Patterns of Multimorbidity in Elderly Veterans

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OBJECTIVES: To determine patterns of co-occurring diseases in older adults and the extent to which these patterns vary between the young-old and the old-old.

DESIGN: Observational study.

SETTING: Department of Veterans Affairs.

PARTICIPANTS: Veterans aged 65 years and older (1.9 million male, mean age 76 ± 7; 39,000 female, mean age 77 ± 8) with two or more visits to Department of Veterans Affairs (VA) or Medicare settings in 2007 and 2008.

MEASUREMENTS: The presence of 23 common conditions was assessed using hospital discharge diagnoses and outpatient encounter diagnoses from the VA and Medicare.

RESULTS: The mean number of chronic conditions (out of 23 possible) was 5.5 ± 2.6 for men and 5.1 ± 2.6 for women. The prevalence of most conditions increased with advancing age, although diabetes mellitus and hyperlipidemia were 11% to 13% less prevalent in men and women aged 85 and older than in those aged 65 to 74 ($P < .001$ for each). In men, the most common three-way combination of conditions was hypertension, hyperlipidemia, and coronary heart disease, which together were present in 37% of men. For women, the most common combination was hypertension, hyperlipidemia, and arthritis, which co-occurred in 25% of women. Reflecting their high population prevalence, hypertension and hyperlipidemia were both present in 9 of the 15 most common three-way disease combinations in men and in 11 of the 15 most common combinations in women. The prevalence of many disease combinations varied substantially between young-old and old-old adults.

CONCLUSIONS: Specific combinations of diseases are highly prevalent in older adults and inform the development of guidelines that account for the simultaneous presence of multiple chronic conditions. **J Am Geriatr Soc 60:1872–1880, 2012.**

Key words: multimorbidity; aged; veterans; age effects

Older adults often have multiple concurrent diseases, and the number and cumulative burden of individual conditions often increases with advancing age. Nevertheless, much remains unknown about patterns of multimorbidity in older adults. The lack of attention to this topic has created substantial difficulties for clinical practice guidelines, because the standard recommendations for a single disease may not be applicable to individuals whose other conditions interact with that disease, both at the level of pathophysiology and with the medications used to treat an individual's ailments.[1–5]

Identifying the most common disease clusters in older adults may help the next generation of clinical practice guidelines explicitly account for common co-occurring conditions so that they can help clinicians avoid drug–drug and drug–disease interactions. Previous work has shed important light on this question by quantifying the number of co-occurring diseases within populations, examining linkages between common conditions, and determining the healthcare outcomes and costs associated with different patterns of multimorbidity,[6–20] but the existing literature has certain limitations. Most of studies in this area have evaluated a limited number of conditions or limited populations, ranked conditions based on costs and outcomes rather than prevalence, focused on two-way disease combinations (and not more-complex patterns of disease co-occurrence), and provide little information on how patterns of multimorbidity may vary between the young-old (e.g., 65–74) and the "old-old" (e.g., ≥ 85).[8,10–12,16–21] Thus, important knowledge gaps remain, particularly in identifying the specific patterns of multimorbidity that are most common in older adults and how these patterns differ between young-old and old-old people.

This study was designed to identify common patterns of multimorbidity in a nationwide sample of community-

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dwelling older adults receiving care in the Department of Veterans Affairs (VA) healthcare system. First, this study aimed to identify the prevalence of common diseases in older male and female veterans and how the prevalence of these conditions varies according to age and sex. Second, the study sought to determine the most common combinations of diseases in older veterans and the extent to which the prevalence of these disease clusters varies between young-old and old-old individuals. In doing so, this study focused on diseases and conditions typically identifiable using large data sources and not on geriatric syndromes, which are critically important to the health of older adults but are more difficult to ascertain using administrative data.

