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Cardiovascular risk factors management in older adults: a clinical consensus statement from the European Association of Preventive Cardiology of the ESC and the ESC Council for Cardiology Practice

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Cardiovascular disease (CVD) currently ranks first in global mortality and morbidity and its prevalence increases with age. The most common risk factors for CVD are hypertension, diabetes mellitus, dyslipidaemias, adipositas, smoking, and physical inactivity, Also, depression, anaemia and frailty can be considered important risk factors for CVD. Incidence and prevalence of risk factors and comorbidities increase with age. Nevertheless, risk factor management in older adults and how intensively they should be treated are challenging for cardiovascular specialists and other clinicians, and an intensive and individual approach is needed, given the limited evidence available to date.

Therefore, in this clinical consensus document from the European Association of Preventive Cardiology of ESC and ESC Council for Cardiology Practice, a modern reappraisal of the evidence on the field is provided, together with simple, practical, and feasible suggestions to achieve the best goal in the clinical setting, focusing on evidence-based concepts.

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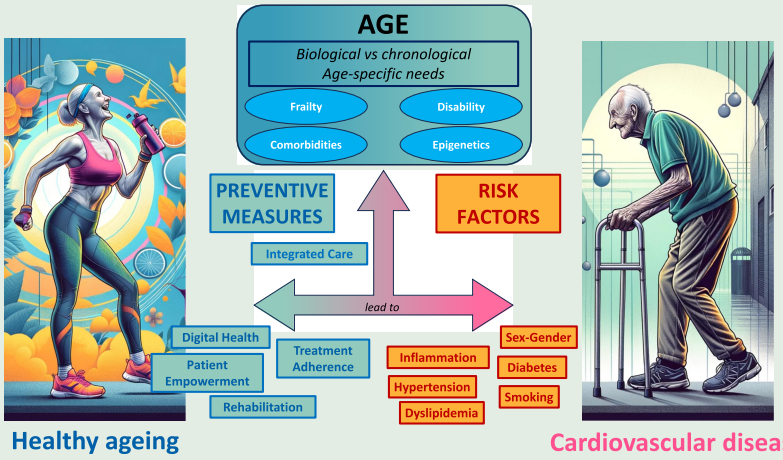
Graphical Abstract



Keywords Elderly • Cardiovascular risk factors • Cardiovascular risk

Introduction

Cardiovascular disease (CVD) currently ranks first in global mortality and morbidity and its prevalence increases with age.[1,2] CVD is the most common cause of death in European Society of Cardiology (ESC) member countries with ischaemic heart disease accounting for 45% of these deaths in females and 39% in males.[2] CVD predominates as the leading health burden for middle-aged and older adults.[1,2]

The most common risk factors for CVD are hypertension, diabetes mellitus, dyslipidaemia, adipositas, smoking, and physical inactivity. Almost one in four people remains affected by elevated blood pressure across ESC member countries, and if declines in total and non-HDL cholesterol concentrations have been recorded in high-income countries, in those with middle-income little change has occurred.[2] The prevalence of obesity has increased steeply across all ESC member countries and now affects more than one in 5 adults;[2] this has been associated with an increased prevalence of diabetes which, in 2019, affected 6.9% and 5.8% of adults in middle-income and high-income countries.[2]

Incidence and prevalence of risk factors and comorbidities increase with age, as do prefrailty and frailty status.[1,2] Nevertheless, risk factor management in older adults and how intensively they should be treated are challenging for cardiovascular (CV) specialists and other clinicians and an intensive and individual approach is needed given the limited evidence available to date.

Purposes

The purpose of this clinical consensus statement is to provide an up-to-date overview of the epidemiology and clinical impact of risk factors on CVD in older patients, including clinical issues relevant to them. If the topic 'older adults' is included in several ESC Guidelines, this Statement will aim to complement topics reported in ESC Guidelines, emphasizing controversial points still present in the field, focusing on therapeutic approaches based on older patients' fitness and biological age. Moreover, the novelty of this paper is that all clinically relevant and state-of-the-art knowledge on this topic is brought together.

Methods

The accumulation of the current evidence was based on a search strategy of English language published research, guidelines, consensus documents, and policy documents, by using electronic databases (MEDLINE, EMBASE, CINAHL), as selected, evaluated, and reviewed by experts from the European Association of Preventive Cardiology of ESC and the ESC Council for Cardiology Practice. Whenever possible, data on older adults were prioritized, in particular within the Scientific Guidelines.

Multidisciplinarity was at the basis of the working group composition including individuals from healthcare professional groups relevant to the care of older heart patients (cardiologists with expertise in ageing, geriatricians, primary care physicians, physiotherapists, and psychologists). The working group did not include patient representatives or methodologists.

The timeline process of the manuscript was the following: (i) composition of the working group, (ii) identification of the table of contents of the document, (iii) submission of the proposal to the EAPC Research Committee, ESC Scientific Document Committee and approval by both the Committees, (iv) assignment of tasks based on each one's experience, a literature search performed by each author independently, contribution by each author to the first draft of the manuscript, sharing of the first draft of the manuscript in the working group, (v) internal review process of the first draft guaranteed by the EAPC Research Committee and the ESC Scientific Document Committee, (vi) incorporation of committees' suggested changes and elaboration of the final draft of the manuscript, and (vii) submission of the final draft to both the Committees for their final approval.

From the collected evidence, consensus advice has been formulated. Any advice was submitted to the revision of all the authors and voted for reaching an agreement. The agreement threshold was ≥75%. In the case of disagreement, it was resolved by reformulating the advice and then repeating the vote. All consensus advice was aligned with current EAPC/ESC position papers or guidelines.

The literature search showed very few prospective randomized controlled trials and mainly allowed to include ESC and other Scientific Societies (ACC, AHA, Canada, ESH, WHO) Guidelines/documents, reviews, and observational series. Consequently, any kind of grading process

or PRISMA selection was unrealistic, making possible only a 'descriptive' approach with a very low level of evidence for any advice.

Epidemiology of cardiovascular risk factors in older adults

The epidemiology of CV risk factors in older adults is not easily evaluable due to the relative scarcity of data. The population studies generally show the incidence and prevalence of CV risk factors without division per age class.

The ESC EURObservational Research Program, and the Cardiovascular Diseases Statistic 2021,[2] when comparing data between ESC member countries, apply age-standardized rates using the European Standard Population to allow for differences in national age structures,[3] using population pyramids.[4] The data are stratified only by national data, sex, and national income status. American data distinguish for age classes only some CV risk factors.[5] World Health Organization (WHO) study group report gives little more information.[6]

Smoking

In Europe, overall smoking prevalence in 17 countries was 11.5% (15.3% in men and 8.6% in women) in 2010, and it was highest in eastern/central Europe for men (20.3%) and northern Europe for women (13.1%).[7] The TackSHS Project based on about 12 000 subjects from Europe showed that compared with subjects aged <45 years, ORs for smoking were 0.97 (95% CI, 0.89–1.07) for 45–64 years, and 0.31 (95% CI, 0.27–0.36) for ≥65 years.[8] In the United States, 8.4% of those ≥65 years of age reported cigarette use every day or some days.[5]

Physical activity

From accelerometer-assessed physical activity observations (NHANES, 2005–2006), in the United States, levels of moderate and vigorous physical activity were lower in older adults (60–69 years of age).[5] Of 58 489 individuals in the SHARE survey, in 19 298 people ≥55 year old (mean age, 67.8), the overall prevalence of inactivity was 12.5%, ranging from 4.9% (Sweden) to 29% (Portugal)[9] All physical activity measures were inversely associated with age ($P < 0.001$), except for time spent in sedentary behaviour ($P = 0.01$) in the Tromso study including 1437 subjects > 70 years of age in a global sample of 5918 subjects.[10]

Obesity

Based on NHANES 2007 to 2014, the prevalence of metabolic syndrome increased with age, reaching 54.9% among people ≥60 years of age.[11] In a sample of 1247 older adults representative of the Italian population between 65 and 95 years in 1990, BMI at the 90th percentile was 31.1 and 34.7 for males and females, respectively.[12] In a Polish population of 604 older adults >65 years, 55.3% of men and 40.1% of women were overweight, and 20.3% and 21.7% were obese, respectively.[13] The overall prevalence of obesity was 19% in women and 15% in men and decreased after the age of 75 years in a cross-sectional study of 2558 men and women aged > 65 years in mid-Sweden.[14]

Hypertension

WHO reports that about one-half of the population > 65 old is hypertensive.[6] Anyway, prevalence varies largely even within regions, as in the WHO-MONICA project, where it may vary fivefold. Most data were casual blood pressure determination, and the real sustained hypertension prevalence has been estimated to be between one-quarter and one-third. In the German KORA-Age1 study, on individuals aged 65–94 years, the overall prevalence of hypertension (≥140/90 mmHg) was 73.8% (74.8% in men and 73.5% in women).[15] American data based on NHANES 2015–2018 report as hypertensive 67.5% of males and 75.7% of females aged 65–74 and 83.6% of males and 84.6% of females > 75 years old.[6]

