Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians

American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity*

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One of the greatest challenges in geriatrics is providing optimal care for older adults with multiple chronic conditions, or "multimorbidity."[1–4] More than 50% of older adults have three or more chronic diseases. The heterogeneous patterns and severity of conditions produce distinctive cumulative effects for each individual.[5]

Multimorbidity is associated with many adverse consequences, including death, disability, institutionalization, greater use of healthcare resources, poorer quality of life, and higher rates of adverse effects of treatment or interventions.[1] Comprehensive strategies for healthcare delivery that are not disease specific, as well as interventions that target geriatric syndromes common in older adults with multimorbidity, show promise for this population,[5–9] although the best approaches to decision-making and clinical management of older adults with multimorbidity remain unclear.

Evidence-based clinical practice guidelines (CPGs) exist for many conditions, but the fact that most focus on the management of a single disease remains a barrier to their application in adults with multimorbidity.[3,9–13] Many CPGs do not address the question of how to integrate care for individuals with multimorbidity. Following single-disease CPGs in older adults with multimorbidity may cumulatively result in care that is impractical, irrelevant, or even harmful.[3,9] The source of this deficiency in many current CPGs is not confined to guideline development and implementation.[3,12] At each phase of the translational path, older adults with multimorbidity are often excluded. These omissions occur in the areas of trial and study design and analysis, synthesis of trial and observational study results in meta-analyses and systematic reviews, and the guideline development process. Because each of these generates the information necessary to support evidence-based care, the exclusion or underrepresentation of older adults with multimorbidity must be acknowledged so that appropriate interpretation of results is possible.

The full spectrum of clinical management of older adults with multimorbidity includes not only treatments and interventions for their conditions, but also screening and preventive and advanced illness care. The best strategies to determine which aspects of this spectrum of clinical management are of the highest priority in a particular older adult with multimorbidity are unknown.

Rather than relying solely on information from the limited evidence-based resources for clinical decision-making, clinicians need a management approach that will consider the multiple problems particular to each individual with multimorbidity. In addition to evidence-based choices, such an approach would reflect an older person's own preferences and goals (in the context of his or her own combination of diseases and conditions), prognosis, and multifactorial geriatric problems and syndromes and the feasibility of each management decision and its implementation. Interactions between treatments or interventions for two different conditions, as well as interactions between treatments or interventions for one condition and coexisting conditions, may factor into decision-making.

The American Geriatrics Society is developing professional tools and public information to support implementation of these principles in clinical care. All tools can be found at www.americangeriatrics.org.

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The American Geriatrics Society (AGS) convened an expert panel with complementary expertise in these topics along with a special interest in older adults with multimorbidity. The goal of the panel was to develop an approach by which clinicians can care optimally for this particular population. It is important to note that this document is not a guideline. A structured literature review was used to inform this work, but unlike a traditional guideline, this document does not issue recommendations based on rigorous evaluation of the quality of evidence for specific clinical questions followed by an assessment of harms and benefits and recommendation statements. By definition, older adults with multimorbidity are heterogeneous in terms of severity of illness, functional status, prognosis, and risk of adverse events even when diagnosed with the same pattern of conditions. Priorities for outcomes and health care also vary. Thus, not only the individuals themselves, but also the treatments that clinicians consider for them will differ. As a result, clinicians must pursue more-flexible approaches to care in these older patients.

This document presents a clinical approach to the care of older people with multimorbidity that describes guiding principles for the clinical management of this population. The goal of this work is also to facilitate the development and growth of an evidence base by which clinicians can make sound care decisions for this population, including the testing of better processes for decision-making. For example, not only must the healthcare community generate better evidence about whether a specific intervention is beneficial, it must also establish effective methods for determining outcome priorities and for deciding what changes are needed to the healthcare system to allow these methods to be accommodated. This is a consensus document, and it is hoped that evidence-based approaches to the care of older adults with multimorbidity will replace it in the future.

A summary of this document, "Patient-Centered Care for Older Adults with Multiple Chronic Conditions: A Stepwise Approach from the American Geriatrics Society,'' is also published in the *Journal of the American Geriatrics Society* and is available online at www.ags-online.org.

There are many relevant clinical concerns that are outside the scope of this project. Questions regarding costs of care, acute care, transitions of care, and the imminently dying are not specifically addressed; instead, the project focuses on older people with life expectancies of months to many years.[14,15] In addition, multimorbidity is associated with high symptom burden and poor quality of life. Management of cumulative illness and symptom burden in multimorbidity is not specifically discussed, although many principles related to patient preferences and treatment complexity can relate to management of symptoms in multimorbid patients. The management of chronic conditions in primary care is the primary focus, although older adults with multimorbidity frequently transition through many care settings, and a variety of provider types, referred to hereafter as clinicians, care for them. The method is relevant across settings and types of clinicians. Many of the principles and literature discussed here may have relevance to younger people with multimorbidity, but this population, and problems unique to younger people with multimorbidity, are not specifically considered.

Any healthcare professional clinically managing an older person with multimorbidity can use this approach, but a primary provider or medical home, with an associated healthcare team, is central to implementation. Clinical management is defined as representing all types of care for chronic conditions provided by clinicians, including pharmacological treatment, nonpharmacological interventions (e.g., referral to specialists, physical and occupational therapy, use of pacemakers), and screening and diagnostic tests and follow-up. Clinicians are the primary intended audience for this document. This work will also inform researchers, public health professionals, payers, policy-makers, and others interested in the care of older adults, because it addresses controversies and challenges to implementing the approach, offers a relevant research agenda, and describes barriers to its adoption.

METHODS

The AGS Clinical Practice and Models of Care Committee convened the expert panel with funding from the AGS. Members of the interdisciplinary panel were selected on the basis of their expertise in different areas relevant to older adults with multimorbidity, with a focus on geographic and training diversity. To ensure that potential conflicts of interest were clarified and addressed appropriately, each member disclosed his or her potential conflicts of interest to the expert panel at the onset. The panelists' potential conflicts of interest are listed at the end of the paper.

Through a one day in-person meeting and a series of conference calls, the panel proposed that the document contain five domains relevant to the care of older adults with multimorbidity: Patient Preferences, Interpreting the Evidence, Prognosis, Clinical Feasibility, and Optimizing Therapies and Care Plans. These domains were used to organize the report, although there is inherent overlap among them. Some of the individual domains apply to multiple steps of the flowchart (Figure 1). In addition to the five domains, a section on Barriers focuses on real-world challenges to implementing this approach in older adults with multimorbidity.

Literature Review Methods

Two distinct literature review strategies were used for this project. The first used a structured PubMed literature search strategy. The second consisted of a citation search of relevant articles.

Structured Literature Search

This is not a systematic review. Four separate literature searches were conducted: one each for the Patient Preferences, Interpreting the Evidence, Prognosis, Clinical Feasibility, and Optimizing Therapies and Care Plans. A separate search was not conducted for the Barriers section. Instead, panel members were asked to look for, and identify, articles that addressed potential barriers and challenges in relation to any of the aforementioned domains.

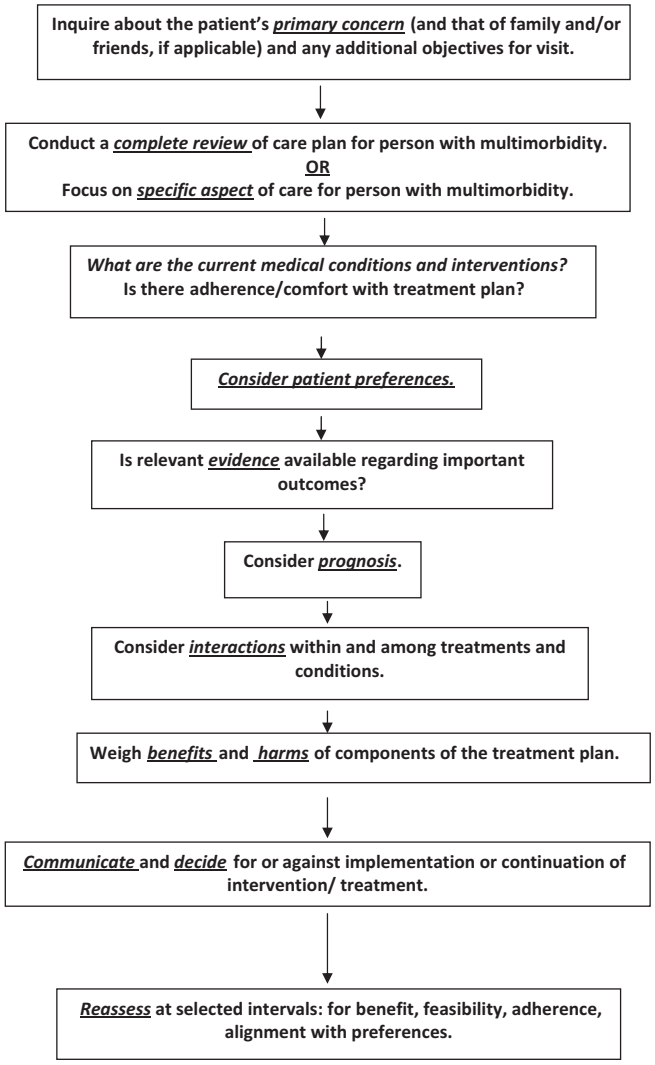

Figure 1. Approach to the evaluation and management of the older adult with multimorbidity.

Panel members recommended a list of domain-specific search terms based on their knowledge of the subject matter, their experience with the literature, and key words found in articles considered to be highly representative of the domain topic. An informationist from the Johns Hopkins Welch Library was consulted on construction of the search strategy. First, all of the appropriate Medical Subject Heading (MeSH) terms that aligned with each of the proposed search terms were identified. Terms without appropriate MeSH headings were added to the search strategy in quotation marks. The overall strategy of the PubMed literature search was to cross the domain-specific concepts with the general concept of multiple chronic conditions, or multimorbidity. Because there are no specific MeSH terms for the concept of "multimorbidity" or "multiple chronic conditions," a list of possible terms related to this concept was created. For each of the four searches, the domain-specific search terms were combined with the search terms related to the concept of multiple chronic conditions through use of the Boolean operator "AND" (Table 1). Only articles published in English since January 2000 were included.

The panel members were provided with the title and abstracts of all of the articles identified using the searches. Each was instructed to reject articles that were not related to the domain topic, not related to patients with multimorbidity, not related to adults, or not relevant for any other reason. Panel members retained articles that were pertinent to any or all of the project domains (regardless of the domain to which they were assigned). They were then provided with the full text of all articles retained for their review and consideration.

Relevant Article Review

In addition to the literature search described above, a search was conducted of articles that panel members determined to be highly relevant to each domain. For each of the relevant articles, we conducted a cited reference search using the Web of Science to find the articles that cited each relevant article. The number of relevant articles per domain, the number of unique citations arising from those articles, and the number of articles retained for review are provided in Table 2. In addition to both of these methods, panelists also reviewed the list of references at the end of each relevant article to capture any additional articles that might have been missed. Major areas of uncertainty or areas where relevant evidence is limited are specifically described, with the goal of highlighting the topics that are most critically in need of future research.

