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Pharmacotherapy in Older Adults with Cardiovascular Disease: Report from an American College of Cardiology, American Geriatrics Society, and National Institute on Aging Workshop

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Abstract

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Author Contributions: Janice B Schwartz, MD, Kenneth E Schmader, MD, and Joseph T Hanlon, PharmD, were conference co-chairs and were responsible for choosing and planning talks and editing summaries of all talks and the final manuscript in collaboration with Planning Committee members and Michael W. Rich, MD, Chair of the Planning Committee. Darrell Abernethy, MD, PhD, Shelly Gray, MS, PharmD, Jacqueline Dunbar-Jacob, PhD, RN, Holly M. Holmes, MD, MS, Michael D. Murray, PharmD, MPH, Robert Roberts, MD, Michael Joyner, MD, Josh Peterson, MD, MPH, David Lindeman, PhD, Ming Tai-Seale, PhD, MPH, Laura Downey, DVM, MSM spoke at the meeting and contributed to preparation of the manuscript.

SUPPORTING INFORMATION

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

Conflict of Interest: No authors report conflicts of interest.

OBJECTIVES: To identify the top priority areas for research to optimize pharmacotherapy in older adults with cardiovascular disease (CVD).

DESIGN: Consensus meeting.

SETTING: Multidisciplinary workshop supported by the National Institute on Aging, the American College of Cardiology, and the American Geriatrics Society, February 6–7, 2017.

PARTICIPANTS: Leaders in the Cardiology and Geriatrics communities, (officers in professional societies, journal editors, clinical trialists, Division chiefs), representatives from the NIA; National Heart, Lung, and Blood Institute; Food and Drug Administration; Centers for Medicare and Medicaid Services, Alliance for Academic Internal Medicine, Patient-Centered Outcomes Research Institute, Agency for Healthcare Research and Quality, pharmaceutical industry, and trainees and early career faculty with interests in geriatric cardiology.

MEASUREMENTS: Summary of workshop proceedings and recommendations.

RESULTS: To better align older adults' healthcare preferences with their care, research is needed to improve skills in patient engagement and communication. Similarly, to coordinate and meet the needs of older adults with multiple comorbidities encountering multiple healthcare providers and systems, systems and disciplines must be integrated. The lack of data from efficacy trials of CVD medications relevant to the majority of older adults creates uncertainty in determining the risks and benefits of many CVD therapies; thus, developing evidence-based guidelines for older adults with CVD is a top research priority. Polypharmacy and medication nonadherence lead to poor outcomes in older people, making research on appropriate prescribing and deprescribing to reduce polypharmacy and methods to improve adherence to beneficial therapies a priority.

CONCLUSION: The needs and circumstances of older adults with CVD differ from those that the current medical system has been designed to meet. Optimizing pharmacotherapy in older adults will require new data from traditional and pragmatic research to determine optimal CVD therapy, reduce polypharmacy, increase adherence, and meet person-centered goals. Better integration of the multiple systems and disciplines involved in the care of older adults will be essential to implement and disseminate best practices.

Keywords

cardiovascular medication; adverse effects; de-prescribing; polypharmacy; adherence

The pathogenesis and incidence of cardiovascular disease (CVD) are mechanistically linked to aging and to exposure to conventional cardiovascular disease risk factors.[1–3] A high prevalence of coronary heart disease, heart failure, valvular heart disease, arrhythmias, peripheral arterial disease, and other CVD processes will inevitably burden the expanding population of older adults, but multiple comorbid conditions and common geriatric syndromes that fundamentally alter the risk:benefit relationship for virtually all diagnostic procedures and therapeutic interventions, including medications proven to be effective in younger, healthier individuals, often complicate caring for older adults with CVD. The multiple healthcare providers involved in managing older adults with multiple conditions further complicates care. Optimal person-centered care for the growing population of older adults thus demands that these multiple complex interactions be better delineated and more

fully integrated into routine clinical decision-making and drug prescribing for older adults with CVD.[4]

These issues were the impetus for a series of workshops supported by the National Institute on Aging (NIA), the American College of Cardiology (ACC), and the American Geriatrics Society (AGS) to identify critical knowledge gaps and research priorities for optimizing person-centered care and outcomes for older adults with CVD. The first workshop, in 2015, focused on multimorbidity in older adults with CVD and identified challenges to and opportunities for advancing principles of multimorbidity, identified research opportunities and resources for integration of multimorbidity into research and clinical care, and identified targets such as practice guidelines and methods to assess and record people's goals and priorities as part of a paradigm shift from disease-focused to person-centered care. A product of the conference was a comprehensive state-of-the-art review on multimorbidity in older adults with CVD targeted to the cardiology community.[5] The workshop also stimulated conceptualization of a rationale and vision for geriatric cardiology that would infuse cardiology practice with expanded proficiencies in diagnosis, risks, care coordination, communications, end-of-life, and other competencies required to best manage older adults with CVD. [6]

