Research Priorities in Geriatric Palliative Care: Multimorbidity

Christine S. Ritchie, MD, MSPH[1–3] and Donna M. Zulman, MD, MS[4,5]

Abstract

With global aging and scientific advances extending survival, the number of adults experiencing multiple chronic conditions has grown substantially and is projected to increase by another third between 2000 and 2030. Among the many challenges posed by multimorbidity, some of the most pressing include how to characterize and measure comorbid conditions, understand symptoms and illness burden, and provide person-centered care in the context of competing health care priorities and increasing complexity. In this white paper emanating from a National Institute on Aging supported conference to discuss research gaps at the geriatrics–palliative care interface, the authors review common definitions of multimorbidity; describe the association between multimorbidity and quality of life, functional status, quality of care, and health care utilization; note content and methodological gaps in multimorbidity evidence; and make recommendations regarding research priorities in this area of expanding public health impact.

Introduction

WITH GLOBAL AGING, rising rates of chronic conditions, and medical advances extending survival, the number of adults experiencing multiple chronic conditions has grown substantially and is projected to increase by more than a third between 2000 and 2030.[1] These trends are requiring clinicians, health systems, and research institutes to shift from their traditional focus on individual conditions to an approach that encompasses a patient's multiple health problems. Among the many challenges posed by multimorbidity, some of the most pressing include how to characterize and measure comorbid conditions, understand symptoms and illness burden, and provide person-centered care in the context of competing health care priorities and increasing complexity.

Definitions and Prevalence

There is no clear definition for the term "multimorbidity." Yancik, in a report for the National Institute on Aging Task Force on Comorbidity, defined multimorbidity as the "the total burden of biological dysfunction."[2] Health services researchers often operationalize the concept of multimorbidity as the coexistence of two or more long-term conditions.[3] However, classification systems vary in terms of what is considered a "condition." For example, affective symptoms (e.g., anxiety, depression); physical symptoms (e.g., pain, shortness of breath); and functional status (e.g., cognitive dysfunction, physical limitations) may or may not be included in counts of comorbidities.[4]

The terms multimorbidity, polypathology, and complexity are often used interchangeably to predict health care utilization, cost, and negative patient outcomes.[4] A number of multimorbidity instruments (e.g., the Charlson Index and Cumulative Illness Rating Scale) have been developed, using a combination of comorbidity counts and severity to generate a single assessment of illness burden.[5–10] Increasingly, there are efforts to capture other patient characteristics including socioeconomic levels and social support infrastructure in defining or describing the implications of multimorbidity.[11,12] For example, Bernabeu-Wittel and colleagues developed a one-year mortality prediction model for multimorbid patients that included specific comorbid conditions along with age, functional status, caregiver status, and health care utilization patterns. Perhaps not surprisingly, his prediction model

[1]Division of Geriatrics, UCSF, San Francisco, California.
[2]San Francisco VA Medical Center, San Francisco, California.
[3]Jewish Home of San Francisco, San Francisco, California.
[4]Division of General Medical Disciplines, Stanford University, Stanford, California.
[5]Center for Innovation to Implementation, VA Palo Alto Health Care System, Palo Alto, California.

performed better than the Charlson Index in identifying those with a high one-year risk for death.[13]

The prevalence of multimorbidity varies depending on the setting (e.g., community, hospital, long-term care) and the conditions included in the multimorbidity assessment. Using ambulatory diagnostic groups (ADGs) to identify International Classification of Diseases 9th Edition Clinical Modification (ICD-9-CM) chronic conditions among Medicare beneficiaries in 1999, Wolff and colleagues found that 65% of participants had two or more types of chronic conditions, 43% had three or more types of chronic conditions, and 24% had four or more types of chronic conditions. The likelihood of having higher numbers of conditions increased with age.[14] More recently, Fried and colleagues used self-report data from the National Health Interview Surveys (NHIS) from 1999–2000 and from 2009–2010 to evaluate the prevalence of nine chronic conditions: hypertension, heart disease, diabetes, cancer, stroke, chronic bronchitis, emphysema, current asthma, and kidney disease. In the 2009–2010 survey, 45% of adults 65 years of age and older reported two or more of the nine conditions, an increase by 37% compared to the 1999–2000 survey.[15]

Available Evidence and Data on Multimorbidity

There is substantial evidence describing the association between multimorbidity and quality of life, functional status, quality of care, and health care utilization.[14,16–20] Using quintiles of multimorbidity determined by the Cumulative Illness Rating Scale, Fortin and colleagues showed that health-related quality of life measured by SF-36 was adversely affected by multimorbidity after adjustment for age, sex, perceived social support, and socioeconomic status.[17] Although Fortin and colleagues' study showed a stronger relationship between multimorbidity and physical (as opposed to mental health) quality of life indicators, Fauth and colleagues' analysis of four Swedish studies of older adults identified multimorbidity as an independent predictor of depressive symptoms.[21]

