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Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design?

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ABSTRACT

Many people living with chronic conditions have multiple chronic conditions. Multimorbidity is defined here as the co-existence of two or more chronic conditions, where one is not necessarily more central than the others. Multimorbidity affects quality of life, ability to work and employability, disability and mortality. Currently, clinicians have limited guidance or evidence as to how to approach care decisions for such patients. Understanding how to best care and design the health system for patients with multimorbidity may lead to improvements in quality of life, utilization of healthcare, safety, morbidity and mortality. The objective of this paper is to review the implications of multimorbidity for the design of health system and to understand the research needs for this population. The consideration of people with multimorbidity is essential in the design and evaluation of health systems. Fundamentally, people with multimorbidity should receive a patient - and family-centered approach to care throughout the health system, and understanding how to deliver this type of care in effective and efficient ways is an enormous challenge, and opportunity, for clinicians, researchers, and policy makers today.

Key words: Multimorbidity, aging, chronic conditions, health system, healthcare, comorbidity.

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INTRODUCTION

Approximately one in four adults have two or more chronic conditions, and half of older adults have three or more chronic conditions.[1-5] The prevalence of multiple chronic conditions (MCC) among individuals increases with age and is substantial among older adults, even though many people with MCC are under the age of 65 years.[5] The number of individuals with MCC will increase dramatically in coming years.[1] Comorbidity is increasingly recognized as a critical clinical issue in medical care, in part because it is an independent predictor of adverse outcomes, including quality of life (QOL), mortality, healthcare, disability, and complications of treatment beyond the effects of the individual conditions.[6-22] Most research and clinical care has considered comorbidity from the perspective of an index condition. In the presence of multiple conditions this perspective becomes an inefficient and perhaps ineffective framework for management of all the chronic conditions of a single person, and may be equally flawed for a health system's approach to people with MCC.[23] The term multimorbidity, capturing multiple, potentially interacting, medical and psychiatric conditions, may be more appropriate and more patient-centered for the older population than consideration from the perspective of a single index condition, which is the traditional approach.[24,25] Currently, clinicians have limited guidance or evidence as to how to approach care decisions for such patients.[26] Understanding how to best care and design the health system for patients with multimorbidity may lead to improvements in QOL, utilization of healthcare, safety, morbidity and mortality.[27] The objective of this paper is to review the implications of multimorbidity for the design of health systems and to understand the research needs for this population.

DEFINITIONS OF COMORBIDITY, MULTIMORBIDITY, AND COMPLEXITY

Feinstein defined comorbidity as "any distinct additional clinical entity that has existed or may occur during the clinical course of a patient who has the index disease under study."[28] By definition, this assumes that one is taking an index disease perspective, with one disease assuming a central place (Figure 1). The usefulness of a framework where one disease is considered central is not clear when considering the optimal care and health system for people with multimorbidity, unless one disease is truly dominant in terms of the care and well-being of the individual.[4,26,29]

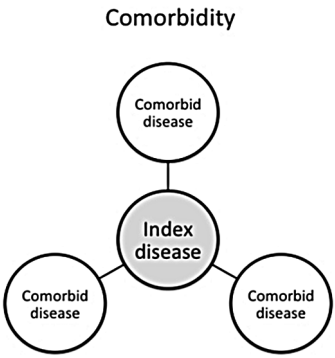

Fig. 1. Conceptual Diagram of Comorbidity: Index Disease, With One or More Comorbid Condition or Diseases Affecting Its Course and Treatment. Comorbidity has often been studied and treated in clinical practice from the perspective of an index disease, and one or more comorbid diseases may typically be considered. These diseases may affect the course and treatment of the index disease to varying degrees (varied weight of connecting bars). This framework may create disjointed treatment plans for each of the diseases and become cumbersome in patients with several co-existing diseases.