The second workshop, "Pharmacotherapy in Older Adults with CVD,", took place February 6 to 7,2017, in Washington, District of Columbia. The main objective was to identify knowledge gaps and research priorities for optimizing pharmacotherapy in older adults with CVD within the areas of polypharmacy, adverse drug effects (ADEs), medication adherence, aligning therapy with individuals' goals, and novel approaches to drug prescribing. Drs. Joseph Hanlon, Kenneth Schmader, and Janice Schwartz co-chaired the workshop. Attendees included leaders from the cardiology and geriatrics communities (officers in professional societies, journal editors, clinical trialists, prominent division chiefs) and representatives from the NIA; National Heart, Lung, and Blood Institute; Food and Drug Administration (FDA); Centers for Medicare and Medicaid Services, Alliance for Academic Internal Medicine, Patient-Centered Outcomes Research Institute (PCORI), Agency for Healthcare Research and Quality, pharmaceutical companies, and selected trainees and junior faculty with interests in geriatric cardiology. This article briefly summarizes the conference proceedings, highlighting challenges to optimal outcomes of medical management related to knowledge gaps, too much medication (age-related changes in medication pharmacokinetics (PK) and pharmacodynamics (PD), multimorbidity, polypharmacy, ADEs), and too little medication (adherence, underprescribing). A discussion of the top priorities for research that workshop participants identified follows. Supplementary Appendix S1 details the topics and speakers, and the presentations are available at https://www.acc.org/membership/sections-and-councils/geriatric-cardiology-section/section-initiatives/workshops.

CVD PREVALENCE AND MEDICATION USAGE

CVD is the leading cause of death, a major cause of functional impairment and loss of independence, and the most common disease in older people in the United States. Prevalence of CVD, including hypertension, coronary heart disease, heart failure, and stroke, is 65% to

70% in persons aged 60 to 79 and 79% to 86% in those aged 80 and older.[7] Because of the high burden of CVD in older adults, cardiovascular drugs are the most commonly used therapeutic classes of drugs in older adults. In the National Social Life, Health and Aging Project home medication survey, 15 of the top 20 most frequently used medications in older adults were cardiovascular drugs. Estimated prevalence of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor use (statins) was 50.1%, of antiplatelet agents was 43.0%, of angiotensin converting enzyme inhibitors was 30.4%, of diuretics was 29.5%, of angiotensin II receptor blockings was 13.2%, of antihypertensive combinations was 12.4%, of calcium channel blockers was 10.5%, and of vitamin K antagonists was 6.4%.[8] The high rate of cardiovascular medication use also reflects benefits that research has demonstrated of pharmacological treatment of hypertension to reduce strokes and cardiac events, cholesterol reduction to prevent initial and recurrent coronary events and strokes, anticoagulation to prevent strokes in individuals with atrial fibrillation or mitral valve disease, renin-aldosterone system inhibition to reduce morbidity and mortality in individuals with reduced ejection fraction heart failure, aspirin to reduce myocardial infarctions, and anti-platelet drugs to reduce cardiac events after interventional revascularization procedures. Nevertheless, as noted previously, the applicability of the results of these studies to older adults with multiple chronic conditions, variable social circumstances, and highly individualized healthcare goals is largely unknown. Furthermore, age-related changes in organ function, PK, and PD fundamentally alter the balance between benefits and risks of drug therapy.

CHALLENGES TO OPTIMAL OUTCOMES AND MEDICATION MANAGEMENT

Benefitting from pharmacotherapy requires selecting the right medication at the right dose administered to the right person at the right time for the right duration (5 R’s of geriatric drug prescribing). To achieve this requires consideration of each medication in the holistic context of each person’s psychosocial and healthcare milieu, with an understanding of and appreciation for the inherent effects of aging on organ function and drug metabolism.