METHODS

Sample

The sample included all adults aged 65 and older receiving care in the VA health system as of October 1, 2006, and who were still alive 1 year later and had two or more visits to primary care medicine clinics or medicine subspecialty clinics or hospitalizations in VA or Medicare in fiscal year (FY) 2007 and FY2008. Discharge diagnoses from hospital stays and encounter diagnoses from outpatient visits in FY2007 and FY2008 were identified using national VA databases. (Trained coders recorded hospital discharge diagnoses, and treating clinicians recorded outpatient diagnoses at the conclusion of clinic visits.) These VA data were merged with equivalent inpatient and outpatient healthcare claims data from Medicare over the same period, using the Medicare Provider Analysis and Review file for discharge diagnosis and the Carrier and Outpatient Standard Analytic Files for outpatient diagnoses. (Additional details about data abstraction procedures are described in Appendix S1.)

Conditions of Interest

A list of 23 common conditions was derived a priori from previous studies and from sources listing the most common chronic conditions in older adults.[6–8,12,22] Conditions were selected that were common, managed with specific and reasonably defined drug therapy regimens, and identifiable using *International Classification of Diseases, Ninth Revision* (ICD-9) encounter codes. The Healthcare Cost and Utilization Project Clinical Classification Software was used to map ICD-9 diagnosis codes for each individual to each of the 23 conditions.[23] These conditions included osteoarthritis and arthritis not otherwise specified (herein called arthritis); coronary heart disease (CHD); cerebrovascular accident (CVA); peripheral arterial disease (PAD; including aortic aneurysms); chronic obstructive pulmonary disease and asthma (COPD); diabetes mellitus; heart failure; atrial fibrillation; depression; hypertension; malignancy other than prostate cancer; prostate cancer; anemia; hypothyroidism; dementia; epilepsy; benign prostatic hypertrophy (BPH); Parkinson's disease; osteoporosis; hyperlipidemia; gout; chronic renal insufficiency; and a combination category of gastroesophageal reflux disease, peptic ulcer disease, and dyspepsia (GERD/PUD). (Details of coding algorithms are provided in Appendix S1.)

An individual was defined as having a condition of interest if he or she had one or more relevant ICD-9 codes during any outpatient visit or inpatient stay over the 2-year study period. Previous validation studies in the VA have identified this approach as highly sensitive and moderately to highly specific for identifying common chronic conditions.[24,25] To maximize fidelity of outpatient diagnoses in VA data, codes were assessed only from encounter types in which a physician or nurse practitioner typically records diagnoses. (This approach does not consider diagnoses associated with radiology, laboratory, or other such visits.) In Medicare data, diagnoses were assessed only from claims arising from physician visits. In sensitivity analyses, a more-conservative method was used that required two or more ICD-9 codes from distinct outpatient visits or one or more codes from hospital discharge diagnoses to identify a disease condition as present.

Analyses

Chi-square tests were used to compare disease prevalence between three age groups (65–74, 75–84, and ≥ 85). Given the presence of multiple hypothesis testing, an a priori significance level was established at $P < .001$, corresponding roughly to the Bonferroni correction given approximately 50 comparisons. To evaluate combinations of diseases, the most common "triplets" (three conditions that coexisted within the same participant) were determined. Three-way disease clusters were chosen as the main unit of analysis because they represented a balance of complexity (multiple conditions) while still maintaining reasonably high prevalence rates within each cluster. A single individual could have more than one triplet; for example, a veteran with hypertension, diabetes mellitus, coronary heart disease, and COPD would have triplets corresponding to each three-way combination of these four conditions. An observed-to-expected approach was used to compare the observed prevalence of three-way disease clusters with the prevalence that would have been expected if all diseases were independent. Analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC).

The Research and Development Committee of the San Francisco VA Medical Center and the Committee on Human Research at the University of California at San Francisco approved this research.

RESULTS

Cohort

The cohort included 1.9 million male veterans and 39,000 female veterans (Table 1). Mean age was 76 ± 7 for men and 77 ± 8 for women. The mean number of chronic conditions (of 23 possible conditions) was 5.5 ± 2.6 for men and 5.1 ± 2.6 for women. The level of disease burden increased with advancing age, with a mean of 4.9 conditions for men age 65 to 74, 5.9 for men aged 75 to 84, and 6.4 for men aged 85 and older ($P < .001$ for difference) and a mean of 4.5, 5.5, and 5.8 conditions for women in the three age groups, respectively ($P < .001$).