External Review

The document was also circulated for peer review to a number of organizations with special interest and expertise in treating older adults with multimorbidity and was posted to the AGS website for public comment. Organizations that participated in peer review are noted in the Acknowledgments section of this document.

APPROACH TO OLDER PATIENTS WITH MULTIMORBIDITY

All clinicians, including primary care providers (physicians, physician assistants, and nurse practitioners), pharmacists, geriatricians, specialists, and other clinicians who take care of older patients with multimorbidity often find themselves challenged on many levels. Of particular concern are complexities involved in clinical management decisions; inadequacy of good evidence for making informed, shared decisions; and time constraints and reimbursement structures that hinder the provision of efficient quality care.[2,16] One approach is illustrated in Figure 1, a flowchart that presents one sequence of questions and considerations useful in the optimal management of older people with multimorbidity. The steps suggested can be taken in other sequences with equal validity, particularly because the best approaches to addressing this population have not been compared, and few approaches of this type appear in the literature.[17,18] For example, in many instances, patient

Table 1. PubMed Literature Search

Domain Name	Domain-Specific Search Terms	Multimorbidity Search Terms[a]	Articles Found, n	Articles Retained, n
Patient preferences	Patient Preference [MeSH] OR "Patient preference" OR "Patient preferences" OR Patient Participation [MeSH] OR Physician-Patient Relations [MeSH] OR "Shared decision-making"		592	102
Interpreting the evidence	Practice Guidelines as Topic [MeSH] OR "Clinical practice guidelines" OR "Practice guidelines" OR "Clinical guidelines" OR Evidence-Based Medicine [MeSH] OR "Evidence based" OR "Evidence-based"	Chronic disease [MeSH Major Topic] OR Comorbidity [MeSH Major Topic] OR "Multiple chronic conditions" OR "Multiple chronic illnesses" OR "Multiple chronic diseases" OR "Multiple morbidity" OR "Multiple comorbidity" OR "Chronic condition" OR "Chronic illness" OR "Multiple conditions" OR "Multiple illnesses" OR "Multiple diseases" OR "Multimorbidity" OR "Multi morbidity" OR "Multi-morbidity" OR "Comorbid disease"	755	113
Prognosis	Prognosis [MeSH] OR "Prognosis" OR "Prognoses" OR "Prognostication" OR "Prognostic" OR Forecasting [MeSH] OR "Life expectancy" OR "Mortality prediction"		926	61
Clinical feasibility and optimizing therapies and care plans	Polypharmacy [MeSH:noexp] "Polypharmacy" OR Inappropriate Prescribing [MeSH:noexp] OR "Inappropriate prescribing" OR "Inappropriate prescriptions" OR Patient Compliance [MeSH] OR Medication Adherence[MeSH] OR Treatment refusal [MeSH] OR "Non-compliance" OR "Non-adherence" OR Drug Interactions [MeSH:noexp] OR Drug Toxicity [MeSH:noexp] OR Pharmaceutical Preparations/adverse effects [MeSH:noexp] OR "Adverse drug "OR Withholding Treatment [MeSH: noexp] OR "Withholding treatment" OR "Withdrawing treatment" OR "Withdraw treatment" OR "Discontinuing treatment" OR "Discontinue treatment" OR "Treatment discontinuation" OR "Medication discontinuation" OR "Dose reduction" OR Medication Therapy Management[MeSH] OR "Clinical feasibility" OR "Clinically feasible" OR "Treatment complexity" OR "Therapeutic complexity" OR "Regimen complexity" OR "Treatment burden" OR "Drug burden"		833	308
Total				584

Although there was no primary literature search for barriers, panelists identified 120 articles while reviewing the abstracts for all of the preceding domains.

[a] The singular and plural forms were used for each term listed.

preferences are best elicited in the context of the patient's prognosis.

The five main domains apply at various steps illustrated in Figure 1. These domains represent themes that must be considered when caring for older adults with multimorbidity. Each domain is discussed below, and each merits a formal review in and of itself. The development of this document was undertaken with the premise that bringing these themes together would be of value to clinicians and would highlight areas for future research in this field.

After describing the five domains in detail, two clinical scenarios are offered, illustrating how the approach can guide clinical decisions for this population. (See Case Examples.)

GUIDING PRINCIPLES

I. PATIENT PREFERENCES DOMAIN

Guiding Principle: Elicit and incorporate patient preferences* into medical decision-making for older adults with multimorbidity.

*By using the term "patient" preferences throughout this section, we aim to keep the patient central to the decision-making process while fully recognizing that family and social supports play a vital role in the management of older adults with multimorbidity and in the decision-making process. Although this is particularly true for the many older adults with multimorbidity who have cognitive impairment, it is also often true for those who maintain decision-making capacity.

Table 2. Cited Reference Search of Relevant Articles

Domain Name	Relevant Articles n	Articles That Cited the Relevant Articles	Articles Retained for Review
Patient preferences	12	119	25
Interpreting the evidence	6	297	65
Prognosis	7	494	49
Clinical feasibility	10	116	131
Optimizing therapies and care plans	10	399	73
Total			343

Although there was no primary literature search for barriers, 30 articles were identified by panelists while reviewing the abstracts of the cited reference search of key articles for all of the preceding domains.

Justification for Principle

CPGs do not routinely search for or include evidence related to patient values or preferences.[19,20] Few references used to construct CPGs address preferences.[20] Consequently, care that is provided in accordance with CPGs may not adequately address this important aspect of medical decision-making.

Older people with multimorbidity are able to evaluate choices and then prioritize their preferences for care, considering pertinent personal and cultural contexts about health and health care. For example, it has been shown that such patients can weigh the risks and benefits of treatment when deciding to take medications[21] and are able to rank health outcomes according to personal health priorities.[22] Some recommendations within CPGs are more preference sensitive than others, and clinicians should be particularly aware of patient preference in these types of medical decisions. Preference-sensitive decisions include choices with more than one reasonable treatment option and possible lifelong implications for chronic disease management or decisions about treatments or interventions that have an important risk or offer uncertain benefit.[23–25]

How to Use in Clinical Practice

All clinical decisions require an assessment of patient preferences. The preferences can be elicited according to the degree of complexity of the situation and the importance of preference to the decision being discussed.[26] The clinician can customize the elicitation of preferences so that decision-making is abbreviated in less-complex situations and more expansive when many options and preferences need to be considered. For clinical management decisions with multiple options, the process of eliciting patient preferences requires several steps.

Recognize when the older adult with multimorbidity is facing a "preference sensitive" decision. In such situations, the clinician must understand what is most important to the patient to determine the best option. Older adults with multimorbidity are more likely to confront these kinds of decisions because of the burdens that the many potential therapies for each condition, the increased risk of adverse events, and the possibility of more limited benefits impose.[3,9] Some examples of "preference sensitive" decisions are therapy that may improve one condition but make another worse (e.g., inhaled corticosteroids to treat chronic obstructive pulmonary disease may exacerbate osteoporosis);[27] therapy that may confer long-term benefits but may cause short-term harm (e.g., medications for primary or secondary disease prevention that have adverse effects such as statins, which decrease cardiovascular risk but may cause cognitive impairment or muscle weakness);[28,29] and multiple medications, each with benefits and harms that must be balanced. Many treatments used in this population can improve individual disease-specific outcomes but may be difficult for the patient to take and be associated with greater risk of falls, weight loss, or dizziness.[30]

Ensure that older adults with multimorbidity are adequately informed about the expected benefits and harms of different treatment options. This step consists of broad consideration of the effects of treatments and interventions on multiple health domains. For example, although clinicians often label adverse medication effects as less important "side" effects than the beneficial outcomes the medications are designed to produce, the individual taking the medication may consider the side effects important outcomes in their own right.[31,32] Therefore, adverse effects in such cases need to be considered as "harms."

Although it is a challenging task, numerical likelihoods should be provided to patients if they are available. It has been shown that words used to convey frequencies, such as "rarely" or "frequently," are interpreted highly variably,[33] and there continues to be a debate about the best way to present numerical information to patients. Generally well-accepted recommendations include presenting the likelihood of the event occurring and the likelihood of the event not occurring, to avoid framing the outcome positively or negatively;[34] presenting absolute rather than relative risks; and providing visual aids, based on evidence that pictographs may be most helpful.[35] Older adults have variable levels of "health numeracy" (capacities to access, interpret, and act on numerical and quantitative health information).[36] Low numeracy may be associated with greater difficulty in understanding risk information.[37] Assessing patients' understanding of the information presented (e.g., using a "teach back" technique) is an important element of this step.

Elicit patient preferences only after the older individual with multimorbidity is sufficiently informed. Various decision aids are available to help inform patients and elicit preferences,[38] but these may fail to account for the likelihood of different outcomes that may vary greatly with different comorbidity and risk-factor profiles.[39] Decision analysis involves the creation of a *decision tree*, which identifies all potential outcomes of each treatment option. The utilities of each outcome are then calculated, based on preference, and assessed using approaches such as the standard gamble and time trade-off.[40–42] Conjoint analysis identifies the characteristics of different treatment options; assigns levels to each characteristic (based on severity of a symptom or likelihood of an outcome); and uses rating, ranking, or discrete choices to determine which

characteristics are most important to an individual.[43] For busy clinicians, a simpler method of eliciting preferences may be to ask patients to prioritize a set of universal health outcomes that can be applied across individual diseases. Typical outcomes would include living as long as possible, maintaining function, and alleviating pain and other symptoms.[44] The individual treatment options are considered in terms of their effects on each of these outcomes, so that a treatment can be selected according to its likelihood of achieving the patient's most-desired outcome or avoiding the least-desired outcome.[21,22]

There are several additional considerations for clinicians to keep in mind when attempting to elicit preferences. First, clinicians need to distinguish between eliciting preferences and making a treatment decision.[45] The former is the process by which patients voice their opinions about the different treatment options in the context of their values and priorities (the process upon which choice of care is based), whereas the latter is the process by which a specific option is chosen. Patients vary widely in their preferred decision-making style. Some patients prefer to make the decision themselves, whereas others leave the decision to the clinician or choose to share the process of decision-making with the physician. Regardless, virtually all individuals want their opinion to guide the decision.[46] Second, patients may want their family, friends, and caregivers to be included in decision-making or even to make the decision for them.[47] For patients with cognitive impairment who are unable to understand the implications of different options, these significant others become surrogate decision-makers who work with clinicians to make decisions on behalf of the patient. Individuals who are cognitively intact may also want their family to be involved. Third, preferences may change over time,[48] so it is important that they be reexamined, particularly when an older adult with multimorbidity has experienced a change in health status. Fourth, the principle of eliciting preferences and involving patients in the decision-making process does not mean that the patient has the right to demand any and all treatment options if these options do not have a reasonable expectation of some benefit.[49]

Controversies and Challenges

There are challenges involved in some aspects of informing older adults and eliciting their preferences. For example, it is often difficult to convey a clear numerical understanding of benefits and harms.[50] Moreover, many studies have demonstrated that the way in which risk information is presented influences patient preferences. Because older adults with multimorbidity may face a large number of preference-sensitive decisions, and the conditions and their clinical management may affect each other, it may not be feasible to use decision tools for each individual choice. Also, data regarding the effects of a given treatment on a range of outcomes, including physical and cognitive function, may not be available. How to communicate uncertainty to patients is challenging in general and is likely to be even more challenging in older people with multimorbidity because the decisions are more complex, and uncertainty may be even greater.[51] In addition, patients may feel burdened by the task of participating in decision-making, particularly in situations in which there are no good outcome data. Finally, clinicians struggle to find time to implement CPGs recommendations for a typical panel of patients with chronic conditions in primary care.[52] Eliciting preferences may make clinical management of older adults even more time consuming.[52]

Ideas for Future Research Agenda

Because the full range of clinical management outcomes shapes preferences, more evidence is needed about the effects of treatment choices on outcomes other than survival, including functional status and quality of life. Risk calculators and other tools may help clinicians inform patients appropriately by providing individualized outcome data according to each person's multimorbidity profile. There have been few studies directly comparing different methods of preference elicitation, and a greater understanding of the feasibility, acceptability, and results of using these methods among persons with multimorbidity is needed.