Aging changes the PK and PD of medications.[9–11] Pharmacokinetic changes include reduction in renal and hepatic clearance and greater body fat, which lead to altered distribution, metabolism, and elimination of drugs, which increases the risk of ADEs in older adults, including cognitive impairment and falls. Age-related pharmacodynamic changes include altered end-organ responsiveness to drugs and reduced cardiac and baroreflex responses.[1–3] The FDA[12] and International Committee on Harmonization[13] recognized the need to consider potential age-related changes in PK and PD during drug development, but it is not required for premarketing drug evaluation or postmarketing surveillance. Large randomized double-blind studies to reduce cardiovascular morbidity and mortality have generally excluded very elderly adults (≥75) and older adults with multiple comorbid conditions or frailty and have enrolled fewer women than men and more Caucasians than other races.[14] The result is that clinicians often prescribe CVD drugs based on guidelines with limited information on benefits and risks in individuals routinely seen in clinical care (aged ≥75, with multimorbidity, women, functionally impaired or frail older persons). Current guidelines also assume that long-term use of cardiovascular drugs entails

benefits and risks that remain constant over time. Current knowledge of and implementation gaps for CVD pharmacotherapy in older populations are summarized in Table 1.

Factors Resulting in Too Much Medication

CVD does not usually exist in isolation in older adults, the majority of whom have multiple comorbid conditions.[5,15,16] Multimorbidity leads to co-administration of multiple medications, and older adults often take vitamins and dietary supplements with pharmacological effects.[17,18] Polypharmacy is the term often used to describe use of multiple concomitant medications. Polypharmacy has varying definitions, but many define it as 5 or more co-administered drugs because there is a steep rise in the number of potential drug-drug interactions when 5 or more drugs are co-administered. Polypharmacy has increased dramatically in the U.S. older population—from 24% in 2000 to 39% in 2012. [19] The number of co-administered drugs has consistently been shown to be the strongest predictor of prescribing problems.[20–24] A phenomenon leading to an increase in medications in older adults has been termed the “prescribing cascade,” which begins when an ADE caused by 1 medication is treated as a new condition, leading to another medication (e.g., hypertension due to a nonsteroidal antiinflammatory drug (NSAID) leading to prescription of an antihypertensive agent), an over-the- counter drug (e.g., acetaminophen or NSAID for statin myalgias), or a recommendation for a medical device to treat the initial ADE (e.g., pacemaker insertion for bradycardia related to cholinesterase inhibitor).[25,26] Drug-disease interactions (e.g., NSAID-induced worsening of heart failure) that might not be appreciated and shifting goals of care arising from the burden of increasing comorbidity and declining functional status further compound problems with polypharmacy, multi-morbidity, and age-related changes in PK and PD.[27,28]

Deprescribing is defined as the process of stopping a medicine or reducing its dose to remedy polypharmacy, minimize risk of ADEs, and improve outcomes.[29,30] Initial targets for deprescribing to reduce ADEs nationally and internationally have largely focused on reducing use of single medications or classes of medications with the highest risk profiles in older adults, such as opioids, sedative hypnotics, and atypical antipsychotics[31] (e.g., Canadian Deprescribing Network, https://desprescribing.org/caden; Australian Deprescribing Network, http://w11.zetaboards.com/ADeN/index/), and have not targeted cardiovascular medications. Experience with deprescribing in older adults with CVD in the United States is limited. Recently, an expert panel developed criteria to define potentially unnecessary polypharmacy in individuals with limited life expectancy,[32] with the hope that eliminating some medications would improve care and quality of life. One randomized trial of statin discontinuation in individuals enrolled in palliative care programs demonstrated feasibility and participant and caregiver acceptance.[33]

Factors Resulting in Too Little Medication

Medication adherence is required to achieve benefits of pharmacotherapy. The International Society for Pharma-coeconomic and Outcomes Research has standard terms to describe adherence: primary adherence (filling an initial prescription for a new medication), adherence persistence, and overadherence.[34,35] The principal methods for measuring adherence include self-report, pill counts, pharmacy refills, and electronic monitoring.

Primary nonadherence is as high as 30% in primary care settings.[36] Nonadherence for chronic cardiac conditions increases over time and is as high as 60% by 3 years.[37,38] Nonadherence has been associated with poor quality of life, high medical costs, and mortality.[39,40] Older age is not a universally accepted independent risk factor for nonadherence, but factors that may affect adherence in older adults include sensory loss, dysphagia, physical or cognitive impairment, attitudes or beliefs about medications, and regimen cost or complexity. Data are sparse on accurate measurement of adherence in older adults with CVD and multiple chronic conditions.

