Cardiovascular Disease in the Elderly: Proceedings of the European Society of Cardiology-Cardiovascular Round Table

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Institution(s) where work performed
CRT Online Plenary Meeting

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Word count: 4,645 (excluding references and abstract); Abstract 211

Abstract

The growing elderly population worldwide represents a major challenge for caregivers, healthcare providers, and society. Older patients have a higher prevalence of cardiovascular (CV) disease, high rates of CV risk factors, and multiple age-related comorbidities. Although prevention and management strategies have been shown to be effective in older people they continue to be under-used, and under-studied. In addition to hard endpoints, frailty, cognitive impairments, and patients' re-assessment of important outcomes (e.g., quality of life versus longevity) are important aspects for older patients and emphasize the need to include a substantial proportion of older patients in CV clinical trials. To complement the often skewed age distribution in clinical trials, greater emphasis should be placed on real-world studies to assess longer-term outcomes, especially safety and quality of life outcomes. In the complex environment of the older patient, a multidisciplinary care team approach with the involvement of the individual patient in decision-making process can help optimize prevention and management strategies. This paper aims to demonstrate the growing burden of ageing in real life and illustrates the need to continue primary prevention to address cardiovascular risk factors. It summarizes factors to consider when choosing pharmacological and interventional treatments in the elderly, and the need to consider quality of life and patient priorities when making decisions.

Keywords: risk assessment, older people, primary prevention, antiplatelet, anticoagulant, coronary revascularization

Introduction

Globally, the population is ageing, with older people becoming a proportionally larger share of the total population.[1, 2] In Europe in 2017, more than 20% of the population was age ≥60 years, and this is projected to increase to 35% by 2050. The incidence of cardiovascular disease (CVD) increases with age from about 40% in adults aged 40-59 years, to 75% in those 60-79 years, and 86% in those >80 years.[3] This has been linked to several factors such as increased oxidative stress, inflammation, apoptosis and overall vascular and myocardial deterioration associated with ageing, as well as to a higher risk for other morbid conditions including frailty, obesity, and diabetes.[3]

While ageing is often measured chronologically (i.e., the number of years since birth), this does not reflect the distribution of functional capacities, health, and productivity within the older population.[4 5] Clinical trials have a need to "categorise" patient populations for analyses, and often use arbitrary cut-offs of over age 65 years, 70 years, 75 years, etc. However, a review of 20 guidelines found that all used the term elderly, but 17 did not define the term in anyway.[6] The 2021 ESC Guidelines on CV prevention, and the Systemic Coronary Risk Estimation 2-Older Persons (SCORE2-OP) risk prediction tool used a cut-off of 70 years of age.[7, 8] Clinically when making management decisions, elderly or older age should be based less on chronological age and more on defining the risk and outcomes for an individual patient.

This article is the product of presentations and discussions during a virtual Cardiovascular Round Table (CRT) workshop organised in May 2021 by the European Society of Cardiology (ESC). It aims to demonstrate the need to continue primary prevention for cardiovascular risk factors, to summarise important factors when choosing treatments for older patients, and the need to consider quality of life and patient priorities when making decisions.

CV risk assessment in older people: Are we over treating or under treating?

Factors to consider when assessing risk of CVD in older people

In older people, the lifetime benefit from CVD risk-factor treatment should consider absolute CV risk, life expectancy, competing (non-CV) risks, and efficacy and safety data from randomised controlled trials (RCT) (Figure 1).[7, 9] Moreover, management decisions should be patient-centric and consider patient preferences, frailty, comorbidities, and polypharmacy.

Risk assessment tools for older people

While age is a strong predictor of risk, the PROSPER trial demonstrated that age alone does not automatically put an individual at high risk, especially in the primary prevention setting.[10] Therefore, risk prediction tools can help identify patients at higher CV risk who may potentially benefit from treatment. Tools designed for the general population can be inaccurate in older people.[7, 11] The relationship between many risk factors and CVD decreases with age, and competing risks become increasingly important.[7] In addition, older patients are generally at higher risk of adverse drug events, so it is important to identify those individuals who benefit from preventive treatment.

In 2021, the SCORE2-OP tool was developed and validated to estimate 5- and 10-year CVD risks of both fatal and nonfatal CVD events (myocardial infarction, stroke), in adults aged ≥70 years.[7] The sex-specific scores include age, smoking status, systolic blood pressure, and high-density lipoprotein cholesterol and are adjusted for competing risks. Therefore, the threshold levels in different risk categories are higher in older age groups, in order to avoid overtreatment in older persons. The decision to initiate preventive therapy should consider that

both benefits and risks of treatments are impacted by age, and therefore, should be made on an individual basis with the patient.[8] In older people the focus should be on the lifetime benefit of treating risk factors rather than 10-year CVD risk.[9] Risk calculators are available online at www.u-prevent.com.[12]

Primary prevention strategies in older people: Is it ever too late?

Given that CVD begins at a young age, primordial and primary prevention strategies to address risk factors should start early to prevent CV events at older age.[13] While, data show that it is never too late to initiate risk factor management strategies, the goal of preventative medicine in older adults is somewhat different; focusing not only on reduction of morbidity and mortality, but more significantly on maintenance of function and preservation of quality of life. The 2021 ESC guidelines on CVD prevention include a section focused on older adults aged ≥70 years, acknowledging the importance of primary prevention throughout the lifespan.[8] This should be delivered in an individualized and patient-centred manner, focusing on outcomes important to the patient, and using interventions with the best evidence and least risk to their day-to-day function.