Hypercholesterolaemia

Although many evaluations of high cholesterol and triglyceride levels are available in young, data about older adults are scarce. Data from NHANES 2007–2018 show a prevalence of hypercholesterolaemia and hypertriglyceridemia, respectively, of 13.4% and 11.4% between 65 and 74 years and 11.7% and 8.6% > 75 years.[16] In two Bavarian villages, 1190 inhabitants ≥ 65 years showed a prevalence of hypertension of 53%, obesity 35%, and hypercholesterolaemia 21%; The prevalence of hypertension increased up to the age groups '75–79 years' in men and '80–84 years' in women, while there was a constant decrease with age for obesity, hypercholesterolaemia, and smoking.[17] In the cross-sectional, national PolSenior survey, of 4101 participants (2136 men; 1965 women) aged 65–104 years, hypercholesterolaemia was present in 62.4% (56.1% of men; 66.3% of women), mainly in those aged 65–69 years.[18]

Diabetes

Twenty per cent of the age group 65–69 years are diabetics according to the International Diabetes Federation.[19] In the USA, > 25% of the population > 65 years has diabetes,[20] and about 40% (39.5%) of the adult diabetic population is aged > 65 years.[21] In 15 095 community-dwelling older people aged ≥75 years in the UK, 1177 people were identified as having Type 2 diabetes mellitus, giving an overall prevalence of 7.8%.[22] Between 2004 and 2013, 180 290 people aged between 40 and 89 years were diagnosed with type 2 diabetes in Scotland, with incidence rates highest at 75 years of age and a decline of incidence in older men during the study period.[23] Data from a Danish diabetes register showed that the age-specific prevalence of Type 1 Diabetes increased till about age 40 in men and 30 in women, while Type 2 Diabetes showed a peak of age-specific prevalence at age 80, with values of 19% in men and 16% in women.[24] A population-based survey in central Spain including 5278 older participants (≥65 years old) showed an incidence rate of Type 2 Diabetes of 9.8/1000 person-years without gender differences.[25]

Ageing process, frailty, comorbidities, sex and gender specificities

Definition of older adults

Although the United Nations defines older people as persons who are > 60 years of age, traditionally, the 'elderly' are those persons aged ≥ 65 years,[26], and some scientific societies proposed to call 'elderly' people ≥ 75 years.[27] Therefore, various studies are performed on patients ≥ 65, whereas some use 70 or 75 years as including criteria. Moreover, most of the guidelines do not clearly define 'elderly' when giving suggestions for the aged patient population. Finally, as for the semantic definition of 'elderly', this word seems to be negatively perceived as being associated with vulnerability, decline and burden and aged people prefer to be called older adults.[28,29] In this document, the consensus was to use the words 'older adults/people/patients' instead of 'elderly'.

Besides the chronological age, it is now well understood that the health condition and life expectancy of older adults are better described by epidemiological or individualized health evaluations.

Various attempts have been made to refine the individual attitude to ageing to identify different trajectories from delayed (associated with successful ageing) to normal and premature vascular ageing.[30]

These include the focus on biological age vs. chronological age, mainly through molecular, epigenetic, and cellular biomarkers, vascular functional and structural parameters, composite predictors including the assessment of frailty, the estimation of ageing by modelling algorithms and evaluating the 'vascular age' and the 'heart age' through online calculators.[31–35]

In addition, the concept of 'prospective age' has been introduced because the different trajectories of death in different countries lead to differently consider subjects as 'old' according to their life expectancies.[36]

In single individuals, vascular age and/or other tools which tend to refine the vascular health status may add information beyond chronological age. Vascular age may be described through an algorithm that considers various parameters such as age, gender, blood pressure values, smoking habits, and cholesterol values.[35,37] whereas other algorithms include measures of vascular stiffness or coronary calcium score.[38]

Moreover, the holistic concept of frailty is crucial in discriminating the various subgroups within the heterogeneity of subjects defined according to chronological age only. For aged people, the comprehensive assessment of functioning is much more relevant than the description of the presence or absence of disease; the definition of frailty, as increased vulnerability to stress and negative health events, better describes the trend towards loss of healthy ageing, including social implications such as loss of independence and disability.[39–44] This approach leads to the concept of 'functional ageing' with multidimensional evaluation and strong integration of various domains such as physical, psychological, cognitive factors, and social functioning, rather than focusing on single causes.[45,46]

Therefore, though considering a chronological age of ≥65 years to define older adults, from a clinical point of view, different expectations of and healthier life depend on being robust or frail (or pre-frail according to some tools to assess frailty), or on having disabilities or multimorbidity. The late CV effects associated with the COVID pandemic such as the worsening of symptoms (dyspnoea) and facilitating arrhythmias may impact the frailty status.[47]

A relevant general protection of older vulnerable individuals against acute illness with implications for the CV system derives from the vaccination strategy (pneumococcal, influenza virus, Herpes Zoster, and SARS-CoV2),[48–50] with environmental aspects such as pollution having an impact on the protective effects of vaccination in older individuals.[51]

Advice 1

- Besides the chronological age, the health condition and life expectancy of older adults are better described by biological age. In single individuals, 'vascular age' and 'heart age' and a comprehensive assessment of physical and mental functioning are crucial in discriminating the various subgroups within the heterogeneity of subjects defined according to chronological age only.[31–35]
- Relevant general protection of older vulnerable individuals against acute illness with implications for the CV system can be obtained by a vaccination strategy (pneumococcal, influenza virus, Herpes Zoster, SARS-CoV2).[48–50]

How to evaluate frailty, multimorbidity, and disability, in daily clinical practice

Frailty is theoretically defined as a clinically recognizable state of increased vulnerability resulting from ageing-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with every day or acute stressors is comprised.[52] Multimorbidity is commonly understood to be the coexistence of multiple health conditions in an individual, often with a cut-off of ≥2; a related term, comorbidity, describes the burden of illness co-existing with a particular disease of interest.[53] Disability is a condition which includes long-term physical, mental, intellectual, or sensory impairments which, in interaction with various barriers, may hinder [a person's] full and effective participation in society on an equal basis with others.[54]

Although frailty, disability, and multimorbidity are distinct concepts, and disability can be present alone even in young people, for instance in Paralympic athletes, ageing is closely related to all these conditions, the frailty trajectory in aged people leads to loss of independence, and the inevitable death.[39,40] Several tools may investigate frailty, multimorbidity and disability, and their evaluation may be partly overlapping.

Frailty is a dynamic phenomenon, and the degree of frailty can be arrested and possibly reverted.[39,55,56] Therefore, evaluating frailty through the identification of frailty domains and components is an essential step to be able to intervene.[39,57]

The evaluation of frailty in cardiology can be done using different tools that range from the evaluation of physical frailty to the accumulation of deficits or using screening or assessment tools focusing on multidomain evaluation.[39] *Figure 1* shows the different conceptual approaches of the operational tools to evaluate frailty.

The more comprehensive view of multidimensional approaches gives a more global evaluation of frailty. A short quick multidomain screening evaluation can be performed through the Essential Frailty Toolset (four items) investigating weakness, cognitive impairment, and laboratory data related to nutritional status (serum albumin) and to a multisystem proxy (serum haemoglobin). The latter screening tool has become widely used in CV patients and may be particularly suitable for vascular patients evaluated in an outpatient setting. Moreover, smartphone applications that include information regarding additional geriatric domains have been recently proposed.[58,59]

The most used tools focusing on multimorbidity are the Charlson Comorbidity Index and the Cumulative Illness Rating Scale whereas the Basic Activities of Daily Living, the Intermediate Activities of Daily Living, and the Advanced Activities of Daily Living scores are the most commonly used tools to assess functional dependence.[39] Regarding CV risk stratification, SCORE2-OP and SMART risk scores are suggested for patients ≥70 years, with no previous CVD or type 2 diabetes or with previous CVD, respectively; the SMART risk score can be used up to the age of 90 years.[60,61]

Recently, a few Guidelines on CVD suggested to use specific tests. For instance, the 2021 ESC/EACTS Guidelines for the management of valvular heart disease suggested the use of the Essential Frailty Toolset in older adults undergoing aortic valve replacement and the Katz Index for evaluating the Independence in Activities of Daily Living whereas the 2024 ESC Guidelines for the management of elevated blood pressure and hypertension state that validated tests should be used for frailty screening/assessment and include the Clinical Frailty Scale (Rockwood).[62–64]