Adherence interventions tested in heterogeneous populations have included patient and caregiver education; enhanced communication with patients, caregivers, and providers; electronic monitoring and reminders; telephone reminders; lottery-based rewards; and multidisciplinary team monitoring.[41] The more complex and multidimensional interventions tend to meet with more success.[42,43] A recent nationwide randomized trial in individuals with myocardial infarction that incorporated electronic pill bottles, lottery incentives, and social support without direct involvement of physicians or pharmacists did not improve medication adherence or reduce cardio vascular readmissions or costs.[44] In general, studies of adherence interventions in older adults have yielded mixed results, with some showing favorable effects on adherence rates and outcomes, some showing greater adherence rates with no effect on outcomes, and some showing no apparent benefit in adherence or outcomes.[45] Individuals with multiple chronic conditions are the least likely to show improvement despite multifaceted interventions.[41] In contrast, there is moderate-strength evidence that policy interventions that lower out-of-pocket expenses reduce but do not eliminate nonadherence to cardiovascular medications.[41] There is little information on behavioral or motivational aspects of adherence specific to older adults that recognize that they may place greater value on quality of life, ability to function independently, and avoidance of ADEs than on delayed potential benefits.

Underprescribing—Medications may also be underprescribed for older adults. Medication underuse, defined as the omission of potentially beneficial cardiovascular medication therapy or inadequate dose or duration, has been demonstrated for aspirin and beta-blockers after myocardial infarction, antihypertensive therapy for hypertension, angiotensin-converting enzyme inhibitors in heart failure, and anticoagulation to prevent strokes in individuals with atrial fibrillation,[46–49] but data are sparse on the effect of medication underuse on clinical outcomes.[50] A recent prospective population- based cohort study that assessed the prevalence, determinants, and outcomes of medication underuse based on the Screening Tool to Alert to Right Treatment (START)[51] found no association between medication underuse and cardiovascular events (fatal and nonfatal) but found a significant association between medication underuse and competing deaths from noncardiovascular causes.[52] Studies of outcomes in relation to “potential” undertreatment in older populations that have been underrepresented in CVD trials are needed.

Patient Engagement and Shared Decision-Making

Older adults with CVD may have goals that are different from outcomes measured in clinical trials of CVD therapies in younger adults. Concerns of older adults with CVD,

especially those with multiple chronic conditions, tend to be about preservation of quality of life, daily function, and maintenance of independence and less about extension of life.[53] Most cardiology practitioners were not trained in the current era of person-centered care or in preparing for difficult medical decisions in advance of acute events. A special issue of *Health Affairs* in February 2013 reviewed emerging evidence suggesting that patient engagement and shared decision-making can help achieve goals of better quality of care, greater cost efficiency, and better population health, although the evidence base for improvement is limited, and even fewer data are available for what does and does not work in promoting patient engagement. It is likely that successful approaches to patient, family, and caregiver engagement will differ substantially between groups and individuals. Tools to assess a person's capacity for engagement will be critical, as well as tools for evaluating patient or caregiver preferences for level of engagement. Research should apply behavioral economic analyses to the supply (prescriber) and demand (consumer) sides of pharmaceuticals. Training will be needed for tools such as the Open Communication intervention,[54] which is being tested on a wide scale, and healthcare systems will need to promote patient engagement and provide the time and means to achieve it. Barriers to shared decision-making include overworked physicians, insufficient provider training, and clinical information systems incapable of prompting or tracking patients through the decision-making process.[55] Methods to improve shared decision-making included using automatic triggers for the distribution of decision aids and engaging team members other than physicians in the process. Substantial investments in provider training, information systems, and process reengineering may be necessary to implement shared decision-making successfully.[55]

Evolving Technologies and Models of Healthcare

Precision Medicine—Numerous academic medical centers and integrated health systems are evaluating implementation of precision medicine, often focusing on individualized dosing algorithms incorporating renal and hepatic drug clearance estimates, as well as considerations of drug interactions to provide person-specific information at the point of care.[56] For example, inpatient clinical decision support for geriatric prescribing has been associated with fewer falls in the hospital.[57] Pharmacogenomic clinical decision support pharmacogenomics to conventional drug selection and dosing models and has been used for tailoring warfarin and clopidogrel therapy in younger individuals,[58–60] with improved ischemic and bleeding outcomes,[61,62] but there has been limited evaluation of outcomes based on pharmacogenomics in older adults with CVD.[63]

Electronic tools that can be used for medication monitoring are rapidly being developed using digital technology. Passive devices that collect information without patient involvement are becoming more feasible and reliable. Electronic devices currently on the market include smart caps and organizer boxes, some of which collect data and upload it, and smart bottles, which measure capacitance or drug weight. Challenges with these devices involve reliability, cost, ease of use, and need for programming. As research tools, adherence monitoring devices can provide more reliable data on adherence and dosing. Reminder applications are low cost and simple to use but are not linked to specific medications and thus rely on active participation by the patient. Patient acceptance, burden, and privacy

concerns are additional challenges. A combination of ingestible event marker sensors embedded into orally administered tablets has also recently entered the market but has limited applications at this time. Technologies that offer speech-level interactions with consumers are on the horizon.