General considerations when using pharmacotherapy in older people: In general, when addressing primary prevention in older adults, the risk of CVD, which is higher by virtue of age, needs to be balanced with the evidence for potential benefit of a medication in an older population, as well as the potential risk of that medication in that individual patient. When doing so, it is important to keep in mind that a number of factors can all lead to well-intentioned, evidence-based medications being poorly tolerated by the older adult or even resulting in harm. Factors that should be considered include changes in pharmacokinetics and pharmacodynamics that occur with age, increased risk and susceptibility to disease-drug interactions, drug-drug

interactions, and adverse events with polypharmacy in older adults, and varied and unexpected clinical response to medications.[14, 15] For example, the prescription of a statin for a high-risk individual could lead to myalgias that prevent performance of activities of daily living, or an antihypertensive medication in an individual with an untreated blood pressure of 160/90 mmHg, may result in orthostatic hypotension that can result in injurious falls.[14, 15] It is important to engage in shared decision-making and practice patient-centred care, providing the best estimate of risks and benefits based on the evidence and discussing the patient's values, preferences, and risk tolerance. Clinicians and patients may inadvertently have opposing goals, with patients being more concerned about symptoms, functional and cognitive status, and quality of life, and clinicians being more interested in preventing major cardiac adverse events or reducing mortality rate.[14, 15] Discussing an individual's values, and when in keeping with their preferences, addressing non-pharmacologic risk reduction, such smoking cessation, diet and exercise and when needed, starting pharmacotherapy at low doses and titrating slowly, can help ensure the best possible outcome in this vulnerable patient population.

In older people, the ability to follow lifestyle or pharmacological strategies can be impacted by cognitive and emotional factors.[8] Cognitive decline shares many risk factors with CVD, including high cholesterol, and high blood pressure, obesity, diabetes, physical inactivity, smoking, and poor diet.[16] In addition, higher levels of cardiac troponin T have been associated with cognitive decline in older adults independent of CVD.[17] The importance of primary prevention is underscored by the fact that CV events have been associated with accelerated cognitive decline over time.[18]

Hypertension: The prevalence of hypertension in older patients is very high, for example, in the U.S. the prevalence in individuals 20-44 years was reported to be 28%,

increasing to 77% in those ≥65.[19] Multiple RCTs in older people have demonstrated the benefits of blood pressure lowering in both fit and frail people, with the greatest absolute benefit being seen in those 75-80 years of age (Table 1).[20-25] However, this benefit is not without some degree of risk, with estimations based on US population data suggesting intensive blood pressuring lowering, such as that in the SPRINT trial, would result in >56,000 episodes of hypotension, >34,000 episodes of syncope and nearly 89,000 episodes of acute kidney injury annually.[23, 26] Therefore, universal implementation of intensive blood pressure lowering has great potential benefit, alongside potential detrimental consequences.

The older adult population is very heterogeneous, with large variation in function, frailty and independence, necessitating a person-centred, rather than a "one-size fits all" approach to balancing the risks and benefits.[27] While older adults with preserved function should often be treated similar to younger adults, those with advanced frailty and functional dependence should have their hypertension management reassessed, with consideration of deprescribing and blood pressure leniency to avoid further functional impairment from adverse effects.[15, 28-30] Clinical decision making for older adults in between these two spectrums is most challenging, requiring a tailored approach considering comorbidities, life expectancy, function, frailty, as well as patient preferences in a process of shared decision-making. The 2018 ESC/European Society of Hypertension guidelines recommend offering antihypertensive treatment to older adults (>65 years, including individuals >80 years with very high systolic blood pressure), taking into account factors such as comorbidities, polypharmacy, frailty and dependence, and not viewing age alone as a barrier to the treatment of hypertension.[31] In addition, the ESC CVD prevention guidelines recommend lowering blood pressure to <140/90 mmHg, and to consider a lower systolic blood pressure target of 130 mmHg in those ≥70 years, if tolerated.[8]

Hyperlipidaemia: The prevalence of hyperlipidaemia is also more frequent in older people. In a European study, hyperlipidaemia was present in 76% in older people (mean age 69 years) compared to 41% in younger (mean age 29 years) people.[32] While evidence supports the benefit of lipid-lowering therapy in older adults with known vascular disease, the evidence for primary prevention in older adults is less clear.[33, 34] A meta-analysis of 8 primary prevention trials in people ≥65 years, at high CV risk, found a significant reduction in the risk of MI and stroke (39.4% and 23.8%, respectively) with statins versus placebo (Table 1).[35] Primary prevention studies in people >75 years are more limited however, and it is difficult to extrapolate data from younger age groups to this population.[33, 35, 36] A meta-analysis of 28 statin trials found a significant reduction in major cardiovascular events (MACE) in all age groups, with a 13% reduction in events per 1.0 mmol/L reduction in LDL cholesterol in patients over 75 years old, however only 8% of participants were in this age group.[33]

While older adults are intrinsically vulnerable to CVD, thereby increasing the potential benefit of statin, they are also susceptible to frailty, sarcopenia, polypharmacy, and multi-morbidity, increasing the risk of statin-related adverse effects and compounding the functional burden of such adverse effects. Additionally, statins have a rather short time-to-harm, with a relatively long time-to-benefit of at least 2-2.5 years, making life expectancy very pertinent when prescribing primary prevention statin.[37, 38] It is unlikely that benefit would outweigh risk in those with a limited life expectancy, however many older adults have an anticipated prognosis of >2.5 years, making shared decision-making and consideration of individual patient's goals and values essential. Current data to inform decisions on primary prevention cholesterol management in older adults are limited, but two large randomized controlled trials are underway. STAREE and PREVENTABLE are both designed to assess the role of primary prevention statins in patients

≥70-75 years and include outcome measures relevant to older adults, such as independence and disability.[39, 40]

The ESC CVD prevention guidelines provide a class IIb recommendation (may be considered) for initiation of statins for primary prevention in older adults aged ≥70 if at high 10-year CVD risk, when assessed using SCORE2-OP, a risk score validated to estimate 5- and 10-year CVD risk in older adults aged ≥70 years.[7, 8] However, the decision to use statin therapy for primary prevention in older adults should be individualised, based on frailty, estimated life expectancy, time to benefit, comorbidities and patient preference.