Highly prevalent chronic diseases (heart disease, diabetes, arthritis, chronic lower respiratory tract disease and stroke) are known to co-occur frequently with each other.[30] Other less prevalent conditions still may occur frequently in combination with these (congestive heart failure, anemia, renal insufficiency, depression).[31,32] While there are varying definitions in the medical literature, **multimorbidity is defined here as the co-existence of two or more chronic conditions, where one is not necessarily more central than the others.**[4,33-35] Multimorbidity includes traditional diseases and syndromes but also may be extended to refer to conditions such as chronic bursitis of the hip, rotator cuff problems, dyspepsia, migraines, sleep disturbances, functional bowel syndrome or constipation, disability, falls, hearing impairment, and sarcopenia, for example.[34] The pathophysiology of these diseases, syndromes, and conditions may overlap and the management of them may interact to varying degrees. The intersection of these factors occurs in a context of biological status and physiologic reserves, as well as psychological health. The ramifications of suffering from multimorbidity unfold for a person within social, educational, cultural, behavioral, economic and environmental circumstances, which in turn affect management. While considering all of these dimensions is essential for patient-centered care,

the best terms for considering how all of these affect clinical decision-making is not known. Multimorbidity needs to be considered within the context of a person, or patient.[25,35] The person with multimorbidity also has individual values and priorities for their life and healthcare, which need to be elicited and factored into treatment plans.

The failure of healthcare to systematically match patient needs to best therapeutic practices partly reflects the challenges of creating an integrated clinical plan for people with multimorbidity.[26] Clinical approaches often focus on one disease at a time or may fail to take into account the interactions between the patient and healthcare system that become increasingly important as individual reserves diminish and the intricacy and intensity of healthcare increases.

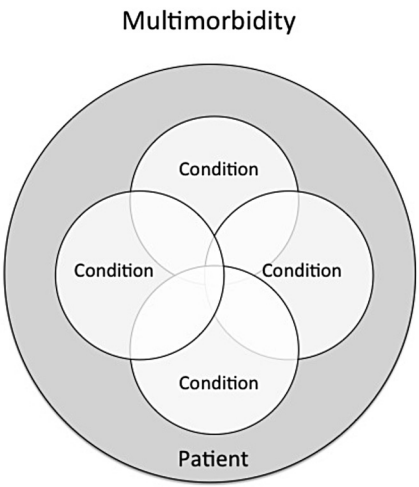

Fig. 2. Conceptual Diagram of Multimorbidity within an Individual Person's Circumstances and Preferences. The perspective of multimorbidity may be useful for treating patients with multiple conditions. Conditions include traditional diseases, but also may reflect conditions such as disability, falls, hearing impairment, and sarcopenia that fall outside the traditional disease model. These conditions may overlap to varying degrees. The intersecting conditions exist within a context of biological health and reserves, as well as the psychological circumstances of a person (i.e., positive affect). The multimorbid conditions also unfold for given people within their social, educational, cultural, economic and environmental circumstances, and these will affect management of the multimorbid conditions. The person with multimorbidity also has individual values and priorities for their life and healthcare, which need to be elicited and factored into treatment plans.

Multimorbidity affects the clinical complexity associated with clinical decision-making and the healthcare system in which clinical decision-making occurs.[31] Clinical complexity results from the factors or elements that should be reconciled or addressed when making decisions about a therapeutic strategy or prevention strategy. Because there is a lack of agreement on definitions of complexity and not all current definitions include non-medical dimensions, this term may be challenging.[36] For people with multimorbidity, the essential element is that decisions must be made within the context of a person (see Figure 2). Some decisions may be reducible to a single decision (i.e., Will a statin benefit this patient, and is she willing and able to take it?) but more commonly they involve several clinical questions at the same time (Should a patient start a statin, anti-depressant, and pursue rehabilitation?). The latter scenario implies the need for prioritization – i.e., what is most important if not everything can be done and what should be done first if everything cannot or should not be done at one time. Some co-occurring conditions may be managed synergistically (i.e., the use of ace inhibitors for diabetes and hypertension), and guidelines and quality standards sometimes recognize this overlap of clinical management. These conditions are thus concordant.[29,37] Discordant conditions are more likely to add to the complexity of clinical decision-making. The care of people with multimorbidity is failed by approaches that do not look at more than one factor or dimension and that may rely on conventional analytic techniques.[38]