II. INTERPRETING THE EVIDENCE DOMAIN

Guiding Principle: Recognizing the limitations of the evidence base, interpret and apply the medical literature specifically to older adults with multimorbidity.

Justification for Principle

CPGs synthesize evidence from multiple types of studies (augmented, in some cases, by meta-analyses and other secondary analyses of clinical trials and observational studies) to provide guidance for clinicians in managing clinical problems according to the best current evidence. However, most studies of treatment effect and CPGs focus on only one to two clinical conditions at a time and address comorbidities in limited ways, if at all.[3,11–13,53] Different conditions coexisting within the same patient may interact in a way that changes the risks associated with each condition and its treatments. For example, a person with heart failure, chronic renal insufficiency, diabetes mellitus, depression, and cognitive impairment may be at greater than average risk for a myocardial infarction but may also be at greater than average risk of adverse events from a particular treatment, as well as at greater risk of morbidity and all-cause mortality,[54] making determining whether the person will benefit from a particular treatment complicated.

The development of thoughtful standardized approaches to interpreting the medical literature,[55,56] known collectively as "evidence-based medicine," provides tools for clinicians to evaluate the applicability of findings reported in the medical literature to each patient. There is increasing consensus about the appropriateness of these methodologies for assessing the quality of evidence supporting GPGs recommendations,[57,58] although one element of such methodologies that must not be neglected is the assessment of applicability of the findings to the specific patient under consideration.[55] Significant gaps exist in the current clinical trials evidence base about interactions of conditions and treatments in patients with multimorbidity.

To provide patient-centered care, clinicians must evaluate the medical literature in terms of its ability to offer conclusions that pertain to this population of older adults.

How to Use Evidence in Clinical Practice

There are several general principles to consider in evaluating clinical evidence. Reviews of evidence should be based on key clinical questions so that it is possible to determine whether a study informs this question or not. Rigorous methods of reviewing the quality of evidence and its applicability to specific populations have been developed and accepted into common usage.[59–63] Although some small differences occur between these approaches, there are a few central concepts in all of them that are consistent and noteworthy. Furthermore, certain questions can be excellent guides to evaluating whether a piece of evidence—regardless of the source—is applicable to an older person with multimorbidity. Although the questions offered below focus on CPGs, they could apply to any piece of scientific evidence. The questions are grouped into five sections: Applicability and Quality of Evidence, Outcomes, Harms and Burdens, Absolute Risk Reduction (ARR), and Time Horizon to Benefit.

Applicability and Quality of Evidence

A fundamental question is whether it is scientifically appropriate to apply the results of a particular study to the population under consideration. In other words, what is the "applicability" of the information? Clinical studies enroll patients drawn from particular populations or subsets of a population. How well the research findings from a particular study apply to older adults with multimorbidity depends upon how closely the individual being considered resembles the research population. Clinicians should try to ascertain whether multimorbid, or even older, people were included in the studies in sufficient numbers to make the study findings applicable to this specific population in a meaningful way. If so, was there evidence of effect modification of intervention effects associated with a factor such as multimorbidity or specific comorbidities?[11,13]

Equally important when considering multimorbid patients is an evaluation of the quality of evidence. Published clinical studies vary considerably in their adherence to accepted principles of clinical research. Even a strongly positive result should be viewed with caution if it is from a poor-quality study, because the results may be attributable to flaws in the study design or analysis.[59,60,63,64] In this regard, a body of evidence is more helpful than a single positive study. Existing approaches to evaluate the quality of evidence are appropriate for older adults with multimorbidity and will be useful to clinicians. In particular for older adults with multimorbidity, clinicians must seek a balance between other aspects of quality of evidence and applicability. For example, well-designed randomized clinical trials diminish the problems of confounding seen in observational studies but often exclude individuals with multimorbidity. Although results from observational studies are often considered weaker than those from randomized clinical trials, such studies are more likely to include older adults with multimorbidity, and they may provide more information about the adverse events associated with an intervention in this population (Table 3).

Outcomes

Clinical trials evaluate many different types of outcomes. For example, trials are often designed to measure intermediate outcomes (surrogates) that are not of immediate importance to patients (e.g., laboratory markers), but there is ample justification in the literature for study designs that evaluate "patient-important outcomes."[59,60,65,66] Intermediate outcomes in themselves may not affect patients directly. An individual might not value a high cholesterol result as highly as a patient-important outcome, such as a stroke or myocardial infarction, although such patient-important outcomes may sometimes be tightly linked to the intermediate outcomes. In addition, outcomes relevant to older patients with multimorbidity may not be addressed in the narrow focus of disease-specific trials. For example, quality of life, physical function, and independent living may matter more to some older adults than progression to end-stage renal disease or other disease-specific endpoints. Individual older adults with multimorbidity and their family members may prioritize outcomes and define quality of life in different ways. An important question for healthcare professionals to consider in evaluating the evidence is whether the outcomes reported are ones that are meaningful for older adults with multimorbidity.[13]

Harms and Burdens

In considering clinical management choices, clinicians must weigh the anticipated benefits against the potential harms and burdens of the treatment, which requires an assessment of information from the medical literature about the harms and benefits of the particular intervention. Several potential pitfalls require special attention in the management of older adults with multimorbidity. For example, short-term efficacy studies may not follow patients long enough to afford an adequate estimate of rates of adverse events and other harms. Also, few clinical trials report the

Table 3. Questions to Ask Regarding the Medical Literature

To what extent were older adults with multimorbidity included in the trials? Is there evidence of effect modification?
What is the quality of the evidence, using accepted evidence-based medicine methodologies?
What are the hoped- for outcomes of the treatment or intervention? Are these outcomes important to patients?
Is there meaningful variation in baseline risk for outcomes that the treatment or intervention is designed to affect?
Are the risks and side effects of the treatments and interventions in older patients with multimorbidity clearly known, so that a decision can be made whether the treatment for one condition will exacerbate another?
What are the comparator treatments or management strategies?
Is it known how long it takes to accrue the benefit or harms of the treatment or intervention?
Does the document give absolute risk reductions or merely relative risk reductions? Is it possible to estimate absolute risk reductions?
How precise are the findings? What are the confidence limits?

burden that patients experience in following the treatment regimen. In addition, following guidelines for one disease may exacerbate another coexisting condition. Accordingly, it is important not only to ascertain whether adverse events associated with an intervention were reported, or were relevant or described correctly, but it is also necessary to evaluate whether the potential for effect on other conditions was studied. Financial costs and the level of difficulty in following the treatment must also be considered, because these often affect adherence.[3,67] Finally, treatment interactions in the clinical management of multimorbidity must be considered.

Absolute Risk Reduction

Study results are often conveyed in terms of relative risk reduction (RRR) rather than ARR, which often suggests strikingly impressive outcomes (e.g., a 50% RRR), but RRR is uninterpretable if the baseline risk is not reported. In contrast, the ARR is based on the risk of an outcome without treatment (or the baseline risk) minus the risk of the outcome with treatment, or ARR may reflect the difference between two comparator treatments. For example, a baseline risk without treatment of 2% minus a 1% risk with treatment would result in a 50% RRR but only a 1% ARR. Clinicians must always consider the baseline risk for the outcome in question for older persons with multimorbidity because the baseline risk for many relevant conditions may be higher or lower than that of the general population. Baseline risk can be ascertained from the control group of clinical trials, from observational studies or registries, or from prognostic indices that may provide for individualized risks. All of these potential sources can be evaluated from the perspective of their applicability to older adults with multimorbidity. A search of the medical literature—including single-disease CPGs practice guidelines and trial reports—may allow clinicians to ascertain the baseline risk for a certain outcome in older adults with multimorbidity and its potential variability.

RRR is often believed or assumed to be constant, regardless of the baseline risk. This suggests that RRR, in combination with estimated baseline risks, can be used to approximate ARR even in people with different baseline risks.[68] In considering the quality of evidence and its applicability to older adults with multimorbidity, it is important to note that variability of RRR in this population has rarely been examined and needs to be tested in multiple clinical scenarios. In the absence of such data, clinicians may interpret results by looking for variability in baseline risks for primary outcomes reported in the literature and use RRR to estimate whether there are meaningful variations in ARR.[69,70] If a study or CPG fails to consider whether there are variations in baseline risk, its results will be difficult to interpret for older adults with multimorbidity.

Time Horizon to Benefit

The medical literature frequently reports results in terms of number needed to treat (NNT) and number needed to harm (NNH), often without consideration of time period to outcome. This can be misleading, particularly when considering older adults with multimorbidity, who typically have more numerous and serious competing risks than older adults with only one or no chronic conditions.[54] NNT and NNH are most helpful in this population when the result includes a time factor (e.g., "The number needed to treat to prevent one death was 50 patients over 5 years of treatment," or "For every 200 people treated in a 5-year period, one will harmed by a myocardial infarction"). In many cases, the reported number of years is simply the duration of the study, despite the fact that there may be statistically significant or clinically meaningful benefits and harms of treatment that occur more rapidly than the preestablished trial length. Although this information may be infrequently discernible from the primary literature or from CPGs, clinicians should look for a time horizon to benefit associated with any treatment when making clinical management decisions.[71,72]

Time horizon to benefit is the length of time needed to accrue an observable, clinically meaningful risk reduction for a specific outcome. Similarly, time horizon to harm is also important. In considering clinical management of older adults, clinicians need to consider the anticipated time until benefits are likely to be realized. For example, antiplatelet treatments can be expected to result in immediate benefit in risk of acute myocardial infarction, and depressed mood usually responds to antidepressant medication within weeks. For some chronic conditions, certain interventions are beneficial only after longer durations of treatment, for example, tight glycemic control in diabetes mellitus and bisphosphonate therapy in osteoporosis. In such cases, clinicians and older persons should decide jointly whether the anticipated benefits warrant a long-term burden and potential harms of treatment for the patient. Because the time horizon to benefit of tight glycemic control in diabetes mellitus is believed to be at least 5–7 years, rigorous control of blood glucose is unlikely to help, and more likely to harm, older adults with multimorbidity who are at high risk of dying from another condition.[73] There is often imperfect information on time horizon to benefit, and study design factors such as the length of follow-up and sample size affect estimations that can be determined from the literature.