Diabetes: The prevalence of type 2 diabetes mellitus increases with age.[41] Metformin has been shown to reduce the risks of MI, CV death, and stroke in overweight patients with diabetes compared to conventional therapy (Table 1),[42] and the both the 2019 ESC guidelines on diabetes and 2021 ESC CVD prevention guidelines recommend it as first-line therapy for primary prevention in patients with diabetes.[8, 43] Two newer classes of medications have been found to lower blood glucose and reduce CVD events in those at high risk: SGLT-2 inhibitors[44, 45] and GLP-1 receptor agonists.[46-48] Post hoc analyses of pivotal trials show that these agents have similar effect on CV outcomes across age categories including those ≥75 years (SGLT-2 inhibitors)[44, 45] and those ≥65 years (GLP-1 receptor agonists).[46-48] ESC guidelines recommend these agents for primary prevention in patients with DM and CKD, and consideration of their use in those at high or very high CV risk.[8, 43]

Aspirin: The evidence for use of aspirin in those with vascular disease (secondary prevention) is unequivocal. However, three more recent randomized controlled trials (ARRIVE, ASPREE and ASCEND) have led to contention about its role in primary prevention (Table 1).[49-52] While two of these trials were not specific to an older adult population, the ASPREE trial

randomized nearly 20,000 patients aged 70 years and above, without known CVD, to aspirin or placebo.[52] After 4.7 years of follow up, the rate of CVD was unchanged (HR 0.95, 95% CI 0.83-1.08) but the rate of major bleeding was increased (HR 1.38, 95% CI 1.18-1.62) with aspirin compared to placebo in these older adults. A 2019 meta-analysis found no reduction in CV mortality with aspirin, but did show a lower risk of non-fatal myocardial infarction (RR 0.82, 95% CI 0.72-0.94) and stroke (RR 0.87, 95% CI 0.79-0.95), with a higher risk of major bleeding (RR 1.5, 95% CI 1.33 to 1.69), intracranial bleeding (RR 1.32, 95% CI 1.12-1.55) and major gastrointestinal bleeding (RR 1.52, 95% CI 1.34-1.73); with a number needed to harm of 222 for major bleeding and a number needed to treat of 357 to prevent one myocardial infarction.[53] The use of aspirin for primary prevention in selected patients at low bleeding risk and high or very-high CV risk remains controversial. However, overall, in the majority of older adults, the increased risk of bleeding appears to outweigh the CV primary prevention benefit, with many national and international guidelines downgrading or eliminating their recommendation for aspirin altogether in older adults.[14, 54, 55] The 2021 ESC CVD prevention guidelines recommend making decisions in healthy individuals <70 years of age with (very) high CVD risk, on a case-by-case basis, with consideration of both ischaemic and bleeding risks.[8] The risk of bleeding may be even more important in older patients, and any consideration of use for primary prevention should be discussed with the patient.[56, 57]

Smoking is a known major cause of CVD, with 1 in 10 CV deaths worldwide being attributable to smoking.[58] Tobacco cessation has been shown to reduce CV risk even among people ≥60 years (Table 1).[59] Excess CV risk decreases with time since tobacco cessation, with benefits accruing within <5 years of quitting.[59, 60] The ESC CV prevention guidelines recommend that clinicians encourage all smokers to quit, including those ≥70 years.[8]

Diet: Dietary modifications have been shown to lower the risk of CV events (Table 1).[61, 62] In the PREDIMED RCT in people 55-80 years at high CV risk, a modified Mediterranean diet was associated with a 28-30% reduction in MACE over a median 5-year follow-up.[61] Similarly, in the EPIC, multicentre cohort study in people ≥60 years without CVD, a modified Mediterranean diet was associated with a significantly longer life expectancy, with benefits increasing with increasing adherence to the diet.[62] The ESC CVD prevention guidelines focus on the importance of maintaining a more plant-based diet, low in saturated fat, high in whole grains, fruit, vegetables, nuts and fish, while reducing red meat, alcohol and sugar-sweetened beverages.[8] These lifestyle recommendations are applicable to all age groups.

Currently, there is insufficient evidence of benefit of vitamin C, D, or E in prevention of CVD.[63-66] Evidence for omega-3 fatty acid supplementation is conflicting. A 2020 Cochrane review suggested little to no effect of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on mortality or CV health.[67] In a more recent meta-analysis (2021), EPA monotherapy was associated with a reduction in cardiovascular mortality, non-fatal myocardial infarction, coronary heart disease events, MACE, and revascularization.[68] While this evidence is not specific to older patients, it suggests that omega-3 fatty acid supplementation, specifically EPA, may be useful for prevention of CVD, however, there was an increased risk of AF and total bleeding events.

