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Review

Global consensus on optimal exercise recommendations for enhancing healthy longevity in older adults (ICFSR)

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Abbreviations: 1 RM, One-repetition maximum; ACE, Acute care of older people; ACSM, American College of Sports Medicine; ADL, Activity of daily living; ADP, Adenosine diphosphate; AHA, American Heart Association; ASCO, American Society for Clinical Oncology; BDNF, Brain-derived neurotrophic factor; BMD, Bone mineral density; BMI, Body mass index; CRF, Cardiorespiratory fitness; CVD, Cardiovascular disease; DPP, Diabetes Prevention Program; DXA, Dual-energy X-ray Absorptiometry; EPESE, Epidemiological Studies of the Elderly; HGS, Handgrip strength; HIIT, High-intensity interval training; IADL, Instrumental activity of daily living; IC, Intrinsic capacity; ICOPE, Integrated Care Program for Older People; LRC, Lipid Research Clinics; MCI, Mild cognitive impairment; MCID, Minimum clinically significant difference; MET, Metabolic equivalent; MI, Myocardial infarction; MICT, Moderate- to vigorous-intensity aerobic exercise; OEP, Otago Exercise Program; PA, Physical activity; PBM, Peak bone mass; PCr, phosphocreatine; PIM, Potentially inappropriate medications; RCT, Randomized controlled trial; PRT, Progressive resistance training; SPPB, Short Physical Performance Battery; T2D, Type 2 diabetes; USPSTF, US Preventive Services Task Force; V̇O2 max, Maximum oxygen uptake; V̇O2 peak, Peak oxygen uptake; VPA, Vigorous physical activity; WHO, World Health Organization.

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ABSTRACT

Aging, a universal and inevitable process, is characterized by a progressive accumulation of physiological alterations and functional decline over time, leading to increased vulnerability to diseases and ultimately mortality as age advances. Lifestyle factors, notably physical activity (PA) and exercise, significantly modulate aging phenotypes. Physical activity and exercise can prevent or ameliorate lifestyle-related diseases, extend health span, enhance physical function, and reduce the burden of non-communicable chronic diseases including cardiometabolic disease, cancer, musculoskeletal and neurological conditions, and chronic respiratory diseases as well as premature mortality.

Physical activity influences the cellular and molecular drivers of biological aging, slowing aging rates—a foundational aspect of geroscience. Thus, PA serves both as preventive medicine and therapeutic agent in pathological states. Sub-optimal PA levels correlate with increased disease prevalence in aging populations. Structured exercise prescriptions should therefore be customized and monitored like any other medical treatment, considering the dose-response relationships and specific adaptations necessary for intended outcomes. Current guidelines recommend a multifaceted exercise regimen that includes aerobic, resistance, balance, and flexibility training through structured and incidental (integrated lifestyle) activities.

Tailored exercise programs have proven effective in helping older adults maintain their functional capacities, extending their health span, and enhancing their quality of life. Particularly important are anabolic exercises, such as Progressive resistance training (PRT), which are indispensable for maintaining or improving functional capacity in older adults, particularly those with frailty, sarcopenia or osteoporosis, or those hospitalized or in residential aged care. Multicomponent exercise interventions that include cognitive tasks significantly enhance the hallmarks of frailty (low body mass, strength, mobility, PA level, and energy) and cognitive function, thus preventing falls and optimizing functional capacity during aging. Importantly, PA/exercise displays dose-response characteristics and varies between individuals, necessitating personalized modalities tailored to specific medical conditions. Precision in exercise prescriptions remains a significant area of further research, given the global impact of aging and broad effects of PA.

Economic analyses underscore the cost benefits of exercise programs, justifying broader integration into health care for older adults. However, despite these benefits, exercise is far from fully integrated into medical practice for older people. Many healthcare professionals, including geriatricians, need more training to incorporate exercise directly into patient care, whether in settings including hospitals, outpatient clinics, or residential care. Education about the use of exercise as isolated or adjunctive treatment for geriatric syndromes and chronic diseases would do much to ease the problems of polypharmacy and widespread prescription of potentially inappropriate medications. This intersection of prescriptive practices and PA/exercise offers a promising approach to enhance the well-being of older adults. An integrated strategy that combines exercise prescriptions with pharmacotherapy would optimize the vitality and functional independence of older people whilst minimizing adverse drug reactions.

This consensus provides the rationale for the integration of PA into health promotion, disease prevention, and management strategies for older adults. Guidelines are included for specific modalities and dosages of exercise with proven efficacy in randomized controlled trials. Descriptions of the beneficial physiological changes, attenuation of aging phenotypes, and role of exercise in chronic disease and disability management in older adults are provided. The use of exercise in cardiometabolic disease, cancer, musculoskeletal conditions, frailty, sarcopenia, and neuropsychological health is emphasized. Recommendations to bridge existing knowledge and implementation gaps and fully integrate PA into the mainstream of geriatric care are provided. Particular attention is paid to the need for personalized medicine as it applies to exercise and geroscience, given the inter-individual variability in adaptation to exercise demonstrated in older adult cohorts. Overall, this consensus provides a foundation for applying and extending the current knowledge base of exercise as medicine for an aging population to optimize health span and quality of life.

1. Optimizing health in an aging population: Leveraging physical activity and exercise

The global population is rapidly aging, with projections indicating that the number of adults ≥65 years will double to 1.5 billion by 2050. At the same time, those ≥80 are expected to triple between 2019 and 2050, reaching 426 million [1], with 80% living in low- and middle-income countries. This demographic shift impacts multiple sectors, including healthcare, social quality of life, retirement planning, and caregiving. More critically, it brings an increased burden of non-communicable diseases and disabilities. Aging is an inevitable, universal process marked by a progressive decline in several physiological functions, although the rate and extent of this decline is highly variable. Human physiological systems exhibit varying peak development timelines: bone mass peaks around age 20, muscle mass often remains stable until approximately age 50, while cognitive functions such as crystallized intelligence, wisdom, and emotional intelligence can continue to develop and improve well into advanced age [2]. Biological aging, characterized by gradual functional declines, begins at different stages for different systems and progresses over subsequent decades. Aging is typically defined as the progressive accumulation of physiological changes and functional decline over time, leading to increased vulnerability to diseases and mortality [3]. This raises an important question: Do health outcomes during the aging process correlate with inherent physiological capabilities?

The “aging phenotype” encompasses the diverse array of observable traits, behaviors, and physiological alterations that lead to a gradual decline in organismal functions and an increased susceptibility to age-related diseases [4]. It is characterized by morphological changes such as wrinkling and greying of hair, more profound functional declines in various organ systems, cognitive modifications, and increased susceptibility to developing chronic diseases. This phenotype illustrates the complex interplay among genetic, cellular, and environmental factors influencing aging [5]. Current research into the aging phenotype is focused on delineating the biological mechanisms underlying these age-associated alterations and developing interventions that could facilitate or delay the detrimental effects of aging, with the ultimate goal of enhancing the quality of life in later years.

Recent advancements in geroscience have focused on potential anti-aging interventions [6]. Researchers have identified twelve interconnected aging hallmarks — genomic instability, telomere shortening, epigenetic alterations, mitochondrial dysfunction, loss of proteostasis, disabled macroautophagy, deregulated nutrient-sensing, cellular senescence, stem cell exhaustion, altered intercellular communication, chronic inflammation, and dysbiosis — that intensify with age [7]. Experimentally targeting these hallmarks offers possibilities for therapeutic interventions that can slow, halt, or even reverse some aspects of biological aging [7]. However, it is critical to effectively evaluate the practicality of targeting these hallmarks [8,9] and also the extent to which these reflect biological aging processes *per se* or are impacted upon by lifestyle factors which accelerate decline. Additionally, maintaining or enhancing functional capacity and increasing the number of years lived without disabilities are vital when considering the impact of life-extending interventions on the health span of older adults [8].

The overlap of features between disuse and biological aging has long been recognized [10], emphasizing the importance of differentiating between the two to optimize aging and prevent or treat diseases and disabilities. As the late Prof. Walter Bortz II, MD, a geriatrician, once stated in his last book at age 94, ‘The mission of medicine is the assertion and the assurance of the human potential’ [11]. Achieving this involves promoting resilience, defined as the capacity to withstand adversity and maintain stability amidst the physical, psychological, and social challenges of aging. It is essential to recognize that resilience is not merely the absence of frailty, just as well-being is more than simply the absence of disease, and true happiness is not simply the absence of depression [12] or the experience of hedonic pleasure, but rather the achievement of ‘eudaimonia’- the Aristotelian concept of flourishing or fulfilling one’s potential as a human being. Therefore, fostering resilience is central to our roles as healthcare professionals and researchers as we work to affirm and ensure human potential [8].

Although there are many paths to optimizing human potential throughout life, regular exercise is one which is widely acknowledged for mitigating cognitive and physical decline, psychological and social challenges often linked with aging [10]. Research suggests that many declines are more likely due to inactivity rather than inevitable biological deterioration, significantly contributing to the aging phenotype [10]. Lifestyle factors significantly influence aging phenotypes, particularly the presence or absence of physical activity (PA) and exercise [13,14]. Tailored exercise programs have proven effective in helping older adults maintain their functional capacities, extending their health span, and enhancing their quality of life [15]. For this consensus statement, “physical activity” is defined as any bodily movement produced by skeletal muscles that increases energy expenditure [16]. The intensity and duration of these activities vary widely. Exercise is defined as a subset of PA, which is characterized by its planned, structured, and repetitive nature that aims to improve or maintain physical fitness components such as aerobic capacity, muscle strength, endurance, balance, coordination, or flexibility [17]. The metabolic equivalent (MET) is a standardized unit used to estimate the energy expenditure during PA. One MET represents the energy expended at rest. Sedentary behavior is defined as any waking activity that involves an energy expenditure of $\leq$1.5 METs typically performed while sitting, reclining, or lying posture. In contrast, a “sedentary lifestyle” refers to a combination of low levels of moderate-to-vigorous PA (equivalent to at least four times the basal metabolic rate) and prolonged sedentary behaviors such as reading, computer use, watching television, office work, and cell phone use [18,19]. Additionally, "insufficient PA" describes individuals who do not meet the physical activity guidelines set by the WHO or country-specific recommendations, which generally suggest 150−300 min per week of moderate-to-vigorous intensity PA [20]. This distinction ensures a more accurate communication regarding the potential health risks associated with physical inactivity and sedentary lifestyles.

Promoting healthy and dignified aging involves supporting healthcare systems to implement evidence-based exercise programs for older adults across the entire aging spectrum, both in community and residential settings. Given the rapid advancements in exercise science related to aging, this consensus document specifically focuses on changes in functional capacity, physical fitness, body composition, quality of life, and disease burden rather than the overall aging process. Understanding the impact of PA patterns is essential for optimizing aging, addressing the concerns of healthcare professionals and caregivers/family members, and ultimately improving outcomes in older individuals. This paper advocates using PA/exercise to enhance health, prevent diseases, and manage existing conditions in older adults. It presents findings from the latest randomized controlled trials (RCTs) that underscore the beneficial effects of specific PA/exercise modalities on age-related physiological changes, disease prevention, and the treatment of chronic ailments and disabilities at advanced age. Additionally, it addresses critical gaps in the previous guidelines and provides updated, evidence-based recommendations tailored to the practicalities of clinical implementation. Thus, this consensus aims to enhance the efficacy, applicability, and comprehensiveness of exercise programs to better meet the current health challenges older individuals face.