Table 1. Characteristics of Participants

Characteristic	All Participants (N = 2,002,693)	Men (n = 1,963,810)	Women (n = 38,883)
Age, n (%)			
65–74	964,773 (48.2)	947,187 (48.2)	17,586 (45.2)
75–84	859,451 (42.9)	844,407 (43.0)	15,044 (38.7)
≥85	178,469 (8.9)	172,216 (8.8)	6,253 (16.1)
Race and ethnicity, n (%)			
White non-Hispanic	1,798,108 (89.8)	1,762,692 (89.8)	35,416 (91.1)
Black non-Hispanic	150,043 (7.5)	147,636 (7.5)	2,407 (6.2)
Other non-Hispanic or unknown[a]	32,419 (1.6)	31,530 (1.6)	889 (2.3)
Hispanic	22,123 (1.1)	21,952 (1.1)	171 (0.4)
Number of conditions (of 23 possible), n (%)			
0	13,392 (0.7)	12,768 (0.7)	624 (1.6)
1–2	193,061 (9.6)	188,454 (9.6)	4,607 (11.8)
3–5	875,219 (43.7)	857,279 (43.7)	17,940 (46.1)
6–8	637,970 (31.9)	626,509 (31.9)	11,461 (29.5)
>8	283,051 (14.1)	278,800 (14.2)	4,251 (10.9)
Number of primary care and medicine subspecialty visits over 2-year study period, median (IQR)[b]	10 (6–17)	10 (6–17)	10 (6–16)
Proportion of outpatient visits occurring in VA, median (IQR)[c]	0.82 (0.30–1.00)	0.82 (0.30–1.00)	0.88 (0.29–1.00)
Number of times hospitalized in 2-year period, n (%)[b]			
0	1,605,570 (80.2)	1,574,939 (80.2)	30,631 (78.8)
1	234,275 (11.7)	229,505 (11.7)	4,770 (12.3)
≥2	162,848 (8.1)	159,366 (8.1)	3,482 (9.0)
Died during second year of study period, n (%)	30,700 (1.5)	30,227 (1.5)	473 (1.2)

IQR = interquartile range.

[a] Includes Native American, Asian and Pacific Islander, other, and unknown.

[b] Combined data from Department of Veterans Affairs (VA) and Medicare.

[c] Number of outpatient visits in VA settings divided by number of outpatient visits to VA and Medicare settings.

Common Conditions and Variation According to Age

Figure 1 shows the prevalence of 23 conditions of interest in men (Figure 1A) and women (Figure 1B) according to age group. The most common conditions were hypertension, present in 85% of men and 82% of women, and hyperlipidemia, present in 78% of men and 72% of women. Many other conditions were also common in men and women, although the frequency varied substantially between the sexes (e.g., coronary heart disease in 46% of men vs 28% of women, arthritis in 29% vs 38%, and osteoporosis in 4% vs 34%, respectively). Most conditions were equally or more prevalent with advancing age, although the prevalence of diabetes mellitus and hyperlipidemia was 11% to 13% lower in men and women aged 85 and older than in those aged 65 to 74 ($P < .001$ for each). (Details are provided in Appendix S2.)

Patterns of Comorbid Burden

The most common triplets (three-way combinations of conditions) are shown in Tables 2 and 3. The leading triplet for men was hypertension, hyperlipidemia, and coronary heart disease, which together were present in 37% of men. The leading triplet for women was hypertension, hyperlipidemia, and arthritis, which was present in 25% of women.

There was substantial variation in the prevalence of each disease triplet between different age groups (Tables 2 and 3). The prevalence of most disease triplets was 1.2 to 1.6 times as high in participants aged 85 and older as in those aged 64 to 74, although there were some notable exceptions. For example, the triplet of hypertension, hyperlipidemia, and diabetes mellitus was substantially less common in men aged 85 and older than in those aged 65 to 74 (24% vs 35%, $P < .001$). In contrast, the triplet of hypertension, hyperlipidemia, and anemia was nearly twice as common in men aged 85 and older (23%) as in men aged 65 to 74 (12%) ($P < .001$). Differences in the underlying prevalence of diabetes mellitus and anemia were predominantly responsible for these age differences.