Although the risk associated with other less proven vitamin supplementation is low, it is important to remember that many older adults already struggle with polypharmacy and pill burden. Therefore, taking pills which are unlikely to provide benefit can result in worsening lack of appetite due to the number of pills ingested, as well as potential for medication non-adherence related to increased pill burden.

Exercise: Multiple observational studies have demonstrated the benefits of exercise for primary prevention of CVD (Table 1).[69-72] The Honolulu Heart Program, a cohort study in men aged 71-93 years, found that those who walked ≥1.5 miles/day had a 50% lower risk of CVD versus those who walked <0.25 miles/day ($p<0.01$).[69] In the Zutphen Elderly Study in men aged 64-84 years, self-reported physical activity proportionally decreased the risk of all cause (23%) and CVD (30%) mortality with increasing levels of activity.[70] Furthermore, maintaining activity levels, or engaging in small increases in the frequency of physical activity (even 1-2 times/week) have been associated with significantly reduced risk for total CVD among older people aged ≥60 years.[71]

Individuals of all ages can benefit from implementation of a safe, tailored exercise routine.[14, 73] While moderate-to-vigorous activity is advised in the ESC CVD prevention guidelines, baseline fitness should be considered.[8] Even frail older adults can benefit by moving from an inactive state to performing any physical activity. Therefore, although 150-300 minutes/week of moderate intensity, or 75-150 minutes/week of vigorous intensity aerobic exercise is preferred, it is recommended that even those who cannot achieve these levels be encouraged to stay as active as their abilities and health conditions allow, while reducing sedentary time to reduce CV risk.[8]

The guidelines also recommend exercise-based cardiac rehabilitation programs for patients for secondary prevention and for patients with HF.[8] Programs should be medically supervised, multidisciplinary, and comprehensive, and home-based interventions can be considered. Exercise-based cardiac rehabilitation should include both aerobic and muscular resistance exercise, address all recognized CV risk factors, and should be individualised.

Treatment decisions: When should we use aggressive interventions vs. medication vs. no treatment?

Decision making for antithrombotic treatments in older people (antiplatelet, anticoagulant, and combination therapy)

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults, and the prevalence is expected to double by 2060.[74] Increasing age is an important risk factor, and approximately 70% of patients are 65-85 years old.[75] However, these patients are also at increased risk of bleeding, which makes the use of antithrombotic therapies one of the most challenging management decisions in older people.[76, 77]

Non-vitamin K antagonist oral anticoagulants (NOACs) have demonstrated improved efficacy and safety compared to warfarin in older people.[78] A meta-analysis of RCTs included 71,683 older people with AF, of whom 30-40% of were ≥75 years.[78] NOACs significantly reduced stroke or systemic embolic events by 19% (relative risk 0.81, 95% CI 0.73-0.91; p<0.0001) compared with warfarin. Although there was a greater risk of gastrointestinal bleeding, NOACs significantly reduced all-cause mortality and intracranial haemorrhage, with a similar risk of major bleeding compared to warfarin. Results were consistent in patients <75 and ≥75 years.[78] Low-dose NOAC regimens yielded similar benefits, with a better safety profile than warfarin, and thus, might be useful for patients who have a high bleeding risk.[78]

Bleeding risk is also a major concern in older patients with AF and concomitant coronary artery disease (CAD) who need both anticoagulant (e.g., NOAC or vitamin K antagonist [VKA]) and antiplatelet therapy (e.g., aspirin or a P2Y12 inhibitor).[79, 80] Dual therapy has been associated with increased bleeding, and increased mortality,[80, 81] and triple therapy (e.g., NOAC, aspirin,

and clopidogrel), has been associated with higher risks compared to dual therapy or monotherapy.[81, 82]

The 2021 European guidelines recommend restricting the use of concomitant anticoagulant and antiplatelet therapy to patients with a clear indication for both (e.g., AF plus PAD, CAD or cerebrovascular disease, particularly if treated with percutaneous revascularization and stent implantation). Further, a NOAC is preferred over a VKA, dual therapy should be continued for only 6-12 months, and duration of use of triple therapy including aspirin should be minimized.[74, 83]

However, the guidelines state that an elevated risk of bleeding is not a reason to withhold anticoagulants or to automatically use lower doses, even for older patients.[74] Rather, therapy should be individualised, modifiable risk factors addressed, and patients should be followed-up more frequently. Similarly, frailty, risk of falls, and cognitive issues are not reasons to withhold therapy.[74] Shared-decision making, with benefit/risk discussions can help in determining the best strategy for an individual.

Decision-making for invasive procedures in older people

Historically there has been a reluctance to perform complex percutaneous coronary intervention (PCI) in older patients. Older people may have more extensive or more severe CAD and be at higher CV risk, and may have a higher risk of post-procedure complications.[84] However, improvements in equipment and techniques have led to high success rates and low complications rates among older patients.[84] Treatment with revascularization and medical devices, such as transcatheter aortic-valve implantation (TAVI) and transcatheter mitral-valve repair (TMVR) can be highly effective in reducing the risk of MACE.[85, 86] In addition, TAVI and

TMVR have not been associated with the risk of major bleeding, even in older patients, compared to that seen with surgical treatment.[85, 86]

Similarly, even among patients ≥75 years, observational studies and RCTs have shown lower rates of MACE and mortality with revascularization (coronary artery bypass graft [CABG] or PCI) compared with medical treatment.[87, 88] In addition, patients experienced improvements in angina severity and quality of life.[88]

When, who, and how to perform revascularization

Myocardial revascularization should be performed to improve prognosis or symptoms as recommended in the 2018 European guidelines on myocardial revascularization (Table 2).[89] Shared-decision-making should include consultation with a heart team, thoroughly informing the patient of the benefits and risks, and consideration of patient preferences.

