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Multimorbidity in Older Adults with Cardiovascular Disease

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Abstract

The demographic of older adults is growing rapidly, a population that is inherently prone to age-related cardiovascular disease (CVD) and to its predictable occurrence in a context of multimorbidity. While multimorbidity can develop at all ages, the number, complexity and diversity of comorbid conditions usually increase with advancing age. Research and clinical care have traditionally been oriented to single disease-specific paradigms, but these approaches adapt poorly to the challenges that arise when CVD occurs with multimorbidity. Concurrently applied guidelines for CVD and comorbid diseases are often contradictory, harmful, and misaligned with patients' own preferences and goals of care. In this manuscript, emerging concepts regarding CVD combined with multimorbidity are reviewed, including recommendations for incorporating multimorbidity into clinical decision-making, critical knowledge gaps, and research priorities with a goal to optimize care in complex older patients with CVD and multimorbidity.

Keywords

aging; multimorbidity; quality of life; frailty; polypharmacy

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The population of older adults is rapidly growing, and accordingly, so is the number of adults with cardiovascular disease (CVD) who survive into later life, as well as the number of older adults who are predisposed to develop incident CVD as a function of normal aging physiologic changes. More than 70% of adults develop CVD by the age of 70 years, among whom more than two thirds also develop non-CVD comorbidities (1,2) . Thus, multimorbidity is endemic among older adults, particularly those with CVD. Current research and clinical practice in CVD have fostered a disease-specific care paradigm focused predominantly on management of a single disease, and that rarely embraces the complexities imposed by multimorbidity. With advancing age, symptoms and priorities of care that are meaningful to most patients become significantly affected by comorbid conditions. Patient-centered priorities for an older patient demographic support the rationale for multimorbidity to become more systematically integrated into the management of patients with CVD. This manuscript reviews emerging concepts regarding CVD in the context of multimorbidity, provides recommendations for incorporating multimorbidity into clinical decision-making, and delineates critical knowledge gaps and research priorities to advance the care of patients with CVD and multimorbidity, especially those of advanced age.

Background

Age-related changes in cardiovascular structure, physiology, and biology increase the susceptibility to CVD, and more adults are surviving into old age with chronic CVD after enduring cardiovascular or other events that would have once ended their lives at younger age (3). This has resulted in a significant proportion of older adults with CVD who, in contrast to younger patients in whom CVD typically presents as a dominant medical condition, are more likely to be challenged with CVD as part of a constellation of chronic conditions (Figure 1). For many older adults with multimorbidity, CVD is not necessarily experienced as the most important of their health and/or healthcare concerns (1,2,4).

While chronological aging is immutable, a mere tally of years alive does not reliably predict health status. It is more meaningful to use metrics that integrate co-existing conditions and their impact on physical, cognitive, and psychosocial function (5–7). Among adults aged ≥80 years, multimorbidity is more common than any single disease, with over 80% of this age group having two or more chronic conditions, and 54% of those age ≥85 years having four or more (8–11). As multimorbidity is a powerful predictor of poor outcome (12) , it becomes an important prognostic metric among older patients.

An additional impetus to promote an integrated approach to treatment for patients with multimorbidity is the alarming fact that the 14% of Medicare beneficiaries who report 6 or more chronic conditions consume 46% of Medicare’s annual budget of over $500 billion. The disproportionate costs associated with multimorbidity are especially relevant given Medicare’s recent mandates to optimize outcomes, value, and efficiency of care.

Responding to this challenge, the American College of Cardiology and the National Institutes on Aging (NIA), in collaboration with the American Geriatrics Society (AGS), convened a two-day multidisciplinary workshop to review the ramifications of multimorbidity on CVD as a unique gathering to update, collaborate and formulate a future

agenda. This workshop, entitled “Multimorbidity in Older Adults with Cardiovascular Disease”, was remarkable for the synergy it generated from a broad cross-section of experts (i.e., cardiologists and cardiology care providers, geriatricians, nurses, epidemiologists and stakeholders from the Centers for Medicare and Medicaid Services [CMS], Food and Drug Administration [FDA], the Agency for Healthcare Research & Quality, and others) to develop strategies to better address this transformative healthcare challenge.

Defining multimorbidity

The definition of multimorbidity established by the Department of Health and Human Services (DHHS), and adopted for this paper, involves two or more medical diseases/conditions each lasting over one year. Yet multimorbidity defined in this way identifies a population that is quite heterogeneous, in part because the number and variety of diseases and other conditions typically increases with age (13), with the burden and impact of multimorbidity usually becoming more severe over time (11,14,15). Most cardiovascular providers routinely face managing multimorbid patients with interrelated pathophysiologies, such as coronary artery disease, hyperlipidemia and hypertension. However in this paper, we focus primarily on the presence of one or more non-cardiac diseases/conditions in older adults with CVD as significant modifiers of care and outcomes. These may include geriatric syndromes, which are broadly defined as multifactorial symptom complexes, usually associated with diminished homeostatic reserve, that are associated with adverse outcomes (e.g., frailty, falls, cognitive and physical impairment, incontinence, sensory dysfunction, and delirium) (16). These syndromes are becoming increasingly familiar to providers who now recognize that geriatric syndromes are more common than many cardiovascular disorders, and often occur in combination with one another, complicating diagnostic certainty and management, while at the same time adversely affecting disease specific and overall outcomes (17).