Differences in the prevalence of triplets between age groups resulted in some meaningful differences in which triplets were more common in each age group. For example, the combination of hyperlipidemia, coronary heart disease, and diabetes mellitus was the fifth most common triplet in men aged 65 to 74 (occurring in 19% of men), the seventh most common triplet in men aged 75 to 84 (21%), and the 21st most common triplet in men aged 85 and older (17%). In the opposite direction, the co-occurrence of hypertension, coronary heart disease, and heart failure was the 31st most common triplet in men aged 65 to 74 (8%), the 20th most common in men aged 75 to 84 (16%), and the sixth most common in men aged 85 and older (21%). Similar effects were seen in women, although overall differences were less predominant between age groups. (See Appendix S3 for details.)

Reflecting their high population prevalence, hypertension and hyperlipidemia were both present in 9 of the 15 most common triplets in men and in 11 of the top 15 triplets in women. To mitigate the dominance of these conditions on the results, the analysis was repeated after excluding these two diseases. Of the remaining 21

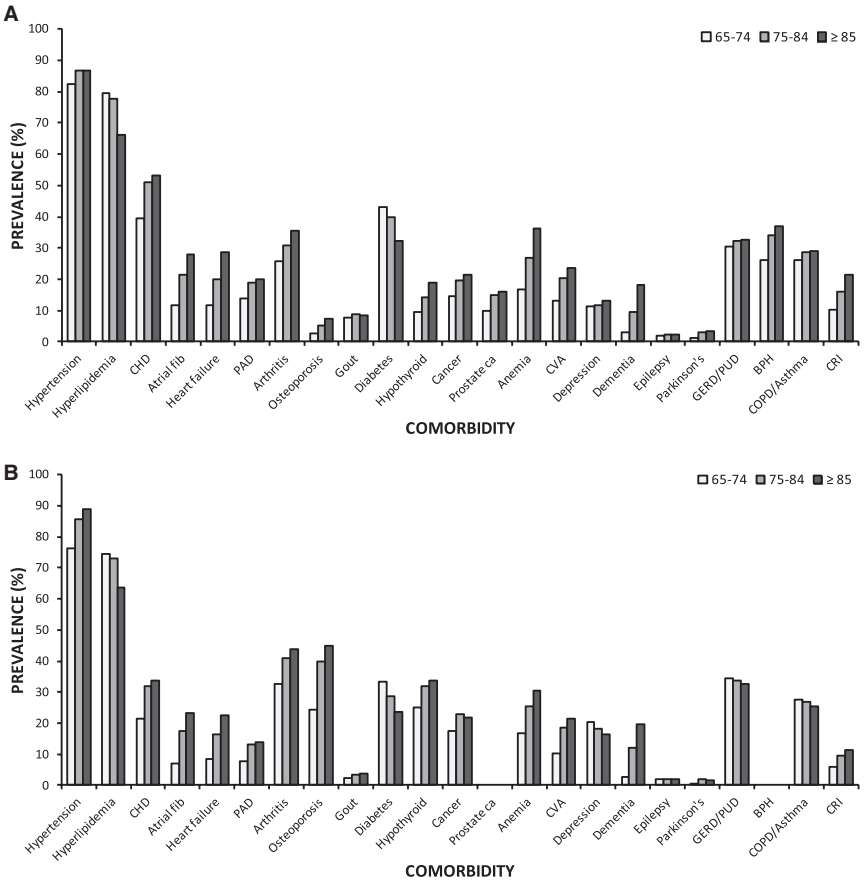

Figure 1. Prevalence of common conditions in (A) male and (B) female veterans according to age group. $P < .001$ for differences in disease prevalence according to age group for all conditions in men and for all conditions in women except epilepsy; gastroesophageal reflux disease, peptic ulcer disease, and dyspepsia (GERD/PUD); and chronic obstructive pulmonary disease (COPD) and asthma. CHD = coronary heart disease; PAD = peripheral arterial disease, CVA = cerebrovascular accident; BPH = benign prostatic hypertrophy; CRI = chronic renal insufficiency.

conditions, coronary heart disease and diabetes mellitus were present in each of the top four disease triplets for men, including these two diseases plus heart failure (7.5% of men), GERD/PUD (7.3%), COPD (7.3%), and anemia (7.1%). For women, GERD/PUD and arthritis were present in each of the top four triplets, including these two diseases plus osteoporosis (6.4%), coronary heart disease (5.8%), COPD (5.6%), and anemia (5.3%). (Further details are provided in Appendix S4.)