CABG has been associated with lower rates of mortality compared to PCI in RCTs in patients with left main disease or triple vessel disease.[90] However, frail patients, especially those with left main disease were excluded from these trials.[84, 91] The guidelines on myocardial revascularization recommend using the SYNTAX score to help guide decisions on whether to perform PCI or CABG.[89, 92] PCI is generally recommended in patients with low SYNTAX scores, mainly because of convenience and cost. CABG is recommended in patients with intermediate or high SYNTAX scores because of with the potential for lower mortality rates.[92] However, the choice should also consider the presence of severe co-morbidities, advanced age (e.g., frailty or reduced life expectancy), and conditions that may affect rehabilitation (e.g., restricted mobility) favour PCI.[89, 92]

When, who, and how to perform aortic or percutaneous mitral valve interventions

Updated European guidelines on valvular heart disease were published in 2021, and a summary of recommendations for the use of interventions in patients with aortic stenosis and mitral regurgitation is shown in Table 3.[93] In addition, the Aortic Valve ReplAcemenT versus Conservative Treatment in Asymptomatic SeveRe Aortic Stenosis (AVATAR) study suggested that surgical aortic valve replacement (SAVR) is beneficial when stenosis becomes severe regardless of symptoms.[94]

TAVI has been associated with reduced rates of all-cause mortality and stroke compared with SAVR, regardless of baseline surgical risk.[95] Stroke may be an important outcome for older people because of the impact on quality of life.

Certain clinical, anatomical, and technical factors should be considered in the decision to perform SAVR or TAVI, and risks and benefits should be discussed with a heart team and an informed patient.[93, 96, 97] SAVR is favoured in patients with complex anatomy, concomitant conditions that require surgery such as significant CAD, or those with endocarditis. Life expectancy, potential quality of life in terms of comorbid conditions or frailty, together with well-informed patient preferences are critical in determining the best management strategy. Delirium can be an important complication after TAVI, especially in older people, who may benefit from early recognition and interventions.[98]

Adding years to life or life to years (making decisions to withhold or discontinue treatment)

The main goals of CV treatments should be to prevent or manage CVD, and to improve the quality and duration of life (healthy active life).[15] Patient preference becomes a primary factor in chronic, incurable, or highly disabling conditions such as advanced HF.[15, 99] Individuals have different beliefs, values, and goals regarding their health care, and these may change over time.[15]

Improved treatments and longer survival in patients with HF is associated with more hospitalizations and an increasingly unmanageable symptom burden.[99] CV risk factors alone should not determine therapy, rather risk minimization strategies should be preferred. Patients may benefit from proactive strategies to address side effects, or from discontinuation of some medications. Studies suggest that reducing the number of drugs in older patients on polypharmacy (including CV and/or non-CV medications) can be done safely, and has the potential to reduce falls, improve quality of life, reduce medication burden, and reduce medication costs.[15, 28-30]

In patients with cancer, palliative care has significantly improved quality of life and survival.[100] In cardiology, palliative care becomes especially important in patients with HF. HF is a progressive, chronic, life-threatening condition that significantly impacts quality of life. In addition, HF is often the end stage of most chronic CV conditions. In a RCT in patients with advanced HF, an interdisciplinary palliative care intervention was associated with significant improvements in quality of life measures, and depression and anxiety scores compared with usual care alone.[101] This illustrates that the risk is actionable and can be influenced.

ESC HF guidelines suggest healthcare providers focus on the quality of life and the symptom burden of patients with advanced heart failure, as well as a timely plan for palliative care based on the patient's needs and beliefs (Table 4).[102] Patients with HF can benefit from palliative care not only to help manage their symptoms, but also to achieve a better understanding of their disease. With the patient's permission collateral information should be obtained from the family (e.g., in patients with cognitive impairment), and relatives should be included in discussions.

Despite favourable scientific evidence, palliative care has not been well integrated into cardiology.[99] Communication requires time, therefore, pathways should be in place for referral to palliative care, incorporating a shared-care strategy.[102] Palliative care should be discussed early in the disease trajectory, and end-of-life discussions should include advance care planning, disease understanding, and the patients' goals of care, with the goal of helping patients understand their disease status, prognosis, treatment options, and facilitate decision-making.[99, 102] In patients with HF who are very debilitated and frail, palliative care can provide psychosocial support in making complex decisions such as device deactivation and place of death preferences.[99, 102] A close collaboration between the palliative care team and the cardiologists is definitively needed, especially with mobile palliative care teams, and should improve the management of elderly patients requiring palliative care. Understanding and expanding the role of palliative care in cardiology is a much needed area for further investigation.

Summary

The growing elderly population worldwide represents a major responsibility, but also a challenge for caregivers, healthcare providers, and society. The life-long exposure to CV risk

factors, as well as age-related comorbidities, promote a high prevalence of frequently complicated CVD in older patients. While prevention and management strategies have been shown to be effective in older people, there continues to be a paucity of robust evidence from dedicated clinical trials. The narrow therapeutic window of some recommended pharmacotherapies, frailty and cognitive impairments, and patients' re-assessment of important outcomes (e.g., quality of life versus mortality), can present management challenges.