PEOPLE WITH MULTIMORBIDITY: PREVALENCE

The prevalence of multimorbidity increases with age, but is not just an issue for older adults. As a result of advances in medical care and public health, a growing proportion of people have multimorbidity.[39] In an Australian cohort study, more than 40 percent of the people with multimorbidity were less than 60 years of age.[40] The prevalence of multimorbidity is striking in studies conducted in several countries in different parts of the world.[1-3,11,12,30,39,41-49] While the prevalence varies, this partially depends on the source of the population studied (patients vs. population based samples), sources of data (e.g., surveys, chart reviews, administrative data), data collection methods, targeted age groups, diagnoses considered and study populations, making the comparability of prevalence estimates questionable.[3] The presence of multimorbidity also indicates higher risk of additional conditions; people with multimorbidity are at a higher risk of being diagnosed with two or more new diseases than those with no disease.[14]

Multimorbidity is even more important when each condition may influence the care of the other condition(s) through limitations of life expectancy, interactions between therapies, and/or direct contraindications to therapy for one condition by other conditions themselves.[23,25,36] Forty-eight percent of older adults have three or more chronic conditions.[1] In younger populations, 35 percent of disabled adults have three or more chronic conditions.[50] Among children, where the definition of a chronic health condition is less clear, prevalence estimates range from less than one percent up to 44 percent of children having multimorbidity.[51]

It can be useful to think about the prevalence of multimorbidity with varied approaches. While it is important to note how many people have multimorbidity, and which specific conditions they have, it is also worth considering reporting data in different ways. For example, among older women participating in the United States nationally representative survey NHANES, examining five major chronic diseases (coronary heart disease, stroke, diabetes mellitus, arthritis, and chronic lower respiratory tract disease) with pattern analyses reveals that less than 20 percent of people with coronary heart disease have that disease alone, and not one of the other four conditions. Similar findings for how often the disease occurs in isolation were found for stroke, diabetes mellitus, and chronic lower respiratory tract disease (all less than 20 percent of the population with each condition, respectively). For arthritis, the prevalence of arthritis alone was 47 percent.[30] These numbers would be smaller if a larger pool of conditions was considered. This work demonstrates that multimorbidity is the norm, not the exception, for many chronic diseases, and may speak to researchers, disease managers, policy makers and providers who have traditionally taken an index disease approach. Researchers have investigated whether specific conditions "cluster," or occur together at greater rates than would be expected by chance alone.[41,52] Such work highlights the need to understand the underlying pathogenesis of multimorbidity, and may identify targets for preventive approaches.

IMPACT OF MULTIMORBIDITY ON PEOPLE

Multimorbidity affects QOL, ability to work and employability, disability and mortality.[4,6-22,42,53-56] The relationship between multimorbidity and QOL is inverse, and the relationship to specific dimensions of QOL is complex.[56] Some specific chronic conditions have a stronger relationship with functional status than others, and there may be interaction between specific conditions, with the risk of disability in people with specific combinations of conditions greater than expected based on risks associated with the

individual conditions alone.[18,57] The accumulation of new chronic conditions is associated with greater disability.[58]

PEOPLE WITH MULTIMORBIDITY AND THEIR FAMILY/SOCIAL SUPPORTS

People living with multimorbidity have greater self-care needs.[59-65] Complex older patients are especially likely to rely on and be affected by caregiver involvement in health management.[66] Family involvement is a key dimension of patient-centered care and several studies substantiate its influence on adherence.[67-72] Aside from their role in dementia care and inpatient settings and with children, the role of caregivers has not been well articulated in chronic care initiatives, but their role is increasingly recognized, particularly for people with multimorbidity.[66,73-75] Caregivers are thus crucial to include in healthcare, public health policy initiatives, health system design, and research on people with multimorbidity. Many important questions remain unanswered in terms of how to optimally integrate caregivers to improve the health of people with multimorbidity.[76]