Pathophysiology and implications of multimorbidity: intersections with CVD

Many of the same age-associated structural, physiologic, and biologic changes that predispose patients to CVD, also predispose them to multimorbidity and compound risks and consequences once diseases occur (18). Physiological stresses from impairment of multiple organ systems in people with multimorbidity may synergistically increase vulnerability and risk for progressive morbidity and mortality (7,8). Mechanistically, accumulating conditions may induce or exacerbate other diseases through common pathophysiology (e.g. chronic inflammatory pathways of CVD increasing the risks of developing diabetes or depression) (9). Furthermore, one condition often impacts other conditions either directly or in respect to their treatment(s) (Figure 2) with unpredictable consequences. Common sequelae of multimorbidity include disease-disease interactions (e.g., heart failure, chronic kidney disease, and hypertension), disease-drug interactions (e.g., heart failure and non-steroidal anti-inflammatory drugs for arthritis), drug-drug interactions (e.g., omeprazole and warfarin), therapeutic competition when a medication for one disease inadvertently destabilizes another (e.g. beta-blocker for heart failure worsening

bronchospastic lung disease), In addition to the interactions of conditions and treatments in multimorbid patients, treatment efficacy versus adverse effects may be further challenged by shortened life expectancy (e.g., statins for primary prevention, such that the time required for anticipated benefit may exceed the remaining lifespan in someone with an end-stage disease) (19). Altered clinical presentations as well as differences in dosing, drug tolerances and therapeutic responses are all more likely as each comorbid condition progresses and/or new ones are added amidst diminished homeostatic reserves. Advancing age, especially beyond 80 years, further worsens risk for adverse outcomes as progressive age-related changes in body composition, metabolism, and drug pharmacodynamics/kinetics are more likely to provoke or worsen co-existing morbidities, geriatric syndromes, and adverse drug effects (20).

Concordant and discordant conditions

Multimorbidity is customarily characterized as concordant and discordant subtypes. Two ‘concordant’ chronic conditions are linked by underlying pathophysiology or by similar management concerns (e.g., heart failure and hypertension) (21). Conversely, ‘discordant’ conditions are less directly related by pathogenesis or treatment, but can still affect one another, directly or via treatment (e.g., heart failure in combination with osteoarthritis, cancer, or frailty). Discordant conditions, which require coordinated care, are often overlooked or, in some cases, not formally recorded in a patient’s record by consulting specialists, despite their impact and relevance for overall care and outcomes.

While concordant cardiovascular conditions often pose considerable challenges for patients and primary care clinicians, such complexity is typically within the skillset of knowledgeable cardiologists and often addressed within specialty guidelines. In contrast, discordant conditions are less frequently acknowledged and integrated in care. Yet CVD and non-CVD conditions impact one another, and cardiology experts have the opportunity to enhance quality and value of cardiovascular care when their attention and insights also extend to comorbid issues. Greater emphasis on non-CVD conditions and increased application of team-based caregiving models are important steps towards enhancing care for patients with CVD and multimorbidity.

Limitations of the current CVD therapeutic paradigm to address multimorbidity

The current approach to clinical care is largely driven by single-disease clinical practice guidelines that are oriented to diagnosis, therapeutics/management, and decision-making (e.g. acute coronary syndrome); yet guidelines become less relevant when diagnosis and care are complicated by multimorbidity (Central Illustration). First, clinical guidelines are based on randomized clinical trials (RCT) that have limited applicability to patients with multimorbidity (22). Most RCTs enroll a relatively homogeneous population with a specific disorder for which the benefits of a specific therapy are assessed. Thus, subjects with multimorbidity are usually deliberately excluded (23,24). Furthermore, the principal focus of many cardiovascular RCTs is on major adverse cardiovascular events, which may be less useful than outcomes that assess overall benefit of a therapy to an older patient, such as

preservation of physical and cognitive function, lack of disability and health-related quality of life.

Second, disease-specific guidelines for multiple conditions lack integration, such that aggregate care for most patients entails considering multiple separate guidelines (25). Decisions regarding discordant conditions are more likely to prompt uncertainty for clinicians and patients (10). Disease-specific guidelines applied concurrently for CVD and discordant comorbid conditions are often contradictory, potentially harmful, and misaligned with the preferences and goals of patients, whose concerns are less likely to be specific measures related to any single disease (e.g., percent change in ejection fraction, reinfarction) (25,26).

Therapeutic competition, where a therapy for one condition can worsen a coexisting condition, is common; it was observed in 22.6% of older adults with multimorbidity (and with CVDs as the most common conditions that competed with others) (27) . As noted above, drug-drug and drug-disease interactions are also common: as the number of medications taken (including non-prescription drugs and supplements) for the many conditions being treated increases, the resultant risk of adverse events and interactions escalates even more rapidly.

Third, disease-specific guidelines promote care oriented to single diseases, with less concern accorded to coordination of care and delineation of a patient's overarching goals of care as the fundamental drivers of management (28). Thus, rather than targeting broad and interconnected patient-directed goals (e.g., improved quality of life, reduced time spent managing medications, and increasing physical function), care often focuses on condition-based targets that may lead to interventions and outcomes that patients may even experience as unsatisfying (e.g., implementing an aggressive blood pressure regimen to achieve guideline-defined goals for a patient who experiences decreased energy, frequent falls (29) and associated hospitalizations) (30). The concept of eliciting patient-preferences is evolving as an important step to improve quality of care and adherence for older adults with multimorbidity (31), yet neither patients nor clinicians are universally trained to discuss, identify, record and implement preferences and goals of care. Severe time constraints imposed by the current reimbursement structure, as well as the narrowed focus of a disease-based approach, pose additional challenges to effectively eliciting care preferences. Furthermore, limitations in patients' cognition and/or sensory capacities (e.g., hearing, vision) may reduce their ability to grasp and/or communicate care preferences.