1.1. Distinctive phenotypes of aging

Engaging in regular exercise, maintaining social connections, keeping the mind active, and consuming a healthful diet while avoiding harmful substances and toxic environmental exposures are essential for promoting good health and well-being at all life stages [8]. Exercise is a preventive and therapeutic measure, synergistically enhancing the benefits of other lifestyle factors [13,14]. At one end of the PA/exercise spectrum are lifelong exercisers and competitive master athletes. Despite a decline in competitive performance, as evidenced by diminishing world records, the absolute levels of physical performance in these individuals are impressive compared to their physically inactive age-matched peers [21,22]. These athletes exemplify how exercise (and likely genotype) can preserve physiological function and enhance human health and functional ability in old age. Thus, PA is fundamental to achieving and maintaining a state of resilience and ensuring full human potential that is age appropriate, despite the social, physical, and psychological challenges of aging [8]. On the other end of the spectrum, with suboptimal levels of PA, aging is more likely to be accompanied by cardiovascular disease, cancer, type 2 diabetes (T2D), obesity, diminished muscular function, Alzheimer's disease and related disorders, depression, frailty, and increased end-of-life morbidity. While PA is generally beneficial, even among the small proportion of individuals who maintain a high level of PA throughout life, some will develop cardiometabolic, musculoskeletal, neurological, or other diseases with age. Overall, the choice, or ability, to engage in PA significantly impacts the trajectory of decline with aging, with PA optimizing physiology and reducing the risk of many chronic diseases, particularly if social determinants of health (economic, cultural, geographic) are favorable. Conversely, a sedentary lifestyle increases susceptibility to these same disorders (Fig. 1).

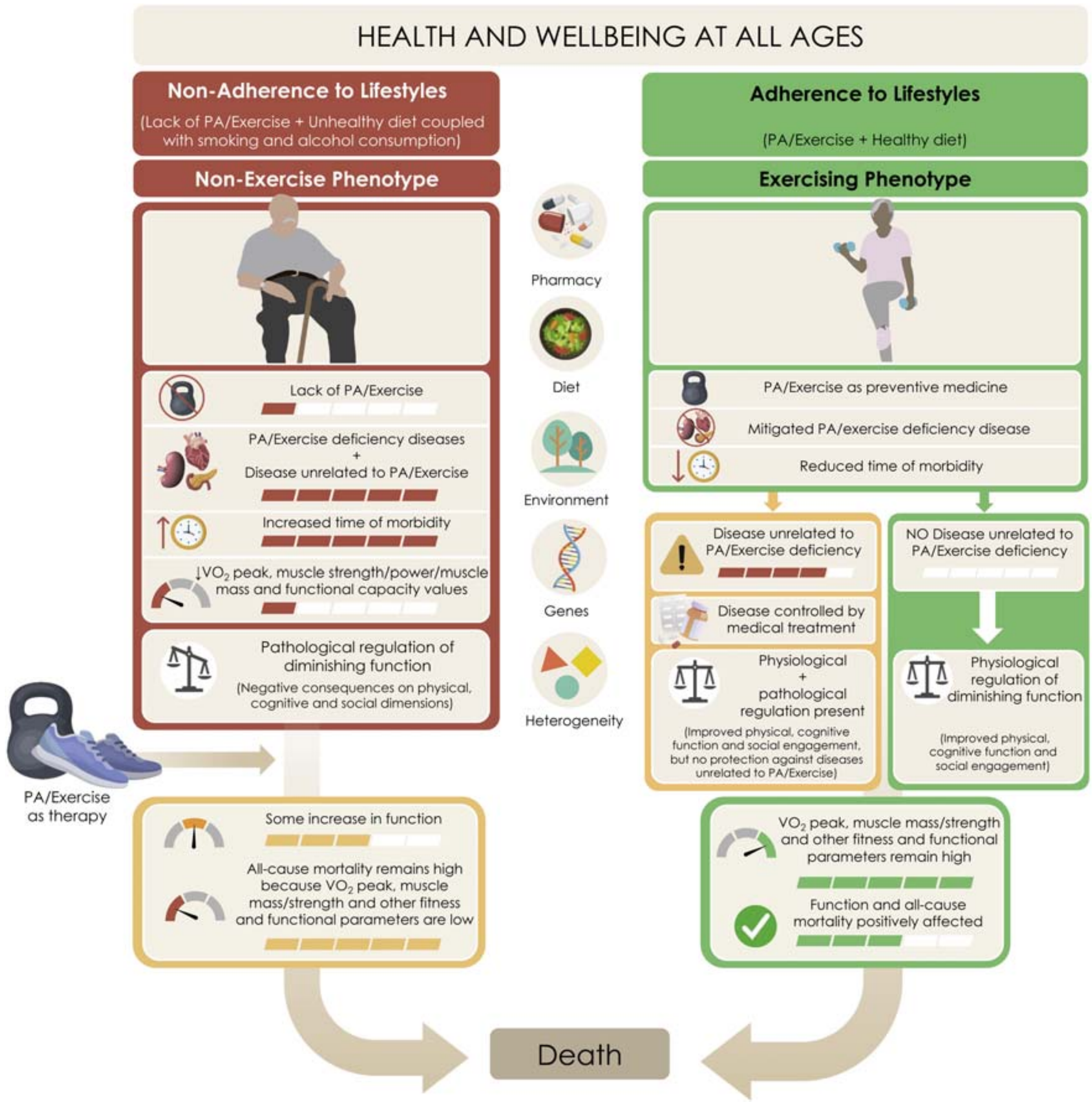

Fig. 1. Evidence shows that being physically active and having a healthy diet (coupled with no smoking and moderate alcohol consumption) are integral to the maintenance of health and well-being at all ages. The left-hand side shows a probable pathway for non-exercisers. These individuals are susceptible to exercise-associated, and diseases not associated with PA. Various pathological processes cause physiological disruption.
Exercise as therapy can potentially reverse some declines, but issues related to low cardiorespiratory fitness (VO_2 peak), muscle strength/power/muscle mass and functional capacity values may persist. The right-hand side illustrates the role of PA as preventive medicine, emphasizing the preservation of effective, albeit gradually diminishing, physiological functions. They are partially protected from exercise-associated diseases but are equally prone to diseases unrelated to exercise. Exercise/PA will have no direct effect on those diseases that are not directly exercise dependent. However, there is evidence that exercise has a protective effect in those diseases whose aetiologies are exercise-dependent. Exercise and PA provide immediate benefits to functionality across a wide range of diseases, irrespective of changes in VO_2 peak. While VO_2 peak improvements may contribute to cardiovascular protection, other outcomes of exercise, such as reducing the risk of falls, fractures, and mortality, are not solely dependent on VO_2 peak enhancement. In the very old, this may not play a crucial role, but in many other patients, VO_2 peak values, because of their inextricable link to all-cause mortality, may be crucial. Although changes in handgrip strength are generally associated with frailty, malnutrition, and mortality risk, rather than being a direct outcome or target of exercise therapy, they may serve as a supplementary marker for assessing overall physiological status during exercise interventions. Both cohorts are experiencing constant decremental changes because of the inherent aging process, but at a different rate due to their PA engagement. The center contains the significant moderators of both pathological and physiological processes. PA = Physical Activity, $\dot{V}O2$ peak = Peak oxygen uptake.

1.2. Lifestyle, genetics, and environment: Interacting determinants of healthy aging

Biological aging and chronic diseases share a bidirectional relationship. Chronic conditions, including geriatric syndromes, can exacerbate age-related decline. Additionally, certain treatments for these conditions may contribute to further health deterioration, especially in older adults. Notably, conditions such as frailty, sarcopenia, and dementia accelerate the onset of age-related disability, posing significant health risks [23]. The World Health Organization (WHO)'s 2015 World Report on Aging and Health defined healthy aging as developing and maintaining functional abilities [24]. Achieving an optimal aging trajectory involves considering an individual's intrinsic characteristics, behaviors, and ecological influences. While homeostatic capacities providing resilience to stressors may diminish with age [25], these factors can be optimized to sustain a person's functional ability and intrinsic capacity throughout their life, especially in older age (Fig. 1).

The primary determinants of health and longevity—genetics, environment, and behavior—interact and influence the manifestations of aging, chronic diseases, and multi-morbidities. This interaction is often evidenced by epigenetic changes to the genome, which can result from lifestyle choices or exposure to maternal or fetal stress/toxins/metabolic abnormalities in utero [26,27]. Insufficient PA and a sedentary lifestyle are major public health issues, together with other modifiable risk factors that have significant beneficial effects across the life course. In this context, the WHO has published the World Report on Aging and Health [24], which describes functional autonomy as the interaction between an individual's physical and mental capacity (intrinsic capacity domains) and the context of each individual's life (environment) [28]. Accordingly, healthy aging depends on intrinsic capacity, socio-economic status, physical environment, as well as the interactions between these factors [29]. The WHO has proposed five domains—locomotion, vitality, cognition, psychological, and sensory—that can be used to evaluate an individual's intrinsic capacity.

The WHO recommends actively addressing these issues to promote healthy aging [30]. Although the specific mechanisms and optimal modalities of PA's health benefits are not fully understood, evidence to date suggests that engaging in PA can substantially enhance domains of intrinsic capacity [31]. This, in turn, reduces mortality, promotes functional ability, and healthy aging [32,33]. However, not all PA is equally effective, as dose-response relationships and exercise modality-specific adaptations exist. There are associations between the intensity, volume, and modality of exercise and many health outcomes [34]. For example, for over three decades [17,35,36], high-intensity progressive resistance training (PRT) has been recognized as a safe and effective means to combat frailty. In contrast, simple stretching exercises do not offer therapeutic benefits for this condition. Therefore, exercise used to promote healthy aging must be prescribed in the same evidence-based manner as any other medicine.