The relationship between multimorbidity and functional decline has been appreciated for several decades. For example, in analyses of 1984 NHIS Study on Aging supplement data, Verbrugge and colleagues found that an individual's number of chronic conditions (excluding Alzheimer's disease and COPD) was directly associated with that person's level of ADL and IADL limitation.[20] In the longitudinal Leiden 85-plus Study (1997–2004), the presence of two or more chronic conditions predicted accelerated ADL disability over time among individuals with normal cognitive function.[22] In addition, several studies have shown an association between multimorbidity and mortality across a range of conditions,[23–26] although this relationship is inconsistent and may be mediated by disability.[27,28]

The quality of care for patients with multiple chronic conditions appears to vary based on both the number and types of conditions involved. In 2007, Higashi and colleagues reported a positive association between number of medical conditions in community-dwelling adults and the quality of care they received (as measured by percentage of quality indicators satisfied, among those for which patients were eligible).[29] Min and colleagues observed a similar pattern for older adults at high risk for functional decline or death.[30] Evaluations of specific conditions, however, have found that quality of care may be adversely affected by the presence of comorbid conditions, particularly if they are discordant or unrelated in terms of management.[31] For example, Turner and colleagues found that the adjusted odds of treatment intensification for uncontrolled hypertension decreased as a patient's number of unrelated conditions (e.g., arthritis, cancer, or depression) increased.[32] Mental health comorbidities, in particular, may negatively impact quality of care for other chronic conditions, a phenomenon that has been observed for a number of diseases including diabetes, heart failure, and arthritis.[33–35]

Health care utilization is generally higher among those with multimorbidity. A study using claims data from 2004 for 123,224 patients aged 65 years and over in Germany found that those with three or more conditions had more than twice as many contacts with physicians (36 versus 16) as those with two or fewer conditions.[36] In Wolff and colleagues' study of 1999 Medicare beneficiaries with multiple chronic conditions, there was an annual increase in Medicare expenditures from $1,154 among individuals with one condition to $2,394, $4,701, and $13,973 among individuals with two, three, and four or more conditions, respectively.[14] More recent data from the Medicare Current Beneficiary Survey between 2000–2005 demonstrated a higher likelihood for ambulatory care sensitive condition hospitalizations among beneficiaries with multimorbidity compared to beneficiaries without multimorbidity (AOR = 1.62; 95% CI = 1.14, 2.30 among those with mental illness and AOR = 1.54; 95% CI = 1.12, 2.11 among those without mental illness).[37]

Content and Methodological Gaps

The growing interest in multimorbidity over the past several years is reflected by the growth in numbers of publications related to the topic. In a search using the term "multimorbidity" filtered by "age > 65 years," "human," and "English language," 237 articles were identified. Of those 237 papers, 57 were published in 2012 alone. Nevertheless, relative to the growing prevalence and impact of multimorbidity among older adults, the gaps in evidence are still large, especially within the field of palliative and end-of-life care.

A large gap in multimorbidity evidence relates to the regular exclusion of older adults and multimorbid individuals from clinical trials[38–40] and the lack of outcomes in clinical trials that are relevant to multimorbid patients.[41] In a review of 284 randomized controlled trials published in high-impact general medical and specialized journals at five-year intervals between 1995 and 2010, Jadad and colleagues found that individuals with multimorbidity were excluded in 63% of studies.[38]

Even when studies include multimorbid patients, they may not evaluate outcomes that are important to older adults with multimorbidity, including changes in quality of life and physical and cognitive function.[40,42] Studies rarely report time horizon to benefit (or harm), which is critical when considering a treatment for someone with a limited life expectancy. Studies also rarely report an intervention's treatment burden (e.g., number of required outpatient visits, length of a hospital stay, extent of testing, or invasiveness of interventions); specific harms and benefits; and absolute risk reduction (versus relative risk reduction), all of which may be of particular importance to multimorbid patients and their providers.

Another gap in multimorbidity research hinges on the taxonomy of conditions and determination of which

conditions "count" in any particular multimorbidity index. Our current taxonomy of conditions has grown in a fragmented way, often guided by reimbursement rather than biology or pathophysiology. There is currently no consensus about the number or types of conditions that should be included in a multimorbidity index, leading to marked variation in the prevalence of multimorbidity across studies. Conditions included in research studies are frequently those that can be identified using claims data, and may not capture sensory deficits, chronic unexplained symptoms, subclinical disease, functional limitations, or cognitive impairment.

