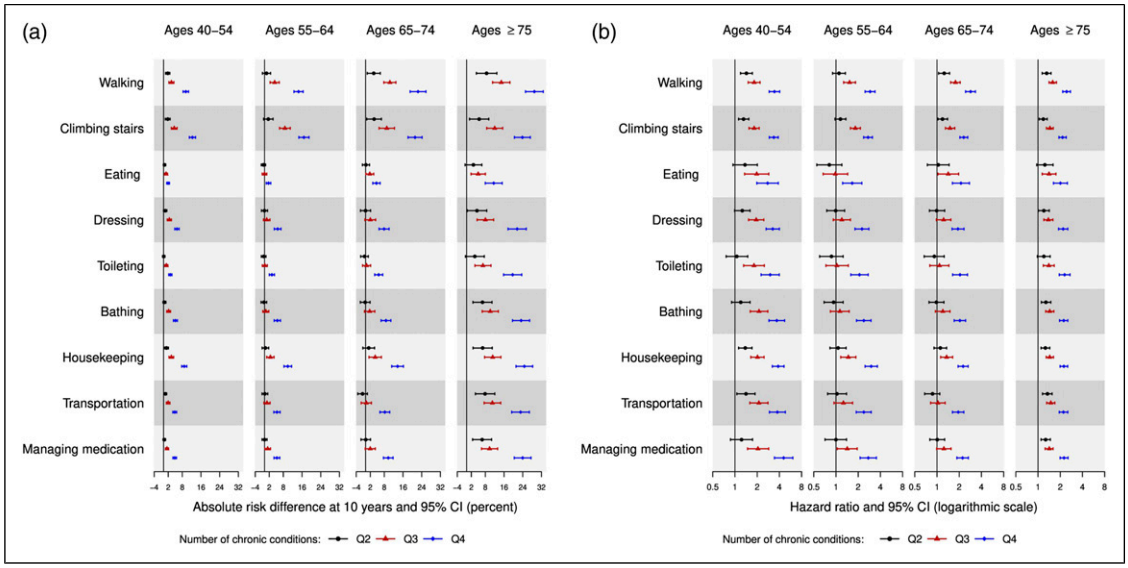

Figure 1. Absolute risk differences (95% confidence interval; panel A) and hazard ratios (95% confidence interval; panel B) for new-onset functional limitations by age-specific quartiles of number of chronic conditions. The age-specific quartiles of number of chronic conditions were 0, 1, 2, and ≥3 for persons aged 40–54; 0–1, 2, 3, and ≥4 for persons aged 55–64; 0–2, 3, 4–5, and ≥6 for persons aged 65–74; and 0–3, 4, 5–6, and ≥7 for persons aged ≥75 years.

Absolute risk differences and hazard ratios were adjusted for continuous age, sex, race (White, Black, Asian, other, unknown), ethnicity (Hispanic, non-Hispanic), marital status (married/committed relationship, not married/committed relationship), and education (less than high school, high school/some college, 4–year college degree/post-graduate studies).

The *p*-value for trend adjusting for the false discovery rate was significant ($p < .01$) for each of the age groups for all functional limitations.

Implications

Persons who have accumulated more chronic conditions compared to their peers may be experiencing accelerated aging and are more likely to develop functional limitations than their peers. Individuals with functional limitations, and particularly the most impaired who need assistance to perform the basic ADLs such as eating, getting dressed, and toileting, also frequently rely on social services, including transportation and home-delivered meals.[35] These persons are also likely to require coordinated care across multiple health care providers because of their complex health problems, and are more likely to experience fragmented care and care that does not meet their needs.[35–38] As a result, persons with both multi-morbidity and functional limitations experience the poorest health care outcomes, including emergency department visits, hospitalizations, death, and increased health care expenditures.[17,18] It is thus critically important to develop strategies to prevent or delay multi-morbidity and to effectively manage multi-morbidity at all ages. One such strategy is to increase physical activity, which may have direct beneficial effects on the development of multi-morbidity and physical deterioration that occurs with aging.[39] Furthermore, systematic assessment of physical functioning is important, given the evidence that interventions targeting progression of disability may improve outcomes, even among persons who have existing functional limitations. In the Lifestyle Interventions and Independence for Elders (LIFE) randomized clinical trial in sedentary persons with physical limitations aged 70–89 years, a moderate-intensity physical activity intervention reduced major mobility disability (loss of ability to walk 400 meters) over an average follow-up of 2.6 years.[40] Furthermore, healthy lifestyle behaviors (including regular physical activity, healthy diet, no smoking, and no/moderate alcohol consumption) have been shown to increase life expectancy even in persons with multi-morbidity.[41]