With the increasing burden of ageing, the time has come to revisit CV research, including increasing use of real-world studies to assess longer-term outcomes. Use of pharmacological and interventional strategies in older patients should focus on quality of life and patient's preferences, with the optimal strategy being determined by a multidisciplinary team who involves the individual patient into the decision-making process.

Acknowledgements

This article was generated from discussions during a virtual Cardiovascular Round Table (CRT) workshop organised in May 2021 by the European Society of Cardiology (ESC). The ESC CRT is a strategic forum for high-level dialogue between 20 industry companies (pharmaceutical, devices and diagnostics) and the ESC leadership to identify and discuss key strategic issues for the future of cardiovascular health in Europe. The authors would like to thank Pauline Lavigne and Steven Portelance (unaffiliated, supported by the ESC) for contributions to writing, and editing the manuscript.

Disclosures

Lettino: Honoraria from Bristol-Meyers Squibb, Pfizer, Sanofi, Boehringer Ingelheim, Daiichi Sankyo, and Edwards Lifescience; advisory board participation for Boehringer Ingelheim and Edwards Lifescience; and a leadership role (President) with a multi-hospital Institutional Review Board.

Mascherbauer: None.

Nordaby: Employment with Boehringer Ingelheim International.

Ziegler: None.

Collet: Grants or contracts from Bristol-Myers Squibb, Medtronic, and Pfizer; and honoraria from Abbott, AstraZeneca, Boston Scientific, and Sanofi.

Derumeaux: Institutional grants to INSERM (RHU CARMMA) from Agence Nationale pour la Recherche (ANR).

Hohnloser: Consulting fees from Bristol-Meyers Squibb, Pfizer, Boehringer Ingelheim, Bayer, and Daiichi Sankyo; and honoraria from Bristol-Meyers Squibb, Pfizer, Boehringer Ingelheim, Bayer, and Daiichi Sankyo.

Leclercq: None.

O'Neill: Honoraria from Servier Canada.

Visseren: Research funding from Amgen.

Weidinger: None.

Richard-Lordereau: Employment with and stock options from Amgen.

Author contributions

All CRT members that were included as authors contributed to design of the CRT meeting and to selection of the topics; ML and IR-L drafted the initial manuscript. All authors critically revised the manuscript, gave final approval, and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Graphical abstract

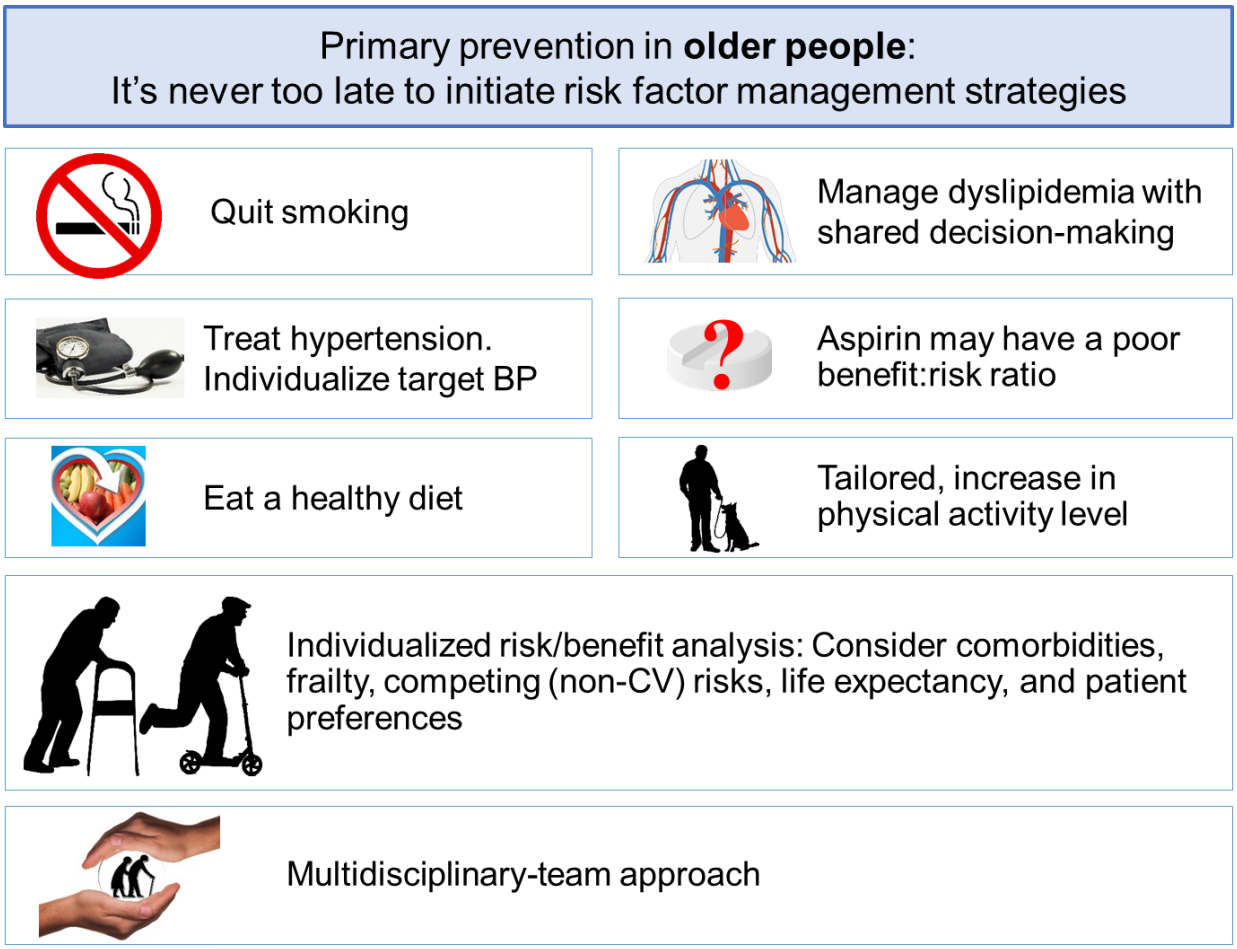

Figure legend

Figure 1: *Individualised decisions on lifestyle changes and risk factor treatment will benefit from a thorough risk analysis and patient involvement*