Telemedicine provides an opportunity to integrate technology with relationship-building and team care to optimize pharmacotherapy and reach patients with mobility and transportation challenges. For example, the U.S. Department of Veterans Affairs telemedicine project, Geriatric Research, Education, and Clinical Center Connect, uses existing infrastructure and a geriatrics multidisciplinary approach to address appropriate prescribing, deprescribing, and polypharmacy. The potential effect of telemedicine on cardiovascular pharmacotherapy in older adults with CVD is unknown, and challenges to its use include reimbursement barriers, lack of standardized and integrated infrastructure, lack of reliable technology, and sustainability.

Models of Care—Innovative models of care may maximize benefit and minimize harms of pharmacotherapy in older adults with CVD.[50] In the outpatient setting, where primary care physicians treat many older adults with CVD, one site participating in the Million Hearts Initiative, a federally sponsored nationwide randomized controlled trial (http://millionhearts.hhs.gov/), is using shared medical appointments to discuss health habits, medications, and how they affect CVD risk. Participants are informed of their Atherosclerotic Cardiovascular Disease score (http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/), participate in individualized shared decision-making, and jointly plan follow-through with the primary care team. In models that included pharmacist-led interventions in hospital, hospital- to-home, outpatient, and community settings, often involving CVD drugs, ADEs were reduced by 35% in older adults.[64] In an early seminal study, a nurse-directed, multidisciplinary model of care improved quality of life, increased medication adherence, and reduced hospital use and medical costs for elderly adults with congestive heart failure.[65,66] The effect of better care coordination in improving CVD prescribing, care, and outcomes has been demonstrated in fully integrated healthcare systems but remains a challenge in the absence of a fully integrated health system or universal medical record access.

RESEARCH DISCUSSION AND KEY RECOMMENDATIONS

Workshop attendees were asked to identify the top research priorities for addressing challenges related to aligning medication prescribing with person-centered treatment goals in older adults with CVD, including tools that are needed to implement patient-aligned drug prescribing in clinical practice; polypharmacy and overuse of medications in older adults with CVD; medication adherence in older adults with CVD; and redesigning drug therapy using novel approaches to prescribing and monitoring in older adults with CVD. The top research priorities for pharmacotherapy in older adults with CVD are presented in Table 1. Discussion of the top research priorities according to theme follows.

Aligning Medication Prescribing with Person-Centered Treatment Goals

Aligning medications with person-centered goals is the foundation of optimal drug prescribing in older adults. To operationalize person-centered care, it is necessary to develop training for healthcare providers for goals-of-care discussions. Development and validation of tools to determine patient preferences and to involve caregivers in decision-making and monitoring are needed. Tools and decision aids for discussing risks and benefits of CVD drugs with patients (incorporating patient preferences) need to be developed and tested with meaningful engagement of patients and families. These discussions and decision-making processes must incorporate patient representatives and take advantage of the skills of specialties and entities committed to person-centered care, including primary care providers, nurses, pharmacists, large pharmacy benefits plans, palliative care, public policymakers, and healthcare administration.

Polypharmacy and Overuse of Medications in Older Adults with CVD

Guidelines for Optimal Prescribing—There is a need to develop medication guidelines for common comorbid conditions that include appropriateness and inappropriateness of prescribing. The guidelines should be based on data from high-quality research studies and interventions. It will be necessary to use traditional (randomized double-blind placebo-controlled trials, cohort studies, registries) and nontraditional study designs (adaptive and pragmatic trials, “big data”) to generate the requisite data. It is also imperative that study outcomes include those relevant to older people, such as quality of life, physical and cognitive function in daily activities, and incidence of common side effects that may limit quality of life. Trials should enroll older adults with CVD and other chronic conditions that commonly occur in combination with CVD and not focus on the less common older adult with few or no comorbid conditions. Analysis and presentation of guidelines should consider the time to benefit and time to harm of therapy with respect to physical and psychosocial function and quality of life in addition to cardiovascular disease morbidity and mortality. Assessment of time to harm versus time to benefit is particularly germane to older adults, because medication ADEs often occur early in the course of therapy (e.g., statin myalgias), whereas potential benefits are often delayed, sometimes for many years. To achieve these goals, patients and caregivers should be included on trial design advisory committees (as PCORI and other organizations advocate), data safety and monitoring boards, and ultimately, guideline committees.