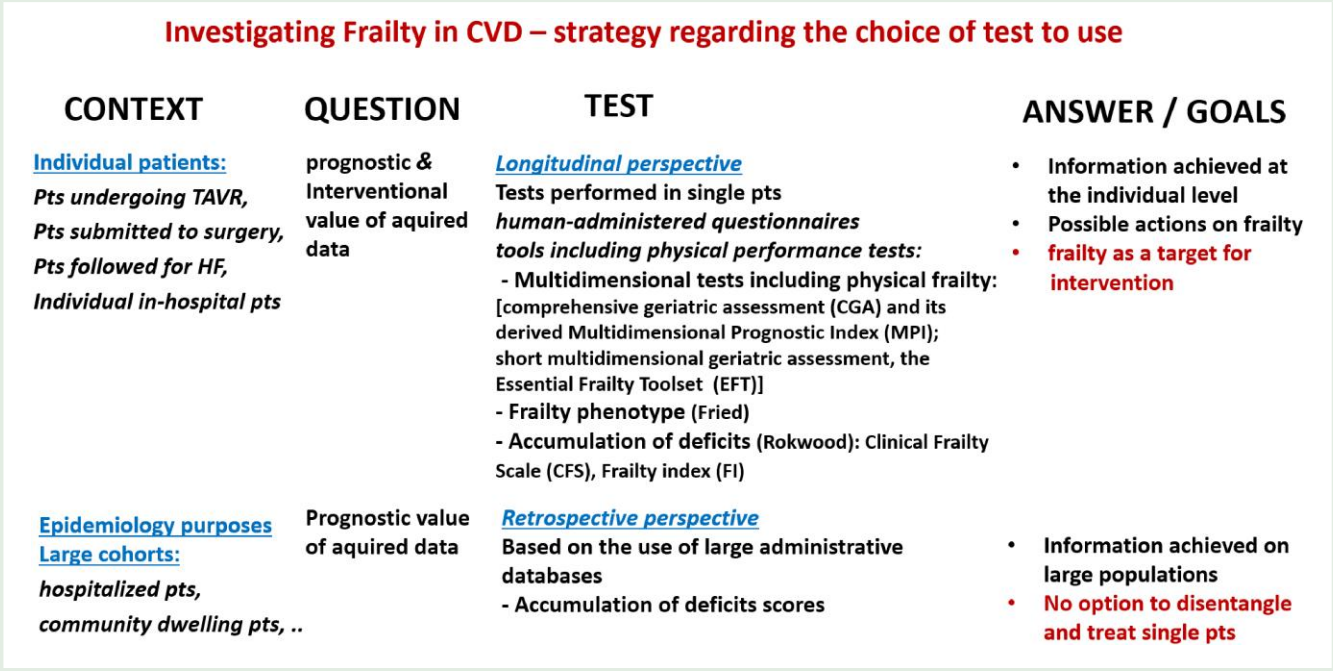


Figure 1 Investigating frailty in CVD—strategy regarding the choice of test to use. HF, heart failure; pts, patients; TAVR, transcatheter aortic valve replacement.

Advice 2

- In daily clinical practice, frailty, burden of comorbidities, and disability must be measured by standardized tools (i.e. Essential Frailty Toolset, Clinical Frailty Scale, Charlson Comorbidity Index, Cumulative Illness Rating Scale, Basic Activities of Daily Living, Intermediate Activities of Daily Living, Advanced Activities of Daily, Katz Index) and not qualitatively evaluated.[39,62–64]
- Comorbidities must be analysed in the management of CVD risk factors, particularly because of polypharmacy and drug-related side effects.

The impact of comorbidities on cardiovascular risk factors management

Chronic kidney disease

Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 mt2, persisting for 3 months or more, irrespective of the cause.[65] CKD is particularly prevalent among older patients, with as much as 30% of adults aged > 70 and 50% of adults aged ≥ 80 years having abnormal renal function.[66] Kidney disease severity is differentiated into stages (categories) according to the level of GFR, albuminuria, and urine albumin–creatinine ratio. In people without manifest CVD or diabetes, kidney dysfunction is causally related to the risk of CVD according to Observational and Mendelian Randomization Analyses in European ancestries participants.[67]

Among persons with CKD, CVD is the leading cause of morbidity and death. Even after adjustment for known CVD risk factors, mortality risk progressively increases with worsening CKD.[68] As GFR declines below approximately 60–75 mL/min/1.73 m^2, the probability of developing CVD increases linearly.

Persons with CKD are also exposed to other non-traditional CV risk factors such as uraemia-related ones, including inflammation, oxidative stress, and promotors of vascular calcification. CKD and kidney failure not only increase the risk of CVD, but also modifies its clinical presentation and cardinal symptoms.[60] Managing risk factors and treating the disease slow its progression and reduce the risk of complications. Smoking cessation in combination with lifestyle optimization and target systolic blood pressure (BP) < 140 down to 130 mmHg, if tolerated, and LDL-C < 1.8 mmol/L (70 mg/dL) in high-risk patients and <1.4 mmol/L (55 mg/dL) in very-high-risk patients are all beneficial.[60] In dialysis patients not receiving statins, there is no indication to start them at that point. SGLT2 inhibitors and finerenone in diabetics, as proven nephroprotective treatments, are promising for handling renal degeneration.

Chronic obstructive pulmonary disease

Although chronic obstructive pulmonary disease (COPD) is recognized and thoroughly investigated as a CVD comorbidity, its role as a cardiac risk factor is not well established.

The high prevalence of CVD in COPD patients may be explained by the fact that both diseases share common risk factors, such as smoking,

ageing, hypertension, and dyslipidaemia. Systemic inflammation and oxidative stress are prominent in COPD, with circulating biomarkers in high concentrations, in association with increased mortality, and promoting vascular remodelling, stiffness, atherosclerosis, and a 'procoagulant' state. Cardiac arrhythmias are common and may be due to the disease-induced haemodynamic effects in combination with the autonomic imbalance and abnormal ventricular repolarization.[60] Acute COPD exacerbations, mainly due to infections, are frequent and are responsible for a four-fold increase in CVD events.[69]

Cancer

Cancer and CVD share many risk factors. In recent years, cancer treatments achieved a dramatic improvement in quality of life and survival in oncologic patients. Consequently, the probability that cancer and CVD coexist is very high in older subjects.[70] However, almost all cancer therapies may expose a Cancer Treatment–Related CV Toxicity (CTR-CVT) in the acute phase of treatment or also after many years, and these toxicities are well shown in the 2022 ESC Guidelines on Cardio-Oncology where the entire chapter is dedicated to their physiopathology, clinical aspects, diagnosis, prevention, and therapy.[70] Their description is out of the scope of the present paper. Some issues may specifically be of interest to older people with cancer. For most cancer treatments the most relevant risk factors for CRT-CVT have been clearly recognized and age *per se* is one of the most important, and considered high > 80 years, independently from any other condition.[71] The baseline risk could be easily evaluated using the calculators in the ESC Pocket Guidelines App. Almost any chemotherapy agents may have different pharmacologic interactions (i.e. CYP450 or CYP3A4), resulting in an increase in plasma levels of both chemotherapy and CV drug treatments. Association of CV drugs and chemotherapy agents should be undertaken after careful evaluation of pharmacokinetic and pharmacodynamics of every drug involved, considering kidney and liver function that may be impaired in older people. Direct oral anticoagulants, antiarrhythmic drugs, antihypertensive drugs, statins, etc., require caution. The correction of common risk factors is required in the prevention and therapy of CRT-CVTs, particularly after treatments affecting the metabolic profile, enhancing the risk of atherosclerotic diseases and left ventricle dysfunction. In older adults may be particularly relevant hormone therapy for prostatic cancer. When a left ventricle dysfunction occurs, a therapy based on ACE inhibitors/sartanes/ARNI, betablockers, gliflozines, etc., is mandatory. It should be continued also in older people in the long term. Supervised exercise therapy (including high-intensity interval training [HIIT]) is safe and well tolerated, attenuates CTR-CVT risk, and improves CV function. Furthermore, HIIT reduces CV risk factors and CV risk in patients with cancer in the pre-, active-, and post-treatment settings.[70] Anyway, HIIT may not be feasible in older and frail patients.[71]

Overall appraisal of sex and gender-specificities

Sex differences and gender, (i.e. the socioeconomic-cultural components), are both crucial factors in the pathophysiology of the ageing CV system.

Ageing influences vascular function leading to endothelial dysfunction and artery stiffening, but also affects oestrogen/androgen production which in turn plays a remarkable effect in the vascular ageing process. During the reproductive years, oestrogens have protective effects on endothelial function, BP, cardiac function, and remodelling but also fat distribution, lipid metabolism and insulin sensitivity. On the contrary, testosterone is pro-hypertensive and likely contributes to the increase in CV risk observed with ageing in males and after menopause in females[72]

Awareness about the prevention and management of CVD remains largely inadequate in women.[73] Worldwide, many women are unaware that CVD is the main cause of death among them, overcoming weight and breast health,[74,75] particularly in those of lower socioeconomic status. Depression and dis-satisfaction with the health care provider are known factors particularly associated with non-adherence in older females, but not in males.[76] In addition, among physicians and healthcare professionals, a great concern is related to inertia regarding the use of guidelines-driven risk assessment in women.[77,78] Older individuals are characterized by multimorbidity and polymedication, entailing risks for adverse events, omissions, and potentially inappropriate medications. Polypharmacy is more prevalent in older women than men and is associated with increased mortality in women only.[77] A recent study reported that female patients were more likely than male to be evaluated for poisoning related to analgesic/opioids and CV medications, while older male patients more frequently received pharmacologic support.[78] Finally, women are less likely than men to receive preventive therapies according to guidelines.[79]

Sex and gender may impact frailty state transitions, multimorbidity, and therapy of CVD.[80] Women have generally been found to be at higher risk of frailty, but they also seem to have a better chance of frailty improvement and lower mortality.[80,81]

Globally, literature on the identification and management of sex and gender-specific differences in older adults is scarce[39] and international consensus documents regarding sex and gender-specific management of CV risk factors in this life period are lacking. Older adult-specific trials including sex-matched individuals are needed, and a sex-specific adaptation of guidelines for drug use among older people is warranted.