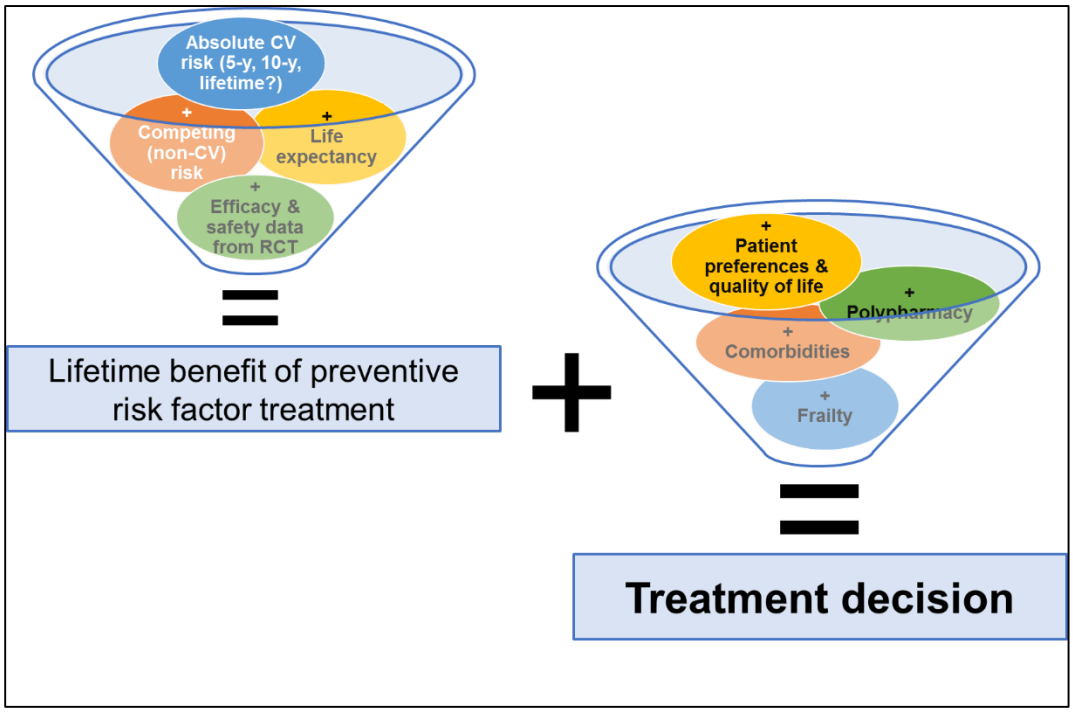

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Table 1: *Summary of important clinical trials of primary prevention strategies in older people*

Risk factor/ interventions	Clinical trials	Findings
Hypertension	SHEP,[20] Syst-Eur,[21] HYVET,[22] SPRINT[23, 26] Intensive SBP targets could prevent ~107,500 deaths/y, at the expense of episodes of hypotension (~56,000), syncope (~34,000), serious electrolyte disturbances (~43,000), and acute kidney injury (~88,000)[26]	• Proven benefit in older people (fit and frail).[24, 25] Maximum benefits in >75-80 y.[25] • Benefits of antihypertensive therapy need to be weighed with risks; increased susceptibility to adverse events in older adults • Treatment targets need to be individualised based on function, frailty, independence to minimise harms[27, 31]
Dyslipidemia	Age ≥65 y: Meta-analyses suggest benefits[33, 35] Limited data >75 y: PROSPER (age 70-82 y), benefits driven by secondary prevention benefit[36]	• Statins appropriate for most healthy older people for prevention of MI/stroke, less evidence of mortality benefit[33, 35] • Consider longer time-to-benefit with statins (~2-2.5 years), as well as patient's anticipated life expectancy[37, 38] • Older people more susceptible to adverse events, and more likely to have co-existing frailty, sarcopenia, polypharmacy; all of which increase potential for harm if adverse effect occurs; thus risk assessment and shared decision making are essential[14]
Type 2 diabetes mellitus	Metformin: e.g., UKPDS[42] SGLT-2 inhibitors: EMPA-REG OUTCOME,[44] DECLARE TIMI-58[45] GLP-1 receptor agonists: SUSTAIN 6,[46] REWIND,[47] LEADER[48]	• Metformin, SGLT-2 inhibitors, and GLP-1 are recommended for older people for prevention of events[43] • Intensive glycemic control not shown to reduce mortality[43] • Tailor targets to individual patient – based on function, frailty, life expectancy[43]