PEOPLE WITH MULTIMORBIDITY AND CURRENT HEALTH SYSTEMS

Patients with multimorbidity and complex healthcare needs often receive care that is fragmented, incomplete, inefficient, and ineffective.[11,23,48,77,78] For example, in addition to associations with high costs and utilization, the risk of potentially avoidable inpatient admissions or preventable complications in an inpatient setting increases dramatically with the number of chronic conditions among older adults.[48,49] Patients with multimorbidity may be particularly susceptible to the hazards of hospitalization, polypharmacy, and post-operative complications.[79-81]

HOW SHOULD AN UNDERSTANDING OF MULTIMORBIDITY INFORM HEALTH SYSTEM DESIGN?

An essential element of health system design that addresses people with multimorbidity is the elimination of the single disease focus. We want to take care of people with multimorbidity, not the individual conditions that add up to multimorbidity. Assuming that an additive process of the single disease approach will meet the needs of people with multimorbidity is flawed and

may even be harmful in many instances. Our health system should focus on people with multimorbidity, and recognize that some of the issues we must address are consequences of the multimorbidity and not diseases *per se*, but may have further adverse effects themselves. For example, polypharmacy is associated with greater rates of adverse events and drug interactions. Falls are most often multi-factorial in etiology, and yet can have dramatic impact on patient important outcomes like function and independence. For both of these examples, evidence-based interventions have been shown to improve patient important outcomes, and yet, neither is considered a "disease".[82,83] Throughout healthcare, the disease-based focus prevails, from the design of clinical trials to the reimbursement structure in many countries.[84]

The Chronic Care Model

The Chronic Care Model (Figure 3), as described by Wagner et al., provides many of the essential elements of a healthcare system optimally designed for people with MCC.[85] It is important to view this model and how it applies from the perspective of multimorbidity, not only a single-disease focus. Many interventions that derived from this model and approach have started with a focus on single conditions, but in recent years, there have been an increasing number of interventions that recognize that most people with one chronic disease have others.[78,86-92]

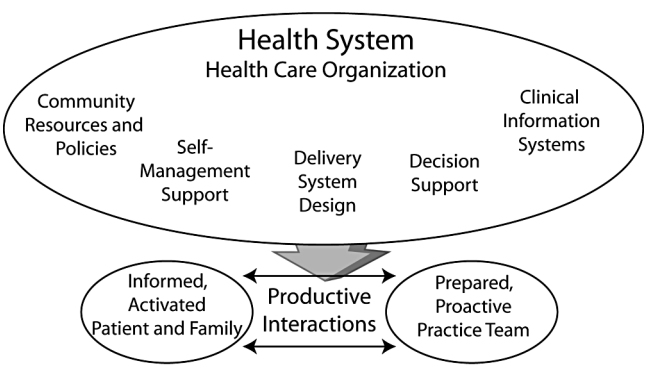

Fig. 3. The Chronic Care Model.
Source: Copyright 1996-2010 The MacColl Institute (with permission). The Improving Chronic Illness Care program is supported by The Robert Wood Johnson Foundation, with direction and technical assistance provided by Group Health's MacColl Institute for Healthcare Innovation.