1.3. Impact of PA/exercise on mortality and age-related diseases

According to the WHO, a sedentary lifestyle and insufficient PA present significant public health challenges that must be addressed to promote healthy aging [30]. While the optimal types, intensity, and mechanisms through which PA exerts its beneficial health effects remain under investigation, epidemiological and empirical data consistently show that PA positively affects aging and mortality rates. The classical study by Blair et al. [37] demonstrated that higher levels of physical fitness, as indicated by maximal oxygen uptake (VO_2 max) values, were associated with reduced all-cause mortality, in a dose-dependent manner [37]. The study identified an optimal aerobic fitness level of 34 ml/kg/min for men and 32.2 ml/kg/min for women, beyond which no additional mortality benefit was observed [37]. More recently, Moore and colleagues [38] reported that higher leisure time PA volumes were associated with enhanced life expectancy across various PA levels and body mass index (BMI) groups in a study of 638,855 men and women aged 40–90 followed over 10 years in pooled data from six prospective cohort studies in the National Cancer Institute Cohort Consortium. Physical activity was categorized by metabolic equivalent hours per week (MET-h/week), a measure that quantifies the intensity and duration of physical activities by comparing them to the energy expended at rest (1 MET). Engaging in 0.1−3.74 MET-h/week of PA, akin to brisk walking for up to 75 min per week, extended life expectancy by 1.8 years compared with no activity. Higher activity levels yielded more substantial benefits, with a 4.5-year increase at 22.5 + MET-h/week (equivalent to brisk walking for 450 + min/week), something reported by only 22 percent of the cohort. Notably, physically active individuals with normal BMI (18.5–24.9 kg/m^2) gained 7.2 years of life expectancy versus inactive individuals with morbid obesity (BMI $\geq$ 35 kg/m^2). It is important to note that the self-reported nature of PA and BMI data has limitations [38]. However, PA is most often over-reported, and this imprecision would attenuate relationships rather than exaggerate them. We now also acknowledge that, despite the inherent limitations of self-reported PA, similar (almost linear) associations between PA and mortality are observed when PA is measured using objective methods. Furthermore, it is important to highlight that the beneficial relationship between PA and mortality persists even in older populations, where changes in PA levels later in life can still exert significant effects on mortality outcomes [39]. Evidence indicates that PA reallocates energy towards healthspan, extending physiological processes by preventing harmful over-accumulation of fat and reproductive tissues and stimulating repair and maintenance mechanisms. This integration of evolutionary and biomedical perspectives explains why PA reduces morbidity and mortality rates, even among modern populations with access to medical care [40]. For example, mortality risk was assessed in a pooled analysis of 6 cohorts [661,137 participants (median age, 62 years; range, 21–98 years), with a median 14.2 follow-up years in the United States and Europe [41], in relation to their adherence to the 2008 PA Guidelines for Americans [42], [a minimum of 75 vigorous-intensity or 150 moderate-intensity minutes per week (7.5 MET h/week) of aerobic activity]. Those who performed some but less than the recommended minimum had a 20% lower risk, a 31% lower risk at 1–2 times the minimum, and a 37% lower risk at 2–3 times the minimum, compared to those reporting no PA [41]. Recently, findings from the 2011–2014 NHANES survey indicate that higher PA intensity, rather than volume alone, is associated with reduced all-cause and cardiovascular mortality risk. These results suggest that integrating PA of higher intensity into daily routines may optimise health [43].

The pathway from higher levels of PA to improved life expectancy noted above is complex and mulitifactorial. However, epidemiological data increasingly demonstrate that cardiorespiratory fitness (CRF) is a stronger predictor of mortality risk than traditional risk factors such as smoking, hypertension, high cholesterol, or T2D. Adding CRF to conventional risk assessment significantly enhances the accuracy of risk stratification for adverse outcomes [44]. The Aerobics Center Longitudinal Study (ACLS) found that the fittest men and women had 43% and 53% lower risks of all-cause mortality and 47% and 70% lower risks of cardiovascular disease (CVD) mortality, respectively, compared with the least fit peers [45]. Similarly, an earlier report from the Lipid Research Clinics (LRC) Mortality Follow-up indicated that each 2 standard deviation decrement in CRF (approximately 2–3 METs) was linked to a 2– to 5-fold increase in CVD or all-cause death rates [46]. Furthermore, Nes et al. [47] reported a 21% lower risk of mortality for every 1-MET increase in CRF in both sexes in a large healthy cohort followed up for over 24 years. Generally, the risk reduction per 1 MET increase in measured CRF is associated with a 10–30% reduction in adverse cardiovascular events [37,48,49]. Optimal PA levels, as measured by METs, indicate that adults with CRF levels below 5 METs face a high mortality risk. As everyone has a 100% mortality risk ultimately, this represents a delay in mortality within a defined period of time. In comparison, those with CRF levels between 8 and 10 METs experience enhanced survival rates [50]. This association of CRF levels and mortality risk was also observed across the entire age spectrum, including septuagenarians and octogenarians, and remained consistently inverse, independent, and graded across men, women, and all races [51].

Despite the strength of the above associations a completely different measure, muscle function, as often extrapolated from handgrip strength (HGS), may serve as an alternative to aerobic capacity for assessing overall physiological status and mortality risk [52,53]. Due to the lack of equipment to uniformly measure muscle strength in various cohorts, HGS has often been used as a proxy for overall muscle function and associated physiological capacities, especially in epidemiological studies. It has been identified as a predictive marker for assessing decline in physical and mental capacity in older adults [54]. Numerous studies have shown that incorporating HGS alongside established cardiovascular disease (CVD) risk factors significantly enhances the precision of risk prediction for CVD morbidity [55], all-cause mortality [56], and cancer mortality [52,56]. Many risk factors and diseases have been correlated with low HGS, including overall strength, upper limb function, bone mineral density, fracture susceptibility, T2D, CVD, mortality, cancer, nutritional deficiencies, cognitive decline, depression, quality of life, and mental health status [57]. However, normative HGS values vary across countries due to differences in ethnicity, sex, age, and nutrition, as well as variable protocols and equipment used to measure for them, complicating the application of reference values to diverse populations. For instance, the European Working Group on Sarcopenia in Older People (EWGSOP) sets the threshold for low muscle strength at two standard deviations below the mean reference value, defined as less than 27 kg for men and less than 16 kg for women [58]. In contrast, the Asian Working Group for Sarcopenia (AWGS) defines low muscle strength as less than 28 kg for men and less than 18 kg for women [59]. Despite this variability in establishing normative values, the potential of HGS as a critical tool for early intervention strategies for disease prevention and health promotion across different populations is widely accepted. Even though the reasons why this simple functional measure is so predictive remain unclear, by including HGS as a vital sign, healthcare practitioners can identify potential health issues earlier, enabling timely intervention and improved patient outcomes.

Both aerobic capacity and muscle strength exhibit substantial genetic influences, with approximately 50% of the variability in VO_2 peak and muscle strength attributable to genetic factors, and the remaining 50% to lifestyle choices and acquired diseases or environmental exposures. This genetic contribution is underscored by findings from Bouchard's HERITAGE Family Study [60], which demonstrated that changes in aerobic capacity in response to training are significantly moderated by genotype, even amongst individuals undergoing identical supervised training regimens. Furthermore, data from the Baltimore Longitudinal Study of Aging (BLSA) reveal that roughly 50% of the age-related decline in V̇O2 peak in healthy individuals can be attributed to the loss of muscle mass, as measured by creatinine excretion [61]. These findings highlight the intertwined nature of aerobic capacity and muscle strength, and their collective impact on mortality risk.

As noted above, both higher levels of self-reported PA, as well as higher levels of CRF and muscle strength are predictive of better survival. Studies which have investigated dose-response relationships of physical activity to health-status have demonstrated that both the intensity and volume of exercise contribute to health benefits [34]. Walking, a fundamental form of moderate-intensity PA, reduces morbidity and mortality risk. Epidemiological studies examining the relationship between daily step counts and health outcomes have produced varied evidence, indicating that beneficial effects can be observed with minimum step counts ranging from 4,000 to 12,000 steps per day [62–65]. Moreover, engaging in short bursts of vigorous PA (VPA), averaging only 4.4 min daily, is associated with lower all-cause, cancer, and CVD mortality risks [66].

The modality of PA performed is also critical for intended health outcomes beyond mortality, as many exercise adaptations are modality-specific. For example, anabolic exercises, such as PRT, are vital for maintaining or enhancing functional capacity in older adults, particularly those who are frail or with conditions such as sarcopenia and osteoporosis, mobility impairment or those hospitalized or in residential care. This importance is underscored by the rapid loss of muscle mass that older adults experience during hospitalization or periods of illness [67], leading to weakened muscle strength/power and function, which in turn increases the risk of falls, disability, morbidity, and mortality [15].

No medications currently enhance fitness, functional capacity or alleviate frailty; thus physical exercise remains the most effective therapeutic intervention for disease prevention and management as well as maintaining functional abilities [68]. The WHO advocates a healthy diet, regular PA, moderate alcohol consumption, and avoidance of smoking as core components of a healthy lifestyle [69]. However, the PA and exercise guidelines for older adults often fail to meet their intended goals due to a lack of evidence-based recommendations. This suggests a need for more precise, adaptable, and personalized guidelines that more effectively address the diverse physiological and health conditions of this heterogenous population, thereby improving their overall health and functional capacity.

Evidence indicates that PA, including structured exercise, profoundly benefits the biological mechanisms essential for healthy aging, even in the oldest populations. These biological mechanisms of aging include chronic mitochondrial dysfunction, inflammation, myokine release, defective autophagy, oxidative damage, cellular senescence, and reduced insulin-like growth factor signaling [68,70–73]. Exercise and PA not only enhance physical function and quality of life but also diminish the burden of non-communicable diseases and premature mortality, including deaths from CVD, cancer, and chronic lower respiratory tract diseases [74–77]. Extensive scientific evidence supports the role of PA and exercise in preventing and/or treating various chronic conditions such as obesity, sarcopenia, T2D, CVD, heart failure, hypertension, cancer, renal failure, pulmonary disease, osteoporosis, osteoarthritis, depression, dementia, and Parkinson's disease, among others [77].

Age-related changes in body composition, marked by significant losses in bone and muscle mass and increases in central and visceral adipose tissue, are closely linked to the effects of PA on aging and chronic diseases. This sedentary lifestyle results in "unhealthy" adiposity with an accumulation of intramuscular, peri-hepatic, intrahepatic, and pericardial/intramyocardial adipose tissue, leading to a range of metabolic and functional impairments, including losses in muscle mass and strength, T2D, and CVD [70,78].

The decline in exercise capacity due to inactivity and a sedentary lifestyle results in significant health consequences, impairing the ability to perform daily activities and maintain independence [70,78]. These declines are also associated with cognitive deterioration, particularly in reasoning, processing speed, attention, executive function, and memory. Such cognitive decline is linked to structural changes in the frontal and medial temporal lobes, including the hippocampus, cingulate cortex, and the amygdala, among others. Exercise not only improves cardiorespiratory fitness, muscle strength, quality, mass, bone density, and mobility in older adults but also positively affects cognitive function, potentially mediated by a myriad of positive influences on brain-derived neurotrophic factor (BDNF), inflammation, insulin sensitivity, dopamine transport, cerebral blood flow, and functional connectivity, as well as associated changes in white and gray matter integrity, cortical thickness, and hippocampal size [79–83].

1.4. Personalizing exercise: understanding the sequencing of the prescription, dose-response and interindividual variability

The data reviewed above on PA and mortality are primarily drawn from large epidemiological studies. Implementing these findings into guidelines to improve health outcomes for individuals in clinical practice is the next step. Personalizing exercise prescriptions is critical in clinical care, especially for older adults, in whom adapting exercise modalities to the unique physiological changes that come with aging is important. As people age, their ability to perform vigorous aerobic exercise decreases significantly, while simultaneously they exhibit declines in muscle mass and function, making anabolic or PRT increasingly necessary. This shift in exercise strategy is not just a matter of preference but a vital adaptation to diminished aerobic capacity and the growing need to preserve muscle mass and strength.