Limitations and strengths

We acknowledge the following limitations. First, we ascertained the number of chronic conditions out of a list of 21 conditions. Some persons may have had other chronic conditions that we did not consider. In addition, we did not analyze individual chronic conditions, and we did not include information on the severity or treatment of the chronic conditions. Second, the count of chronic conditions may have been affected by coding practices and by the degree of access to the health care system. Third, we excluded 23% of persons in our community due to missing baseline information and 6% due to missing follow-up information. Fourth, functional limitations may differ in severity, and some may be temporary (e.g., difficulties with

Table 3. Absolute risk differences and hazard ratios for new-onset functional limitations by age-specific quartiles of number of chronic conditions.

Functional limitation Age stratum	Absolute risk at 10 years, % Q1	Absolute risk difference (95% CI) at 10 years, %*			Hazard ratio (95% CI)*, †		
		Q2 – Q1	Q3 – Q1	Q4 – Q1	Q2 vs. Q1	Q3 vs. Q1	Q4 vs. Q1
Walking							
40–54	0.96 (0.95, 0.96)	1.78 (0.87, 2.69)	3.36 (2.29, 4.43)	9.52 (8.36, 10.68)	1.43 (1.19, 1.72)	1.82 (1.51, 2.19)	3.43 (2.91, 4.04)
55–64	0.91 (0.90, 0.92)	0.82 (−0.92, 2.56)	4.32 (2.37, 6.27)	14.53 (12.57, 16.49)	1.10 (0.90, 1.34)	1.53 (1.27, 1.84)	2.90 (2.48, 3.38)
65–74	0.84 (0.83, 0.86)	3.48 (0.69, 6.27)	10.39 (7.81, 12.97)	22.42 (19.05, 25.79)	1.25 (1.05, 1.48)	1.78 (1.53, 2.06)	2.85 (2.44, 3.32)
≥75	0.55 (0.52, 0.58)	8.54 (4.17, 12.91)	14.82 (11.11, 18.53)	28.97 (25.17, 32.77)	1.31 (1.14, 1.50)	1.58 (1.41, 1.78)	2.44 (2.16, 2.75)
Climbing stairs							
40–54	0.94 (0.93, 0.95)	1.77 (0.74, 2.80)	4.56 (3.33, 5.79)	12.35 (11.03, 13.67)	1.31 (1.12, 1.54)	1.82 (1.55, 2.13)	3.36 (2.92, 3.86)
55–64	0.88 (0.87, 0.89)	1.60 (−0.42, 3.62)	8.69 (6.38, 11.00)	16.83 (14.65, 19.01)	1.15 (0.97, 1.36)	1.83 (1.57, 2.14)	2.72 (2.37, 3.12)
65–74	0.78 (0.76, 0.80)	3.62 (0.49, 6.75)	9.05 (5.75, 12.35)	21.15 (18.15, 24.15)	1.19 (1.03, 1.39)	1.50 (1.30, 1.74)	2.30 (2.04, 2.61)
≥75	0.42 (0.40, 0.45)	5.36 (1.25, 9.47)	12.01 (8.60, 15.42)	23.84 (20.44, 27.24)	1.18 (1.04, 1.33)	1.45 (1.30, 1.61)	2.15 (1.92, 2.41)
Eating							
40–54	0.99 (0.99, 0.99)	0.42 (−0.08, 0.92)	1.08 (0.47, 1.69)	1.95 (1.37, 2.53)	1.37 (0.94, 2.01)	1.97 (1.35, 2.87)	2.77 (1.98, 3.87)
55–64	0.97 (0.97, 0.98)	−0.49 (−1.41, 0.43)	−0.04 (−1.02, 0.94)	1.68 (0.71, 2.65)	0.81 (0.55, 1.20)	0.98 (0.67, 1.44)	1.66 (1.23, 2.24)