There is also a need for guidance regarding the illness burden that is generated by common combinations of conditions, and interactions among those conditions. While a number of tools have been developed to measure multimorbidity,[5–7] they do not provide a sufficiently comprehensive assessment of illness burden (Yancik's "total burden of biological dysfunction") to effectively guide treatment decisions or routine clinical management. Methods are needed to evaluate multimorbidity burden from the patient's and caregiver's perspective and provide insight on what elements of illness (symptoms, costs, life disruption, etc.) influence their goals for care.

There are also a number of opportunities to improve communication around the topic of multimorbidity. Few studies have directly compared differing approaches to preference elicitation from multimorbid patients and caregivers. Approaches that determine patients' preferences regarding life-extending versus symptom-directed care[43,44] are useful first steps but do not fully capture the complex array of goals and options that patients and families routinely navigate in the context of multimorbidity. There is also often uncertainty about prognosis and treatment outcomes for patients with multiple chronic conditions. Few prognostication tools incorporate comorbid conditions, and it is unclear how these tools should be applied (and their results communicated) to multimorbid patients.

Finally, more information is needed about the most effective and efficient strategies for engaging patients with multimorbidity in clinical settings, including optimal workflow approaches, team members, and educational methods. Better approaches are also needed for translating general clinical practice guidelines to specific individuals with multiple conditions in a way that aligns performance measures with high-quality personalized care. This will require the use of strategies that prioritize multiple, sometimes discordant, recommendations, and help determine the value (and potential harm) of medications, diagnostic tests, and interventions for individual patients.

Priorities for Research (See Table 16)

There is a need for standardized approaches to multimorbidity measurement. A conceptual framework that recognizes the complexity of comorbidity assessment, while at the same time incorporating key comorbidity domains, would advance work in multimorbidity. While this framework should be guided by research to date, it should also be guided by patients' and caregivers' experiences. A standardized framework for multimorbidity could help advance quality and provider performance metrics to better reflect optimal care for patients with multiple chronic conditions.

With respect to inclusion of patients with multimorbidity in clinical trials, the Food and Drug Administration, the National Institutes of Health, and the pharmaceutical industry

TABLE 1. RESEARCH PRIORITIES FOR MULTIMORBIDITY

Research priority	Study objective	Study setting	Sample	Study design
Develop consensus around measures of multimorbidity	Develop a framework for multimorbidity to encourage standardization of measures across research, clinical guidelines, and policy	Community, institutional, long-term, or acute care (ideally longitudinal, across settings)	Medium to large sample size, representing the overall older adult population	Systematic review, validation studies
Improve communication with multimorbid patients	Develop enhanced communication methods and tools around topics related to multimorbidity and goals of care	All settings of care	Small to medium with attention to both patients and caregivers	Qualitative and quantitative studies; observational studies and clinical trials
Advance prognostication and clinical care for patients with multiple chronic conditions	Elicit new knowledge about multimorbidity from structured and unstructured data	All settings of care	Database from large health care system or insurer	Data mining
Promote research practices that will yield evidence that is relevant to multimorbid patients	Develop study protocol recommendations (e.g., inclusion/exclusion criteria, outcomes, analytic methods) to optimize the relevance of clinical trial findings to multimorbid patients	All settings of care	Dependent on research question	Observational studies using propensity matching, pragmatic clinical trials

will need to make a concerted effort to increase participation of multimorbid patients and include outcome measures (such as quality of life) that are relevant and important to individuals with multiple complex medical conditions. Studies should also be encouraged to evaluate benefits and harms of therapy discontinuation, and report treatment burden and time horizon to positive and adverse outcomes.

With the increasing availability of "big data," priority should be given to research that uses sophisticated data mining techniques to elicit new knowledge from structured and unstructured data, and to develop personalized prognostication models that can help guide care for patients with multiple chronic conditions.

Summary

Multimorbidity is increasing among older adults, and is associated with high rates of health care utilization and declines in quality of life and function. There is a need for consistent definitions and standardized measures of multimorbidity, as well as better prognostic tools, enhanced communication techniques, and refined quality of care and performance metrics for patients with multiple chronic conditions. Additionally, research will need to systematically explore optimal approaches to provide care for older adults with multimorbidity, especially as their illnesses become more advanced.

Acknowledgments

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Address correspondence to:
Christine S. Ritchie, MD, MSPH
University of California San Francisco
School of Medicine
3333 California Street, Suite 380
San Francisco, CA 94143-1265

E-mail: christine.ritchie@ucsf.edu

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