Clinical observations indicate that in older adults who have developed advanced frailty and multiple comorbidities resulting in mobility and functional impairment, it is often difficult or impossible to implement robust, moderate, or high-intensity aerobic exercise capable of improving fitness or disease pathophysiology. However, such individuals remain very capable of undertaking high intensity PRT, even in the tenth decade of life [35,84]. This shift in both feasibility and rationale highlights the urgent need for healthcare providers to recalibrate exercise recommendations, tailoring them to meet the specific capabilities and needs of the aging population.

Adopting a personalized approach and prescribing PRT as a cornerstone of physical activity for older adults, combined with aerobic and balance training where indicated and feasible, holds the potential to maintain functional autonomy and enhance quality while mitigating the risk of various age-related conditions. The integration of this personalized strategy into routine clinical practice will likely yield substantial health benefits, enabling our aging population to enjoy a fuller and more active later life (Fig. 2).

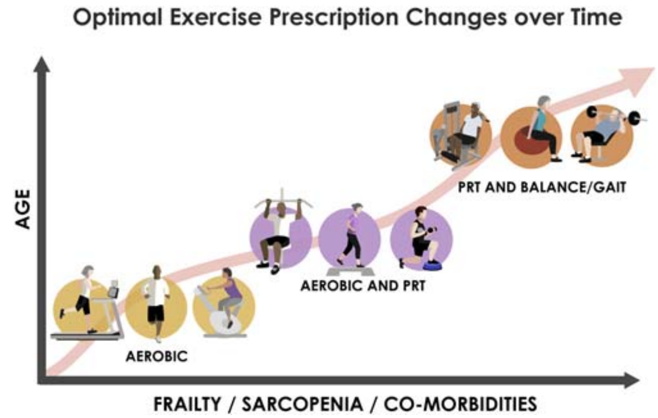

Fig. 2. Sequential exercise programming for individuals with severe frailty should align with the physical requirements necessary for mobility. The process begins with PRT, emphasizing basic movements such as standing up from a seated position or negotiating steps, as these are fundamental for lifting body weight and initiating movement. Following sufficient strength development, the focus shifts to balance exercises to maintain upright positions. Finally, endurance training is introduced to support walking and other daily activities over extended periods. This progression mirrors the natural demands of movement, minimizing the risk of falls and promoting safe ambulation. PRT = progressive resistance training.

Exercise prescriptions for health-related outcomes must consider the relationship between dose and response, volume, intensity, and the specific adaptations necessary for the desired outcomes. For example, resistance, aerobic, balance, and mobility training can specifically target age-related deficits. Multicomponent exercise programs that integrate cognitive tasks effectively improve frailty characteristics, such as low muscle mass, strength, endurance, mobility, PA level, and energy, while also enhancing cognition to optimize functional capacity during aging [85,86]. It is also recommended that older adults participate in multicomponent exercise training, emphasizing functional balance and moderate-to-high intensity PRT at least three times per week to prevent falls [15].

Power training is an additional modality that assumes ever greater importance with advancing age. The relationship between muscle power output—the product of the force of contraction and speed of movement—and physical function in daily tasks is profound [87]. The significant loss of muscle power, attributed to fast-twitch (Type II) fiber atrophy and changes in neural recruitment associated with aging, supports the inclusion of explosive PRT, also known as power training, whenever possible. This training modality involves rapid and forceful concentric (shortening) muscle contractions to optimize functional outcomes for fit and frail older adults [88]. Sarcopenia, which consists of losing muscle mass, strength, and function with aging, necessitates high-intensity PRT for optimal adaptation, underscoring the importance of modality and intensity in managing this widespread condition [58], and training techniques to simultaneously optimize both strength and power outcomes (fast velocity at moderate-to-high intensity loading) are therefore ideal [89].

However, evidence is scarce to support the optimal quantity of muscle-strengthening activities in older adults. Notably, data supporting specific dosages and intensities of PRT needed to enhance strength, power, muscle mass, bone density, and overall functional capacity is not yet fully defined [4,5]. The minimum clinically important difference (MCID) in various outcomes and populations after PRT has also yet to be entirely determined. This includes factors such as recommended intensity (percentage of maximal voluntary contraction or velocity-based), volume (sets and repetitions), frequency (number of training days), and rest periods between repetitions or sets [8,9].

One factor that further complicates the definition of the optimal exercise prescription in older adults referred to above is the notable interindividual heterogeneity in physiological responses and adaptations to PA and exercise. Current debate concerns the categorization of individuals as "responders," "non-responders," or "adverse responders", but uniform definitions of these groupings are not yet available or consistent across exercise modalities [90–92]. For example, genotypes predictive of aerobic adaptation do not predict anabolic adaptation to PRT [60,93]. The relationship between exercise intensity and strength gains is well-established, with higher intensities of PRT leading to more significant improvements in muscle strength. Contrary to the idea of "non-responder" status, low strength gains in older adults are more often attributable to improperly prescribed or inadequately progressed PRT rather than an individual's inability to respond [94]. While some individuals may show variable functional performance outcomes despite strength gains, the lack of strength improvement is typically linked to suboptimal training intensity or exercise prescription rather than an inherent lack of response. Exercise should be considered a form of treatment, with PA or structured exercise prescriptions tailored to the intended outcomes, whether for primary prevention, enhanced fitness or functional status, or disease treatment. It is critical to personalize, adjust, and manage these prescriptions, as with any medical treatment, considering external (exercise variables) and internal (acute response to exercise) factors influenced by personal, genetic, functional, psychosocial, and environmental factors [95] (see Fig. 1). Thus, the need for precision in exercise prescriptions remains a significant area of further research.

1.5. Physical activity and exercise: global health recommendations

Strategies to increase population-level PA and optimize adherence increasingly focus on integrating exercise into daily life. Simple actions, such as choosing stairs over elevators, standing on one leg while doing dishes, or sitting and standing without using arms, are practical ways to incorporate aerobic, balance, and strengthening exercises into routine activities. Research is currently exploring whether these lifestyle-integrated prescriptive methods lead to greater exercise adherence and better outcomes than traditional approaches, particularly in preventing falls in older adults [96,97].

The World Health Organization (WHO) recommends that adults aged 65 and older engage in at least 150 min of moderate-intensity or 75 min of vigorous-intensity aerobic activity weekly, plus muscle-strengthening activities on two or more days per week [20]. Similarly, the US Department of Health and Human Services (HHS) advises older adults to undertake multicomponent exercise training that includes balance, muscle strengthening, and moderate-intensity aerobic activities three or more times per week for 30–45 min per session to enhance functional ability in those with frailty [98]. However, adherence to these guidelines is low; data from the Behavioral Risk Factor Surveillance Survey indicate a modest increase from 17% to 23% in U.S. adults meeting aerobic and resistance exercise guidelines between 2015 and 2019 [99–101]. A sedentary lifestyle combined with insufficient PA is a precursor to conditions such as sarcopenia, frailty, obesity, and chronic diseases [14,102–105], and not meeting PA recommendations is linked to approximately 1.3 million premature deaths annually worldwide [106].

The role of exercise in disease prevention and management, particularly for age-related conditions in which medication effectiveness is debatable, is increasingly recognized. Substantial evidence supports PA and exercise as preventive and therapeutic measures for CVD, T2D, and obesity; these activities improve muscle function, mental health, and quality of life and reduce mortality [107,108]. Moreover, the combination of balance and PRT has proven to be the most effective intervention for reducing falls and PRT for treating sarcopenia [14,109–112], where pharmacological treatments have shown limited or no benefits [112].

A detailed comparison of the effectiveness of exercise versus pharmacological treatments across a broad spectrum of health conditions and physiological domains is presented in Fig. 3. It categorizes these into four main areas: optimization of peak body composition and fitness, prevention of risk factors for chronic disease, treatment of chronic diseases, and prevention of age-related changes in physiology and function. The figure indicates whether exercise, drugs, or both are effective treatments for each health condition listed. This comparative

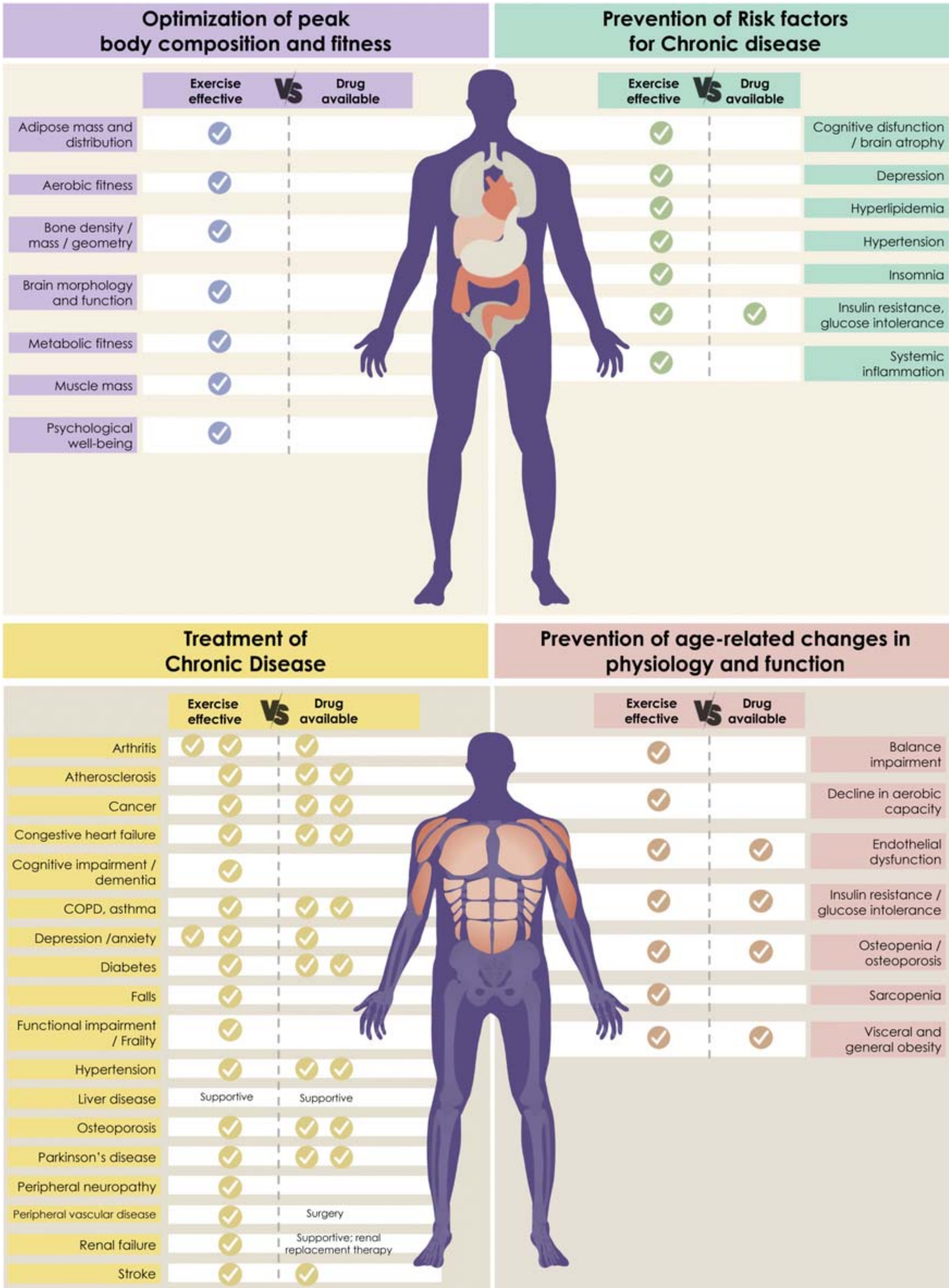

Fig. 3. Comparative Efficacy of Exercise and Pharmacological Treatments Across Health Domains. This figure outlines the effectiveness of exercise and drug treatments across various health-related domains, categorized into four primary sections: Optimization of Peak Body Composition and Fitness, Prevention of Risk Factors for Chronic Disease, Treatment of Chronic Disease, and Prevention of Age-Related Changes in Physiology and Function. Each health condition listed under these categories is evaluated for the effectiveness of exercise and available drug treatments, clearly marked to indicate whether exercise, drugs, or both have been found effective. The comparison aims to assist healthcare providers in devising comprehensive, evidence-based treatment plans that integrate physical activity and pharmacological interventions as needed. The presence of two tick marks indicates a higher level of effectiveness, while a single tick mark reflects a lower level of effectiveness. This differentiation is used to visually represent varying degrees of outcome strength.