Lifestyle components as risk factors

Physical inactivity and sedentary behaviour

According to the WHO, physical inactivity and sedentary behaviour are considered major CV risk factors and important contributors to all-cause mortality and patients' disability.[82,83]

Ageing is usually associated with a progressive decline in physical activity and a large amount of older people, 2/3 of individuals, show a sedentary lifestyle.[84]

The causes of such a reduction in physical activity are multiple and include but are not limited to the presence of chronic illness, reduced mobility, reduced muscular mass, chronic pain, depression, and loneliness.[9,85] Also environmental, social, and cultural aspects may play a role; a cross-sectional study investigating physical activity in older individuals across Europe reported huge differences among countries. In the SHARE study, significantly associated with insufficient physical activity were socioeconomic factors such as low educational and financial difficulties, and a number of chronic diseases.[86]

Sedentary behaviour in older adults has been associated with negative outcomes, especially in terms of all-cause mortality, metabolic syndrome, and overweight.[87]

The benefits of exercise in terms of improving CV outcomes and reducing morbidity and mortality have been demonstrated by large

population studies and even individuals with CV conditions may safely be involved in leisure time physical activity with appropriate prescriptions.[60,88–90]

A meta-analysis of 147 studies reported that physical activity interventions on older adults in residential care were associated with a significant improvement in the functional capacity of the patients, according to the volume of exercise.[91] Other than CV and metabolic effects, physical activity shows beneficial effects in terms of functional independence, prevention of falls, well-being, cognitive function, social interaction, and sleep quality.[91]

There is no single type of physical activity that is suitable for older adults, and healthcare professionals prescribing exercise must adapt the prescription to the characteristics of the person, considering their desires (walking, dancing, and swimming), functional limitations, and general physical condition, introducing the exercise gradually and with realistic goals. Aerobic activity, muscle strengthening, and balance exercises should be included.

The intensity of physical activity is described in terms of the metabolic equivalent of Task (METs) where 1 MET is the metabolic expenditure of sitting quietly.[92] A sedentary behaviour has a very low metabolic expenditure in the range of 1.0 to 1.5 METs, and mild physical activity is in the range of 1.5–3.0 METs. Moderate physical activity is in the range of 3.0–6.0 METs and includes among others, stair climbing, brisk walking, cycling, golfing, and dancing. A high-intensity physical activity is characterized by >6.0 METs and includes high metabolic demanding physical activities like jogging, callisthenics, and rope jumping.

Physical activity, to produce significant changes and improvements in health status, should ideally include exercises of at least moderate activity. A summary of the specific 2020 WHO recommendations for people over 65 years of age is shown in *Table 1*.[83]

Advice 3

- Sedentary behaviour in older adults has been associated with negative outcomes, especially in terms of all-cause mortality, metabolic syndrome, and overweight.[87]
- Physical activity is associated with a significant improvement in the functional capacity of older adults.[91]
- It is important to adapt an individualized approach including aerobic activity, muscle strengthening, and balance exercises, according to 2020 WHO recommendations.[83]

Smoking and older adults

Age does not appear to diminish the benefits of quitting smoking. Smoking cessation interventions like counselling interventions, clinician advice, buddy support programmes, age-tailored self-help materials, telephone counselling, and nicotine replacement have been effective in both the general population and older smokers.

The disease consequence of smoking occurs disproportionately among older adults because of the long duration of the cumulative injury or change that underlies the bulk of tobacco-caused disease. Older smokers are less likely than younger smokers to attempt quitting, but they are more likely to be successful in the attempts that they make to quit.

Advice 4

Age does not appear to diminish the benefits of quitting smoking. Smoking cessation interventions are effective in both the general population and older smokers.

Table 1 2020 WHO recommendations for physical activity in people over 65 years of age.[83]

1) The amount of time spent sedentary should be limited to the minimum
2) At least 150–300 min of moderate-intensity aerobic physical activity or 75–150 min of vigorous physical activity or a combination of the two should be performed per week, if tolerated
3) Muscle-strengthening activities should also be performed at least two days per week
4) At least three times per week exercise for balance and muscle strength should be performed to reduce the risk of falls

Diseases as risk factors

Arterial hypertension (with a specific focus on older and frail patients)

Hypertension is the most common cause of heart failure,[93] a strong predictor of coronary heart disease,[94] and a risk factor for late cognitive impairment and dementia.[95]

Beneficial effects of drug treatment in adults > 65 years have been established by several randomized trials.[96–99] Nevertheless, the definition of hypertension, the thresholds, and the goals for treatment are controversial.[100]

Treatment should be decided on absolute CVD risk, risk modifiers, comorbidities, estimated benefit of treatment, frailty, and patient preference.[60] ESC guidelines[63] consider starting pharmacological treatment in adults with BP values > 140/90 mmHg, with caution in patients with orthostatic hypotension, moderate-to-severe frailty, limited life expectancy, and in those aged ≥85 years. Nevertheless, these values vary considerably between the international guidelines (*Table 2*),[63,101–104,106] particularly concerning the very old ones.

Considering the benefit/harm ratio is crucial in older patients,[107,108] but this should not overlook that high BP remains an important risk factor even at the most advanced ages.[63] As seen in *Table 2*, most of the guidelines are to reach a SBP < 140 mmHG. An intensified BP therapy, targeting SBP < 120 mmHg, seems superior when compared with a target of systolic BP (SBP) < 140 mmHg.[109,110] This is reflected in the recommended ESC target of BP < 120/80 mmHg and AHA/ACC target of BP < 130/80 mmHg, whatever the age (*Table 2*).[63,102]

The ESC hypertension guidelines recommend a 'BP target corridor' of 120–129/70–79 mmHg.[63] Likewise, the recent ESH guidelines advise not to decrease SBP/DBP < 120/70 mmHg.[105] This may call for the J-curve phenomenon, which describes increased CVD risk among patients with the lowest BP. Although recent data advocate that this phenomenon is rather a marker than a casual process, non-CVD side effects (orthostatic hypotension, syncope, and renal injury) observed in case of BP target <120/70 mmHg, push to maintain the 'BP corridor' rules in asymptomatic old (>65 years) patients, and to lower BP only 'as low as reasonably achievable' (ALARA) in the older (>85 years) and frail ones.'[63]

Checking drug tolerance is crucial, as the intensity of treatment is associated with adverse effects. Polypharmacy, multi-comorbidity, and poor hydration, frequent in the older population, reflect the high prevalence of biological disturbances, fatigue, confusion/delirium, and falls. Orthostatic hypotension (in which neurodegenerative diseases, such

Table 2 Threshold values and targets (mm Hg) for drug treatment in the hypertensive older adults among recent guidelines

Publication	Threshold values (mmHg)		Targets (mmHg)
(Year)	Age: 65–79 years	Age >80 years	Age > 65 years
ESC (2024)[63]	**>140/90** >130/85 if CAD or Stroke	**>140/90**	**120–129/70–79** if well tolerated Personalized Therapy if: >85 years, Frailty, OH.
Heart Foundation (Australia) (2016)[101]	**>140/90** >160/90 if low risk	**>140/90** >160/90 if low risk	**<140/90** <120 if no DM and well tolerated
AHA/ACC (2017)[102]	**>130/80** >140/90 if moderate–low CV risk	**>130**	**<130/80**
Hypertension Canada (2018)[103]	**>140/90** >130/80 if high CV Risk, DM, or >age 75 >160/100 if low CV risk	**>140/90** >130/80 if high CV Risk, DM, or >age 75 >160/100 if low CV risk	**<140/90** <120 if high risk <130/80 if DM
NICE (UK) (2019)[104]	**>160/100** >140/90 if high CV risk	**>160/100** >150/90 advised	**<140/90** (***<150/90*** *if Age > 80)*
ESH (2023)[105]	**>140/90**	**SBP > 160** >159–140 advised	**SBP: 130–140** (130/80 if well tolerated) *(SBP: 140–150 if Age > 80)*

CAD, Coronary artery disease; DM, diabetes mellitus; OH, orthostatic hypotension.

as diabetes and Parkinson's disease are confounding factors),[111] increases mortality in older people[112] and must be systematically sought. Frailty represents an even more confusing situation, as antihypertensive treatment may contribute to frailty, while frailty itself may increase the risk of drug-induced side effects; in addition, these patients (as nursing home residents and individuals with dementia) are usually excluded from randomized controlled trials.[113] In very old/frail patients, life expectancy may be shorter due to competing causes of death.[114] Finally, clinical judgment, patient preference, and, if necessary, a geriatric approach might be useful, keeping in mind that, even if one patient does not reach the designated target, any decrease in BP results in a reduction of both morbidity and mortality', justifying the 'ALARA' strategy.[63,100]