Controversies and Challenges

Clinicians looking for the types of information suggested here may find the effort challenging and time consuming, but the more requests that are made for relevant data from GPGs, clinical recommendation papers, clinical trials, observational studies, and speakers, the more likely it will be that these concerns will be addressed in future study designs, systematic reviews, and meta-analyses or that their absence will be noted. Unfortunately, it is likely that incomplete information will continue to challenge clinicians given the heterogeneity of older adults with multimorbidity and the complexity of the clinical questions that arise. It may be unrealistic to expect that data that fully describes the marginal risks and benefits of specific management decisions in this population will ever be available. Observational studies may provide the most data because it is unlikely that randomized controlled trials will be designed and powered to test for heterogeneity of treatment effects in all relevant groups of patients, but it is challenging to determine whether the results of observational studies are unbiased and true.

Controversy exists regarding how far to extrapolate study findings to patients whose clinical characteristics place them outside a defined study population. There is also debate about the extent to which it is appropriate to base clinical practice on biological plausibility in the absence of clinical trial data. Another major controversy stems from concern about the lack of reproducibility of many experimental results.[74]

Even where GPGs are available, clinicians may have insufficient time to read them carefully enough to remember and apply them with individual patients.[75,76] Although there is general agreement that treatment regimens involving large numbers of medications are unwieldy and potentially hazardous, there is no clinical consensus about the optimal method for prioritizing the multiple possible treatment recommendations. Such prioritization often occurs implicitly.

Ideas for Future Research Agenda

Clinicians need a stronger evidence base that is relevant to older adults with multimorbidity. Research on clinical management of conditions common to such individuals should include substantial numbers of these older adults with multimorbidity or, better still, focus primarily on this population, using appropriate analytical strategies in both cases.[70] Outcome measures of clinical trials should include measures of functional status, well-being, and other health-related quality-of-life assessments. In addition, time horizon to benefit needs to be routinely considered in the design and reporting of clinical trials.[71,72]

Research is needed regarding how best to communicate relevant evidence and uncertainty about it to older adults and their caregivers. Similarly, more information is needed about the best and most-efficient methods of conducting clinical encounters with older adults with multimorbidity. Different kinds of interventions, such as the provision of educational materials before visits, redesign of the clinical workflow within clinicians' offices, and more-effective involvement of nonphysician healthcare team members may facilitate better communication.

Better methods are also needed to help clinicians apply GPGs appropriately to older adults with multimorbidity. Where electronic health records are in use, automated clinical decision-support systems that make use of the full range of relevant patient data may provide assistance with complex decision-making, but further research is needed on clinical decision-support methods when several GPGs apply to the same person. Methods for prioritizing multiple recommendations need to be studied for clinical decision-making in older individuals with multimorbidity.

III. PROGNOSIS DOMAIN

Guiding Principle: Frame clinical management decisions within the context of risks, burdens, benefits, and prognosis (e.g., remaining life expectancy, functional status, quality of life) for older adults with multimorbidity.

Justification of the Principle

Clinical management decisions necessitate the evaluation of prognosis to adequately assess risks, burdens, and benefits.[77] Although prognosis has traditionally focused on remaining life expectancy, functional disability and quality of life represent additional outcomes of particular relevance for older persons with multimorbidity.[78,79]

In addition to overall prognosis, clinicians need to evaluate individualized risks for specific conditions in individuals with multimorbidity. One example is the use of aspirin (initiation or continuation) for primary prevention of cardiovascular disease in men.[80] Benefits include lower cardiovascular risk, but aspirin use also increases the risk of gastrointestinal hemorrhage, and this risk increases with age and the presence of other common risk factors such as previous gastrointestinal bleeding or concomitant nonsteroidal anti-inflammatory drug use. Such condition-specific risks are part of the process of prognostication for older adults with multimorbidity.

Each person's prognosis informs, but does not dictate, clinical management decisions within the context of their preferences.[77] As mentioned above, the time horizon to benefit for a recommended treatment may be longer than the individual's projected life span. In diabetes mellitus, not only are many years of tight glycemic control required for benefits to become evident,[81] unnecessary overtreatment of diabetes mellitus can also harm patients because of greater risks of hypoglycemia, polypharmacy, drug–drug, and drug–disease interactions. These risks may be of even greater consequence in persons with multimorbidity than in those with a single disease process.[81] Similarly, screening procedures such as prostate-specific antigen testing, mammography, and colonoscopy may not be beneficial or may be even harmful if the time horizon to benefit is longer than remaining life expectancy, especially because the harms and burdens associated with many of these tests increase with age and comorbidity.[68]

A discussion about prognosis can serve as a springboard for difficult conversations with older people with comorbidity and families and may thus facilitate shared decision-making and advance care planning.[77,82] For example, the prognosis of a patient with cancer, a solid tumor, and poor performance status usually worsens when chemotherapy is administered; these individuals tend to get sicker and possibly die sooner than those who do not receive chemotherapy.[83] Also, if the cancer has progressed during first- and second-line therapies, treatment response is less likely.[83] A discussion about hospice, alternatively, offers patients and their families additional support and services at home, improves quality of life, and may be associated with longer survival.[84] Therefore, evaluating and discussing prognosis can often inform several facets of care simultaneously, including elucidation of patient preferences, mitigation of treatment complexity, and prioritization of therapies most likely to benefit an individual.

How to Use in Clinical Practice

Clinicians need to consider various factors when developing an approach that will incorporate prognosis into clinical decision-making: framing a focused clinical question; determining the outcome being predicted (e.g., remaining life expectancy, functional ability, quality of life, or a condition-specific risk such as stroke); selecting a prognosis measure, while recognizing its strengths and weaknesses;

estimating prognosis; and integrating this information into the decision-making process.

Regardless of ethnicity, a majority of older adults wish to discuss prognosis, but a minority do not. Clinicians should offer to discuss prognosis, but not all older adults with multimorbidity may wish to do so. A culturally sensitive manner is always recommended, because culture often influences priorities in treatment and care.[85,86] One helpful tool, *Doorway Thoughts*,[87] offers "clinical pearls" to clinicians, as well as specific considerations for particular ethnic groups to facilitate the approach to this conversation. The dialogue that ensues needs to follow the ethical principles of autonomy (patient self-determination), beneficence (promotion of patient well-being), nonmaleficence (avoidance of harm), and justice (protection of vulnerable populations and fair allocation of resources).

Specific situations in which a determination of prognosis may help inform clinical decision-making include disease prevention or treatment (e.g., whether to start or stop a medication or insert or replace a device), disease screening (e.g., for cancer, cognitive decline, osteoporosis), change in a patient's clinical status (e.g., functional decline, weight loss, falls), and type of health service to use (e.g., whether to hospitalize a patient or provide aggressive intensive care unit treatment).[68,77,82] The specifics about which prognostic measure to include and what prognostic information to share with patients and families are part of the total integrated process of decision-making, in conjunction with an evaluation of the evidence and patient-stated preferences.[88]

When attempting to integrate prognosis into clinical decision-making, it is helpful to prioritize decisions based on life expectancy or other outcomes.[77] Using this approach, decisions are categorized as short-term (within the next year), midterm (within the next 5 years), and long-term (beyond 5 years).[88] A patient with limited life expectancy would focus efforts on relevant short-term decisions such as appropriate intensity of glucose control and monitoring, use of physical therapy for strengthening and endurance, consideration of advance directives, and whether to continue to live alone. Midterm or long-term decisions would have lower priority and might include decisions related to lipid or breast cancer screening. In this way, prognosis can inform clinical decision-making by helping to prioritize elements of the care plan and inform treatment decisions so that patients consider treatments and interventions from which they are most likely to receive benefit and reduce the chance of experiencing harms without benefit.

Although the science of prediction and forecasting in medicine continues to evolve, some evidence exists to help clinicians estimate prognosis. Published tools are usually developed and tested in specific settings, potentially limiting the measure's validity in other settings.[89] For example, it is likely that a measure estimating remaining life expectancy developed in the community would lack validity in the nursing home or hospital. Also, clinicians need to consider which type of measure to incorporate and how well it applies to older individuals with multimorbidity. Tools developed for estimating remaining life expectancy have been the most widely studied and include measures for specific diseases (e.g., congestive heart failure, cancer, chronic obstructive pulmonary disease, dementia),[82,90–92] as well as life tables broken down according to age, sex, and distribution of life expectancy for specified ages.[68,77] Others include measures of functional status (e.g., self-report and performance based),[79,93] integrated measures or indices (e.g., Vulnerable Elders Survey or index based upon National Health Interview Survey),[94–97] and measures of advanced illness (e.g., palliative prognostic score and palliative performance scale).[98–100] Unfortunately, fewer measures are currently available to help predict functional disability and future quality of life, even though clinicians and patients frequently cite this as an important determinant in clinical decision-making.[78,101]

Controversies and Challenges

Although GPGs frequently recognize the importance of prognosis when considering a recommendation, they rarely provide clinicians with ways to assess prognosis adequately. This is important, because different prognosis measures for the same patient may yield conflicting results. For example, a community-dwelling 85-years-old with end-stage chronic obstructive pulmonary disease (dyspnea at rest on oxygen with cor pulmonale); diabetes mellitus; mild dementia; tobacco use; and difficulty paying bills, managing medications, and ambulating has a disease-specific mortality of 5% at 1 year (the Body Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index),[91] a 64% likelihood of dying at 4 years using a different prognostic index,[94] 145-days survival based upon the Palliative Performance Scale,[99,100] and a 50% likelihood of dying within 6 months based upon hospice criteria for chronic obstructive pulmonary disease.[102] At the same time, clinical management decisions, particularly in older persons with multimorbidity, may simultaneously improve one outcome (e.g., survival) and diminish another (e.g., quality of life or functional status). Moreover, it may become overwhelming for clinicians and patients with multimorbidity to evaluate prognostic information, because many potential treatments for multiple conditions may need to be considered concurrently with a need to weigh which treatment for which disease gives best results from among the many possibilities.

Another consideration is that available tools to help estimate prognosis are based upon point estimates, whereas a patient's health status is dynamic and changes over time. As a result, clinician efforts to incorporate prognosis need to match the measure and underlying disease trajectory to the patient's individual situation (e.g., whether to start or stop a therapy, pursue cancer screening, or discuss hospice).[77] In addition, clinicians need to consider the validity of the prognosis measure itself.[89,103] For instance, the noncancer clinical criteria for hospice eligibility (e.g., presence of congestive heart failure, chronic obstructive pulmonary disease, and dementia) do a poor job of establishing 6-month prognosis, because the guidelines were primarily developed according to expert consensus.[102,104,105] Empirically based prognosis measures have noteworthy shortcomings as well.[89,103] The discriminate ability (area under the curve analysis) of many prognosis measures remains suboptimal. At the same time, most published prognosis measures have not been

evaluated outside of their validation cohort, limiting their generalizability to other populations.