Finally, most disease-specific RCTs rely primarily on objective, quantifiable outcomes relevant to that disease, such as recurrent myocardial infarction, revascularization, readmission, or cardiovascular death. Such disease-focused endpoints are difficult for a patient with multimorbidity to weigh against other repercussions and burdens of a treatment (e.g., medication side effects, costs, or procedural risks) and are often disconnected from day-to-day concerns that matter most to patients (e.g., the ability to take care of household tasks or care for a spouse) (2,32).

Typical priorities among older adults include physical and cognitive function, symptom control, reduced burden of therapy, health related quality of life, maintenance of independence and overall well-being (33). Thus, a major shift is required from our disease-oriented clinical standards to strategies that better respond to the clinical realities and concerns of patients, which ideally should be integrated into future research as outcomes of importance (4,33,34).

A multidimensional approach to multimorbidity

The American Geriatrics Society has established 5 guiding principles for the care of older adults with multimorbidity that contrast with traditional disease-specific models of care: [1] eliciting and incorporating patient preferences into medical decision-making; [2] applying evidence from the literature, but acknowledging limitations of the evidence base; [3] framing clinical management decisions in a context of risks, burdens, benefits and prognosis; [4] assessing treatment complexity and feasibility; and [5] choosing treatments that optimize benefit, minimize harm, and enhance quality of life (35). Applying these concepts in usual care is complex, and research is essential to overcome many obstacles.

As previously noted, research is needed to refine and validate multimorbidity frameworks (concordant and discordant), including basic steps to develop a consensus definition and taxonomy for classifying multimorbidity and other geriatric syndromes. Related priorities include initiatives that lead to improved clinical study design, enhanced assessments of patient preferences and goals, enriched clinical decision-making assessments/tools, improved care coordination and communication among providers and patients, and refined metrics for quality of care.

Changing the clinical approach to better respond to multimorbidity

Addressing CVD in the context of multimorbidity presents an opportunity to build a model of care based on patient-centered medicine, and to manage diseases and conditions in ways that are oriented to patients and their goals (36,37). The central patient-directed question shifts from ‘what is the matter?’ to ‘what matters to you?’ (38) Patient-centered care has been described as a “systems biology approach” that accounts for patients’ physical, psychosocial, and environmental experiences (39,40). It incorporates patients’ preferences and values, and empowers patients to work as partners in decision-making with their interdisciplinary care teams. This approach is consistent with the National Academy of Medicine’s (formerly the Institute of Medicine) six key domains for high quality care, i.e. care that is safe, effective, personalized, timely, efficient and equitable (41,42). Furthermore, it aligns with changes to reimbursement initiated by the CMS toward a system that rewards value-based care. This approach requires a shift in focus from traditional, reductionist, disease-specific outcomes to one focused on goal-oriented outcomes, such as function or specific tasks (2,6). The new care approach also emphasizes communication and collaboration across multiple providers and care settings (i.e., outpatient, inpatient, skilled nursing facility, specialist, primary care), and sectors (i.e., academic, industry, government, community).

Knowledge gaps and research priorities

Table 1 provides an overview of research gaps and unmet needs pertaining to the care of older adults with multimorbidity. To best inform the shift in clinical care that multimorbidity mandates, advances in multiple domains are necessary.

Given the high prevalence of multimorbidity in older patients with CVD, several study designs have evolved. Some of these efforts have concentrated on improving understanding and care of patients with 2–3 chronic conditions by studying specific disease dyads or triads (such as coronary artery disease in combination with diabetes and depression) as they affect specific outcomes (43). However, the marked heterogeneity of multimorbidity also implies a need for strategies that can address more complex disease and condition combinations (44,45).

While the traditionally rigid inclusion and exclusion criteria in RCTs have limited the applicability of many CVD management precepts to real-world older adults with CVD and multimorbidity (22), this could be modified. RCTs could enroll more subjects of advanced age (e.g., ≥80 years), enlist more patients with multimorbidity, and employ design strategies such as clustering and stratification. It may be particularly practicable to recruit patients with specific patterns of multimorbidity (e.g., dyads or triads) that are associated with the CVD that is being studied. Conversely, enrolling a more heterogeneous population carries the price of an increased sample size and potentially higher cost, implicating a need for innovative study designs (46).

Multimorbidity can also be studied using clinical data from national registries, cohort studies, administrative databases and clinical studies. These rich sources of ‘real world’ subjects could improve understanding of practice patterns and provide insight into benefits and harms associated with specific interventions among key subgroups of the population with various multimorbidity combinations (47,48). For example, a study using the Transcatheter Valve Therapies Registry found that outcomes at 30 days and one year following transcatheter aortic valve replacement were worse in patients with end-stage renal disease, suggesting that this procedure should be used sparingly in these patients (49).

Pragmatic trials with cluster randomization can enroll large numbers of persons with multimorbidity, including under-represented and under-served populations, to study the effectiveness of conventional CVD interventions or therapies (46,50). Further, innovative pragmatic study designs can employ prospective registries as an economical platform. A targeted set of pertinent data elements can be measured longitudinally on a large real-world population to ascertain the impact of various risk factors, multimorbidity, and geriatric syndromes on clinical and/or holistic outcomes (e.g., function, cognition, independence) or in respect to a specific intervention. To that end, very large and comprehensive ‘big data’ networks representative of broad populations have been or are in the process of being generated by CMS, the Veterans Administration, National Institutes of Health (NIH) Health Care Systems Research Collaboratory and a Patient-Centered Outcomes Research Institute (PCORI) data network, (PCORnet), or by pooling electronic health records from multiple health systems (Healthcare Systems Research Network) (51,52). However, standardized

metrics of multimorbidity, as well as validated measures of physical and cognitive function, health related quality of life, activities of daily living, geriatric syndromes (particularly frailty) (53,54), independence, self-efficacy, and other patient-oriented factors pertinent to older adults are still being refined. Inconsistency among definitions and measures, as well as the time and costs required to integrate such measures into established databases, registries and cohort studies have slowed this evolution.