analysis highlights exercise as a universally beneficial intervention, particularly effective in enhancing aerobic fitness, muscle mass, metabolic fitness, and psychological well-being. It also underscores exercise's role in preventing and managing chronic conditions such as hypertension, diabetes, and arthritis. In contrast, drug treatments are specified for conditions where pharmacological intervention is necessary, such as managing lipid levels, insulin resistance, and systemic inflammation, respiratory illness, atherosclerosis, cancer, or providing supportive care in diseases like renal failure. By mapping out the efficacy of exercise versus drugs, the figure guides clinicians to tailor the most appropriate and holistic treatment plans for their patients, emphasizing the critical role of exercise in maintaining health and managing diseases.

It appears counterintuitive to rely on pharmaceutical interventions that target specific aging syndromes when the underlying problems involve broader physiological and neurological pathways. Currently, no pharmacological treatments effectively slow aging or its associated conditions like frailty, mobility impairment, disability, sarcopenia, and dementia. Notably, even when medications are available for treating common psychological issues such as depression, insomnia, and anxiety, they may lead to adverse events such as falls, hip fractures, delirium, and worsening cognitive impairments. By contrast, exercise also effectively treats depression, insomnia, and anxiety while at the same time reducing the risk of falls, hip fractures, and cognitive decline [113]. Thus, a risk: benefit analysis clearly favors exercise over drugs for these conditions.

Therefore, the actual value of *exercise as medicine* includes 1) preventing diseases for which treatments are available, 2) supplementing effective medical or surgical interventions, 3) substituting less safe treatments with exercise, a safer alternative, and 4) mainstreaming exercise in the management of conditions without other effective treatments, including addressing the most debilitating conditions affecting older adults globally, such as sarcopenia, frailty, disability, and dementia.

Despite these benefits, exercise prescription is far from fully integrated into geriatric medicine, nor is it a core part of training for healthcare professionals, including geriatricians [68,97,114]. The scarcity of research on tailored PA guidelines that maximize exercise-related effects on functional abilities, daily living activities, and cognitive, psychological, sensory, locomotion, and vitality aspects in older adults is a significant gap [97]. Tailored interventions should also consider behavioral and social factors to enhance adherence and motivate PA, emphasizing the benefits of an active lifestyle and boosting self-efficacy [97,115,116]. Moreover, addressing not only the behavioral causes of ill health (such as tobacco use, alcohol consumption, unhealthy diet, and physical inactivity) but also inequity (social determinants of health) by improving social and environmental support for exercise is essential to enhance PA levels in older adults. For instance, implementing strategies to improve access to PA facilities (e.g., providing free transportation) and modifying public and private spaces (such as workplaces for people who choose to work in later life) to promote PA and reduce sedentary behavior are necessary to promote an active lifestyle [97,117].

1.6. Preserving exercise capacity with age via habitual engagement in physical activity/exercise

Regular PA and exercise can significantly mitigate the decline in aerobic exercise capacity typically associated with aging. A notable exception is the age-related decrease in maximal heart rate, which is attributed to the reduced sensitivity to β-adrenergic stimulation in the aged heart [118]. While older adults may achieve lower peak exercise workloads, cardiovascular and musculoskeletal adaptations from long-term aerobic exercise enable them to maintain higher submaximal workloads with reduced cardiorespiratory responses (heart rate, blood pressure, and dyspnea) and less musculoskeletal fatigue. Although there is some overlap, exercise adaptations are specific to the chosen modality. The greatest improvements in aerobic capacity are elicited by moderate-to-vigorous-intensity aerobic exercise (MICT), with the most significant effects observed with high-intensity interval training (HIIT, 85–95% peak heart rate for 1–4 min intervals [119,120]). High-intensity PRT is considered optimal for treating sarcopenia and contributes to improved balance [121]. An exception to this specificity of modality principle is the evidence that high-intensity PRT improves aerobic capacity in older adults nearly as well as moderate-intensity aerobic exercise [122]. Thus, a comprehensive exercise prescription that combines aerobic and resistance exercises addresses two significant age-related changes in exercise capacity.

By contrast, aerobic exercise alone does not enhance strength or balance and is thus insufficient as a standalone modality for older adults. Similarly, while isolated balance training leads to improved balance [123,124], and is associated with reduced falls and fall-related injuries, as well as improved functional mobility [110,125,126], as does Tai Chi in some studies [127–129], these do not address aerobic capacity or sarcopenia. On the other hand, multicomponent exercise programs that incorporate PRT, balance, and functional exercises [84,123,130,131], have been demonstrated to effectively reduce the incidence of falls in older adults compared to control groups, and the largest benefits for falls are generally seen with the combination of moderate to high intensity PRT and challenging balance training in sufficient quantities [123].

Although stretching is commonly included in exercise guidelines [17,132], evidence supporting its effectiveness in achieving significant clinical outcomes remains limited. Flexibility exercises are best utilized during the cooldown routine after the exercise sessions. Acute stretching before exercise, particularly before PRT, has not been shown to reduce musculoskeletal injuries and may even decrease muscle performance, potentially diminishing the strength gains from PRT [133,134]. The most effective warm-up, particularly before PRT, involves performing a lower-intensity version of the forthcoming activity, such as walking slower or performing weightlifting repetitions with lighter loads [114]. This recommendation aligns with evidence suggesting that stretching prior to exercise may not provide substantial benefits and could even reduce performance outcomes.

However, regular static stretching exercises have been associated with modest improvements in muscle strength, though it is important to note that these findings are largely derived from studies with predominantly younger samples (median age of 22) [135]. While some older participants were included, these studies were not primarily focused on older adults, and the effect sizes reported were negligible to small. Moreover, many of the strength outcomes measured involved maximum voluntary contraction (MVC) during isometric contractions, which may simply reflect a training effect of the static stretching itself rather than a meaningful improvement in dynamic strength. More robust data on dynamic outcomes, such as 1RM testing, are needed.

Flexibility benefits from stretching are directly related to a higher number of repetitions per exercise, longer time under stretching per session, and a longer total time under tension [135]. However, a recent meta-analysis of 38 studies (n = 1134) comparing stretching and foam rolling with other interventions (e.g., walking, vibration, cycling, calisthenics, strength training, electrical stimulation, heat pack passive warm-up, and cryotherapy) found no significant differences in range of motion or stiffness reduction when compared to these other methods [136]. More high-quality studies are needed to investigate the specific benefits of stretching and foam rolling.

1.7. Bridging the gap: from research to clinical implementation in exercise prescription for older persons

Despite the numerous advantages of exercise, its integration into mainstream medical practice for older adults remains limited. Most healthcare professionals, including geriatricians, need more training to incorporate exercise directly into patient care [15]. Progress has been made in including exercise counseling for older adults within healthcare settings. Yet, it is often reserved for those without significant physical or mental limitations and generally promotes only mild activities such as walking, often at dosages and intensities not supported by the current evidence [8,9]. This cautious approach seems to stem from an unfounded fear of exercise-related injuries or the perceived risks of more vigorous activities for older adults, whereas, in reality, *sedentariness is the lethal condition* [15].

Prescribing non-evidence-based exercise intensities and/or volumes should be viewed similarly to knowing prescribing sub-optimal medication dosages [8,9]. In pharmacology, a "placebo" effect is not considered sufficient, yet this seems prevalent in physical exercise prescriptions, especially concerning PRT [8,9], where often low-intensity/light and non-progressive exercise is prescribed. This inconsistency highlights the need for rigorous standards in exercise prescriptions to ensure their effectiveness. Given the substantial benefits of exercise and its low risk of harm for older adults [15], it is imperative to make optimal exercise recommendations a standard part of health prescription for all older people, individually adapted to their level of function. This includes incorporating exercise into the care provided in hospitals, clinics, and aged care facilities [105] and promoting active lifestyles through community programs, public health policies, and societal initiatives. Enhancing our understanding of how exercise mitigates the biological hallmarks of aging [7] could solidify its central role in the care of older adults. The sections below provide much of the rationale for this role.

2. Evidence for types of exercise recommendations in older adults

An extensive body of evidence from epidemiological studies and experimental trials supports integrating basic exercise prescription training for all physicians, including geriatricians, to enhance their patients' health-related quality of life [114] (Table 1). While physicians may not act as personal trainers, they need the knowledge to explain and understand the benefits of PA/exercise and refer patients to appropriate PA/exercise professionals for personalized exercise programs. Substantial evidence demonstrates that exercise training is practical for managing various chronic diseases and associated comorbidities such as cognitive impairment, frailty, sarcopenia, falls, and mobility impairment [77,104]. Promoting PA in older adults is a multifaceted issue that involves not only geriatricians but also family doctors, health fitness trainers/physiotherapies, policymakers, health agencies, insurance companies, and urban planners. The effective promotion of PA requires a collaborative approach and the development of environments and policies that encourage active lifestyles among older adults.

Screening for sedentary behavior and insufficient PA is recommended during all healthcare interactions, as they are major risk factors for a range of conditions, including all-cause and cardiovascular mortality, obesity, sarcopenia, hypertension, insulin resistance, progression of chronic kidney disease, CVD, diabetes, stroke, colon, breast, prostate, and other cancers, depression, dementia, osteoarthritis, osteoporosis, recurrent falls, frailty, and disability [68,97]. Additionally, an appropriate exercise prescription should be included whenever feasible in healthcare recommendations.

Exercise recommendations should be customized and tailored to specific goals, and personalized according to the type of activity, frequency, duration, and intensity. They should have support systems in place to monitor progress and provide feedback. Although there has been progress in providing exercise counseling during healthcare encounters with community-dwelling older adults, the advice is often limited to those without significant physical or mental impairments. Given the strong evidence supporting the benefits of exercise for older adults across different functional levels, excluding exercise prescriptions from clinical practice is sub-optimal care. A major future challenge is integrating exercise programs as a core component of care for older persons, whether in hospitals, outpatient clinics, or institutional care settings [105].