In short, uncertainty exists regarding the use of prognostic measures in clinical practice, particularly in persons with multimorbidity. At the same time, studies that delineate the "best" approach to communicating prognosis in the effort to support "optimal" clinical decision-making are lacking. Moreover, clinicians may not feel comfortable discussing prognosis and instead choose to focus their efforts on a discussion of additional treatments and interventions. Finally, the majority of prognosis measures that exist focus on remaining life expectancy instead of outcomes that may be more relevant to the individual, such as physical and social function and quality of life.

Ideas for Future Research Agenda

Prognosis is an important consideration in the process of planning clinical management. The use of prognostic measures to facilitate clinical decision-making is in its infancy, and more research in this area is needed, particularly with regard to older adults with multimorbidity. Measures need to be developed, refined, externally validated, and tested for feasibility and effect on clinical outcomes for this population.[89,103,106] Another area that requires further investigation is understanding of clinician-related factors, such as how clinicians use prognosis to inform treatment plans and what methods are used to communicate this information to the individuals concerned and their families. More research is also needed to identify the "best" approaches for incorporating prognosis into clinical decision-making for older adults with multimorbidity.

IV. CLINICAL FEASIBILITY DOMAIN

Guiding Principle: Consider treatment complexity and feasibility when making clinical management decisions for older adults with multimorbidity.

Justification for Principles

Treatment complexity and burden must be acknowledged and addressed in older adults with multimorbidity. Some guideline organizations, such as the Grading of Recommendations Assessment, Development and Evaluation working group, now encourage their routine consideration when making recommendations,[107] but the definition of these concepts has been inconsistent within clinical practice and the existing literature.

A framework has been developed to break down treatment complexity and interpret it through the use of measures such as steps in the task, number of choices, duration of execution, informed consent, and patterns of intervening distracting tasks.[108] These measures provide a list of factors to consider when attempting to simplify individual components of multitask processes such as management of medications or adherence to a heart-healthy diet. The Medication Regimen Complexity Index also identifies multitasks that need to be considered when an older person is confronted with medication complexity. This tool not only records the number of medications, it also evaluates the dosage forms, frequency of dosing, and administration instructions.[109]

The more complex a treatment regimen, the higher the risk of nonadherence,[110] adverse reactions (e.g., falls, decreased cognition),[111] poor quality of life, and economic burden,[3,112] as well as greater strain and depression in caregivers.[113] Medication adherence is dynamic, in that situational factors and patient perceptions of which conditions are most important over time—perceptions that are constantly changing and being renegotiated—affect daily decisions.[114] Patients do not typically use evidence-based methods when they choose which medication to take; rather they often base their decision on a single factor, such as cost or their assessment of need.[115,116]

The disconnect between the approaches of patient and clinician can be daunting for the healthcare team because it requires ongoing education and monitoring to ensure appropriate medication use. The fact that individuals in general recall as little as 50% of the discussion from a typical medical encounter poses an additional challenge.[117] Also, cognitive impairment is common in older adults and affects adherence, particularly to complex regimens. Therefore, education and assessments need to be multifaceted, individualized, and delivered using a variety of methods and settings outside the examining room.[117]

How to Use in Clinical Practice

Because treatment complexity often increases with multimorbidity, an interdisciplinary team should assess the ability of older adults with multimorbidity to manage or adhere to a treatment plan or medication regimen on an ongoing basis. Various tools exist that measure medication management capacity, including the Medication Management Ability Assessment (MMAA), Drug Regimen Unassisted Grading Scale (DRUGS), Hopkins Medication Schedule (HMS), and the Medication Management Instrument for Deficiencies in the Elderly (MedMaIDE).[118] Regardless of the evaluation tool used, the assessment needs to be individualized, and a patient-centered discussion must be held in collaboration with the support system (e.g., family, caregivers). These steps will help guide optimal treatment approaches and options for the individual. Emerging evidence illustrates that consistent medication regimens, as well as medication management support, results in fewer hospitalizations.[119–121] Various interventions to optimize medication management have been studied (e.g., medication packaging, reminder systems, education) with varying degrees of effect on clinical outcomes.[106]

In older adults with multimorbidity, evidence-based medicine alone does not provide an adequate guide to the best clinical management. Furthermore, the use of condition-specific GPGs to dictate practice leads to regimens that are overly complex, burdensome, and unrealistic for adherence.[3] When approaching a complex treatment regimen, clinical feasibility and individual preferences should inform choices about treatment. This emphasis on concordance between clinician and patient in the development of a treatment plan may lead to improvements in motivation, persistence, and adherence.[122] It may also help

to improve the clinicians' perspective on medication prescribing.[123,124]

It is imperative to identify treatment complexity through discussions about adherence and the individual preferences of older adults with multimorbidity. These discussions will help frame the approach that is needed to avoid adverse drug reactions with problematic medications such as anticoagulants, overuse or underuse of which can lead to hospital admissions.[125] The individual's own resolution to adhere to medications, change eating patterns, engage in exercise, or make other medical and lifestyle decisions are manifestations of their desire, willingness, and ability to achieve a given outcome or goal. There a is growing literature on education programs that teach patients self-management skills. These help patients set realistic goals and realize the self-efficacy necessary to achieve them.[126]

In the development of patient-centered, feasible treatment plans, there is always the possibility of conflicts arising between what clinicians want and what an individual with multimorbidity is willing to accept. Such conflicts will require ongoing consideration, education, and reevaluation. Care transitions are important opportunities to reevaluate treatment complexity, especially in light of the high incidence of nonadherence.

Controversies and Challenges

Because the treatment regimen and the older person's unique characteristics both influence "treatment complexity" and "feasibility," it is difficult to define a uniform threshold at which a treatment becomes overly complex or no longer feasible. A continuum from "simple" to "complex" that incorporates objective measures, such as frequency of treatment dosing, as well as subjective measures, such as an individual's ability to incorporate the regimen into his or her lifestyle, may be more useful to clinicians as they prioritize the issues that need to be addressed. Even with tools to help clinicians prioritize, addressing treatment complexity is time consuming. It requires a strong grasp of all of the patient's conditions and an appreciation of each one's unique concerns to address treatment complexity effectively. Many clinicians lack the necessary training to identify and address treatment complexity systematically in their practice.

Ideas for Future Research Agenda

More work is needed to develop sound and practical measures for describing treatment complexity in older adults with multimorbidity.[118] Measures have not been tested widely in this population, nor have they been systematically compared between themselves. None of the measures generated so far, even those that are easy to administer, have been systematically integrated into clinical practice and evaluated for sustained use.

At this time, most of the measures available have focused only on medication complexity, rather than on the complications that patients experience from pharmacological and nonpharmacological aspects of clinical management. More measures need to be developed to understand overall treatment burden and how it affects perceived burden, adherence, and patient-important outcomes.

V. OPTIMIZING THERAPIES AND CARE PLAN DOMAIN

Guiding Principle: Use strategies for choosing therapies that optimize benefit, minimize harm, and enhance quality of life for older adults with multimorbidity.

Justification of Principle

Older adults with multimorbidity receive many interventions of various types, most significantly medications, and are therefore at risk of polypharmacy, suboptimal medication use, and potential harms from various interventions. Clinicians who treat individuals with multimorbidity need to prioritize treatments and interventions, with the goal of optimizing adherence to the most essential pharmacological and nonpharmacological therapies. With this approach, clinicians can hope to minimize risk exposure while maximizing benefit. Important therapeutic omissions may occur as a consequence of polypharmacy, when necessary medications need to be added.[127,128] Polypharmacy is associated with less benefit from otherwise beneficial medications or even harm in older adults with multimorbidity. Nonpharmacological clinical management (e.g., implantable cardiac electronic devices) may prove more burdensome than beneficial if, as happens in some cases, it is inconsistent with the preferences of the individual.[129]

Multimorbidity and the presence of specific comorbidities, including cancer, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease, and heart failure, are significantly associated with a greater number of medications.[130] Persons with multimorbidity are more likely than those without to experience adverse drug reactions (ADRs) as a consequence of polypharmacy.[111,131] ADRs may result from clinically significant drug interactions and from inadequate monitoring of medications that have a narrow therapeutic range. Greater medication number contributes to the risk of such drug interactions and ADRs.[132,133] Even without polypharmacy, older adults are at higher risk of ADRs because of normal age-related changes in pharmacokinetics and pharmacodynamics.[134,135] Reducing the medication number, in particular targeting those most likely to be harmful, could reduce the risks associated with medication overuse.

How to Use in Clinical Practice

In attempting to reduce the number of interventions, the first step is to identify treatments that may be inappropriate in older adults or in persons with multimorbidity. Several consensus statements and expert-derived criteria exist to identify potentially inappropriate medications (PIMs) in older adults (Table 4). Drugs that should be avoided are suggested in the Beers list,[136] whereas explicit indicators for prescribing are offered in the Screening Tool to Alert to Right Treatment and Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (START/STOPP).[137] Medications that are consistently considered inappropriate in multiple criteria include benzodiazepines and tricyclic antidepressants.[138] Similar strategies may be used in choosing procedures and nonpharmacological therapies. Also, a clinician who is considering the use of an

implantable cardiovascular electronic device can refer to an expert-derived consensus statement, which recommends consideration and reevaluation of the benefits and risks of the therapy including clear discussion with patients and families of their preferences, keeping functional status and quality of life in mind.[129]

Other approaches for identifying PIMs include the application of algorithmic tools[139] such as the Medication Appropriateness Index (MAI),[140,141] as well as sedative and anticholinergic indices.[142,143] The goal of these approaches is to identify medications associated with a greater risk of adverse events (falls, impaired cognition, and other geriatric syndromes) and detect greater healthcare use and costs due to these adverse events.[144,145]

Applying these principles in clinical practice can be particularly challenging because older adults with multimorbidity are at greater risk for healthcare transitions and use. A recent evaluation of PIMs and actually inappropriate medications (AIMs) noted that 66% of older adults were admitted to the hospital using one of these medications and that 85% were taking these medications at discharge. Approximately 50% of the AIMs were started in the intensive care unit.[146] This finding, in addition to others, speaks to the importance of evaluating medication appropriateness during reconciliation of medications at hospital admission and at intensive care unit and hospital discharge.

Identifying interventions that should not be initiated or should be stopped can be a complex process in this population. Factors to consider include the likelihood of benefit in terms of altering the person's baseline risk for the particular outcome, the risk of harm, and a comparison of the time horizon to benefit and the patient's likely remaining life expectancy (prognosis). For older adults with advanced disease or limited remaining life expectancy, achievable benefits are unlikely to offset the risks and burdens of clinical management.[147–153] For example, secondary prevention interventions in diabetes mellitus to reduce risk of long-term complications are unlikely to provide meaningful benefit in this context. In older adults with multimorbidity, clinicians would be advised to avoid starting this type of clinical management or to stop the intervention if it has already been initiated. In cases in which a therapy has been ongoing for a significant length of time, benefits may persist after discontinuation, moderating any harm that withdrawal of the treatment might create.