Older adults with multimorbidity might also be more successfully recruited into trials with creative study designs that reduce the burden of study participation (e.g., fixed study duration or remote data collection). Furthermore, including patients with multiple conditions and/or their patient representatives in the phases of study conception, design and implementation will likely help ensure that feasibility, subject compliance and retention, burdens and outcomes of the study are better aligned with patient-centered priorities in respect to both process and endpoints (55).

Risk prediction models need to better gauge benefits and harms attributable to multimorbidity to enhance understanding of the risks and benefits of treatment options and to facilitate shared decision-making. Risk prediction tools may potentially distill complex information into actionable scores. Although the Thrombolysis in Myocardial Infarction risk stratification model predicts risk for all-cause mortality and cardiovascular events over 14 days (56), it and many other cardiology-directed tools overlook risk from multimorbidity or geriatric syndromes, which limits their accuracy and applicability among ‘real world’ older CVD patients (57). The development of risk assessment tools that incorporate the impact of patients’ baseline health parameters (e.g., multimorbidity, physical function, frailty, life expectancy) on the risk of interventions or treatments, and tools that assess outcomes aligned with older patients’ goals and preferences will markedly improve the ability of providers, patients and caregivers to meaningfully engage in shared decision-making. Other efforts are focusing on machine learning and phenomapping as alternative strategies to “match” individual patient characteristics with treatments most likely to achieve the patient’s goals and align with their care preferences (58,59).

Yet, even as research considerations regarding multimorbidity evolve, scalable methods to align goals with measurable outcomes still need to be developed. Likewise, translational deliverables such as policies, guidelines, appropriate use documents, and performance metrics will then need to be structured in order to integrate multimorbidity into customary care.

Clinical guidelines

As previously noted, contemporary clinical guidelines still largely omit the impact of multimorbidity on time to benefit/time to harm, health related quality of life, patient preferences, and tradeoffs in achieving goals (25). The burden of care that derives from following multiple non-integrated guidelines is substantial (60,61) and potentially dangerous. Nonetheless, guidelines could play a pivotal role in highlighting the prevalence of multimorbidity and other geriatric syndromes (particularly frailty and cognitive impairment) and underscore their potential to transform precepts of care (10,22,62).

Recent collaborative work conducted with the guideline development community has addressed specific approaches to improve the applicability of guidelines to older adults with multimorbidity (10,19,62–65). Specific considerations include commenting on adults with multimorbidity, either throughout the guideline or in a specific section, in which the guideline [1] acknowledges the prevalence of multimorbidity and its implications; [2] considers the limits of evidence to patients with multimorbidity; [3] introduces specific recommendations for patients with multimorbidity, including options for deprescribing and palliative care, and [4] provides specific information necessary for clinicians to undertake decision-making that incorporates patient preferences.

Quality metrics and performance measures

Many publicly reported quality measures fail to adequately consider the nuances of caring for patients with multimorbidity, including the complexity of decision-making, lack of standards for evidence-based care in the setting of multimorbidity, care preferences, and difficulties in coordination of care (66). Quality metrics and performance measures generally reflect consensus opinion on what represents “standard of care” in relatively broad clinical contexts (e.g., prompt reperfusion therapy in ST-elevation myocardial infarction). Although such measures allow for non-use of recommended interventions if an appropriate rationale is documented in the medical record, this decision is often based on “gestalt” rather than on clear evidence in multimorbid patients. The American College of Cardiology (ACC) criteria defining satisfactory performance measures for ST- and non-ST-elevation myocardial infarction call for measures that are evidence-based, interpretable, and feasible (67). Acknowledging the limitations of performance measures in certain patient populations, including those with multimorbidity, a consortium that included the ACC has called for performance measures that are integrated, relevant to the complexity of care, and attentive to patients’ needs and goals, (62,68,69) emphasizing shared accountability among patients, clinicians, and health systems (70).

Government organizations

Governmental agencies have roles in the development and funding of research, and in some cases, its translation to practice and policy. The NIH and Agency for Healthcare Research and Quality, as well as philanthropic, non-profit organizations (e.g., PCORI) and the medical and device industry, are promoting research and innovations aimed at improving care for older adults with multimorbidity. The FDA and CMS play a more prominent role in policy development. Synergy across agencies can accelerate common themes to improve clinical care (71). FDA and NIH have encouraged RCTs with expanded inclusion and fewer exclusion criteria, which might permit assessment of treatment effects in older populations with multimorbidity. The FDA has also increased efforts to describe treatment effects by baseline risk and demographic factors (72). CMS initiatives play a key role in translating research into reimbursement policy and in developing incentives for providing high value care. As the healthcare payment system evolves, there is growing recognition that compensation to providers for the time and expertise required to manage patients with multimorbidity can enhance efforts to deliver optimal patient goal-directed care.