Current recommendations and guidelines for PA in older adults generally advocate a multifaceted exercise regimen that includes aerobic, PRT, balance, and mobility training through structured and casual (integrated lifestyle) activities [17,35,36,114,137]. It is advisable to start with a single exercise modality to allow sedentary older adults to gradually adapt to a new exercise routine before introducing additional components [138]. Research indicates that even small amounts of PA can provide health benefits, especially among those who are most physically inactive [139], and engaging in some PA is generally preferable to none, but this is not the final goal. Tailoring exercise prescriptions to the individual is essential, considering risk, medical history, functional capacity, tolerance, and personal preferences. Before initiating any structured aerobic training, it is important first to assess and address significant deficits in muscle strength, balance, and joint range of motion (ROM), as these factors are crucial for optimizing overall physical performance. Aerobic training alone may not sufficiently improve musculoskeletal strength. Therefore, incorporating a multicomponent training program, including resistance exercises for strength, as well as gait and balance training, is necessary to enhance musculoskeletal health and minimize the risk of frailty-related outcomes, such as falls and fractures.

2.1. Principles of exercise prescription for older individuals with mobility challenges

Several fundamental principles can guide the development of exercise prescriptions for older individuals, emphasizing the importance of sequence, specificity, and safety in enhancing mobility and reducing risk factors. These recommendations are intended for healthcare professionals working with frail individuals facing mobility challenges. A comprehensive geriatric assessment is essential for identifying each patient's needs and capabilities before developing an exercise program. This multidisciplinary approach involves collaboration between physicians, physical therapists, occupational therapists, and other healthcare providers to ensure a holistic plan.

The process begins with a physician conducting the initial assessment and prescribing the exercise program. A team of professionals manages follow-up and adjustments over time, monitors the patient's progress, and adapts the program as needed. Patient empowerment is crucial; understanding previous PA levels, preferences, available equipment, and social context, such as accessibility and cultural/ethnic sensitivities, helps tailor the program to enhance adherence and enjoyment. Whether exercises are performed in groups or individually, expectations such as pleasure, performance, and social interaction should be taken into consideration to ensure that the program meets the holistic health needs of individuals. By adhering to these principles, exercise programs can comprehensively address various factors contributing to frail individuals' mobility, health, and overall well-being. These practices emphasize that exercise prescription is not solely about enhancing physical capabilities but also about improving an individual's holistic health and self-perception of well-being.

Sequencing and progression: When working with individuals living with frailty, it is essential to approach exercise sequencing based on the physical requirements underpinning mobility. Specifically, standing up requires strength and power, staying upright involves balance, and walking at any distance requires endurance. This sequence follows a logical progression. Attempting to ambulate those who cannot lift their body weight out of a chair or maintain a standing balance will likely fail and increase the risk of falls [114]. Therefore, exercises that enhance strength should be prescribed at the beginning of the program to train in basic movements, such as standing up from a seated position or negotiating steps. Once an acceptable strength gain is achieved, the focus should be placed on balance to maintain upright positions. Finally, endurance training should be incorporated to enable walking or daily activities over a longer time span. The sequence should follow the natural progression of movement demands.

Starting with low-intensity exercises, the duration, frequency, and intensity are gradually increased. This approach allows individuals to adapt to the new physical demands and reduce the risk of injury or excessive fatigue.

Table 1
Exercise recommendations for optimal aging and maintenance/improvement of functional capacity in older adults.

	Resistance training	Aerobic exercise training	Balance training
Frequency (days per week)	2 – 3	3 – 7	1 – 7
Volume	1–3 sets of 8–12 repetitions, 8–10 major muscle groups	• In continuous exercise: ○ 20–60 minutes using large muscle groups / session • In HIIT: ○ Short bouts of high-intensity exercise lasting from 30 seconds to 4 min.	1–2 sets of 4–10 different exercises emphasizing static and dynamic postures/movements
Intensity	• Start at 50% of 1RM and progress to heavier loads of 70–80% 1 RM (15–18 on Borg Scale[a]) over the first 2 weeks of training. Progress loading via interim 1RM testing every 2−4 weeks and using Borg Scale in-between 1RMs to keep relative intensity high • 1−3 min rest between sets • Power training at 60–80% of 1RM	• In continuous exercise: ○ 12–14 on Borg Scale[a] (55–70% heart rate reserve or maximum exercise capacity) or 4−5 on a modified RPE scale (range 0–10) • In HIIT: • Intensity levels ranging from vigorous effort (70–89% of HR peak, 60–79% of VO_2 peak) to very hard effort ($\geq$ 90% of HR peak, $\geq$ 80% of VO_2 peak), interspersed with rest periods of up to 90 seconds	• Progressive difficulty as tolerated[b] • Narrowing the base of support • Perturbation of ground support • Decrease in proprioceptive sensation • Diminished or misleading visual inputs • Movement of the centre of mass of the body away from the vertical or stationary position • Dual tasking: adding a cognitive distractor or secondary physical task while practising a balance task • Functional movements and activities that mimic real-life situations, such as reaching, carrying objects, navigating obstacles, and transitional movements (e.g., sit-to-stand, gait initiation/termination)
Specific physiological adaptations	• Strength • Power • Hypertrophy • Endurance	• Maximal aerobic capacity • Sub-maximal endurance • Cardiac contractility/stroke volume • Peripheral oxygen extraction • Arterial stiffness • Heart rate variability	• Dynamic stability
Exercise examples	• Multiple and single joint exercises (free weights and machine) with slow to moderate lifting velocity • Bench press and squat • Knee extensions and knee curls • Exercise selection can be varied through alterations in body posture, grip, hand and foot stance, unilateral vs bilateral exercises • Once body weight no longer serves as a sufficient source of overload, additional resistance can be provided by machines or free weights as needed to ensure progression.	• Walking with change in pace and direction • Treadmill walking • Hiking • Jogging / running • Cross-country skiing • Swimming • Cycling • Stair climbing • Dancing • Step-ups May start with 5−10 mins and progress to 15−30 mins. The intensity is proportional to heart rate and/or perceived exertional scales if on B blockers or has pacemaker and can be increased from moderate to vigorous depending on fitness.	• Tai Chi • Standing yoga or ballet movements • Tandem walking • Standing on one leg, stepping over objects, climbing slowly up and down steps • Turning • Standing on heels and toes, walking on a compliant surface such as foam mattresses • Maintaining balance on a moving vehicle, such as a bus or train • Dual-tasking: adding cognitive distractor while maintaining balance Many conditions in older adults require balance training before aerobic exercise/gait retraining
Safety tips:	• **Consult with a healthcare professional,** especially if you have pre-existing health conditions or concerns about specific exercises. • **Screen for joint conditions:** Pay special attention to volume, progression, positioning, and repetitive loading to avoid exacerbating joint problems.	• **Ensure adequate hydration:** Adequate hydration is crucial for maintaining effective thermoregulation during physical exertion and helps prevent both dehydration and overheating, thereby supporting cardiovascular function and reducing the risk of adverse events. • **Select appropriate clothing:** Wearing appropriate clothing, such as	• **Start with a stable support:** Begin balance exercises near a stable support, such as a wall or sturdy chair, to provide safety and confidence until balance improves. • **Wear appropriate footwear:** Use supportive, non-slip shoes to enhance stability and prevent falls during balance training exercises.

(continued on next page)

Table 1 ***(continued)***

	Resistance training	Aerobic exercise training	Balance training
	• **Monitor techniques and form:** Utilize a qualified trainer to ensure exercises are performed correctly, reducing the risk of strain or injury. • **Control velocity and range of motion:** Avoid sudden, jerky movements and maintain a controlled pace. • **Breathe regularly:** Do not hold your breath during strength exercises. Instead, practice regular breathing (inhale before lift or push, exhale on concentric phase, inhale again on eccentric lowering of load) to avoid increased blood pressure and other complications. • **Warm-up and cool down:** Always include a proper warm-up before and a cool-down after your resistance training sessions. This prepares the muscles for exercise and aids in recovery, reducing the risk of injury.	moisture-wicking fabrics and layers, can help regulate body temperature. Also appropriate footwear. • **Warm-up and cool down:** Gradual warm-up increases blood flow to muscles, while cool-down helps in gradual recovery of heart rate and blood pressure. These measures reduce the risk of dizziness, chest pain, and muscle stiffness. • **Monitor intensity:** Using perceived exertion scales or heart rate monitors can help ensure exercise intensity remains within safe limits. • **Be aware of surroundings:** Exercising in a safe environment, free from traffic and hazards, is important. This includes being aware of weather conditions and choosing safe paths or tracks to prevent falls and injuries. • **Use safety equipment:** Utilizing appropriate safety equipment, such as supportive footwear and, if necessary, assistive devices, can prevent injuries. Use Nordic sticks while walking to reduce the risk for falls	• **Progress gradually:** Increase the difficulty of exercises slowly, starting with basic movements and advancing to more challenging ones as balance improves. • **Focus on core strength:** Incorporate exercises that strengthen the core muscles, as a strong core is essential for maintaining balance and stability. • **Monitor environment:** Ensure the exercise area is free from hazards, such as loose rugs or clutter, to reduce the risk of tripping and falling. • **Use a spotter if needed:** For added safety, especially when attempting new or challenging exercises, have someone nearby to assist and provide support if necessary.

1RM = One repetition maximum; HIIT = High intensity interval training; HR peak: highest heart rate an individual achieves during maximal exercise; $\dot{V}O2$ peak = Peak oxygen uptake; RPE = Rate of perceived exertion.

[a] Borg Scale of Perceived Exertion from 6 (easy) to 20 (maximal).

[b] Intensity is increased by decreasing the base of support (e.g., progressing from standing on two feet while holding on to the back of a chair to standing on one foot with no hand support); by decreasing other sensory input (e.g., closing eyes or standing on a foam pillow), perturbing the center of mass (e.g., holding a heavy object out to one side while maintaining balance, standing on one leg while lifting the other leg out behind the body, or leaning forward as far as possible without falling or moving feet), or by dual-tasking (adding a secondary cognitive (e.g., naming animals) or physical (e.g., juggling) task while tandem walking).

Specificity of training: Tailor exercise programs to address specific functional deficits identified in an individual. The most effective approach is paying attention to the physiological determinants of transfer ability and ambulation and targeting these aspects with an appropriate exercise prescription when reversible deficits are identified. For instance, if triceps strength is a limitation for transferring from a wheelchair to a bed, exercises targeting arm and upper body strength should be prioritized [140]. Similarly, low-impact, seated resistance exercises that do not exacerbate joint pain should be considered instead of high-impact, weight-bearing, aerobic activities for those with severe knee osteoarthritis. In such clinical conditions, aquatic-based resistance exercises could also be a low-impact exercise alternative as they have shown promising results in improving strength and muscle mass in older individuals [141,142], as well as metabolic health in patients with non-communicable diseases [143,144].

Safety and risk mitigation: Evaluate the risks associated with different exercise modalities, given the individual's specific health conditions. For example, in some cases, a chronic health condition may benefit equally from resistance or aerobic training (e.g., depression). In such instances, the prescription should be based on the individual's ability to tolerate one form of exercise over another or the presence of a second disease that requires a specific prescription. For example, severe osteoarthritis of the knee, recurrent falls, and a low threshold for peripheral ischemia may make PRT safer/more feasible than aerobic training as an antidepressant treatment. Ensure that the exercise environment is secure and that the individual is always within their capability to perform exercises without the risk of injury.