Polypharmacy associated with multimorbidity may also be burdensome in other ways for patients. Adding medications to treat multiple conditions is likely to lead to a reduction in overall drug benefit and an additive effect of harms and side effects.[154] While acknowledging the benefits of medication, persons with multimorbidity express concerns about burdensome side effects with multiple medication use.[155] Side effects become especially problematic when they lead to greater medication use; one definition of polypharmacy or medication overuse is the misidentification of drug side effects as a new medical condition leading to a new prescription—the so-called "prescribing cascade."[156] Nonpharmacological therapies such as physical therapy or lifestyle modification should be considered as alternatives to medication to limit side effects.[157] Finally, drugs are costly, and the additional financial stress may generate a significant burden in itself.[158,159]

Older adults with multimorbidity need good information to help them make decisions about clinical management, including clear explanations regarding uncertainty about potential benefits and harms. Individuals are often less informed about possible adverse effects than about the benefits of their medications.[160] Although it may be easier to frame a discussion around stopping or not starting interventions that are harmful, discussions and decision-making about interventions with a higher risk-to-benefit ratio or about a long-time horizon to benefit may be more difficult and time consuming. Ultimately, choices should be made after careful discussion with the individual with multimorbidity, and the reasons for arriving at the decision should be documented.

A detailed plan for safe discontinuation needs to follow any decision to stop a medication but little evidence from well-designed trials is available to guide this process for specific therapies. Many medications can be safely discontinued without the need to taper dosages or withdraw slowly to avoid significant adverse events attributed to medication termination.[141] However, certain drug classes, especially those that act on the cardiovascular or central nervous system, need to be discontinued cautiously, because these are most often associated with adverse drug withdrawal events, including exacerbation of underlying disease.[161] If there is uncertainty about discontinuing a medication, a time-limited withdrawal can help clarify whether the medication was needed in the first place.[162] Medications should ideally be stopped one at a time.[162] When further assistance is needed, clinicians should partner with pharmacists and other clinicians to optimize medication selection and management.[163,164]

Controversies and Challenges

The lack of good evidence to guide clinicians in the avoidance or discontinuation of treatments in older people with multimorbidity makes this a particularly challenging and time-consuming process. Conversations with patients and caregivers on this topic may be complex. Mutual understanding is necessary between the patient (or caregiver) and the clinician when discussing the benefits and burdens of management choices and patient priorities in the context of limited life expectancy. In addition, clinicians may fear liability regarding underuse of therapies and may continue medications even when the benefit, in the context of the patient's overall health status, is unclear. The consideration of these concepts for nonpharmacological interventions is underdeveloped.

Ideas for Future Research Agenda

More emphasis needs to be placed on research that will help clinicians recognize indications for discontinuing therapy and situations in which therapies should not be initiated at all. Similarly, research is required that will evaluate specific patterns of medication use and their adverse drug effects and highlight medications that warrant particular scrutiny.[138,145] The studies with the greatest effect would be those that focus on drugs that are com-

monly recommended but are of diminishing benefit, especially at the end of life.[165] There is emerging evidence of the feasibility and safety of discontinuing medications,[166,167] but more work needs to be done, particularly on approaches for discontinuing medications. Good evidence could be efficiently acquired in this area if future treatment trials incorporate a discontinuation arm or post-discontinuation follow-up.

CASE EXAMPLES

To illustrate the application of these principles, two cases are described, using the flowchart in Figure 1 to guide their implementation. These cases highlight several important points. First, the order of implementing the principles may vary, so that the flowchart sequence, and therefore the sequence for these cases, is just one possibility. Second, for the sake of illustrating these principles, the cases have been distilled, but actual patient care based on these principles is a complex, dynamic process. Third, specific pieces of evidence are described as examples, but systematic reviews that include protocols for finding and including an entire body of evidence that meets prespecified criteria have not been conducted. Finally, there are numerous barriers to implementation of the guiding principles, some of which are beyond the individual clinician's immediate control. These barriers include those described in previous sections discussing Controversies and Challenges and Future Research for each guiding principle, as well as barriers that may require policy level solutions (described in the next section).

Approach to the Evaluation and Management of Older Adults with Multimorbidity

Case Example 1

Current Concerns and Objectives for This Visit

An 87-year-old man presents to your clinic. His son and daughter have accompanied him on this visit. He and his children are concerned that he is excessively fatigued and is taking too many medications. His children are his healthcare agents and wish to make sure that their father is safe and will be able to stay in his own home, where he lives alone. He has the Medicare Part D Prescription Plan to pay for his medications, but the expense of nonprescription medications and copayments is a financial burden.

Review the Overall Clinical Management Plan

What Are the Current Medical Conditions and Interventions?

Current medical conditions

- Probable Alzheimer's disease
- Congestive heart failure
- Osteoarthritis
- Osteoporosis
- Insomnia
- Type 2 diabetes mellitus
- Benign prostatic hyperplasia

Current medical data

- Mini-Mental State Examination (MMSE) score: today, 23/30; 6 months ago, 25/30.
- Blood pressure: sitting, 110/70; standing, 100/60; pulse: sitting, 54 beats per minute; standing, 56 beats per minute.
- Glycosylated hemoglobin (HbA1c): today, 6.8%; 3 months ago, 7%.
- Echocardiogram approximately 1 year ago: ejection fraction, 30%.
- Lipid panel: total cholesterol, 180 mg/dL; low-density lipoprotein cholesterol, 70 mg/dL; high-density lipoprotein cholesterol, 50 mg/dL; triglycerides, 300 mg/dL.
- Notable from today's basic metabolic panel: blood urea nitrogen, 40 mg/dL; creatine, 1.7 mg/dL; glucose, 100 mg/dL.

Interventions

Medications

- Metformin (500 mg; 1 pill twice daily)
- Glyburide (10 mg; 1 pill twice daily)
- Enteric coated aspirin (325 mg; 1 pill once daily)
- Donepezil (10 mg; 1 pill at bedtime)
- Memantine (10 mg; 1 pill twice daily)
- Furosemide (40 mg; 1 pill twice daily)
- Metoprolol (100 mg; 1 pill twice daily)
- Lisinopril (20 mg; 1 pill twice daily)
- Tamsulosin (0.4 mg; 1 pill in the evening)
- Acetaminophen (325 mg; 2 pills twice daily)
- Tramadol (50 mg; 1 pill twice daily and as needed for severe pain)
- Calcium and vitamin D (600 mg and 500 IU; 1 combination pill twice daily)
- Alendronate (70 mg; 1 pill once weekly)
- Zolpidem (10 mg; 1 pill at bedtime)
- Simvastatin (40 mg; 1 pill in the evening)

Other clinical interventions

- Blood sugar checked three times per week
- Exercise: goal is a daily 1- to 2-mile walk

Is the Individual Comfortable with, and Adherent to, the Clinical Management Plan?

This older man admits that:

- He often forgets his evening medications because he is tired
- He does not check his blood sugar regularly because the fingerstick hurts

What Are the Preferences of the Individual and His Family?

This patient and his children express the following priorities:

Table 4. Commonly Cited Tools to Optimize Medication Therapy in Older Adults in the Outpatient Setting

Criteria, Publication Year (Country) Target Group Basis of Criteria	Definition of the Content Validity of the Criteria	Content of the Criteria and Amount of Clinical Patient Information Included	Evidence of Association with Outcomes
Beers, 2012 (United States)[87] Persons aged ≥65 Literature (published 2001–2011 in English)	Modified Delphi consensus panel consisting of 11 interdisciplinary experts in geriatrics and pharmacotherapy, using a mail survey, conference calls, and in-person meeting followed by conference calls for final consensus	53 medications or classes of medications in three categories: PIMs to avoid in older adults, PIMs to avoid in certain diseases and syndromes, and medications to be used with caution	Studies utilizing prior versions of the Beers criteria show conflicting evidence: studies link higher numbers of PIMs with drug-related problems, adverse drug events, hospitalization, and other adverse outcomes,[208–210] but multiple studies have found no association between PIMs on the Beers list and adverse outcomes.[211–215] Of hospitalizations for adverse drug reactions, Beers list medications accounted for only 6.6%, more than half of which was due to digoxin.[216]
STOPP and START, 2008, (Ireland)[217] Persons aged ≥65 Evidence-based literature (not defined exactly in the article) Clinical experience of the investigators	Two-round mail survey based on Delphi method with 18 experts (9 teaching hospital consultants in geriatric medicine, 3 clinical pharmacologists, 1 old-age psychiatric, 2 senior academic primary care physicians, 3 senior hospital pharmacists with interest in geriatric pharmacotherapy)	STOPP: 65 criteria focusing on prevalent problems associated with commonly prescribed medicines in older adults arranged according to physiological systems (42 criteria concerning avoidance of medications in certain disease states or conditions, 4 criteria concerning specific drug combinations to be avoided, 12 criteria concerning duration of drug therapies, 2 criteria concerning doses, 3 criteria concerning avoidance of prescribing without indication, 2 criteria concerning need for additional therapy) START: 22 evidence-based explicit prescribing indicators for common diseases in older adults	Use of STOPP and START was associated with improvement in appropriate prescribing based on MAI and the Assessment of Underutilization.[218] No studies linking improvements in STOPP and START criteria prescribing and health outcomes[218]
MAI, 1992, Summated 1994 (United States)[135,140] Developed in persons aged ≥65, but use not restricted to older adults Literature (Medline and manual search) published 1982–1990 Clinical experience of a clinical pharmacist and an internist geriatrician	MAI: convenience sample of 10 academic clinicians judged MAI items to be definitely important or moderately important, providing an independent validation of their suitability. Summated MAI: applying summated MAI to 105 medications prescribed to 10 elderly veterans. The results reflected the putative heterogeneity in prescribing appropriateness of 1,644 medications prescribed to 208 elderly veterans in the same clinic	10 criteria (indication, effectiveness, dosage, correct directions, drug–drug interactions, drug–disease interactions, practical directions, costs, duplication, duration) worded as questions to assess the appropriateness of each prescribed drug with instructions for use and operational definitions for each criterion	Most studies using this tool have used the MAI score as the outcome of interest. Decrease in MAI score during an in-patient intervention was linked with decrease in hospital readmission or emergency room visits 3 months after hospital discharge.[219] Higher MAI score linked with greater risk of adverse drug events in primary care patients.[220] Higher MAI scores in Veterans Affairs outpatients associated with greater numbers of subsequent hospital admissions and unscheduled visits[221]

(*Continued*)

Table 4. (Contd.)

Criteria, Publication Year (Country) Target Group Basis of Criteria	Definition of the Content Validity of the Criteria	Content of the Criteria and Amount of Clinical Patient Information Included	Evidence of Association with Outcomes
Good Palliative-Geriatric Practice algorithm, 2007, Israel[222] Developed for use in disabled and frail older persons, no clear age recommendation provided Based on clinical practice as applied in nursing homes (not clearly defined in the article)	Not validated	Flow diagram of items to evaluate (quality of evidence, valid indication, risk versus benefit ratio, possible symptoms or signs due to adverse reaction, alternative therapies, and feasibility of dose reduction) that aid in decisions to stop or switch a drug or reduce its dose	Study in nursing homes and geriatric centers in Israel showed less mortality and need for acute care in those randomized to receive an intervention using the algorithm.[222] An outpatient study in 70 older persons demonstrated the ability to stop medications as recommended by the algorithm, with a low risk of adverse effects resulting from stopping medication[141]

Adapted with permission from Dimitrow MS, Airaksinen MSA, Kivela SL, Lyles A, Leikola SNS. Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. J Amer Geriatr Soc 59:2011:1521–1530. PIM, potentially inappropriate medication; STOPP, Screening Tool of Older Person's Prescriptions; START, Screening Tool to Alert doctors to Right Treatment; MAI, Medication Appropriateness Index.