Individuals with common disease triplets also had a number of other conditions. In older adults with the 15 most common triplets, the mean number of conditions per person ranged from 6.9 to 8.5 in men and 6.7 to 8.3 in women. Thus, on average, the three conditions constituting the triplet represented fewer than half of the total number of chronic conditions present in a given individual.

Some conditions clustered together more commonly than would be expected according to their overall prevalence in the population, reflecting a shared etiology or risk factors. Nevertheless, such effects were small for most combinations. The ratio of observed to expected prevalence for each of the 15 most common triplets ranged from 1.0 to 1.4 for men and women. These effects became much more prominent after excluding hypertension and hyperlipidemia from the mix of possible combinations. (See Appendix S4 for details.)

Sensitivity Analyses

Sensitivity analyses were conducted using a more-stringent coding definition based on ICD-9 diagnoses being present at two outpatient visits or in one hospital discharge diagnosis. Across the 23 conditions, the median reduction in the assessed prevalence of conditions was 25% for men and 24% for women when using the more-stringent coding criteria. These reductions in disease prevalence using the more-restrictive definition ranged from a 6% lower prevalence of hypertension in men and women to a 38% lower prevalence of osteoporosis in men and a 39% lower prevalence for gout in women. Overall, the prevalence of triplets decreased by approximately one-third in men and women, although in general, the relative prevalence of triplets (and their rank order of frequency) was similar to the main analyses. (See Appendix S5 for details.)

DISCUSSION

In this national study of older men and women receiving care in the VA healthcare system, multimorbidity was common, and the prevalence of most individual diseases and the total number of conditions increased with advancing age. Nevertheless, there were notable exceptions, with

Table 2. Most common 3-way combinations of conditions among male veterans age 65 years and older (n = 1,963,810)

Rank order of combination	HTN	LIP	CHD	DM	GERD	OP	THYR	BPH	ARTH	COPD	ANEM	CA	CVA	PAD	DEP	Prevalence of combination (%)	Prevalence by age group (top 65-74, mid 75-84, bottom 85+) 0 10 20 30 40	Total number of conditions Mean (SD)
1	X	X	X													37.4		7.3 (2.4)
2	X	X		X												32.6		6.9 (2.5)
3	X	X			X											22.4		7.4 (2.5)
4	X	X						X								21.1		7.2 (2.5)
5	X		X	X												20.4		7.9 (2.4)
6	X	X							X							20.2		7.3 (2.5)
7		X	X	X												19.5		7.8 (2.4)
8	X	X								X						19.0		7.8 (2.5)
9	X	X									X					16.7		8.3 (2.5)
10	X		X		X											15.0		8.2 (2.4)
11		X	X		X											14.5		8.2 (2.4)
12	X		X							X						14.0		8.5 (2.4)
13	X	X											X			13.8		8.1 (2.5)
14	X	X												X		13.5		8.2 (2.5)
15	X		X					X								13.3		8.1 (2.4)

Total number of conditions = mean number of conditions (out of 23 possible) among men with each 3-way combination of conditions.

HTN = hypertension; LIP = hyperlipidemia; CHD = coronary heart disease; DM = diabetes mellitus; GERD = gastroesophageal reflux disease, peptic ulcer disease, dyspepsia; OP = osteoporosis; THRY = hypothyroidism; BPH = benign prostatic hypertrophy; ARTH = arthritis; COPD = chronic obstructive pulmonary disease, asthma; CA = cancer, non-prostate; ANEM = anemia; CVA = cerebrovascular accident; PAD = peripheral arterial disease; DEP = depression.