Effective prioritization involves evaluating the risks and benefits of each exercise modality and considering the individual's current health status and physical fitness level. When one exercise modality addresses multiple conditions, it is generally preferred over a more limited option. For instance, in individuals with osteoporosis and depression, PRT is a more suitable option than aerobic exercise, which research indicates can only target depression [114].

Personal preference and individualization: Consider an individual's preferences regarding the exercise setting (group vs. individual), type of exercise (structured vs. lifestyle activities), level of supervision required, and specific likes or dislikes of certain exercise modalities. Conducting a comprehensive assessment of physical, cognitive, and functional status is essential for developing an appropriate exercise plan that aligns with an individual's goals, preferences and unique needs. This personalized approach ensures that the exercise regimen is effective for achieving health and fitness goals as well as sustainable and enjoyable for the individual, increasing the likelihood of long-term adherence and positive outcomes.

Holistic health consideration: When designing an exercise program, consider the individual's overall health status and physical fitness level. For frail individuals, particularly those with multiple chronic conditions, it is essential to select exercises that can effectively address several health issues simultaneously. This economical approach ensures that the exercise regimen not only meets the specific needs of the individual but also maximizes the benefits across various aspects of their health, efficiently enhancing overall well-being and functional capacity.

Multicomponent approach: An effective exercise program should ultimately include various exercises, such as strength, aerobic, balance, and flexibility training. Each component targets different aspects of physical function, improving overall health and mobility, and they can be introduced sequentially based on feasibility and priority of adaptations desired.

Functional training and emphasis on balance and fall prevention.

Focus on exercises that simulate daily activities such as standing, walking, and carrying objects. Functional training enhances the ability to perform activities of daily living, promotes greater independence, and improves quality of life.

Exercises that challenge and improve balance, coordination, and proprioception should be included to reduce the risk of falls and promote independence in mobility.

Cognitive engagement: Incorporating cognitive elements, such as multi-tasking or memory exercises, enhances mental function and promotes adherence to the exercise program.

Social support: Encouraging social interaction and support through group exercise sessions or involving caregivers, family members or friends may enhance motivation and adherence.

Ongoing evaluation and adaptation: Regular assessment of an individual's progress is essential. The exercise program should be adjusted to meet the individual's needs, ensure progression, prevent plateaus, and optimize benefits.

Supervision and monitoring: Close supervision and monitoring should be provided, especially during the initial stages of the exercise program. This ensures proper technique, safety, and appropriate progression based on an individual's response to exercise.

Adaptive equipment and modifications: Use adaptive equipment, such as chair-based exercises, water aerobics, handrails or stability balls to accommodate mobility limitations and enable safe and effective exercise execution.

2.2. Gait training

Several studies have investigated the effects of exercise interventions on gait stability in older adults with frailty, yielding conflicting results. Some studies reported gait improvements after physical training [84,145,146], while others found no benefits [84]. Notably, most studies that showed improvements utilized multicomponent exercise programs [84,109,146–148], in contrast to those that only employed resistance exercises [149] or combined aerobic training with yoga [150].

Gait speed is a strong predictor of survival in older adults [151], and its maintenance should be prioritized. Gait variability predicts fall risk in healthy and clinical cohorts [152,153]. Practical exercises for enhancing gait stability, velocity, and mobility include walking with changes in pace and direction, treadmill walking, step-ups, and stair climbing, as well as balance training [154].

Weight-bearing aerobic activities that mimic real-life activities are preferable when possible. For individuals with severe osteoarthritis or balance impairments, alternatives such as aquatic exercises, seated steppers, or recumbent cycles may be more suitable exercise modalities initially, but they will not directly benefit gait stability. Generally, seated resistance, strength, and power training should be prioritized for those who cannot independently support their body weight, but then progression to ambulation and aerobic exercise should be attempted as soon as feasible.

2.3. Aerobic training

Aerobic training is a form of exercise primarily focusing on improving cardiovascular endurance and overall health through rhythmic and continuous activity. It typically involves activities such as walking, cycling, and swimming. Aerobic training consists of thousands of repetitions of low-resistance muscle contractions rather than a few contractions against moderate-to-high resistance. It generally involves the use of large muscle groups, particularly in the legs, but may also include the arms, or rely solely on the arms for individuals who cannot use their legs due to conditions such as amputation, stroke, neuropathy, pain, or injury.

The exercise component should start with durations of 5–10 min (or less) during the initial weeks of training and may extend to 20–30 min over time. The intensity of this exercise is typically proportional to the heart rate [usually approximately 50% of the heart rate reserve (HRR), equivalent to the % of the difference between the maximum (peak) heart rate and the resting heart rate of an individual], which is then added to the resting heart rate to determine the target HR zone. It can be increased from moderate (40–60% HRR) to vigorous intensity (60–85%) as the individual's fitness and confidence improve. Clinicians should utilize perceived exertion scales if the heart rate is not a reliable indicator of exercise intensity due to conditions such as arrhythmias, treatment with beta-blockers, or functioning pacemakers. Thus, employing a subjective scale of perceived exertion is essential to accurately gauge workout intensity in aerobic exercise, allowing for personalized and adaptive exercise regimens that reflect real-time cardiovascular demands. For example, the Borg Scale [155] is widely used for measuring the perceived intensity of effort during PA. It allows individuals, coaches, and health professionals to estimate and adapt the exercise intensity based on individual needs and performance. Additionally, it is essential to monitor non-cardiac signs of cardiac distress, such as unusual shortness of breath, dizziness, or excessive fatigue, which may necessitate prompt medical evaluation (for detailed safety tips, please refer to Table 1).

In addition, ensuring adequate hydration and selecting appropriate clothing are essential for maintaining effective thermoregulation during physical exertion. These measures help prevent both hyperthermic and hypothermic states, which can adversely affect cardiovascular function and potentially lead to serious adverse events. By implementing these strategies, individuals can enhance their cardiovascular fitness safety by engaging in aerobic activities.

2.4. High-intensity interval training

High-intensity interval training (HIIT) is an increasingly popular form of aerobic exercise that involves short bouts of high-intensity exercise, lasting from seconds to minutes, interspersed with periods of rest [156]. Recently, HIIT has gained recognition as an effective exercise method for older adults due to its numerous health benefits, including improvements in cardiovascular health [120] and muscle mass [157] and cognitive function [158,159]. However, further research is necessary to establish definitive conclusions about its safety and benefits [160–163]. Published HIIT protocols for older adults typically involved less than 12 weeks of training, two to three sessions per week, each lasting 20 min. These sessions consist of several short bouts of high-intensity exercise lasting from 30 seconds to 4 min, with intensity levels ranging from vigorous effort (70–89% of peak HR, 60–79% of peak VO_2) to very hard effort (≥90% of peak HR, ≥ 80% of peak VO_2), interspersed with rest periods of up to 180 seconds [160]. Due to these widely varying prescriptions, there is no consensus on which HIIT protocol is the most effective for older adults.

Studies have shown that HIIT can be safely implemented in carefully selected older adults in supervised settings, including those at low-moderate risk of CV events and with pre-existing cardiovascular diseases, without significantly raising the risk of adverse events over moderate-intensity continuous training (MICT) [164–168]. According to a systematic review and meta-analysis of the effectiveness and safety of HIIT compared to MICT in improving cardiorespiratory fitness (CRF) in patients with lifestyle-related chronic diseases, HIIT offers CAD patients some aerobic fitness training stimulus advantages compared with MICT (e.g., VO_2 peak, submaximal exercise performance and cardiac performance [120,167,169–171]). This is particularly relevant in populations looking for time-efficient training methods, as HIIT demands significantly less time commitment while offering comparable, if not superior, cardiorespiratory benefits. Studies consistently show that HIIT elicits significant enhancements in VO_2 peak, with increases ranging from 15% to 20%, making it a promising option for those seeking to improve aerobic performance in a condensed format [120,164–166]. A five-year RCT of older adults in Norway (mean age 72 years who were generally in good health and active at baseline) showed that HIIT (mostly unsupervised in community) was a feasible and safe exercise modality, with no significant differences in recurrent cardiovascular events compared to MICT or control groups following national physical activity guidelines [172]. However, the generalizability of these findings to clinical cohorts in other countries with chronic co-morbidities or frailty is not known. Moreover, HIIT shows similar benefits compared to MICT in lipid profiles, blood pressure (BP), body fat, and overall cardiovascular disease (CVD) risk reduction [120,167,169–171].

However, the current literature does indicate a slightly elevated risk of adverse cardiovascular events associated with HIIT, particularly in patients at high risk for cardiovascular events. For example, Rognmo et al. [173] retrospectively analyzed cardiovascular adverse events in 4,846 patients with CAD and found that there was one case of fatal cardiac arrest per 129,456 patient-exercise hours for MICT and 1 per 23,182 patient-exercise hours for HIIT. Notably, most existing studies on HIIT have been conducted under clinical supervision and largely exclude high-risk cardiac patients) [120,164–166]. This makes the applicability of HIIT in unsupervised or non-clinical settings in higher risk patients unproven, necessitating further investigation before its broader adoption.

Emerging evidence suggests that older adults' perceived capability to engage with PA is influenced by their functional capacity and their perceived risk of injury from PA [174]. Additionally, the short-term sensations of pleasure or discomfort experienced during high-intensity physical activities may play also a role, though this effect may vary across individuals, particularly in older adults [175–177]. While research shows that as ventilation increases—reaching the first ventilatory threshold (VT), and/or blood lactate threshold—most individuals report a decline in pleasure and an increase in discomfort [178], this is not universally the case. For older adults, exercise around VT, whether administered during an exercise or self-selected, will likely result in positive affective responses [176]. Furthermore, many adults report a state of reduced pain sensitivity, sedation, euphoria, and decreased anxiety during or after endurance training, often referred to as the well-known "runner's high" [179]. Some have also emphasized a lost sense of time and feelings of effortlessness [180]. These positive effects can enhance mood and contribute to a sense of accomplishment.

Fatigue and muscle soreness, typically driven by the accumulation of hydrogen ions (H^+) and inorganic phosphate (Pi) during intense exercise, which reduces pH, can impair muscle contraction and energy production, leading to both peripheral and central fatigue [181,182]. However, many older adults view these effects positively, finding pride in their ability to participate in HIIT or high-intensity power training. They value the physical and psychological benefits not achieved through low-intensity exercise. This sense of accomplishment can enhance self-efficacy and promote long-term adherence.

It's important to avoid generalizations that all older adults prefer to avoid vigorous effort. HIIT can be particularly rewarding for many, including frail individuals, as it provides significant physiological and psychological benefits that contribute to continued participation in exercise programs. There is also evidence that negative psychological responses to catecholamine release, which may deter some individuals from high-intensity exercise, are genetically mediated [177]. This genetic predisposition may explain why specific individuals experience discomfort with vigorous exercise while others find it enjoyable and rewarding.