- To stay alive
- To optimize quality of life
- To reduce out-of-pocket expenses since the patient lives on a fixed income
- To remain safely in his home despite the mild Alzheimer's disease first noted 3 years ago

What Evidence Is Available Regarding Intervention Effects?

Example of the type of evidence that is useful:

The cholinesterase inhibitor, donepezil, has had only modest success in delaying institutionalization and in maintaining functional status, and results are mixed.[168–172] Many existing studies do not examine these outcomes.[173] Memantine has shown no benefit alone or in combination therapy for mild Alzheimer's disease.[174]

Data from the Fracture Intervention Trial Long-Term Extension (FLEX) study of women with osteoporosis taking alendronate for longer than 5 years suggest that fracture protection exists for up to 5 more years after stopping it.[175]

Tight glycemic control may result in more harm than benefit, and the appropriate HbA1c target may be 8% to 9%.[176]

What Is the Prognosis?

Given this individual's age and multimorbidity, life expectancy is estimated to be 2–3 years.[94,177] Ongoing cognitive decline is likely, with an average loss on the MMSE of 2–3 points per year. He will probably experience progressive dependence in his instrumental activities of daily living (IADLs) (driving, medication management, and finances).

Are There Interactions with Medications and Medical Conditions?

There are concerns that some drug interactions may be contributing to this individual's complaints and medical conditions. The following is a list of his health concerns and what potential interactions his provider can consider.

Fatigue: The patient enjoys exercise but has been feeling more fatigued lately. His bradycardia may be due to the increased dose of metoprolol, especially in combination with donepezil. Both agents can slow the heart rate.

Suboptimal regulation of his type II diabetes mellitus, resulting in unstable blood glucose, may also be affecting his energy levels. Also, glyburide should be avoided in older individuals because of the greater risk of hypoglycemia than with other agents in its class.

Fatigue may also be an adverse effect of statin therapy. Considering this individual's prognosis and this possible source of fatigue, a reevaluation of the simvastatin treatment for dyslipidemia is warranted.

Insomnia: Donepezil may cause nightmares, especially when taken at bedtime. Zolpidem, although possibly helpful for falling asleep, may not keep him asleep for the night and can also cause excessive somnolence during the day.

Congestive heart failure: Metformin should be avoided in patients with heart failure and compromised renal function because of the risk of lactic acidosis.

Alzheimer's disease: Agents such as zolpidem have been found to worsen dementia and can also increase the risk of falls—primary safety concern for this older individual with osteoporosis living alone.

Osteoporosis: Concern about this patient's renal function and duration of alendronate therapy suggests a reevaluation of the bisphosphonate administration.

Does the Balance of Benefits and Harms Favor the Intervention?

In light of the effect of treatment complexity and medication burden on feasibility, adherence, and quality of life, several things that can influence clinical management must be considered.

In this case, clinical management decisions merit reevaluation in several areas, including treatment of the type II diabetes mellitus, insomnia, dyslipidemia, congestive heart failure, cognitive decline, and osteoporosis.

Communicate and Discuss Decisions About Clinical Management with the Individual and Family

In the discussion of clinical management options, consider the feasibility of the approach, the patient's and family's preferences, and their outcome priorities. Ensure that the individual understands and agrees with the clinician's recommendations, which should be based on the individual's outcome values. Including the patient in the discussion and decision-making process is likely to improve adherence to clinical management and therefore to improve health outcomes.

Ideally, share written explanations with the individual in question and the family to ensure that all significant members of the healthcare team fully understand the rationale for clinical decisions.

The following is an example of an appropriate approach for a discussion of options regarding glycemic control:

"We understand that you prefer to remain at home and in your community and avoid hospitalization, are not concerned about outcomes 5–10 years in the future, are at risk of low blood sugar and its consequences, would like to feel more energetic, and would like to decrease expenses. We therefore suggest that you reduce some of your medications and relax your effort to achieve tight control of your blood sugar levels."

Possible revisions to the treatment plan, with consideration of patient and family preferences.

In general, medication changes should not be made concurrently. The following possibilities would ideally be done in stepwise fashion.

Bradycardia: Reduce the metoprolol twice daily to one lower dose in the morning only (see Congestive Heart Failure below). This dose reduction will help to minimize pill burden while still addressing the bradycardia. Family members will monitor his complaints of fatigue and energy levels.

Insomnia: Donepezil will be taken in the morning rather than at bedtime. The zolpidem will be reduced from 10 to 5 mg at bedtime, to be used only if needed. Complete discontinuation of zolpidem is the goal.

Congestive heart failure: Because all his heart failure medications are taken once daily, all should now be taken in the morning. This is likely to improve adherence, because he habitually skipped evening medications. The following modifications should also improve adherence:

furosemide (40 mg; 1 pill in the morning)
lisinopril (20 mg; 1 pill in the morning)
metoprolol XL (50 mg; 1 pill in the morning)
aspirin (reduced from 325 to 81 mg daily)

Alzheimer's disease: Published evidence does not support the use of memantine in the mild stages of Alzheimer's disease, but this man's family is resistant to change in the case of memantine and feels strongly that it is helping him maintain his independence. Because his estimated creatinine clearance is approximately 30 ml/min, the memantine dosage should be reduced to 10 mg once daily rather than twice daily. Again, this limits medication administration to the morning, which should improve adherence.

Because this older man with mild dementia takes frequent walks, suggest that he obtain Alzheimer Association's Safe Return® identification.

Type II diabetes mellitus: This individual's target HbA1c should be less restrictive, at approximately 8% to 9%. Although much higher blood sugar levels may add to his confusion and contribute to other problems such as blurred vision, his control may be too tight. Also, some oral agents increase his risk for hypoglycemia. It would be reasonable to discontinue the metformin and glyburide. Because the patient has been avoiding fingerstick glucose monitoring three times per week, suggest that he monitor his glucose levels only if he is feeling symptomatic. HbA1c should be tested every 3 months; adding a low dose of an oral agent may be needed at that time

Dyslipidemia: In light of this older man's prognosis, uncertain benefit, unreliable adherence, and complaints of fatigue, the clinician recommends discontinuing simvastatin.

Osteoporosis: Because this individual has been taking alendronate for many years. Data from the Long-term Extension of FIT (Fracture Intervention Trial) FLEX study of women with osteoporosis taking alendronate for longer than 5 years suggest that he can stop the alendronate and still have fracture protection for up to 5 more years.[175] This is relevant in light of his estimated life expectancy of 2–3 years. Although there is evidence to support bisphosphonate use in men, the evidence from the FLEX trial for stopping therapy comes from a large study of women with osteoporosis. Vitamin D blood levels should also be checked. Adherence to the calcium and vitamin D supplement regimen will probably improve if taken only once daily. Suggest greater dietary intake of calcium and vitamin D.

Medication management: One of the children or another family member should be chosen who can take responsibility for filling pillboxes each week. Give written instructions detailing the new regimen, including the indications for use and directions for monitoring. This will help the children to be participatory in their father's care and encourage close oversight. Except for the zolpidem,

the medications should be stored in the family member's home, rather than with the patient.

Communicate and make clinical management decisions with other members of the healthcare team.

By prioritizing the older individual's preferences in this case, it is likely that fewer consultations and communications with other specialists will be necessary. Although valuable for the care of patients with multimorbidity, such efforts are time consuming for the coordinating clinician. Changes in reimbursement structures for this activity are therefore indicated and discussed below in Promising Approaches to Overcoming Barriers to Implementation of Guiding Principles in the Care of Older Adults with Multimorbidity.

Reassess at Selected Intervals for Benefit, Feasibility, Adherence, and Alignment with Patient Preferences

Case Example 2

Current Concerns and Objectives for This Visit

A 72-year-old woman presents to your office for a routine follow-up visit, accompanied by her daughter. She lives alone in an apartment complex for seniors and requires daily assistance from outside caregivers, including home health aides and friends, because of limitations in instrumental activities of daily living (IADLs). She manages her basic activities of daily living (ADLs) independently. She is physically frail, has difficulty walking, uses a walker to get around, and has a history of frequent falls. She lives on a small, fixed income.

Her daughter notes that her mother appears to be "slipping" in her general capabilities.

The older woman has heard of osteoporosis, is concerned, and wonders if she has it. She would like to know whether this is an important concern for her and whether anything should be done about it.

Focus on a Specific Aspect of Clinical Management

The broad management approach needs to be reviewed, with a focus on this older individual's personal concern about osteoporosis.

What Are Her Current Medical Conditions and Interventions?

Current medical conditions

- Moderate to severe chronic obstructive pulmonary disease
- Smoking habit
- History of transient ischemic attacks and lacunar infarcts (several hospital evaluations for stroke)
- Peripheral vascular disease: carotid stenosis and right subclavian steal syndrome
- Hiatal hernia
- History of major depression and suicide attempt
- Mild cognitive impairment
- Hyperlipidemia.

Current medical data

Forced expiratory volume in 1 second/forced vital capacity = 60%.
MMSE score 22/30.

Interventions
Medications

- Albuterol/ipratropium inhaler (1–2 puffs every 6 hours)
- Escitalopram (20 mg, 1 pill daily)
- Esomeprazole (40 mg, 1 pill daily)
- Clopidogrel (75 mg, 1 pill daily)
- Simvastatin (10 mg, 1 pill at bedtime)
- Multivitamin with calcium (twice a day).

Is the Individual Comfortable with, and Adherent to, the Clinical Management Plan?

This older woman reports that she has some trouble taking her medications. Her primary care provider has noted that she also has difficulty keeping appointments.

When you review medications and refill patterns with the individual and her daughter, it becomes clear that her adherence is poor. When you make this observation, she complains about having to take too many medications.

The likelihood of good adherence to additional medications is poor. Initiating a new medication such as a bisphosphonate, with its complex pattern of safe administration, will be challenging.

What Are the Preferences of The Individual and Her Family?

The patient prefers to stay in her apartment and to live independently. Her daughter is somewhat involved, visiting two or three times each month. She agrees that her mother needs care, but the family is generally limited in their ability to provide greater oversight. She is concerned that her mother's abilities seem to be becoming more limited. Generally, the family favors a simple management approach that will allow this older individual to stay in her apartment and maintain her independence.

What Evidence Is Available Regarding Intervention Effects?

Osteoporosis is associated with fracture risk. Estimates of this woman's 10-year risk of major osteoporotic fracture or hip fracture are 12% and 4%, respectively, according to Fracture Risk Assessment Tool (FRAX), a diagnostic tool used to evaluate the 10-year probability of bone fracture risk developed by the World Health Organization.[178] Bone mineral density (BMD) assessment (e.g., dual X-ray absorptiometry) can detect bone loss and osteoporosis and is covered by Medicare.