Tools and resources to address research needs

Table 2 enumerates existing resources to support research on multimorbidity in older patients with CVD. One notable partner is the PCORI, which was created as part of the Affordable Care Act to support comparative effectiveness research and to engage patients and other stakeholders throughout the research process. As an institute specifically focused on patient-centered priorities, improving care for individuals with multimorbidity is among PCORI's top concerns. To that end, a pilot study co-sponsored by PCORI and the John A. Hartford Foundation is examining the effects of patient-priority aligned care integrated into routine cardiology practice in a large Accountable Care Organization in Connecticut (ProHealth). The study will assess the extent to which patients perceive that they receive care consistent with their health priorities. PCORI is also interested in supporting trials, observational studies, and pragmatic studies to examine the heterogeneity of treatment effects across subgroups. The PCORI sponsored data network, PCORnet, serves as a platform for pragmatic studies and trials.

The DHHS and NIH have prioritized research on multimorbidity in their strategic framework to optimize health and quality of life. NIH Common Fund initiatives on multimorbidity include the NIH Health Care Systems Collaboratory, a large pragmatic trial network studying patients with multimorbidity. The NIA has also funded several initiatives to improve understanding and care of patients with multimorbidity, including support for the Health Care Systems Research Network (9), which comprises several large health care systems, diverse health care delivery models, and the Claude D. Pepper Older American Independence Centers to conduct interdisciplinary multimorbidity research. NIA has funded basic research in animal models to elucidate common biological pathways that may underlie and link multimorbidity. In collaboration with the NIH GeroScience Initiative, the NIA is investigating potential singular therapeutic targets to prevent, alleviate or treat multimorbidity (51). The Agency for Healthcare Research and Quality supported the Multiple Chronic Conditions Research Network platform. Another potential partner, the ACC's National Cardiovascular Data Registry (NCDR), is a portfolio of registries that can serve as a global, patient-centered platform for RCTs, cost-effectiveness research, and post-approval studies. NCDR data can be used alone or merged with longitudinal administrative databases to examine short-term and long-term outcomes in subgroups of patients with CVD and to inform quality improvement. NCDR and the ACC Foundation have established the National Cardiovascular Research Infrastructure to provide a stable clinical research platform, standardize and harmonize CV data collection, coordinate and facilitate data transfer to existing and future registries, and develop enduring educational content to train clinical investigators and site personnel. Currently, the NCDR is considering inclusion into all its registries of a parsimonious set of standardized data elements relevant to older adults, including multimorbidity (specifically heart failure, atrial fibrillation, chronic obstructive lung disease, cancer, diabetes, depression, and liver disease), home functioning variables (cognition, use of a walking assistive device, and activities of daily living), body mass index, and key laboratory data (creatinine, hemoglobin, albumin). Other notable partners include professional societies and funding agencies oriented to nursing, pharmacy and physical and occupational therapy that are involved both in conducting research and in translating

findings into practice, as well as stakeholders in the pharmaceutical and medical device industries.

One approach that might help moderate the burden of the multitude of disease-specific guidelines would be for professional societies to collaborate on cross-disciplinary guidelines (73), perhaps starting with dyads and triads of common conditions (73), and coordinating efforts across disciplines (e.g., internal medicine, geriatrics, hospital medicine, emergency medicine, and surgery), but then evolving beyond specific groupings to address issues with overarching approaches.

A recent evolution of federal and private research initiatives reflects the escalating prioritization of integrating the realities of multimorbidity into specialty care. The DHHS has launched an initiative on multimorbidity, which advances some of the themes introduced at ACC/NIA/AGS workshop: [1] Multimorbidity: a strategic framework; [2] inventory of multimorbidity activities: database of programs, tools, and research initiatives to address the needs of individuals with multiple chronic conditions & the innovative profiles report; [3] evaluation of the strategic framework; [4] multimorbidity among Medicare beneficiaries; [5] multimorbidity measurement framework; [6] multimorbidity research network; [7] implementation actions by DHHS agencies. Related funding initiatives include the NIA RFA-AG-17-059, Multimorbidity in Alzheimer's Disease Impacts Choice of Ancillary Treatments; Agency for Healthcare Research and Quality NOT-HS-16-013, Optimizing Care for People Living with Multiple Chronic Conditions through the Development of Enhanced Care Planning; and PCORI Informing Patient-Centered Care for People with Multiple Chronic Conditions , and Research Spotlight on Multiple Chronic Conditions..

Integration into clinical practice

The management of patients with multimorbidity is an evolving field, with inherent complexities and heterogeneity that challenge basic precepts of single-disease management. Nonetheless, given the significant impact of multimorbidity on CVD care and outcomes, steps to integrate multimorbidity into contemporary CVD standards and management seem fundamental. Table 3 recapitulates some of the key opportunities to integrate multimorbidity into CVD care to better ensure that management is aligned with patient-specific goals. The American Geriatric Society's Guiding Principles for the Care of Older Adults with Multimorbidity provides a broad framework for these objectives (35), but the integration to specialty care remains an ongoing challenge, especially because it modifies a predominantly disease-focused approach to care that cardiologists have relied upon for many decades (74). Additionally, performance measures must also achieve the subtle balance between promoting standardized principles of care and allowing sufficient flexibility to accommodate idiosyncrasies of each multimorbid patient (69,75).

Conclusions and Future Directions

Multimorbidity is endemic in older adults with CVD and substantially impacts the clinical features, diagnosis, management and outcome of the majority of older cardiac patients. The ACC/NIA/AGS workshop on multimorbidity in older adults with cardiovascular disease

highlighted the challenges and opportunities implicit in advancing patient-centered care for the growing population of older patients with CVD and multimorbidity, fostered several collaborations between participants and stakeholders, and advanced the concept of care aligned with individual patient goals as a cardiovascular priority.