Stop smoking and lifestyle recommendations are recommended for all >70 years old.[60] Weight loss is beneficial for BP control.[115] However, in older adults, a catabolic state and inactivity may result in sarcopenic obesity.[116] Equally, comorbidities have a catabolic dominance. In these cases, nutritional restriction should be avoided or done with great caution and physical activity proposed, in adapted individualized programmes.[117] Added salt and high-salt foods should be avoided.[105] Combination therapy should be initiated at the lowest available doses, preferably as a single-pill combination, with a close monitoring of symptoms of orthostatic hypotension. Although the American guidelines suggest thiazide diuretics or/and a calcium channel blocker as the first antihypertensive drugs in older adults,[102] the five major classes can be used (ACE inhibitors, Angiotensin receptors blockers, calcium channel blockers, thiazide/thiazide-like diuretics, betablockers), the choice depending on efficacy, tolerability and the presence of specific comorbidities. Loop diuretics and alpha-blockers should be avoided, and renal function should be frequently assessed. In very old and frail patients, it may be appropriate to initiate treatment with monotherapy,[63] and ambulatory BP monitoring might contribute to optimize treatment.[63] Non-steroidal anti-inflammatory drugs should be avoided.[118] Randomized controlled trials need to be performed in very old/frail hypertensive patients, particularly those with frequent falls, marked cognitive impairment, multiple comorbidities, or living in nursing homes.[119]

Dyslipidaemias (with a specific focus on lipids treatment in older adults)

Low-density lipoprotein cholesterol (LDL-C) levels represent a major CV risk factor and the main recommended treatment target in guidelines for atherosclerotic cardiovascular diseases (ASCVD) prevention.[60,120] The absolute benefit of lowering LDL-C depends on the absolute risk of ASCVD, so even a small absolute reduction in LDL-C may be of value in high- or very-high-risk patients.[121] The 2021 ESC SCORE2-OP allows to stratify the risk in patients ≥70 years.[60] However, as data on ASCVD prevention come from studies including only a few older people, the evidence is scarce in this population, while the continuous worldwide increase of individuals >70 years makes this issue critical in developing its management.[122]

Statins still represent the first ASCVD preventive medication, as they reduced CV events and mortality in a wide range of individuals.[121,123,124] According to the 2019 ESC guidelines on the management of dyslipidaemias, statins are recommended in older adults with ASCVD in the same way as in younger patients.[125] According to these guidelines, the recommended LDL-C goal is < 1.4 mmol/L (55 mg/dL) and to be lowered by > 50% from baseline. In case of recurrent ASCVD within 2 years, a target LDL-C < 1.0 mmol/L (40 mg/dL) is recommended.

There is less evidence of benefit in the primary prevention setting.[121] The number needed to treat (NNT) with a moderate-intensity statin to prevent a CV event over 5 years was lowest for individuals 70–100 years, with the NNT increasing with younger age.[121] Initiation of statin therapy in apparently healthy people >75 years may be considered in patients at high or very high risk, defined by SCORE >5% or SCORE2-OP >7.5%, according to both the 2019 and 2021 guidelines,

respectively.[60,125] A stepwise initiation of lipid-lowering medication is recommended, starting with a statin, adding on ezetimibe if LDL-C goals are not obtained, and further adding a PCSK9-inhibitor. Long-term adherence to statins is poor and adherence problems are significant in older age.[126,127]

If LDL-C goals are not obtained, bempedoic acid (a pharmacological inhibitor of ATP citrate lyase), can be initiated. It has shown a significant reduction in CV events in patients with high CV risk and statin therapy intolerance in the CLEAR outcomes trial.[128,129]

Globally, defining an age threshold concerning statin prescription is highly discussed, even if statin-related adverse effects may be higher in older patients facing multimorbidity, frailty, polypharmacy, and decline in hepatic and renal functions.[130] To be noted, however, statin use was not associated with incident dementia or declines in individual cognition.[131] Reduction for CVD after statin therapy was seen in patients ≥ 75 years without increasing risks of severe adverse effects. Of note, the benefits and safety of statin therapy were consistently found in adults aged ≥85 years.[132] Further, discontinuation of statins resulted in increased risk of ASCVD events in older patients.[133,134] Efficiency and safety of lipid-lowering medications need to be addressed in studies focusing on older persons.[135]

Diabetes Mellitus

The treatment of hyperglicaemia remains the key aim of antidiabetic treatment, also in older patients. According to 2023 ESC guidelines, reducing HbA1c decreases microvascular complications, particularly when achieving near-normal levels.[106] Nevertheless, in geriatric patients, the management of the therapies must avoid any worsening of the patient's functional status and quality of life. In this regard, hypoglycaemia is a common, unpredictable, and potentially dangerous side effect of antidiabetic treatment. Episodes of hypoglycaemia are particularly dangerous in older patients, whose care is complicated by chronic medical illness, frailty, isolation, or a shortened life expectancy. Moreover, prior research has also suggested a link between hypoglycaemia and fall-related fractures in older patients with type 2 diabetes. Fractures are the most common non-fatal outcome of falls; nevertheless, also damage to internal organs, traumatic brain injuries and even death can occur.[136]

For all these reasons, physicians should try every possible effort to reach adequate glycaemic control without causing hypoglycaemia.[137] A glycated haemoglobin ($HbA1_c$) goal < 7.0–7.5% for self-sufficient patients, with generally good conditions and an expectation of life of at least 8–10 years represents the target. According to the 2023 ESC recommendations, it is important to individualize HbA1c targets according to comorbidities, diabetes duration, and life expectancy, taking into account a higher target ($HbA1_c$ < 8.5%).[106]

Another strategy to reduce hypoglycaemia is using an adequate antidiabetic treatment. Regarding sulfonylureas, glinides, and insulin, it is necessary to pay maximum attention in older patients, also for an increased risk of CV events. Metformin monotherapy is effective and associated with a low risk of hypoglycaemia which is infrequent also with dipeptidyl peptidase 4 inhibitors, because they act in a glucose-dependent manner. Thiazolidinediones have a low incidence of hypoglycaemia and can be also used in severe forms of CKD; however, they are contraindicated in patients with heart failure.

Type 2 diabetes mellitus is common among patients with ASCVD or at the highest risk of CVD. The converse is also true: ASCVD is common in patients with type 2 diabetes mellitus.[106] Given these relationships, it is key to consider the presence of type 2 diabetes mellitus when deciding strategies to mitigate CV risk.[106] Glucagon-like peptide-1 agonists and sodium-glucose cotransporter 2 inhibitors are reference drugs for this purpose.[106]

Glucagon-like peptide-1 (GLP-1) agonists are recommended in the 2023 ESC guidelines for their effectiveness in reducing CV outcomes.[106] These drugs resulted in reducing the risk of CV and all-cause death and in lower rates of diabetic kidney disease.[106] In older patients, they combine not only their effectiveness in reducing outcomes but also a CV safety and a low risk of hypoglycaemia. They also lead to weight loss and may be particularly useful in diabetic patients with associated obesity. Taking GLP-1 agonists could lead to nausea and vomiting, especially during first administrations, with a progressive reduction up to the disappearance of gastrointestinal symptoms.

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) did not cause hypoglycaemia and improve CV and renal outcomes;[106]; due to their diuretic properties, they also have positive effects on the BP. These drugs can cause genitourinary infections; therefore, it is useful to avoid prescribing such drugs to patients suffering from recurring urinary tract infections.[137]

In conclusion, it is important to minimize the risk of hypoglycaemia and prioritize the use of glucose-lowering agents with proven CV benefits, all independent of glucose-control, like GLP-1 agonists and SGLT2i, over agents without proven CV benefits or proven CV safety. Nevertheless, according to the results of a meta-analysis of randomized controlled trials to evaluate the effects of SGLT2i on sarcopenia in patients with Type2 diabetes mellitus, if SGLT2i have positive effects on weight loss predominantly derived from reduction of fat mass, a negative influence on muscle mass is parallel to the reduction in fat mass and body weight, and the consequent increased risk of sarcopenia is noteworthy, especially as patients are already predisposed to physical frailty.[138] It is important to conduct large-sample and long-term follow-up studies to better understand the risk of sarcopenia and explore strategies for preserving lean mass and improving physical function.[138]

Advice 5

- Treatment of arterial hypertension, dyslipidaemias, and diabetes is essential in older adults considering that CVD worsens the quality of life and frailty status. Therapeutic strategies and targets are discussed in the text.
- In case of difficulty in achieving the pressure targets, especially in older (>85 years) and frail patients, an individualized therapeutic approach based on clinical judgment, patient preference, and geriatric advice might be proposed.[63,100]

Targeting inflammation as an untraditional CVD risk factor

Ageing is associated with proinflammatory mediators and is termed inflammageing. It is uncertain whether inflammageing is related to ageing itself or a result of comorbidities common in older age.[139] The mechanisms that connect inflammageing with CVD are poorly understood, although inflammation plays a critical role in atherothrombosis.[140,141] Four large double-blind trials have compared the effects of anti-inflammatory agents vs. placebo in patients with ASCVD optimally treated with lipid-lowering medication.