Table 3. Most common 3-way combinations of conditions among female veterans age 65 years and older (n = 38,883)

Rank order of combination	HTN	LIP	CHD	DM	GERD	OP	THYR	BPH	ARTH	COPD	ANEM	CA	CVA	PAD	DEP	Prevalence of combination (%)	Prevalence by age group (top 65–74, mid 75–84, bottom 85+) 0 10 20 30 40	Total number of conditions Mean (SD)
1	X	X							X							24.7		6.9 (2.3)
2	X	X		X												23.6		6.7 (2.4)
3	X	X			X											22.9		7.1 (2.3)
4	X	X	X													22.0		7.6 (2.3)
5	X	X				X										20.5		6.9 (2.4)
6	X	X					X									19.3		7.0 (2.4)
7	X	X								X						17.3		7.5 (2.4)
8	X	X									X					15.5		7.9 (2.4)
9	X				X				X							13.8		7.5 (2.3)
10	X	X										X				12.8		7.2 (2.4)
11		X			X				X							12.4		7.5 (2.3)
12	X	X													X	12.1		7.4 (2.4)
13	X					X			X							12.0		7.3 (2.4)
14	X	X											X			11.6		7.8 (2.4)
15	X		X						X							11.0		8.3 (2.3)

Total number of conditions = mean number of conditions (out of 21 possible, not including benign prostatic hypertrophy or prostate cancer) among women with each 3-way combination of conditions.
HTN = hypertension; LIP = hyperlipidemia; CHD = coronary heart disease; DM = diabetes mellitus; GERD = gastroesophageal reflux disease, peptic ulcer disease, dyspepsia; OP = osteoporosis; THRY = hypothyroidism; BPH = benign prostatic hypertrophy; ARTH = arthritis; COPD = chronic obstructive pulmonary disease, asthma; CA = cancer, non-prostate; ANEM = anemia; CVA = cerebrovascular accident; PAD = peripheral arterial disease; DEP = depression.

the prevalence of hyperlipidemia and diabetes being 11% to 13% lower in men and in women aged 85 and older than in those aged 65 to 74. Certain three-way combinations of diseases (triplets) were also highly prevalent; for example, more than one in three men had concurrent hypertension, hyperlipidemia, and coronary heart disease, and one if four women had the combination of hypertension, hyperlipidemia, and arthritis. Hypertension and hyperlipidemia dominated disease combinations for men and women, reflecting their high population prevalence. These results confirm and expand upon previous studies of multimorbidity in older adults and highlight the high prevalence of multimorbidity in older adults and the potential utility of considering disease clusters as a framework for addressing the care of older adults with complex comorbid conditions.[12,18]

There is emerging recognition of the importance of considering the full spectrum of disease burden in older adults, rather than managing each condition in isolation.[5,22] This is particularly pertinent for clinical practice guidelines and other tools to aid disease management, which have historically provided little guidance on how to manage a given disease in individuals with multiple comorbid conditions.[5] Nevertheless, guidelines cannot reasonably address management of every possible combination of diseases. In this light, these results may be particularly helpful in identifying which are the most common combinations of diseases, for older adults in general and separately for the young-old and old-old, so that guidelines may focus their attention on scenarios that are most commonly encountered in clinical practice.

These results suggest several important lessons for such efforts. First, they emphasize the importance of hypertension and hyperlipidemia as concurrent diseases. Thus, guidelines for a disease whose management is conceivably interrelated with drugs and interventions used to lower blood pressure or lipids should address how these co-interventions may affect care of the index disease. Such interactions may arise in unexpected ways. For example, management of neurological conditions is not typically considered to interact with management of hyperlipidemia, but drugs such as phenytoin and carbamazepine have clinically significant drug–drug interactions with simvastatin, lovastatin, and atorvastatin.[26] Moreover, aggressive management of hyperlipidemia may be less appropriate for individuals with limited life expectancy.[27,28]

Because hypertension and hyperlipidemia so dominated the most common disease triplets (a pattern consistent with previous studies), patterns of concurrent comorbidities were evaluated after excluding these two conditions.[18,21] Here, important sex differences emerged, with coronary heart disease and diabetes mellitus rising to the top sources of comorbidity in men and arthritis and GERD (and related syndromes) in women. These common disease clusters highlight numerous potential drug–drug and drug–disease interactions. For example, use of nonsteroidal anti-inflammatory drugs to manage arthritis has important implications for individuals with heart failure, hypertension, and chronic renal insufficiency, whereas the effect of proton pump inhibitors on absorption of aspirin and on fracture risk is important to address in individuals with coronary heart disease and osteoporosis.[29–31] Although these supplementary analyses shed additional light, it is important not to discount the importance of hypertension and hyperlipidemia, which were excluded from these supplementary analyses precisely because they were so dominant that they obscured other underlying patterns.