Patient-Centered Care

Primary care (or generalist care) is essential when considering how a health system should care for people with multimorbidity. Patient-centered care for patients with chronic illness is care which (1) is attentive to patient's psychosocial as well as physical needs, (2) explores the patient's concerns and priorities for care, (3) conveys a sense of partnership between the patient and physician, (4) facilitates active patient involvement in decision making, and (5) is coordinated across professionals, facilities, and support systems.[93,94] This type of patient-centered care in a "medical home" may not need to be provided by a generalist or primary care provider, but should include the essential elements of a holistic approach to these patients and their healthcare and not focus inappropriately on one condition over others.[94] In some instances, one condition may be dominant, or be so complex or serious that it eclipses the management of other conditions either in the short-term or over the long-term.[29] As described by Piette and Kerr, examples of this would include end-stage disease, severely symptomatic, or recently diagnosed conditions. When one condition is not dominant, patient-centered care would ideally balance all of a person's conditions and allow for an integrated approach to their healthcare. This presents enormous challenges, as work by Yarnall et al. and Ostbye et al. demonstrates that a typical family practitioner in the US with a standard panel would not have adequate time in a typical day to deliver the services currently recommended for chronic disease management or preventive services.[95,96] This work highlights two issues. First, the responsibility for patient education and follow-up of protocols and guidelines should be shared within an integrated healthcare system and community-based health programs to also engage physician assistants, nurse practitioners, professional and neighborhood health educators to provide education, counseling, and guidance.[97-99] Second, the generation of evidence, the synthesis of evidence in guidelines, the development of quality standards, and the setting of healthcare system policy need to account for these issues, and prioritize across conditions and approaches to healthcare for those elements that are most important for improving the well-being of people with multimorbidity.[26,96]

Sites of Care and Transitions Between Them

People with multimorbidity are seen frequently, and in multiple sites of care, including emergency rooms, hospitals, outpatient settings, specialty clinics, nursing home and rehabilitation facilities, assisted livings, and home healthcare. People with multimorbidity are thought particularly vulnerable to suboptimal quality care.[1,100] Central then to the design of care

for these patients is the communication and connections between these traditional silos of care. Patients with multimorbidity may be most vulnerable to the adverse consequences of transitions of care, and thus the optimal health system would allow for facile communication across sites of care to avoid duplicate testing which may be harmful, allow for medication reconciliation, and transfer of essential information about allergies, medication, recent and past history, decision-making capabilities and contact information for healthcare agents (surrogates). Work on transitional care has included both disease specific approaches and those that do not focus on a particular condition.[100-105] However, much of this work has focused on the transitions between the hospital and post-hospital settings, but transitions between outpatient providers may be equally important for the long-term management of people with multimorbidity.

Reimbursement Structure

Reimbursement systems are varied across countries, and often even within the same country. Therefore, we will focus on identification of general principles for reimbursement structures considering the design of health systems and people with multimorbidity.

The goals of structuring a reimbursement system include the following key issues. These are not meant to be exhaustive in terms of considering all of the goals of reimbursement systems, but rather those issues that are particularly salient to people with multimorbidity.

- To encourage providers to want to care for people with multimorbidity (as opposed to avoiding them).
- To reward the cognitive processes and shared decision-making believed very important in making thoughtful, patient-centered decisions about healthcare.
- To reward the cognitive aspects of medicine, not just procedures and technology.
- To minimize overuse and underuse of therapies and maximize appropriate use.
- To attract adequate numbers of highly qualified individuals to primary care or care of people with multimorbidity.
- To reward a patient – and family – centered approach over a disease based-approach (with incentives based largely on disease specific quality standards).
- To reward care coordination and communication between providers across sites of care, as well as with patients and families.

It is critical that the effects of changes to reimbursement systems be rigorously evaluated, particularly in regards to the most vulnerable populations, which include those living with multimorbidity. While there are many success stories,[106] there are also many examples of unintended consequences resulting from changes in how we approach the reimbursement structures for healthcare.[107-111]

Role of Family and Friends

While the importance of family and friends in chronic care has been increasingly recognized, the optimal ways to engage family members in the care of people with multimorbidity are not yet known, yet many of these patients are likely to be accompanied to medical visits, and many of these medical visit companions likely assume roles in the management of healthcare tasks for these people.[66,76,112-114] The term "patient- and family-centered care" is increasingly used, but it is yet to be a reality in many chronic care outpatient settings.[115,116]