Bisphosphonates: In the presence of osteoporosis, bisphosphonates have been shown to improve BMD (not a patient-important outcome) and prevent all major osteoporotic fractures (patient-important outcome), including silent vertebral fractures.[179] Bisphosphonates such as alendronate have been shown to reduce the incidence of spine and hip fractures by 50% over 3 years. If this patient's baseline risk of a major osteoporotic fracture is 12% over 10 years, and the assumption is made that risk

is constant over that time, her 3-year risk of major osteoporotic fracture is 3%. With bisphosphonate treatment, her ARR would be approximately 1.5% over 3 years. If she has a T score that is worse than –2.5, the NNT to prevent any fracture is 18 at 4 years, with a likely time horizon to some incremental (nonsignificant) benefit at approximately 18 months.[180] If this woman already has subclinical vertebral fractures, her ARR for major osteoporotic fracture with treatment would be even greater, with benefits beginning after 9–12 months of treatment, but bisphosphonates also have the potential for adverse events. In this woman's case, bisphosphonate administration could aggravate her hiatal hernia and increase her risks of atypical fractures and osteonecrosis. Also, because her adherence has been suboptimal in the past, it is likely that she will have difficulty keeping to the stringent instructions that must be followed when taking bisphosphonates.

Other interventions for osteoporosis: Calcium intake of at least 1,200 mg/d, vitamin D intake of at least 1,000 IU/d (with calcium), weight-bearing exercise, and fall prevention strategies are all associated with lower fracture risk.

Prevention of hip fractures can improve quality of life, support the continuation of independent living, and decrease costs associated with fractures (e.g., hospitalization and physical therapy). The data are less clear for the prevention of vertebral fractures.

What Is the Prognosis?

According to published studies, this patient has a 64% risk of dying within 4 years[94] and a 30% risk of dying within 15 months.[181]

Are There Interactions with Medications or Medical Conditions?

In the case of this older woman with multimorbidity, there are many examples of interactions between medications and her medical conditions. For example, concurrent use of clopidogrel and escitalopram can increase the risk of bleeding. Also, esomeprazole may decrease the clinical effectiveness of clopidogrel, resulting in greater risk of thrombosis.[182]

Proton pump inhibitors such as esomeprazole lower stomach acid levels, decreasing calcium absorption and increasing fracture risk.[183] Escitalopram also increases serotonin levels, resulting in less osteoblast activity and subsequent bone loss.[184] Selective serotonin reuptake inhibitors may more than double the risk of fractures and have even higher risks if used over the long term.[185]

Does the Balance of Benefits and Harms Favor the Intervention?

This older woman's ability to reliably take—and her likelihood of tolerating—a weekly or monthly dose of bisphosphonate is low. Her history of irregular adherence and inability to keep appointments suggests that difficulties will arise in her attempts to follow instructions regarding bisphosphonate administration.

Yearly intravenous bisphosphonate administration might be a better option, but the high cost precludes it for this patient. It is also possible to propose other forms of intermittent doses of bisphosphonate and enlist the help of the daughter if possible.

Communicate and Discuss Decisions About Clinical Management with the Individual and Family

In considering these factors, it was emphasized to the patient and family that certain "trade-offs" are inevitable. Benefits and harms may be associated with opting for or against antiresorptive therapy. For example, a hip fracture might threaten or even terminate this woman's independence, and bisphosphonate treatment would be the most effective way to decrease this risk, but the ARR associated with treatment is small, and the treatment itself is complicated and expensive and comes with its own health risks. When these considerations were discussed with the patient and her daughter, the incremental benefits of bisphosphonate therapy were not considered to be worth the possible harms.

Because the patient decided not to begin bisphosphonate therapy, her BMD was not tested.

Possible revisions to the treatment plan, with consideration of patient and family preferences.

Following your recommendations, this woman chose to continue and optimize oral calcium and vitamin D supplementation and to undertake a daily walk, as tolerated.

Communicate and make clinical management decisions with other members of the healthcare team.

Document clinical management decisions and share this information with this woman's other clinicians, including physician specialists, nurses, and pharmacist, whenever possible.

Reassess at Selected Intervals for Benefit, Feasibility, Adherence, Prognosis Including Functional Status and Fall Risk, and Alignment with Patient Preferences

PROMISING APPROACHES TO OVERCOMING BARRIERS TO IMPLEMENTATION OF GUIDING PRINCIPLES IN THE CARE OF OLDER ADULTS WITH MULTIMORBIDITY

There are important barriers to implementing these guiding principles in clinical practice. Few interventions have been developed that systematically and simultaneously address the restructuring of the healthcare delivery process, changes in clinician behavior, and the support that patients and their caregivers need, with the ultimate goal of improving the quality of care in this population.[186] A clinician who aims to implement the guiding principles described above needs an effective healthcare team made up of interdisciplinary clinicians, as well as family, friends, and paid caregivers across sites of care, including the home; adequate training; reimbursement structures that reward patient-centered medical care; and an evidence base relevant to older adults with multimorbidity. These components, which are beyond an individual clinician's immediate control, must also change to fully address the healthcare needs and outcomes of older adults with multimorbidity.

Coordination of Care and Patient-Centered Medical Home

Because individuals with multimorbidity consult more clinicians (generalists and specialists),[187] implementing these guiding principles can be difficult without adequate systems of primary care medicine and central care coordination. Although the limited geographic availability of healthcare resources also restricts access to primary care and geriatricians,[188] having an identified "primary" provider or practice, such as a patient-centered medical home, may help older adults with multimorbidity (and when applicable, their family or social supports) make more-informed decisions about their priorities and improve coordination of care among clinicians. Consequently, these principles may guide the development and implementation of an effective patient-centered plan of care. In turn, such a plan can facilitate care coordination and integration of healthcare services and support services within and between sites of care.

Primary care providers may not have established relationships with collaborative partners, such as pharmacists, who are helpful for the implementation of these principles. Similarly, the presence of mental illness highlights the need for integration of mental health services in clinical healthcare management for these individuals.[189] Effectively working with specialists may be challenging for some primary care providers because of the lack of effective communication systems and inadequate access to appropriate types of specialists. Also, specialists may not recognize serious problems facing older adults with multimorbidity, including the importance of coordinating with a primary provider and the complexity of managing multiple conditions. These are challenges that the development of true patient-centered medical homes will help address, although all clinicians need more training in the care of older adults with multimorbidity to achieve optimal management of these individuals.

Workforce Training: The Need for Curriculum Development and Training

Adequate evidence-based patient-centered care for older people with multimorbidity will likely require greater partnership between government agencies, professional organizations, and academic institutions to develop the ability to care for older adults with multimorbidity. Clinicians are often insufficiently trained to care for these individuals.[190] Because education programs usually focus on single-disease entities, there is a need for new curricula with an emphasis on care of people with multimorbidity.[191] Investing resources in education will stimulate the development and implementation of such curricula across healthcare disciplines.

Older adults with multimorbidity may have a particular need for assistance with ADLs and IADLs, in addition to healthcare management tasks.[192] Without adequate support, many older adults with multimorbidity may base treatment decisions on their inability to perform daily care. One example of such a situation would be that of an individual with diabetes mellitus who is unable to check his or her own blood sugar because of an essential tremor. In such a case, self-monitoring would not be an acceptable part of the treatment plan. Although family members, friends, and other caregivers accompany many older adults when they visit their clinician, and despite the fact that this involvement tends to persist over time,[193] many clinicians do not know how to integrate family or friends into an effective partnership for healthcare management.[194] Emerging evidence is focusing on care facilitation by caregivers.[195–197] New interventions, such as the Guided Care Program for Families and Friends (GCPFF), have been developed to support caregivers of older adults with complex health-related needs.[186] Such work is a promising first step in the development of comprehensive models of chronic care delivery for this population.[186]

Inadequate communication skills and educational materials are also barriers to the care of older adults with multimorbidity. Because conversations about prognosis and preferences can often be difficult for clinicians, training of all healthcare team members must address communication skills. Ethnic and cultural factors may also affect management. Cultural sensitivity on the part of the provider may improve treatment adherence and outcomes, particularly if the older adult has a different ethnic background from that of the healthcare professional.[52,198–201] A problematic "mismatch" can also occur if clinician–patient management styles differ. For example, a clinician who practices in a paternalistic style may unintentionally antagonize an older individual who prefers shared decision-making, or vice versa.[201] Illiteracy (including healthcare illiteracy), language barriers, and hearing and visual impairments may also affect outcomes. As ethnic and racial diversity of older Americans increases, printed educational materials in preferred languages may not always be available for every chronic condition. Thus, facilitation of communication will require investment in curricula for communication skills and development of patient educational tools that address these barriers.

Reimbursement Structure

To care for older people with multimorbidity adequately, there must be changes in the current reimbursement structure to provide incentives to the provision of quality care. All necessary team members need to receive appropriate compensation, which will allow adequate time to be spent with patients and families to help them become well-informed participants in this patient-centered approach. Unfortunately, the current reimbursement structure rewards acute, episodic, and specialist care for "quantity" of patients seen, not for "quality" of care delivered.[202] Therefore, the current systems of patient care need to be modified to allow more time and resources for patients and their families and caregivers.[6,52] Also, care that is organized around single diseases may be inadequate because single-disease rehabilitation, support, and education groups are not able to meet the needs of complex, heterogeneous patients.[3,203] In addition, GPGs pertaining exclusively to a single disease or condition may be used to determine clinician compensation in pay-for-performance formats. The focus on provider performance of process indicators for common single, chronic diseases may influence clinicians to provide unnecessary or potentially harmful care to older adults with multimorbidity.[52,204] Thus,

development of performance standards appropriate for older adults with multimorbidity that are adequate for trial use in pay-for-performance demonstrations is imperative.[205,206]

Performance criteria should also be developed to reward approaches known to improve patient health outcomes, functional status, and quality of life. Because Medicare and Medicaid are the main payment sources for health care in older adults with multimorbidity, they are the most appropriate agencies to implement innovative demonstration projects in payment system reform efforts. The Centers for Medicaid Medicare Innovation have solicited proposals to do so. As the number of older adults living with multimorbidity increases, the need to identify and support effective clinical management approaches will become more acute.[207]

Building a Better Evidence Base

The lack of research focusing on the needs of older adults with multimorbidity has held back optimal clinical management and the development of needed tools to educate these patients and their families and friends. Healthcare systems can develop better approaches over time through a greater effort to collect relevant data. This information could provide insight into treatment effects and adverse consequences in this population. With increasing use of electronic medical records, patient outcomes and system performance can be monitored, and quality improvement strategies, reimbursement options, and new performance measures can be developed and evaluated.

CONCLUSION

The adoption of these guiding principles for clinical decision-making and the management of older adults with multimorbidity may improve their health care and outcomes. Patients should be evaluated, and care plans should be designed and implemented according to the individual needs of each patient, with the recognition that few studies are currently available that have rigorously evaluated the effectiveness of approaches related to these guiding principles. For this reason, nonadoption of these principles should not imply medical liability or malpractice. These principles are intended to help guide clinicians through the complex process of managing older adults with multimorbidity. They highlight the urgent need for more research in the optimal management of the growing population of older adults with multimorbidity.

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