65–74	0.96 (0.95, 0.97)	0.16 (−1.35, 1.67)	1.80 (0.12, 3.48)	4.63 (3.07, 6.19)	1.04 (0.74, 1.46)	1.42 (1.03, 1.96)	2.11 (1.62, 2.75)
≥75	0.86 (0.84, 0.88)	2.91 (−0.67, 6.49)	4.95 (1.88, 8.02)	11.59 (7.97, 15.21)	1.24 (0.96, 1.60)	1.41 (1.14, 1.75)	2.01 (1.62, 2.50)
Dressing							
40–54	0.97 (0.97, 0.98)	0.69 (−0.03, 1.41)	2.47 (1.58, 3.36)	5.73 (4.80, 6.66)	1.26 (0.99, 1.60)	1.94 (1.53, 2.46)	3.25 (2.64, 4.00)
55–64	0.95 (0.94, 0.96)	−0.04 (−1.34, 1.26)	0.92 (−0.47, 2.31)	5.58 (4.16, 7.00)	0.99 (0.75, 1.31)	1.20 (0.92, 1.57)	2.25 (1.81, 2.79)
65–74	0.90 (0.90, 0.92)	−0.02 (−2.16, 2.12)	2.01 (−0.28, 4.30)	7.90 (5.76, 10.04)	0.99 (0.79, 1.27)	1.23 (0.98, 1.54)	1.92 (1.60, 2.32)
≥75	0.70 (0.68, 0.73)	4.44 (0.28, 8.60)	8.02 (4.48, 11.56)	21.61 (17.73, 25.49)	1.20 (1.01, 1.42)	1.38 (1.20, 1.59)	2.19 (1.90, 2.53)
Toileting							
40–54	0.98 (0.98, 0.99)	0.09 (−0.43, 0.61)	1.19 (0.53, 1.85)	2.90 (2.22, 3.58)	1.06 (0.76, 1.49)	1.81 (1.31, 2.50)	3.00 (2.26, 3.99)
55–64	0.97 (0.96, 0.98)	−0.40 (−1.40, 0.60)	0.10 (−0.97, 1.17)	3.12 (2.02, 4.22)	0.87 (0.60, 1.25)	1.03 (0.73, 1.47)	2.08 (1.59, 2.73)
65–74	0.94 (0.93, 0.95)	−0.47 (−2.09, 1.15)	0.42 (−1.30, 2.14)	5.60 (3.88, 7.32)	0.92 (0.67, 1.25)	1.08 (0.80, 1.45)	2.05 (1.63, 2.59)
≥75	0.77 (0.75, 0.80)	3.52 (−0.51, 7.55)	6.98 (3.54, 10.42)	19.68 (15.80, 23.56)	1.20 (0.98, 1.46)	1.40 (1.18, 1.66)	2.29 (1.94, 2.71)
Bathing							
40–54	0.98 (0.98, 0.98)	0.39 (−0.23, 1.01)	2.18 (1.37, 2.99)	5.08 (4.24, 5.92)	1.20 (0.90, 1.60)	2.12 (1.61, 2.79)	3.69 (2.89, 4.71)
55–64	0.96 (0.95, 0.97)	−0.29 (−1.48, 0.90)	0.53 (−0.75, 1.81)	5.44 (4.11, 6.77)	0.93 (0.69, 1.25)	1.13 (0.84, 1.51)	2.38 (1.90, 2.98)
65–74	0.90 (0.89, 0.92)	−0.17 (−2.24, 1.90)	1.74 (−0.47, 3.95)	8.71 (6.62, 10.80)	0.98 (0.78, 1.24)	1.20 (0.96, 1.50)	2.04 (1.71, 2.44)
≥75	0.63 (0.61, 0.66)	6.78 (2.70, 10.86)	10.11 (6.66, 13.56)	23.28 (19.63, 26.93)	1.28 (1.11, 1.49)	1.44 (1.27, 1.64)	2.23 (1.96, 2.53)
Housekeeping							
40–54	0.97 (0.96, 0.97)	1.26 (0.45, 2.07)	3.32 (2.32, 4.32)	8.84 (7.76, 9.92)	1.38 (1.12, 1.70)	2.02 (1.64, 2.48)	3.85 (3.21, 4.62)
55–64	0.94 (0.93, 0.95)	0.35 (−1.05, 1.75)	2.48 (0.92, 4.04)	9.92 (8.30, 11.54)	1.07 (0.83, 1.37)	1.47 (1.16, 1.86)	3.00 (2.48, 3.64)
65−74	0.87 (0.85, 0.88)	1.32 (−1.18, 3.82)	4.10 (1.45, 6.75)	13.67 (11.17, 16.17)	1.11 (0.91, 1.35)	1.35 (1.12, 1.63)	2.26 (1.93, 2.64)
≥75	0.54 (0.52, 0.57)	6.85 (2.75, 10.95)	11.16 (7.69, 14.63)	24.68 (21.12, 28.24)	1.26 (1.10, 1.44)	1.44 (1.29, 1.62)	2.24 (1.99, 2.52)

(continued)

Table 3. (continued)