The workshop identified challenges and opportunities to advance precepts of multimorbidity, identified research opportunities and resources to integrate multimorbidity into research and clinical care, and identified targets such as practice guidelines and methods to assess and record patients' goals and priorities as part of a paradigm shift from disease-focused to patient-centered care. Research to support this transition is already underway, and opportunities abound for novel research designed to test specific interventions and programs aimed at moving the field forward.

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Abbreviations

ACC	American College of Cardiology
AGS	American Geriatrics Society
CMS	Centers for Medicare and Medicaid Services
CVD	Cardiovascular disease
DHHS	Department of Health and Human Services
FDA	Food and Drug Administration
NCDR	National Cardiovascular Data Registry
NIA	National Institute on Aging
NIH	National Institutes of Health
PCORI	Patient-Centered Outcomes Research Institute
RCT	randomized clinical trial

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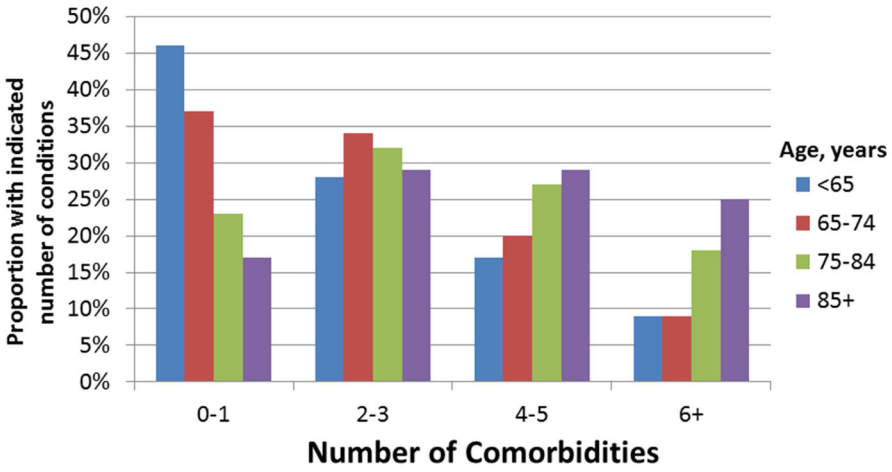


Figure 1. Prevalence of multimorbidity by age

Among Medicare fee-for-service beneficiaries**, t**he number of coexisting chronic conditions increases with age (11). Just over half of beneficiaries <65 years have two or more chronic conditions compared to 63% of those 65–74 years, 77% of those 75–84 years and 83% of those ≥ 85 years.

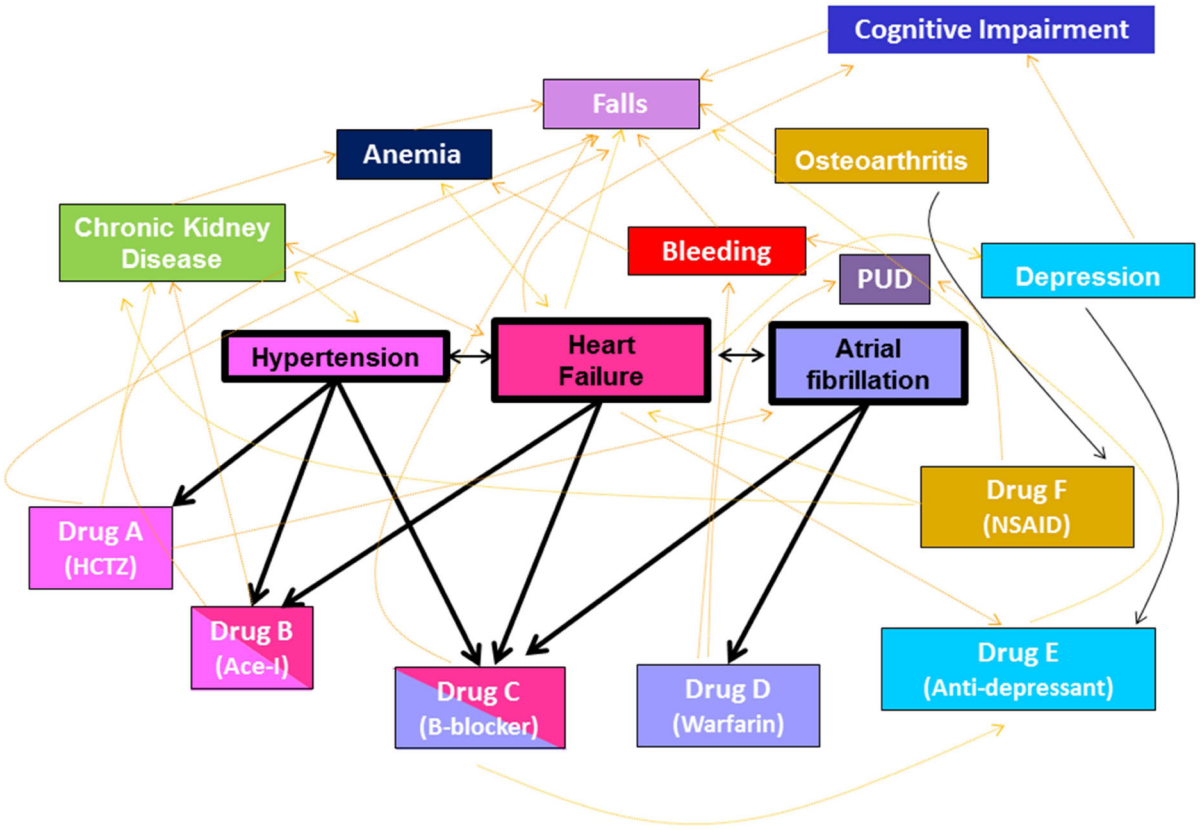
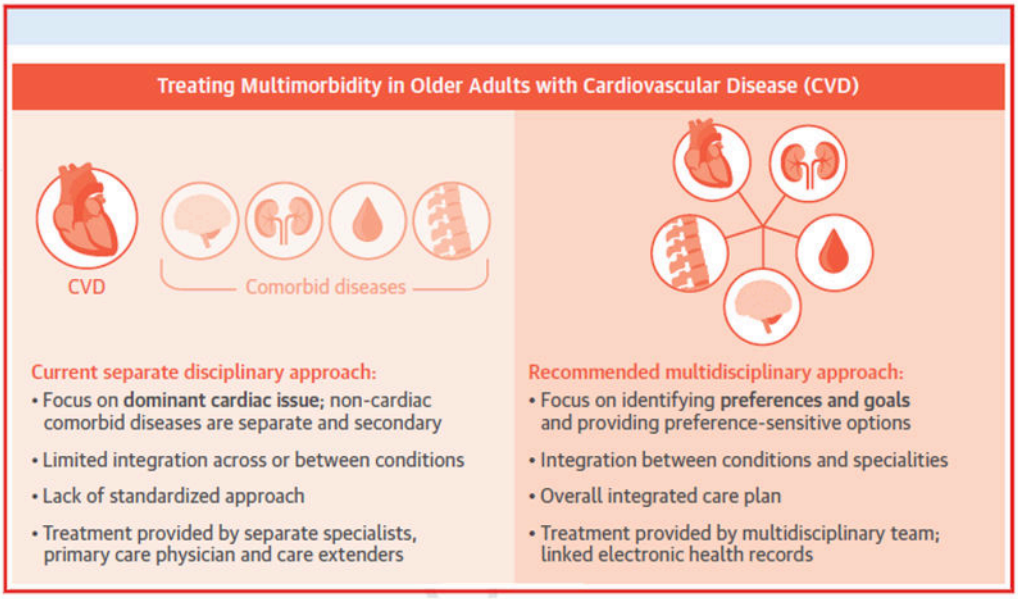