Clinical Practice Guidelines

Table 1

Summary of Review of CPGs Applicability to Older Adults with Multimorbidity

Issue	Number of CPGs addressing the issue
Quality of evidence for older adults with multimorbidity	2/9
Guidance on treatment of index condition in context of single comorbid condition	7/9
Guidance on treatment of index condition in context of multiple comorbid conditions	4/9***
Information on time needed to treat in order to achieve benefit	1/9
Discussion of QOL issues	7/9*
Discussion of short-term vs. long-term goals	0/9
Recommendations for incorporating patient preferences	7/9**

* for two of these, QOL is addressed for only a single symptom119,120

** patient preferences are discussed only in regard to end-of-life for the congestive heart failure CPG119

*** guidance given for three of these conditions is only for multiple cardiovascular conditions

Source: Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: Implications for pay for performance. JAMA. 2005;294:716-24.[26]

The applicability of clinical practice guidelines (CPGs) to older adults with multimorbidity is limited.[26,117,118] A review of nine common chronic conditions and selected primary care and specialty CPGs recommended by national or international organizations demonstrated inadequate attention to this population.[26] The CPGs were abstracted by two reviewers for components relevant to the care of older patients with multimorbidity. Thus as shown in Table 1, few of the nine CPGs address these issues of high relevance for older adults, particularly those with multiple conditions, and none of the guidelines that were reviewed comprehensively addressed these issues.

Applying relevant CPGs to a hypothetical 79 year old woman with moderate severity osteoporosis, osteoarthritis, diabetes mellitus, hypertension, and chronic obstructive pulmonary disease leads to a complex and potentially harmful treatment regimen.[26] Implementing CPGs for these conditions, and choosing generic, long-acting drugs with the least side effects, she would be prescribed 12 unique medications, requiring a complex regimen of 19 doses of medication per day, and 14 non-pharmacologic treatments (self-monitoring, diet, exercise, healthcare visits, and laboratory testing). There were many potential drug-condition, drug-drug, and food-drug interactions. Non-pharmacologic recommendations also contradict. This work identifies a high level of complexity, cost, and potential burden for such a treatment regimen. Complete adherence would not be feasible for many multimorbid adults, and, as shown above, the evidence for effectiveness for this patient population is often lacking.[26]

With rare exceptions, guidelines focus on the management of a single disease, and do not address how to optimally integrate care for individuals whose multiple problems may make guideline-recommended management of any single disease impractical, irrelevant or even harmful.[26,121] The root of this problem, however, is not narrowly confined to guideline development and application, but is inherent throughout the translational path from the generation of the evidence to the synthesis of the evidence upon which guidelines depend. Recently, emphasis has been placed on the role of "pragmatic" clinical trials to guide the care of real world populations. It is essential to note that without appropriate analytic techniques to account for heterogeneity of treatment effect, the results of such trials may be misleading about whether specific patients benefit more or less from therapies than the average patient.[122,123] Efforts are currently underway to increase the applicability of our evidence-base and clinical practice guidelines to people with multimorbidity.[124,125]

Quality Standards

The applicability of current CPGs is therefore poor for patients with multimorbidity.[26] The translational path culminating with guideline development for patients with multimorbidity is flawed and has implications for the development and application of performance measures. Basing standards for quality of care and pay for performance on existing CPGs could lead to inappropriate judgment of the care provided to individuals with multimorbidity and could create perverse incentives that emphasize the wrong aspects of care for this population and diminish rather than improve the quality of their care.[26] Defining and measuring quality of care in a patient-centered manner is essential for complex patients.