Aspirin	ARRIVE,[49] ASCEND,[50] ASPREE[51, 52]	• Minimal or no net clinical benefit in older people (risk of bleeding vs. MACE/mortality)[49-51] • Not recommended for primary prevention[14, 54, 55] • Beers Criteria recommends additional caution when using ASA in older adults, due to risk of bleeding[54]
Smoking	Meta-analyses[59, 60]	• CV risks decreased with time since cessation becoming significant within <5 y, and reach non-smoker level at ~20 y[59, 60] • Cessation is important at any age[14]
Diet	PREDIMED,[61] EPIC[62] Meta-analyses and RCTs suggest no benefit for vitamin C, D, or E Meta-analyses for omega-3 fatty acids conflicting	• Mediterranean diet reduced risk of MACE • No apparent benefit of vitamin supplements • Omega-3 fatty acids, particularly EPO may be considered
Exercise	Honolulu Heart Program,[69] Zutphen Elderly Study[70]	• Reduction in CVD risk[14, 69, 70, 73] • Tailor to individual's needs and ability[14, 73]

CVD; cardiovascular disease; EPO; eicosapentaenoic acid; MACE, major cardiovascular events; SBP, systolic blood pressure. Note abbreviations for trials can be found in the references.

Table 2: *Summary of extent of disease indicating a need for revascularization in patients with stable CAD and documented ischaemia or a haemodynamically relevant lesion from the 2018 European guidelines on myocardial revascularization*

Goal of improving prognosis

• >50% stenosis in
  ○ Left main CAD
  ○ Proximal left anterior descending CAD
  ○ 2- or 3-vessel disease with LVEF ≤35%
  ○ Sole remaining patent coronary artery
• Extensive ischaemia on functional testing (>10% LV) or abnormal invasive fractional flow reserve

Goal of improving symptoms
• Haemodynamically significant stenosis in patients with limiting angina on optimised medical therapy

Adapted from reference.[89] CAD, coronary artery disease, LVEF, left ventricular ejection fraction

Table 3: Summary of interventional strategies for patients with aortic stenosis or chronic severe secondary mitral regurgitation from the 2021 European guidelines for valvular heart disease

Recommended indications for intervention in aortic stenosis
• Symptomatic
  ○ Intervention recommended if severe, high-gradient aortic stenosis (mean gradient ≥40 mmHg, Vmax ≥4.0 m/s and valve area ≤1.0 cm^2)
• Asymptomatic
  ○ Intervention considered if severe and LVEF <55%, without another cause
  ○ Intervention considered if LVEF >55% with a normal exercise test and any of the following:
  • Very severe (mean gradient ≥60 mmHg or Vmax ≥5 m/s)
  • Severe valve calcification and Vmax progression ≥0.3 m/s/year
  • Markedly elevated BNP levels by repeated measurements, without another cause

Recommended mode of intervention (SAVR, TAVI) in patients with aortic stenosis • Heart team should assess risks and benefits based on evaluation of clinical, anatomical, and procedural factors, in consultation with informed patient • SAVR recommended in younger patients (<75 years) at low surgical risk, or patients unsuitable for transfemoral TAVI • TAVI recommended in older patients (≥75 years), or in those at high surgical risk • SAVR or TAVI recommended for remaining patients based on clinical, anatomical and procedural factors • Non-transfemoral TAVI considered in patients who are unsuitable for SAVR or transfemoral TAVI

Indications for mitral valve intervention (SAVR, TAVI, TEER) in chronic severe secondary mitral regurgitation (SMR)
• Surgery/intervention recommended in patients with severe SMR who are symptomatic despite optimal therapy in consultation with heart team
• Patients with concomitant CAD or other cardiac disease requiring treatment
  ○ In symptomatic patients. PCI (and/or TAVI) possibly followed by TEER (if persistent severe SMR) considered in those not appropriate for surgery based on assessment by heart team
  ○ Valve surgery recommended in patients undergoing CABG or other cardiac surgery
• Patients without concomitant CAD or other cardiac disease requiring treatment
  ○ In selected symptomatic patients, TEER considered in those not eligible for surgery with a high likelihood of response
  ○ In selected high-risk symptomatic patients not eligible for surgery and unlikely to respond to TEER, consider a TEER procedure or other trans-catheter valve therapy, after evaluation for ventricular assist device or heart transplant by heart team

Adapted from reference.[93]

BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; SMR, secondary mitral regurgitation; TAVI, transcatheter aortic valve implantation; TEER, transcatheter edge-to-edge repair; Vmax, peak transvalvular velocity

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• Patients with concomitant CAD or other cardiac disease requiring treatment
  ○ In symptomatic patients. PCI (and/or TAVI) possibly followed by TEER (if persistent severe SMR) considered in those not appropriate for surgery based on assessment by heart team
  ○ Valve surgery recommended in patients undergoing CABG or other cardiac surgery
• Patients without concomitant CAD or other cardiac disease requiring treatment
  ○ In selected symptomatic patients, TEER considered in those not eligible for surgery with a high likelihood of response
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Table 4: *Considerations for palliative care in patients with advanced HF from the 2021 European guidelines for the management of acute and chronic heart failure*

Indications (despite optimal therapy)
• Progressive functional decline and loss of independence • Severe HF symptoms and poor quality of life despite optimal therapy • Frequent episodes of serious decompensation or hospital admissions despite optimal therapy • Not suitable for heart transplantation or mechanical circulatory support • Cardiac cachexia • Close to end of life (clinical assessment)
• **Key components**
• Focus on optimising quality of life of the patient and family until death • Frequently assess symptoms (including dyspnoea and pain) and focus on symptom relief • Facilitate access for the patient and family to psychological/spiritual support as needed • Assist with advanced care planning, including preferences around death and resuscitation (may require multidisciplinary team decisions)

Adapted from reference.[102]