Figure 2. Diseases and medications impacting one another in multimorbidity

Disease and medication interactions may inadvertently induce detrimental effects in the context of multimorbidity. In this schematic, concordant hypertension, heart failure and atrial fibrillation occur in association with discordant osteoarthritis and depression. Whereas the dark lines indicate relatively straightforward intent of treatment in a disease-based model, the orange lines show the many possible interactions between diseases, between drugs, that are likely to escalate instability and adverse outcomes (e.g., inducing secondary renal deterioration, bleeding, anemia, falls, and cognitive decline). Although the figure is complex and difficult to navigate; this mirrors the inherent clinical challenges of managing patients with multimorbidity.



Central Illustration. Redefining cardiovascular disease as a clinical challenge amidst multimorbidity

Differences between current a disease-specific paradigm and the emerging patient-specified goal directed care approach: the latter seeks to address issues emanating from cardiovascular disease in a context of multimorbidity.

Table 1

Selected research gaps and unmet needs in the care of older adults with multimorbidity

I. Research

Ia. Study design

- Inadequate enrollment of older adults and other underserved populations with multimorbidity and geriatric syndromes in clinical trials and registries
- Insufficient inclusion of functional and quality of life outcomes, including maintenance of independence/avoidance of institutionalization
- Lack of studies that address longitudinal care and outcomes across multiple care settings and care transitions
- Limited studies on interactions between disease burden, functional status, family dynamics/social support, and shared decision-making

IIb. Research infrastructure

- Methods to routinely include data elements relevant to multimorbidity in clinical and administrative datasets
- Infrastructure that facilitates pragmatic trials embedded in routine clinical care focused on multimorbidity and patient centered outcomes
- Harmonization of data collection, particularly in extra-cardiac domains, to allow direct transfer from EHR to large registries
- Engagement of patients and caregivers in study design including but not limited to selection of meaningful endpoints
- EHRs able to synthesize patient data across venues, including hospitals, transitional and long-term care facilities, out-patient offices and laboratories, pharmacy, home health, implanted and potentially wearable devices

Ic. Risk prediction models

- Models that incorporate geriatric conditions (e.g. multimorbidity, cognitive function, frailty) for assessing risk and predicting outcomes
- Models that incorporate discordant conditions (e.g. arthritis, neurological disorders) for assessing cardiovascular and non-cardiovascular outcomes (e.g. mobility/function, mood/affect, overall quality of life)
- “User-friendly” patient-specific risk models comprehensible to patients and caregivers

Id. Gaps related to cultural and socioeconomic factors

- Studies on impact of cultural, socioeconomic dimensions (e.g. education, income, living situation, social support), and geographic factors on preferred health outcomes and willingness to participate in research among older adults with multimorbidity
- Studies on health disparities in the care of vulnerable older adults with multimorbidity
- Studies on methods to elicit and incorporate culturally sensitive approaches to care of older adults with multimorbidity in clinical and research environments

II. Clinical Care

IIa. Assessment of patient preferences and goals

- Tools or methods for presenting choices and assisting patients in deciding among options while acknowledging uncertainty
- Methods to incorporate preferences into clinical practice across care settings and providers