The methods used in this study are important to consider in interpreting the results. First, the study population comprised individuals receiving at least some care in the VA healthcare system. Previous work has shown that, on average, VA patients have greater illness burden and lower socioeconomic status than people who receive care exclusively through Medicare.[32,33] Thus, the generalizability of the results to the general population of older adults in the United States is uncertain. In addition, the method used to ascertain diagnoses can affect estimates of multimorbidity.[14,22] One concern is that the accuracy of administrative diagnoses varies between conditions and depending on who is doing the coding (e.g., professional coders for hospital discharge diagnoses vs clinicians for outpatient encounter diagnoses).[24] The study aimed to maximize sensitivity for identifying conditions by requiring the presence of only one pertinent ICD-9 code to establish a diagnosis. In a previous validation study of VA data, the sensitivity of the one-diagnosis approach for common conditions such as coronary heart disease, diabetes mellitus, and benign prostatic hypertrophy ranged from 70% to 96%, with specificity of 86% to 94%.[24] As expected, the sensitivity analyses that used more-stringent criteria for identifying conditions found a lower prevalence of individual diseases and disease combinations, but the overall disease patterns did not substantively differ from the original analyses.

It is also important to consider that certain diagnoses may "crowd out" other underrecognized or quiescent conditions such as mental health conditions and geriatric syndromes so that the true prevalence and burden of these conditions is not captured in the results. Undercoding may also result from other conditions being prioritized or from coding fatigue. For example, it is possible that some of the lower prevalence of diabetes mellitus and hypertension in the oldest-old adults may be due to undercoding of these diagnoses because of more-pressing complaints in these individuals. (Another likely explanation may be remission of hypertension and diabetes mellitus as individuals lose weight with advancing age or a healthy survivor effect whereby individuals with these conditions are less likely to survive into older age.[34]) Conversely, certain diseases may be preferentially coded in the presence of other conditions, thereby increasing the observed clustering between related conditions. For example, clinicians may be more aggressive about diagnosing and coding hyperlipidemia in a individual with coronary heart disease because treating the former can reduce risk of future coronary events.

Finally, the analytical approaches used cannot capture the full complexity of disease status in older men and women. Participants with each of the 15 most common three-way disease combinations had a mean of approximately seven to eight conditions so that the three-way combinations identified in the analyses represents less than half of their measured disease burden (not to mention additional conditions not captured by the measures). Moreover, clinical complexity goes far beyond simple

disease counts, including disease severity and subjective symptoms, geriatric syndromes such as falls and cognitive impairment, and dependence in basic and instrumental activities of daily living.[35–37] Thus, developers of guidelines should interpret these results as primarily evaluating the role of "traditional" medical comorbidities and should not neglect the important role of mental health conditions, geriatric syndromes, and other important conditions that have critical effects on people's well-being.

Accounting for common patterns of multimorbidity is essential for developing systematic approaches to disease management that reflect the clinical reality of older adults. Although decision-making needs to be customized to the unique preferences and clinical characteristics of each individual, clinicians, guideline developers, and policy-makers should consider commonly co-occurring conditions to minimize drug–drug and drug–disease interactions and create an integrated plan of care that accounts for the multiplicity of diseases that often exist within the same individual.

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SUPPORTING INFORMATION

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

Appendix S1. Data extraction procedures.

Appendix S2. Data tables for disease prevalence by age group.

Appendix S3. Most common disease combinations by age group.

Appendix S4. Most common 3-way combinations of conditions–excluding hypertension and hyperlipidemia.

Appendix S5. Sensitivity analyses.

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