Functional limitation	Absolute risk at 10 years, %	Absolute risk difference (95% CI) at 10 years, %*			Hazard ratio (95% CI)*, †		
Age stratum	Q1	Q2 – Q1	Q3 – Q1	Q4 – Q1	Q2 vs. Q1	Q3 vs. Q1	Q4 vs. Q1
Transportation							
40–54	0.98 (0.98, 0.99)	0.73 (0.12, 1.34)	1.97 (1.21, 2.73)	4.78 (3.97, 5.59)	1.41 (1.06, 1.87)	2.11 (1.59, 2.80)	3.76 (2.93, 4.82)
55–64	0.96 (0.95, 0.97)	0.14 (−1.08, 1.36)	1.04 (-0.28, 2.36)	5.28 (3.94, 6.62)	1.03 (0.77, 1.39)	1.26 (0.94, 1.68)	2.38 (1.88, 3.00)
65–74	0.90 (0.89, 0.91)	−1.29 (−3.34, 0.76)	0.30 (-1.87, 2.47)	8.22 (6.13, 10.31)	0.87 (0.68, 1.09)	1.03 (0.82, 1.29)	1.94 (1.62, 2.31)
≥75	0.63 (0.60, 0.65)	7.90 (3.75, 12.05)	11.02 (7.47, 14.57)	23.06 (19.29, 26.83)	1.34 (1.15, 1.55)	1.49 (1.31, 1.69)	2.21 (1.94, 2.53)
Managing medication							
40–54	0.99 (0.98, 0.99)	0.32 (−0.22, 0.86)	1.46 (0.78, 2.14)	4.77 (4.00, 5.54)	1.23 (0.87, 1.73)	2.05 (1.48, 2.86)	4.57 (3.43, 6.08)
55–64	0.97 (0.96, 0.97)	-0.01 (−1.08, 1.06)	1.32 (0.11, 2.53)	5.25 (4.03, 6.47)	1.00 (0.71, 1.39)	1.42 (1.04, 1.94)	2.74 (2.12, 3.53)
65–74	0.91 (0.89, 0.92)	0.06 (−1.97, 2.09)	1.99 (-0.17, 4.15)	9.70 (7.65, 11.75)	1.01 (0.80, 1.27)	1.24 (0.99, 1.55)	2.22 (1.86, 2.66)
≥75	0.62 (0.59, 0.64)	6.61 (2.55, 10.67)	9.81 (6.37, 13.25)	23.95 (20.36, 27.54)	1.27 (1.10, 1.47)	1.42 (1.25, 1.60)	2.25 (1.99, 2.55)

Absolute risk differences and hazard ratios are adjusted for continuous age, sex, race (White, Black, Asian, other, unknown), ethnicity (Hispanic, non-Hispanic), marital status (married/committed relationship, not married/committed relationship), and education (<high school, high school/some college, 4-year college degree/post graduate studies). Quartile 1 served as the reference (absolute risk difference of 0; hazard ratio of 1.0).

*The age-specific quartiles of number of chronic conditions are 0, 1, 2, and ≥3 for persons aged 40−54; 0−1, 2, 3, and ≥4 for persons aged 55−64; 0−2, 3, 4−5, and ≥6 for persons aged 65−74; and 0−3, 4, 5−6, and ≥7 for persons aged ≥75 years.

†The *p*-value for trend adjusting for the false discovery rate was significant ($p < .01$) for each of the age groups for all functional limitations.

walking or climbing stairs after a knee or hip replacement surgery). We did not have information to categorize the severity of the functional limitations or to identify persons with temporary limitations. Finally, our population includes a small proportion of non-whites and Hispanics, and our results may not be generalizable to more diverse populations.

Our study also has several strengths, including the comprehensive data capture with patient-reported information on functional limitations. Patient-reported functional limitations are not routinely available in electronic health records. In addition, the large sample size of our cohort allowed us to conduct analyses stratified by age group. We also created age-specific quartiles of number of chronic conditions which allowed us to compare the development of functional limitations among people who have accumulated more chronic conditions than peers in their same age group.

Conclusions

At all ages, persons who accumulate more chronic conditions compared to their peers experience increased risks of developing functional limitations. For the majority of functional limitations, the absolute risk differences were largest among persons aged ≥75 years, with a larger than 20% absolute risk difference at 10 years for the highest compared to lowest chronic condition quartile. For all age groups and functional limitations, an approximately twofold to threefold relative increased risk was observed among persons in the highest chronic condition quartile compared to the lowest quartile. These findings underscore the importance of assessing health status and employing interventions to prevent and effectively manage multi-morbidity at all ages.

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Supplemental Material

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