In CANTOS, an anti-interleukin (IL)1-beta monoclonal antibody, canakinumab, reduced the combined endpoint outcome in over 10 000

patients with previous myocardial infarction and C-reactive protein (CRP) ≥ 2 mg/L,[142] but the drug was not further developed for this indication because of the risk of fatal infections and high costs.[142]

In CIRT, low-dose methotrexate (15–20 mg once weekly) did not reduce the final composite endpoint in 4786 patients with previous myocardial infarction or very high CV risk.[143]

Low-dose colchicine (0.5 mg daily) was compared to placebo in 4745 patients with recent myocardial infarction, regardless of CRP values (COLCOT)[144] and in 5500 patients with atherosclerotic coronary artery disease, stable since at least 6 months (LODOCO2).[145] In both studies, Colchicine had favourable effects on ASCVD outcomes. In addition, in a recent meta-analysis including over 12 000 patients with ASCVD,[146] colchicine reduced the risk of myocardial infarction, stroke, and unstable-angina-driven revascularization, with no significant effect on CV death and all-cause death. No increase in gastrointestinal events was noted with a daily dose of < 0.5 mg.

Patients with inflammatory joint diseases (Rheumatoid Arthritis and Axial Spodyloarthritis) have an increased risk of ASCVD,[147,148] possibly due to the excess of systemic inflammation.[149] Some modern anti-rheumatic medications targeting inflammation, especially methotrexate, Tumour Necrosis Factor inhibitors, and Interleukin-6 (IL-6) inhibitors, seem to improve various biomarkers of CVD and reduce ASCVD in observational studies in Rheumatoid Arthritis cohorts,[149] However, these current results are not stratified by age, and in addition, it is uncertain whether these observations are due to specific atheroprotective effects.

Anti-inflammatory therapies targeting NOD-like receptor protein 3 (NLRP3) inflammasome (colchicine) and IL-1/IL-6 pathway may seem promising for secondary prevention of ASCVD in older patients. ZEUS, the Zlitivekimab Cardiovascular Outcomes Study which is still ongoing, will compare ziltivekimab (an IL-6 inhibitor) to placebo among 6200 patients with stages 3–4 CKD and elevated hsCRP to formally test whether reducing circulating IL-6 reduces CV event rates.[150] Unfortunately, these results cannot be extrapolated to all older patients, as this study only included patients with a mean age of 69–72 years. Furthermore, the four major randomized controlled trials on anti-inflammatory medication excluded patients with inflammatory joint diseases. Thus, more data are needed on the effect of anti-inflammatory medication in secondary CVD prevention in older patients, both with and without inflammatory joint diseases.

The role of epigenetics in cardiovascular risk factors in the older adults

Epigenetic alterations (DNA methylation or hydroxymethylation, histone modification, and non-coding RNA expression) form an important link between the intrinsic genetic landscape and extrinsic environmental influences ultimately regulating gene expression.[151,152]

Most CV risk factors induce epigenetic modifications, and these accumulate during ageing.[152] In DNA methylation, enzymes add a methyl group to cytosine bases, altering chromatin structure and thus modulating gene expression. Smoking induced changes in 22 DNA methylation sites in a study on monozygotic twins.[153] Chemical modifications to histone proteins, influencing chromatin structure and gene expression, were found when analysing several genetic mutations associated with dyslipidaemia.[154] Several non-coding RNAs, transcripts that are not coded into proteins but regulate gene expression and chromatin structure through alternative mechanisms, are implicated in the renin-angiotensin-aldosterone system, with implications for arterial hypertension.[155]

Based on the 'information theory', ageing results from the accumulation of genetic and epigenetic errors. Because epigenetic modifications are intrinsically reversible, CV ageing can potentially be reversed.[156] This could be achieved by either halting the responsible maladaptive epigenetic modifications, through control of CV risk factors or by inducing beneficial epigenetic changes. Many studies suggest that the latter can be achieved through exercise training, healthy nutrition, and pharmaceutical intervention in primary as well as secondary prevention of CVD.[157] For example, muscle-specific changes in DNA methylation, histone modifications, and non-coding RNAs regulate skeletal muscle and myocardial interactions during and after exercise.[158,159] The positive CV effects of a Mediterranean diet could also be mediated by epigenetic changes.[160,161]

Nutraceutical polyphenols such as resveratrol or cocoa polyphenols may interfere with genome-wide epigenetic modifications in humans.[162] Epigenetic drugs have shown the potential to prevent vascular inflammation, endothelial dysfunction, and atherosclerosis, and some have been translated into clinical studies.[157] In a meta-analysis of randomized studies, apabetalone (a drug modifying an epigenetic reader protein) was shown to reduce CV events in patients with established CVD by improving high-density lipoprotein levels.[163] Resveratrol treatment improved diastolic function and natriuretic peptide levels (both hallmarks of ageing) in patients with ischaemic heart disease.[164,165] Finally, administration of a micro-RNA 132 inhibitor (CDR132L) decreased cardiac dysfunction and fibrosis in patients with heart failure, which indicates the potential for treating CVD risk factors.[166]

Our current understanding of epigenetic regulation during ageing in the CV system remains incomplete and based on associations. Whereas the independent effects of ageing and CV risk factors on the epigenome have been defined, we still have little evidence exploring a coupled and potentially unique interaction. Therefore, the direct contribution of ageing-related epigenetic changes to CVD onset is still poorly understood and large randomized trials will need to establish their definite role.

Psychosocial status, therapeutic adherence, rehabilitation, digital health and society

Psychosocial status

Ageing entails multiple changes in the individual psychosocial status, which significantly impact the management of complex conditions like CVD. Cognition is a critical area for its impact on how individuals age, determining their ability to live independently, move safely, and adhere to medication regimens.

Normal ageing is typically accompanied by cognitive declines,[167] and, with a growing ageing population, nearly 50 million individuals worldwide suffer from dementia, a number projected to rise to 152 million by 2050.[168]

There is mounting evidence suggesting that adopting healthy lifestyles may mitigate the rate of cognitive decline associated with ageing and delay the onset of cognitive symptoms in age-related diseases.[169] These include maintaining a proper diet, increasing physical activity, avoiding excessive alcohol consumption, and treating mood disorders.

Among mood disorders, depression represents one of the most prevalent mental health issues among older adults worldwide.[170] The estimated global prevalence of depressive disorders among older adults

ranges 10–20%,[168] with 40% of all individuals diagnosed with mental illness also suffering from depression.[171] Depression is associated with an increased risk of global morbidity and mortality, heightened suicide risk, declining cognitive and social functioning, and an elevated risk of dementia in later life.[172] Depression and CVD are mutually causative conditions and exert reciprocal effects on each other, constituting a significant health concern.[173] Overall, the prevalence of depressed patients with coronary artery disease is 20–40%, significantly higher than the average prevalence among healthy individuals.[174] Depression exacerbates functional disabilities caused by the illness, interferes with treatment and rehabilitation, and leads to unhealthy lifestyle choices and dysfunctional coping strategies, such as emotional suppression and problem avoidance.

Isolation and social withdrawal are among the multiple factors contributing to the onset of depression.[175] Epidemiological data indicates that over 20% of older adults living in the community are identified as socially isolated. Being unmarried, male, having lower levels of education, and having a low income were all found to be independently associated with this condition.[176] Social withdrawal and isolation are closely associated with feelings of loneliness and lack of social support, both emotional and instrumental, which are also recognized as further risk factors for CVD.

Frailty is often associated with lower socioeconomic status, which encompasses factors such as education, income, wealth, housing, and occupation. This relationship holds true across different geographical regions, regardless of the frailty measure used, and remains consistent even after adjusting for age, sex, and other relevant factors.[177] The interplay between frailty and socioeconomic status is bidirectional, with each influencing the other and potentially intensifying over time. Additionally, various mediators may moderate this relationship, including behavioural factors (e.g. health-related behaviours), health-related factors (e.g. multimorbidity), social factors (e.g. social network size), material factors (e.g. access to healthcare), and mental factors (e.g. cognitive function).[178]

Advice 6

- Adopting healthy lifestyles may mitigate the rate of cognitive decline associated with ageing and delay the onset of cognitive symptoms in age-related diseases.[169]
- Depression is a severe mood disorder representing one of the most prevalent mental health issues among older adults worldwide.[170] Depression exacerbates functional disabilities, interferes with treatment and rehabilitation, leads to unhealthy lifestyle choices and dysfunctional coping strategies.
- Isolation and social withdrawal are among the multiple factors contributing to the onset of depression.[175]
- Psychosocial risk factors must be evaluated in the global assessment of older patients and appropriately managed, tailoring the treatments to the patient's conditions.