Deprescribing and Potential for Decreasing Medication Overuse and ADEs—Deprescribing has been suggested as an approach to address polypharmacy and ADEs in elderly adults, and research in the area of deprescribing was ranked as high priority. Barriers to widespread application of CVD deprescribing include lack of data on the appropriate duration of cardiovascular pharmacotherapy, including time to benefit and time to harm, and on the effectiveness of cardiovascular medications in older adults with multimorbidity. In addition, clinicians are not well trained in shared decision-making to incorporate patients’ goals of care and functional status when considering complex cardiovascular medication regimens.[67–69]

Deprescribing trials are needed in multiple care settings, in diverse patient subsets to identify those most likely to benefit, and across the range of CVD medication classes. Initial targets should be individuals aged 75 and older with CVD and trials could include patient-activated strategies. Important components would include determining barriers to implementation of deprescribing and optimal strategies to incorporate patient goals and preferences, as well as methods for monitoring and evaluating adverse withdrawal events and therapeutic failures with deprescribing. A by-product of this conference and one of the first steps to stimulate more work in this area is the recently announced NIA funding opportunity to create a collaborative network to advance deprescribing research for older adults with multiple chronic conditions (https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-19–005.html).

Although dietary and exercise interventions as alternatives to or in conjunction with drug therapy are underrepresented in the literature on treatment of CVD in elderly adults, they may provide benefits affecting other conditions than CVD. Comparisons of nonpharmacological and pharmacological interventions for common types of CVD in older persons should also be a high priority as a way to decrease the number of medications prescribed.

Once sufficient data have accumulated, studies are needed to develop, test, and identify the most effective methods of dissemination and implementation of best prescribing practices. To facilitate implementation, it will be necessary to develop standardized medication review and management tools to assess the status of therapy. This will require enhanced communication and interoperability between electronic health record (EHR) systems and between EHR systems and community pharmacies, as well as development of systems to facilitate instant, integrated, efficient communication between systems and between healthcare providers at the point of care. To engage patients in the implementation process, it is critical that communication tools be developed that can be customized to individual characteristics and incorporate individual preferences.

Medication Adherence in Older Adults with CVD

Accurate methods for measuring adherence in older adults are needed. Electronic prescribing has brought new opportunities and challenges. Methods will need to involve merging multiple sources of data from pharmacies, medical records in hospitals and clinics, and patients and caregivers. It is also necessary to determine ways to incorporate adherence measures into clinical care and the EHR.

Once adherence can be accurately assessed, nonadherence can also be identified, and it will be essential to develop methods to determine underlying reasons for nonadherence in older adults and to predict nonadherence. Behavioral drivers need to be determined, and strategies for behavioral change in older patents need to be evaluated. Incentives individualized for patients, clinicians, and healthcare systems should be considered. A priority should be determining the most effective and cost-effective methods and technologies to improve adherence. This will need to be determined for specific patient groups (disease, sex, race, health literacy), for specific care settings, and during care transitions. It will also be important to explore factors related to medication packaging, instructional content and method of messaging and delivery, person(s) providing instructional content, recipient of the

education (patient, caregiver), and patient preferences for learning and medication management. In other words, adherence interventions must be person-specific, recognizing patients' needs, cultural backgrounds, and varying circumstances; healthcare professional, patient, and caregiver collaboration is essential; and time and reimbursement are needed for these efforts.

Redesigning Drug Therapy Using Novel Approaches to Drug Prescribing and Monitoring

The medical care system in the United States is undergoing change that could promote better CVD medication therapy in elderly adults. Most hospitals and healthcare systems have adopted patient-focused telemedicine, whereas telehealth that focuses on populations has been less uniformly adopted. These systems are neither standardized across domains within a system nor integrated across systems and do not use standard platforms. Major needs are coordination of care within and between health-care sites and caregivers and development of tools (technological, paper, social networks) to facilitate communication and medication prescribing, review, and monitoring. Components for investigation include "medical homes" with clear designation of primary prescribers, provision of point-of-care real-time digital data, including pharmacogenomic information (drug clearance, risk related), over-the-counter medications and dietary supplements, care goals, and physical function and cognitive status to guide medication prescribing and evaluation. Efficient, easy-to-use interfaces for data need to be created. Care teams for follow-up and patient education that incorporate nurses, pharmacists, medical assistants, and peer groups, including healthcare navigators, should be evaluated. A largely unexplored area in this age group is the potential role for social media and digital medicine (e.g., cellphone or computer applications, wearable devices) in monitoring medication effects and improving medication use. For digital medicine to be used in many older persons, strategies to address health and computer literacy will be needed, along with device adaptations to accommodate age-related limitations related to arthritis, vision loss, decreased hearing, and mobility as well as lack of universal internet or computer accessibility.