Comprehensive consideration of these issues is important for a framework for measuring performance for people with multimorbidity. Performance measurement for patients with multimorbidity has not been adequately developed.[126] Importantly, most research on quality of care in people with multimorbidity has not employed simultaneous assessment of both patient-reported quality of care and technical quality of care. While disease-specific performance standards are achieved in many multimorbid adults, patient reports of quality of primary care may be worse.[127-129] Limited prior work suggests that these two perspectives are often poorly correlated and that patient evaluations of care are critical in understanding performance.[130,131] However, existing tools do not adequately capture the needs and complexity of people with multimorbidity, and it is unknown how to best measure performance for these patients.[132]

Quality of care may be defined using the Institute of Medicine's six aims for healthcare: safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity.[133] No one has developed and employed an assessment of multimorbidity-specific quality. Assessing Care of Vulnerable Elderly (ACOVE) measures and the Patient Assessment of Chronic Illness Care have been used to measure care for people with multimorbidity, but neither capture all of the elements important for performance for people with multimorbidity.[134] Measurement of this comprehensive definition of quality of care would ideally capture optimal medical decision making with treatment appropriately individualized based on preferences and a relevant evidence base, and minimize both underuse and misuse.[29,60,126,135] Goals of care for individuals with multimorbidity include patient-centered care, with a well-informed patient and provider understanding his/her individualized risks and incorporating patient preferences. The goal is to avoid causing harm from adverse consequences of treatments, and to reduce morbidity and mortality without compromising function while maximizing other patient-important outcomes.

Patients with multimorbidity are seen in multiple sites of care and by multiple providers, and measurement of performance will need to address these issues.[136] Patients with multimorbidity may benefit most from processes that target the aggregate effect of multiple conditions, such as processes related to reducing polypharmacy, fall risk, and minimizing adverse drug reactions. Over time, the framework for thinking about all of a person's conditions may need to vary, to recognize that severity, prognosis and symptom burden will change.[29] Also, patients with multimorbidity often choose or need to involve family or friends in their healthcare and decision-making.[66]

Many patients with multimorbidity receive interventions for which there is little evidence of benefit and are at high risk for adverse health events. Performance measures are available for specific conditions and are sometimes used in patients with multimorbidity in the absence of evidence that they are appropriate, and further development is needed. Many conceptual issues in performance measurement for patients with multimorbidity require further development.

Approaches Specifically Using a Multimorbidity Perspective in Primary Care

A recent review of US models of care serving older adults with multimorbidity found similarities between the programs including: comprehensive assessment, development of a comprehensive care plan that incorporates evidence-based protocols, implementation of the plan over time, proactive monitoring of the patient's clinical status and adherence to the care plan, coordination of primary care, specialty care, hospitals, emergency departments, skilled nursing facilities, other medical institutions, and community agencies, facilitation of the patient's transitions from hospitals to post-acute settings, facilitation of the patient's access to community resources, such as meals programs, handicapped-accessible transportation, adult day care centers, support groups, and exercise programs.[77] Key differences between the programs reviewed include the year in which the program began, whether an established physician or new physician was involved, the type of setting where it was provided, eligibility for the program, the frequency of contact, and reimbursement structures.[106,137-139] International work has identified other models with promise.[140-143] Much work is needed in this area, particularly to understand the optimal health systems for younger people with multimorbidity, as well as how to transform typical primary care practices to meet these needs. In addition, little is known about how community, neighborhoods, and environments can best

support people with multimorbidity, although information from the broader chronic disease literature is potentially informative for understanding the necessary research agenda.

CONCLUSION

The consideration of people with multimorbidity is essential in the design and evaluation of health systems. Fundamentally, people with multimorbidity should receive a patient- and family-centered approach to care throughout the health system, and understanding how to deliver this type of care in effective and efficient ways is an enormous challenge, and opportunity, for clinicians, researchers, and policy makers today.

Acronyms list:
MCC = Muliple chronic condiditons
QOL = Quality of life
CPGs = Clinical practice guidelines

Terms and definitions list:
Multimorbidity: The co-existence of two or more chronic conditions, where one is not necessarily more central than the others.

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