Treatment adherence in older adults

Lifestyle measures and/or guideline-directed medical therapy remain too poor.[79] Medication adherence ranges from 50% for primary CVD prevention to 66% for secondary prevention; of all medication-related hospital admissions in the United States, 33% to 69% and approximately 9% of CVD cases in Europe can be attributed to poor medication adherence.[79]

In this regard, sufficient treatment adherence is a key element for improving prognosis in CVD, reducing the burden of morbidity and mortality associated with CVD, and decreasing costs due to rehospitalizations.[79]

Despite the beneficial effects of prevention programmes, including cardiac rehabilitation, on clinical outcomes in older patients with CVD, participation and adherence significantly decrease with age.[79] The main reasons include transport difficulties and a lack of referral by healthcare providers. Also, older patients are more likely to assume that lifestyle changes would not improve their health.[79] Key factors include supervision, social support from staff and peers, and individualization.[79] Moreover, it is important to provide adequate information about benefits and potential risks, identifying perceived barriers and facilitators, as patients with realistic expectations of change are more likely to be adherent.[79] This may also increase patients' self-efficacy which is related to achieving lifestyle goals. Enjoyment is an immediate reward that is closely related to intrinsic motivation and could lead to better adherence than delayed rewards, such as health benefits in the long term.[79] Many secondary prevention services have not specifically been designed for the older adults.[79] A comprehensive geriatric assessment including not only CV function but also peripheral functional evaluation (strength, balance, coordination, and aerobic capacity), assessment of disability and comorbidities, nutritional, cognitive, and psychosocial components is suggested.[79]

Multimorbidity and the associated use of multiple medicines (polypharmacy) is common in the older population. According to a systematic review conducted to identify and summarize polypharmacy definitions in existing literature, the most commonly reported definition of polypharmacy was the numerical definition of ≥5 five medications daily.[179] Polypharmacy is common in the older population and is associated with some adverse clinical outcomes and increases healthcare burdens.[180] Nearly 40% of the older population is exposed to polypharmacy, and its prevalence is significantly higher in older individuals aged ≥70.[180] Many medications have side effects, require additional monitoring, and serve as a consistent reminder of the patient's illness. All these factors might reduce the patient's persistence/adherence.[181] Furthermore, complicated dosing regimens can lead to inconvenient administration times and contribute to forgetting to take medications. It is important to focus on avoiding inappropriate polypharmacy in the older population to address the growing burden of polypharmacy.[180] Finally, a study addressed the critical challenge of medication non-adherence in healthcare by pinpointing indicators related to medication adherence across 39 European countries and Israel showing an high variability of country-specific data among the countries, highlighting the need for more comprehensive data collection and research for developing targeted, country-specific interventions to improve adherence.[182]

Advice 7

- Lifestyle measures and/or guideline-directed medical therapy remain poorly implemented, particularly in older patients.[79]
- It is important to provide adequate information to patients and caregivers, identifying perceived barriers and facilitators, as patients with realistic expectations of change are more likely to be adherent.[79]
- Polypharmacy is common in the older population, and it may reduce the patient's persistence/adherence.[180]
- It is important to focus on avoiding inappropriate polypharmacy in the older population to address the growing burden of this phenomenon.[180]

The role of digital health in cardiovascular prevention in older adults

Digital health (DH) certainly has to be adapted to the needs of old and frailty patients and cannot simply replace the intense direct interaction between health care professionals, patients, and caregivers. Nevertheless, DH technology may hugely contribute to the health management of patients living with limitations due to ageing, mainly in cases of frailty, disability, and poly-pathology. The tools provided by DH may be simple messages sent via SMS or mApp or have progressive more complex technology, based on information through biological sensors or monitoring with sensors-based systems or video recording.[183,184] Simple text message programmes proved their efficacy in the management of CV risk factors modification, like smoking interruption, weight reduction, nutrition, physical activity improvement, and mainly in BP control and diabetes care.[185]

Smoking cessation

Some data suggest that the use of mApps usage for smoke quitting correlates negatively with age,[186] while other studies didn't find any significant relationship between demographics and propensity in the usage of a smoking cessation app.[187,188]

Physical activity

Waist-worn accelerometer sensors allow digital monitoring of walking speed and wrist-worn sensors may be used to assess precisely the level of physical activity in the older adults and used to improve their adherence to prevention programmes based on it.[189,190]

Hypertension

Although data about the DH methodology used for telemonitoring, the clinical setting, and the characteristics of the patient's samples, are highly heterogenous, all show an improvement in BP control.[191–193] The 2018 EHS Guidelines suggest that telehealth strategies can be useful adjuncts to interventions shown to reduce BP.[194]

Diabetes

Many mApps provide reminders for regular measurement of the required parameters and medication adherence and the transmission of glycaemic values from patients to the physicians may use SMS, e-mail, or web-based services. The controls may use the support of Bluetooth-enabled glucose metres (BlueStar™[195,196]) or continuous glucose monitoring patches (Freestylen™ LibreLink™ app Abbott Laboratories, Abbott Park, IL).[197] Meta-analyses indicate that mobile phone interventions reduced slightly haemoglobin HbA1c (0.2–0.5% over 6 months,[198] and the 2023 ESC Guidelines on diabetes and CV diseases underline that large-scale glycaemic studies are required, using continuous glucose monitoring to assess glucose levels, to establish whether optimizing glycaemia in patients with CVD and diabetes improves clinical outcome.[106]

Underutilization of DH may be related to an incomplete understanding of its value due to inertia, misunderstanding of its potential role, lack of resources of health care providers, and lower usage and comprehension of digital devices by older subjects. Also, the lack of manufacturers' attention to older age needs, like devices of simple usage with large screens allowing large text sizes, can play a role.[59] Anyway, a survey of 2017 by the Pew Research Center showed that about 42% of subjects > 65 years old own smartphones, increasing from 18% in 2013, 67% have Internet access, 42% have home broadband, 32% have tablets, and 34% use social media.[199] In another survey from the ESC Council for Cardiology Practice and the Digital Health Committee, 57% of 559 respondents graded their knowledge about DH as 'fair' using the most frequently clinical information systems, mHealth Apps, and telemedicine.[200]

Advice 8

- Digital health technology may contribute to the management of patients living with limitations due to ageing, mainly in cases of frailty, disability, and poly-pathology.
- The available tools include progressively more complex technology;[183–185] therefore, standardization of their use in daily clinical practice is needed.

The role of cardiac rehabilitation in the older adults

The benefits of cardiac rehabilitation are well documented in several clinical conditions such as coronary artery disease and heart failure.[201,202] Cardiac rehabilitation can also improve the level of frailty[203]; thus, it is an essential component in the continuum of care of older patients with CVD.[204,205] The higher prevalence of comorbidities,[206] geriatric syndromes,[207] frailty,[207] the more adverse CV risk profile[208], and lower exercise and functional capacity[209] compared to their younger peers underscore the need for sustained cardiac rehabilitation. The benefits for older patients are well-documented[210] and include improvements in functional capacity and strength,[211–213] quality of life,[214] modification of CV risk factors[208] but also enhanced compliance with secondary prevention medication regimens. Therefore, the main goals of cardiac rehabilitation in older adults are the preservation of mobility independence and mental function, prevention of sarcopenia and frailty, prevention and treatment of anxiety and depression, encouragement of social adaptation, and return of the patient to the same lifestyle as before the event.[204] However, given the age-related clinical complexities, the implementation of cardiac rehabilitation in older patients requires a higher degree of individualization[204] which includes the diagnosis and treatment of not only CVD but also other chronic diseases,[205] targeted prevention of non-CV events and CV complications, and[206] efficient assessment of the functional impact of CV conditions on the patient's quality of life and independence.[204,210]

Advice 9

- The benefits of cardiac rehabilitation are well documented in several clinical conditions such as coronary artery disease and heart failure.[201,202] Cardiac rehabilitation can also improve the level of frailty[203]; thus, it is an essential component in the continuum of care of older patients with CVD.[204,205]
- The main goals of cardiac rehabilitation in older adults are the preservation of mobility independence and mental function, prevention of sarcopenia and frailty, prevention and treatment of anxiety and depression, encouragement of social adaptation, and return of the patient to the same lifestyle as before the event.[204]