SUMMARY

Drug prescribing in older adults with CVD is complex (Figure 1). Optimal prescribing requires an approach that addresses the whole person. Older adults with CVD often have multiple medical conditions, and treatment risks and benefits must be balanced across multiple diseases. The medication regimen and potential treatment benefits should be considered in the context of the person's life expectancy and healthcare preferences. Challenges are to acquire novel data on best ways to achieve these goals, to educate and disseminate the information, and to develop systems and funding mechanisms to implement optimal CVD medication management strategies. To accomplish these objectives, substantial involvement will be needed from prescribers, patients, healthcare systems, researchers, and entities providing infrastructure for these efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Knowledge and Implementation Gaps for Interventions to Reduce ADEs

- Best and most efficient methods for detection and prevention of ADEs
- Prioritization of efforts to reduce ADEs
- Funding for drug safety research, education and dissemination, and implementation efforts

Knowledge and Implementation Gaps for Optimizing Adherence in Older Adults

- Best and most efficient methods for detection of nonadherence
- Best and most efficient methods for individualized multidimensional approaches to improve adherence to person-centered therapies (healthcare teams, individual and caregiver education and support, technology-based platforms)
- How to incorporate successful techniques into clinical care (implementation into systems, overcome financial and efficiency obstacles)

Knowledge and Implementation Gaps for Newer Approaches to Care in Older Adults with CVD

- Dosing models that include a broad range of personalization factors
- Cognitive and interventional studies to learn how best to incorporate elements of precision medicine in routine clinical care
- Evaluation of new technologies such as telemedicine and wearable devices to improve CVD therapy in older adults
- Effectiveness, cost-effectiveness, implementation, and integration of multidimensional and interdisciplinary care models in routine care
- Practical methods to integrate health care services, provide universal access to healthcare information, and optimize coordination of care programs