IIb. Tools/methods for assessment of health status and quality of life

- Tools to assess health status and quality of life in the context of multimorbidity
- Scalable methods to assess function, health status and quality of life in clinical practice without increasing burden through utilization of EHR
- Methodologies to present and assess trade-offs in health status and quality of life with respect to care options
- Approaches to incorporate health status, function and quality of life data into shared decision-making

IIc. Alternative models of care

- Evaluation of care teams for optimizing care across disciplines and settings (e.g. using the heart valve team model)

- Evaluation of patient-centered medical home as alternative to traditional care for older patients with multimorbidity
- Evaluate telemedicine and wearable devices as means for improving care and outcomes
- Evaluate “health care coach” or “patient navigator” to improve care and outcomes
- Develop and evaluate simple pragmatic care approaches to enhance self-care and preserve function and independence
- Evaluate impact of early introduction of palliative care on clinical outcomes, including patient and caregiver satisfaction

III. Implementation

IIIa. Logistic and methodological limitations to assessing outcomes and aligning outcomes with patient goals

- Approaches for aligning care with desired health outcomes defined by individual patients
- Methods to harness the EHR to facilitate care across multiple providers and venues
- Methods to coordinate care in patients with multimorbidity and ensure that treatment across venues is aligned with patient preferences and without therapeutic competition
- Systems to efficiently communicate relevant information to patients and multiple caregivers in ways that are concise, comprehensible, and sensitive to individuals’ health literacy
- Incorporating life expectancy, time-to-benefit and time-to-harm into shared decision-making

IIIb. Performance measures

- Performance measures that assess quality and value of care provided to older adults with multimorbidity
- Integrate multimorbidity into the EHR
- Modify existing performance measures to account for complexity and patient preferences

CVD: cardiovascular disease; EHR: electronic health record

Table 2

Resources for research on older adults with cardiovascular disease and multimorbidity *

Registries and clinical databases
National Cardiovascular Data Registry (all components)
American Heart Association registries
Veterans Affairs databases
Centers for Medicare and Medicaid Services databases
Healthcare Utilization Project
Clinical trials, cohort studies, and cross-sectional studies
Framingham Heart Study
Atherosclerosis Risk in Communities Study
Multi-ethnic Study of Atherosclerosis
Cardiovascular Health Study
Silver-AMI
Baltimore Longitudinal Study of Aging
Health and Retirement Study
National Health and Nutrition Examination Survey
Duke Databank
NHLBI-sponsored clinical studies (biolincc.nhlbi.nih.gov)
Yale Open Data Access project
Networks
PCORnet
Health Care Systems Research Network
FDA Sentinel
NIH Health Care Systems Collaboratory
Models and tools
PREPARE for advance care planning (prepareforyourcare.org)
Time to Harm and Benefit Assessment
NIH Toolbox/PROMIS (healthmeasures.net)
ePrognosis (ePrognosis.org)
Funding agencies and partners
National Institutes of Health
Patient-Centered Outcomes Research Institute
American Heart Association
American Federation for Aging Research
Longer Life Foundation
Retirement Research Foundation
John A. Hartford Foundation
Robert Wood Johnson Foundation

AMI: acute myocardial infarction; FDA: Food and Drug Administration; PCOR: Patient-Centered Outcomes Research; NIH: National Institutes of Health; NHLBI: National Heart Lung and Blood Institute

*Note that this list is not intended to be all-inclusive

Table 3

Approaches for Integrating Multimorbidity into Clinical Practice

I.	Consider multimorbidity and geriatric syndromes in designing care		
	A.	Routinely assess for the presence of multimorbidity and geriatric syndromes	
		1.	Maintain list in the EHR of all chronic conditions for each patient
		2.	If appropriate, consider screening for frailty and geriatric syndromes (e.g., http://frailtytool.com)
	B.	Evaluate potential impact of concordant and discordant conditions on CVD management	
		1.	Is the presence of comorbid conditions likely to reduce the benefit or increase the risk of CVD interventions (e.g., severe osteoarthritis may diminish the potential benefits of revascularization or heart failure therapies on functional capacity)?
		2.	How will the presence of geriatric syndromes affect response to therapy (e.g., cognitive impairment may reduce adherence to medication and lifestyle interventions; urinary incontinence may reduce adherence to diuretic therapy)?
	C.	Recognize polypharmacy and intervene proactively	
		1.	Discontinue or reduce non-essential medications (e.g., deprescribe)
		2.	When starting a new medication, consider potential drug-drug and drug-disease interactions
II.	Assess patient priorities and goals of care		
	A.	Elicit patient priorities for health care	
		1.	Relative importance of quality of life vs. length of life
		2.	General sense of how aggressive to be in pursuing goals
	B.	Identify patient-specific goals (e.g., maintenance of independence, not becoming a burden, avoiding nursing home, avoiding hospitalization)	
	C.	Engage in shared decision-making	
		1.	Considering the patient's priorities and goals, discuss realistic care options in a non-judgmental manner, outlining potential benefits and risks
		2.	Communicate uncertainty in available data while avoiding any sense of abandonment.
		3.	Come to a joint decision on how best to proceed that is aligned with the patient's priorities and goals
III.	Guidelines and performance measures		
	A.	Guidelines	
		1.	Clearly acknowledge the limitations of guidelines in patients with multimorbidity and offer more flexibility in care options for these patients
		2.	Emphasize the importance of shared decision-making, especially in patients for whom the evidence base is not robust
	B.	Performance measures	
		1.	Develop more robust methods for identifying patients for whom performance measures are applicable and excluding those to whom the measures do not apply
		2.	Develop novel performance measures that specifically assess quality of care in patients with multimorbidity

CVD: cardiovascular disease; EHR: electronic health record