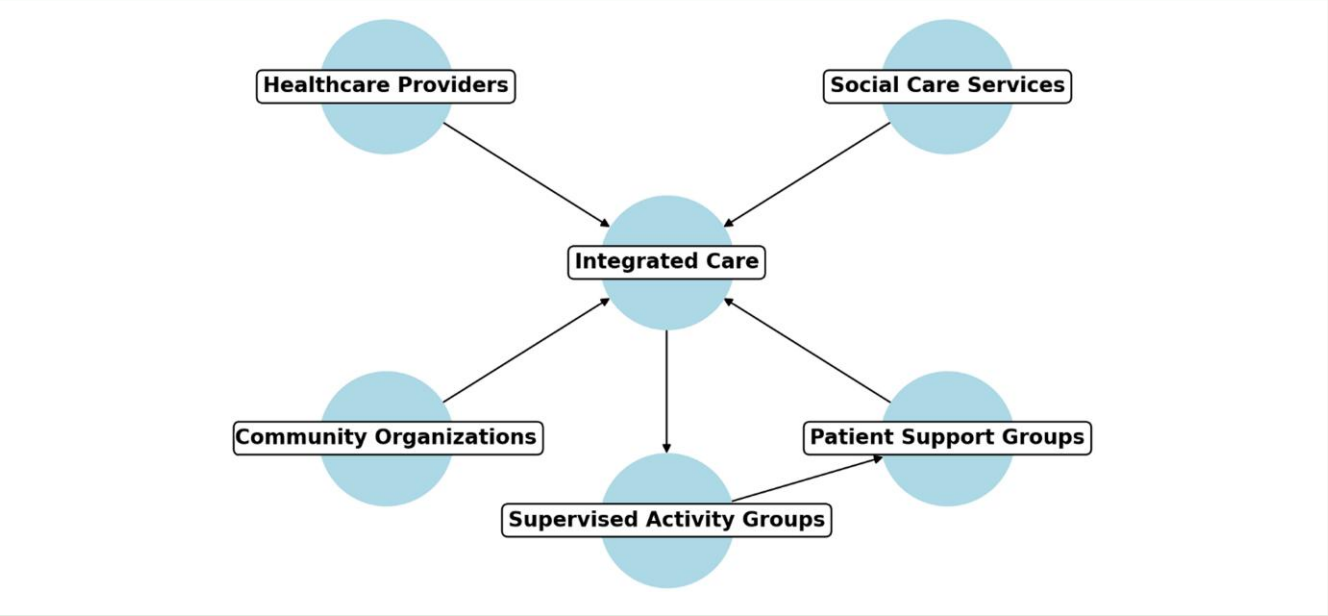


Figure 2 Integration of care.

Integration of care (including cooperation with other professionals and social support)

Integrated care aims to provide a coordinated and personalized approach to healthcare, reducing inequalities and improving quality of life, and requires the collaboration of different disciplines and sectors.[215] Professionals should use a simple routine to transition towards person-centred care and initiate a patient narrative and partnership. In a more integrated approach, staff should advocate for collaboration with other key sectors to decrease fragmentation, ensuring comprehensive early discharge planning and transdisciplinary care processes.[216] Building strong leadership skills within the healthcare and social care workforce, alongside developing cross-disciplinary competencies, is crucial for implementing holistic CV care. Furthermore, team-based training enhances communication, coordination, and collaboration across healthcare and social services.[217]

Health service, local government, and community organizations should establish integrated care systems that deliver well-coordinated services closer to individuals' homes, while simultaneously reducing hospital admissions and wait times. This approach should integrate person-centred care, transdisciplinary collaboration, and technology-supported interventions.[217] Following the acute phase, comprehensive management that accounts for common medical needs and age-specific health concerns is crucial in reducing duplication, enhancing coordination, and minimizing costs for both patients and healthcare systems.[218]

A critical component of optimizing CV care pathways, particularly for older adults, is the incorporation of frailty screening and prevention strategies. Identifying frailty at an early stage enables targeted multidisciplinary interventions, which contribute to improved health outcomes, preservation of functional independence, and a reduction in hospital readmissions. Moreover, for older patients, it is essential to balance the need for individualized treatment with social interactions, which can serve as a crucial motivational factor. Long-term 'activity groups,' whether supervised or not, may support the maintenance of lifestyle changes and adherence to therapeutic recommendations, thereby improving long-term compliance with treatment. These strategies (*Figure 2*), coupled with holistic and interprofessional approaches, are essential for enhancing the quality of care within integrated healthcare systems.[216–219]

Empowerment of patients and family caregivers

Several barriers impede the effective empowerment of patients within healthcare systems, where empowerment refers to the process of equipping patients with the knowledge, skills, confidence, and autonomy necessary to actively participate in their care and make informed health decisions. The misalignment between often contradictory strategies and socioeconomic conditions hamper patients' ability to engage in their care effectively.[218]

Additionally, limited financial resources and bureaucratic processes may impede the implementation of patient empowerment strategies for chronic diseases.[220] At the hospital level, the constraints on time allocation for patient education prevent healthcare providers from sharing crucial information. Yet, family caregivers are critical in empowering patients, especially in the self-management of CVD. Their contribution should be therefore recognized and supported. This includes providing caregivers with adequate education, emotional support, and access to resources that enable them to assist in medication adherence, symptom monitoring, and lifestyle modifications. Structured training programmes and caregiver involvement in medical consultations can further enhance their role in patient empowerment.[221] Hurdles in healthcare delivery, like long waiting times, poor service quality, and mistreatment of patients and their families hinder patient empowerment efforts. Moreover, the lack of culturally sensitive care, inadequate health literacy support, and the absence of shared

decision-making frameworks further weaken patient empowerment efforts. Establishing patient advocacy programmes and incorporating patient-centered care models can mitigate these challenges. Healthcare professionals, as critical points of contact between patients/families and the healthcare system, can unintentionally contribute to patient disempowerment. Respectful relationships, involving patients and families in treatment decisions, may foster empowerment and improve health outcomes.[218]

Patients' engagement in the empowerment process may be hindered by losing loved ones and perceiving being out of control. However, some patients are motivated to take control of their CVD and adopt new habits for recovery.[221] The unavailability or misuse of appropriate medical resources might be a barrier. Additionally, inadequate budget allocation and lack of health insurance compound patients' and families' challenges, particularly in low- and middle-income countries. Financial insecurity and out-of-pocket expenses often force patients to prioritize immediate financial survival over long-term health management. Policymakers should consider expanding subsidized healthcare programmes, offering financial counselling, and improving access to affordable medication and rehabilitation services.[220] Gender dynamics, referring to the social and cultural roles, expectations, and power relations between genders, also play a significant role in patient empowerment. These dynamics influence access to healthcare, decision-making autonomy, and adherence to medical recommendations. Beliefs shaped by gender norms can both empower and hinder patients. Beliefs that support patient autonomy contribute to empowerment, while beliefs attributing the illness to spiritual forces may hinder the necessary lifestyle changes. For example, in some cultural contexts, seeking medical intervention might be perceived as secondary to faith-based healing, which could delay critical care. Educating patients and communities about the complementarity of medical treatment and spiritual beliefs could help address this challenge. Addressing health beliefs is essential for empowering patients effectively.[222] Patient satisfaction serves as an essential indicator of service quality.[223] Positive patient experiences with medical staff contribute to higher satisfaction levels, which, in turn, are associated with an increased commitment to follow-up care and the development of self-management abilities. Encouraging a culture of patient-centered communication, empathy, and shared decision-making within healthcare institutions can enhance trust and strengthen patients' commitment to their care plans.[222]

In conclusion, patient empowerment faces numerous obstacles within healthcare systems. Addressing these barriers is crucial for fostering empowerment and improving health outcomes. Healthcare systems must recognize these challenges and implement strategies to empower patients actively in their care and enable them to make informed decisions.[220]

Advice 10

- Integrated care in older adults is needed to provide a coordinated and personalized approach to healthcare, reducing inequalities and improving quality of life. It requires the collaboration of different disciplines and sectors.[215]
- Patient empowerment faces numerous obstacles within healthcare systems. Addressing these barriers is crucial and healthcare systems must implement strategies to empower patients actively in their care and enable them to make informed decisions.[220]

Future perspectives (daily clinical practice, clinical research, translational research)

Ageing has a transformative bearing on CVD such that standards applied to younger adults become relatively less reliably aligned with the preferences of geriatric patients. Therefore, in daily clinical practice, our focus on 'disease-specific outcomes' must be shifted in the geriatric population to a more intense focus on quality of life by improving functionality and reducing daily symptoms.

In the field of clinical research, the management of the geriatric patients is encumbered by the lack of clinical trial data. Whereas most clinical recommendations remain premised on standards oriented to morbidity and mortality, geriatric patients' concerns may change to include or even to prioritize qualitative and/or functional objectives. Therefore clinical trials focused on older patients and including outcome dimensions like symptomatic status, frailty, avoidance of dependency and maintenance of independence, individual patient outcome goals and the impact of sex and gender are strongly needed. Also, the role of digital health technology has to be further evaluated in older patients.

Regarding translational research, most older individuals develop inflammageing, a condition characterized by elevated levels of blood inflammatory markers that carries high susceptibility to chronic morbidity, disability, frailty, and premature death.[139] Whether early modulation of inflammageing prevents or delays the onset of CV frailty should be tested in clinical trials,[139] as well as the effect of anti-inflammatory medication in CVD prevention in older patients, both with and without inflammatory joint diseases. The direct contribution of ageing-related epigenetic changes to CVD onset is yet poorly understood and large randomized trials will need to establish their definite role.

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Author contribution

R.F.E.P. conceived the idea for paper, led the work group, drafted sections of the text, and provided editorial oversight. M.F. shared the idea for paper, co-led the work group, drafted sections of the text, and provided editorial oversight. L.G. shared the idea for the paper, drafted sections of the text, reviewed, and commented on a final draft of the paper. R.A./A.B.G./T.S.B./S.C./V.A.C./R.C./G.D./F.D./D.K./E.O./D.R./A.G.S./P.S. drafted sections of the text, reviewed, and commented on a final draft of the paper. All authors agreed to the final version of the paper.

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