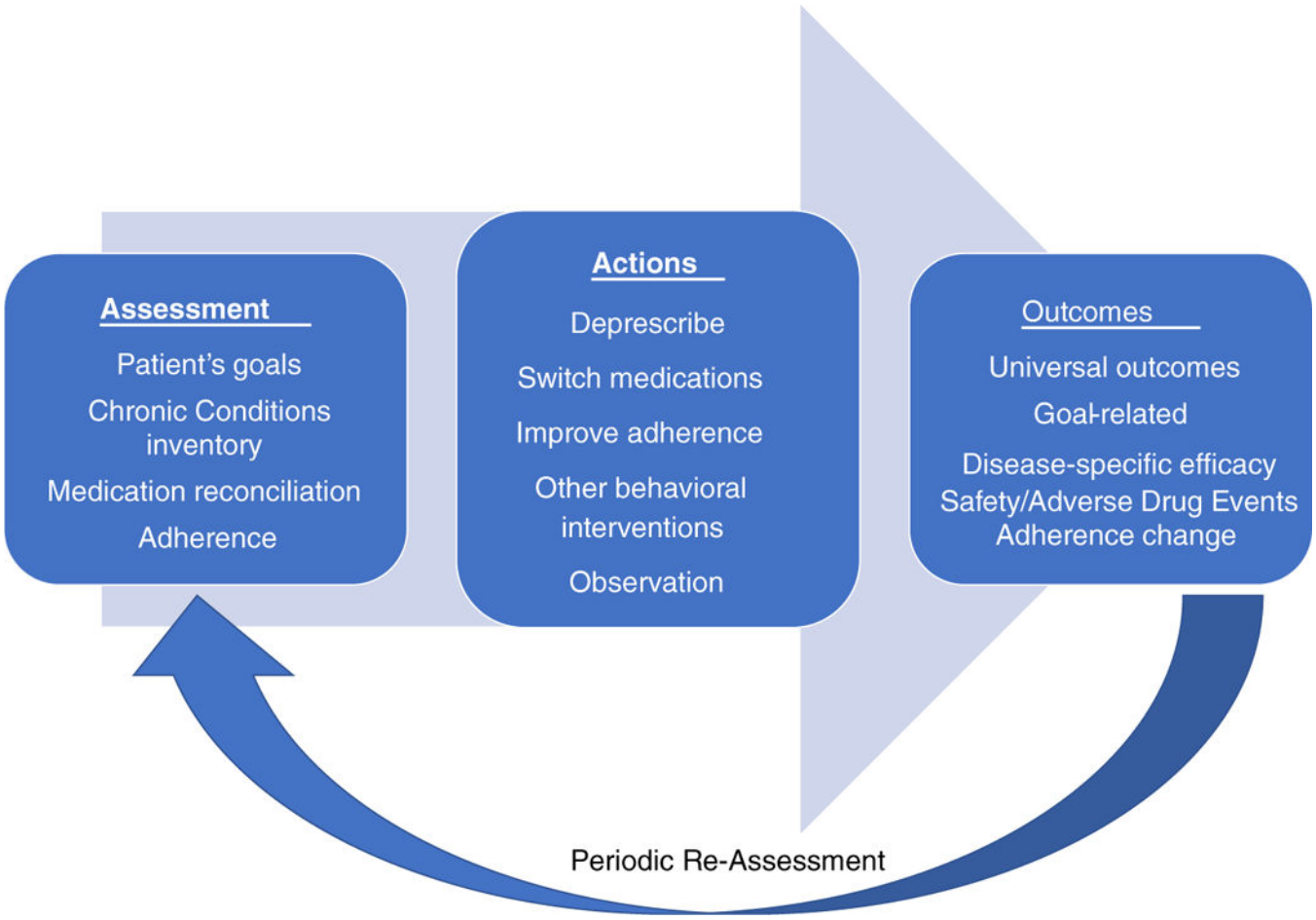

Figure 1.
Steps in management of medications in older adults with cardiovascular disease.

Table 1.

Research Knowledge and Implementation Gaps and Top Priorities for Research

Knowledge and Implementation Gaps	Top Research Priorities
Benefits of Cardiovascular Pharmacotherapy in Older Populations	
• Pharmacokinetic and pharmacodynamic data for dosing of effective CVD therapies • Efficacy trials in elderly adults reflective of entire population • Data to determine appropriateness of use or underuse of cardiovascular drugs in multimorbid, frail, and very old adults	• Develop medication guidelines for older adults with CVD and multiple chronic conditions based on: a. Trial data (current and new), when available b.Consensus in absence of trial data • Determine best methods for dissemination and implementation of best prescribing and monitoring practices
Aligning prescribing with person-centered goals	
• Assessment of individual goals in older adults with CVD • Assess patient priorities related to health care • Patient perceived tradeoff of benefit vs risk regarding CVD therapy	• Develop training for goals-of-care communication skills • Develop and validate tools to determine patient preferences
Interventions to reduce ADEs from CVD pharmacotherapy	
• Best, most efficient methods for detection and prevention of ADEs • Prioritization of efforts to reduce ADEs • Funding for research, education and dissemination, and implementation efforts	• Perform clinical trials of deprescribing in patient subsets and medication classes (define benefits and potential harms; time to benefit or harm; behavioral, communication, and implementation methods) • Comparison of nonpharmacological strategies and pharmacological interventions
Optimizing adherence in older adults with CVD	
• Best, most efficient methods for detection of cardiovascular drug nonadherence • Best, most efficient methods for individualized multidimensional approaches to improve adherence to person-centered therapies for CVD • Incorporation of above techniques into clinical care • Interventions to improve adherence to appropriate cardiovascular medications in elderly adults	• Develop accurate, efficient methods to measure adherence • Determine underlying factors responsible for nonadherence • Determine best methods to optimize adherence
Approaches to care in older adults with CVD	
• Dosing models that include a broad range of personalization factors • Cognitive and interventional studies to learn how to best incorporate elements of precision medicine in routine clinical care of older adults with Cvd • Evaluation of new technologies such as telemedicine to improve CVD pharmacotherapy in older adults • Effectiveness, cost-effectiveness, and implementation and integration of multidimensional and interdisciplinary care models to improve CVD pharmacotherapy in routine care • Practical methods to integrate health care, provide universal access to healthcare information and coordination of care programs	• Develop standardized medical review and management tools that can be individualized for individual characteristics and preferences • Develop methods to improve communication interoperability between electronic health record systems, prescribers, and pharmacies and between all systems to the point of care • Develop methods to achieve person-centered CVD care for older adults that involves multidisciplinary collaboration

ADE = adverse drug effect; CVD = cardiovascular disease.