Additionally, a meta-analysis comparing psychological responses to HIIT versus moderate-intensity continuous training (MICT) supports the notion that individual responses vary, with many older adults experiencing greater psychological benefits from HIIT [183]. Addressing these individual differences in responses to exercise, rather than assuming uniformity, may lead to more effective, tailored HIIT prescriptions, improving both adherence and outcomes by promoting individualized exercise recommendations. Strategies to enhance physical activity participation among older people should include raising awareness of the benefits and minimize the perceived risks of physical activity [184].

The feasibility of HIIT for populations with frailty or mobility impairments also remains uncertain. For example, treadmill-based HIIT may not be feasible for individuals with gait disturbances. At the same time, cycle ergometry, though an alternative, may not be optimal as it is non-weight-bearing and does not improve balance, prevent falls, or enhance bone mineral density (BMD) [120]. Therefore, caution is warranted when considering HIIT for elderly individuals or those with significant mobility restrictions.

Regarding muscle metabolism, HIIT is known to stimulate anabolic adaptations and hypertrophy, making it potentially valuable for skeletal muscle health [162,185–187]. However, whether clinically significant improvements in muscle size and strength occur in older adults remains to be established. More research is needed to determine whether these metabolic benefits translate to functional improvements in populations prone to sarcopenia. In summary, while HIIT presents many advantages in efficiently improving aerobic capacity and other cardiovascular outcomes, its safety, particularly in high-risk populations, and its utility in older adults with frailty or mobility issues, require further research before it can be widely recommended.

2.5. Progressive resistance training

Evidence dating back to 1990 has shown that high-intensity PRT is both feasible and effective for older adults who are severely frail [35]. To maximize musculoskeletal adaptations and time efficiency, PRT programs should be performed 2–3 times per week, beginning with one to two sets and advancing to two to three sets of eight to twelve repetitions. These exercises should target the major muscle groups involved in function and mobility, incorporating both multi-joint exercises (such as leg presses and chest presses) and single-muscle group exercises (e.g., triceps, knee extensors, and hip abductors). Typically, 6–10 exercises make up the whole routine, but this can be reduced to 3−4 exercises per set for beginners. A minimum of one day of rest between sessions is recommended for muscle recovery and hypertrophic adaptations following eccentric muscle damage [188]. Resistance training for individuals with frailty should also include functional exercises, such as progressively more difficult sit-to-stand exercises, to mimic daily activities closely. Difficulty can be increased by lowering the seat height, eliminating use of the arms, standing up with one leg, and if possible, jumping up with one leg as strength, power and balance improve.

Studies comparing training frequencies have shown that twice-weekly and thrice-weekly sessions yield similar improvements in muscle power, strength, mass, quality, and cardiorespiratory fitness in previously trained healthy older men [189,190]. This indicates that twice-weekly sessions are time-efficient for achieving optimal adaptations. However, higher frequencies may benefit clinical populations like diabetes patients [108,191,192], in whom more frequent exercise may help better manage glucose levels, or those with depression who benefit psychologically from higher doses of exercise [193].

There is no need to delay the introduction of high-intensity training in older adults with frailty. High-intensity efforts can start by assessing muscle strength with a one-repetition maximum (1 RM) to determine the maximum weight an individual can lift in a single repetition for a specific muscle group. Initial training sessions can use weights of 50% of 1RM and progress continuously to 60, 70, and 80% of 1RM over the initial 2−3 weeks of training. Studies have indicated that PRT guided by 1RM testing [194], and performed at 70–80% of 1RM is more effective in promoting strength gains than training at lower intensities [195,196] or using only perceived exertion to guide progression (Table 1). During subsequent training sessions, the load can be adjusted based on perceived exertion scales, maintaining exertion in the hard-to-very-hard range (15–18 on the original Borg scale) [155], or preferably by sequential 1RM testing over time as well [194]. Importantly- if only the initial 1RM is used to guide the intensity, the *relative* load will be progressively lower, rather than maintained or higher over time as the individual gains strength- which is the opposite of the intent of *PRT*. This approach (repeating the 1RM every 2 weeks and using the Borg Scale each session to adjust loads in between 1RMs) has been effectively and safely used in many clinical cohorts including, for example, nursing home residents up to 103 years old and in older adults recovering from hip fractures 12 weeks after surgery [140]. Special care should be taken during the program's initial phase because even minor injuries can lead to significant setbacks, necessitating a return to pre-injury exercise levels (for detailed safety tips, please refer to Table 1). Although the absolute weights may be low, the relative intensity is high, and frailty is not a barrier to engaging in robust exercise; it is, by contrast, a crucial reason for prescribing such activities.

We recognize that delayed onset muscle soreness (DOMS) may occur after PRT, particularly in response to eccentric contractions, which are a normal part of the adaptive process leading to muscle hypertrophy [197]. Instead of attempting to avoid DOMS, it is important to educate participants on its physiological basis, enabling them to differentiate between typical soreness and potential acute injury during exercise. Notably, in older adults, including novice lifters engaging in higher intensity workouts, DOMS is generally less frequent and not severe [197]. Emphasizing this distinction can help alleviate unnecessary concerns and promote continued adherence to PRT programs.

2.6. Power training recommendations

Power training is a specific type of muscle training that targets both the force production and velocity components of muscle power. Unlike traditional PRT, which involves overcoming resistance using a high force at slow speed during the concentric (shortening) phase, power training emphasizes overcoming resistance at maximal volitional speed [198]. Muscle power declines significantly with age, leading to an increased risk of physical impairment, falls, disability, and mortality [8,15]. The ability to perform daily activities is closely linked to muscle power output and the rate of force development [199–201], with research showing strong correlations between these metrics and performance in functional capacity tests in healthy older adults [199–201]. Recent studies have also linked muscle power and explosiveness to enhanced functional capacity and reduced incidence of falls in frail, oldest-old populations [200–202].

Aging-associated physiological changes, such as the loss of type II fast-twitch fibers and deficits in neural recruitment, can diminish power output in ways that traditional slow-velocity strength training does not address, such as the early onset of muscle force and the maximal rate of force development [15]. Power training can significantly enhance physical capabilities in older adults by promoting the recruitment of fast-twitch fibers and improving neuromuscular coordination through high-velocity contractions, optimizing motor unit firing rates, and enhancing muscle activation and intermuscular coordination, which are vital for daily tasks [15,88]. Although evidence indicates benefits for individuals ranging from robust to frail, including hospitalized older persons, power training remains underused in clinical practice [8,15,203].

Bodyweight exercises, such as quick standing from a chair, can initially provide resistance (as long as it is safe; i.e., there is no diagnosis of orthostatic hypotension, instability/severe pathology of hip or knee joints, or balance problems). Individuals may start these exercises slowly with assistance and progress to performing them by themselves and quickly. This method can easily be implemented in hospital rooms, long-term care facilities, and at homes. If an individual's body weight does not provide a sufficient load, additional weights or machines can be introduced to ensure progression. Both free weights and specialized PRT machines are used for power training, showing similar improvements in neuromuscular [84,204,205], functional, and overall fitness [84,204,205]. Studies employing pneumatic resistance machines specifically designed for power training have shown comparable benefits [206–208].

An alternative way to increase intensity without PRT machines is to change from bilateral to unilateral body weight exercises such as lunges, which can also be performed at increasing speeds during the concentric phase. Monitoring movement speed is essential because power training relies on explosiveness, whereas endurance methods focus on repetition. Plyometric training, such as jumping onto platforms or boxes, which children and athletes have traditionally used, may be an alternative when power training machines are unavailable. However, lower extremity or spinal arthritis, osteoporosis of the spine, and balance impairment frequently preclude the use of lunges or plyometrics by many older adults with frailty, who are the individuals most in need of improvement in muscle power.

Power training should include fast concentric (shortening lifting) and controlled eccentric (braking or lowering) phases for optimal gains, focusing mainly on the lower extremities [15]. Explosive resistance training sessions can be combined with traditional PRT in the same workout, avoiding concentric failure and maximizing effectiveness and safety [15,205,209,210]. The ideal intensity for these sessions might range from 60% of the maximal load for upper-body exercises and 80% for lower-body exercises [132,211]. A dose-response study [132] indicated that peak muscle power improved similarly across light (20%), moderate (50%), and heavy (80%) resistance levels, but the 80% load provided the best improvements in strength as well. There is a known correlation between training intensity and muscle strength and endurance improvements, with higher intensities yielding better results. However, moderate-intensity power training (60% of 1RM) [84,212,213] can lead to superior functional capacity adaptations. Caution is advised with low-load power training, as it may increase injury risk owing to undiagnosed joint issues exacerbated by the very high velocity of the movement [214,215]. Starting with a minimal dose for the first few 2−3 weeks is recommended, particularly for older participants [15]. This is especially advisable for frail older adults who might not tolerate high training volumes due to fatigue. Two–three sessions per week are typically sufficient to achieve significant neuromuscular and functional benefits [198] (see Table 2 for specific examples of power training prescriptions for older adults).

In muscle power training, the concentric phase is ideally performed as rapidly as possible; however, care is required to prevent musculoskeletal injury. Therefore, screening for musculoskeletal and joint conditions, such as tendinopathy or osteoarthritis, before initiating power-based training may contraindicate such activities or require specific adjustments. In addition, if free weights are used, instructions to avoid the use of momentum (swinging the weight) to achieve high velocity is critical, as this will both minimize the muscle adaptation as well as increase the likelihood of tendon or cartilage tears in open chain exercises with unrestricted end ranges (such as knee extension, overhead or bench press movements) or back strain in standing biceps curls for example. While the risks associated with power training are generally low and comparable to those associated with traditional PRT, careful screening and exercise selection are essential to minimize injury risk and ensure safety [198]. In some cases, these injuries may preclude power training in older adults; however, traditional slow-velocity resistance exercise remains an option.

As noted above, two potential adverse events related to muscle power training are injury to tendons/cartilage, particularly of the rotator cuff and knee, where degenerative tears are commonplace [215], and exacerbations of abdominal/inguinal hernias [89]. These may also occur with traditional PRT. Interestingly, a systematic review of the effects of PRT, including power training in frail older adults reported only one case of shoulder pain related to PRT interventions in 20 studies and 2544 subjects [131]. It is essential to screen for these issues to mitigate injury risks and ensure the continuity of the benefits of exercise. Exercise prescriptions should carefully manage workload, volume progression, heavy and repetitive workloads, and unfavorable positions that could exacerbate conditions, such as the military press or lat pulldown in rotator cuff disease. Thus, screening for joint conditions and exercising caution when selecting exercises for volume, progression, positioning, and repetitive loading is essential. The risk of injury can be reduced by

Table 2
Power training recommendations in older adults (Adapted from ref. [198]).

Assessment and training variable	Recommendations
Clinical assessment	• Assessment of the orthopedic and rheumatologic history, including surgery surgical procedure • Screening for joint conditions is critical, especially for degenerative tendon and cartilage injuries like rotator cuff tears and knee osteoarthritis, which are prevalent in older adults.
Velocity of movement	• The concentric (shortening) phase should be performed with maximal or near maximal intended velocity, followed by a controlled eccentric (lengthening) phase. Triggering the repetition with a verbal or tactile cue and coaching the person to imagine moving the weight as fast as possible during the rest interval between repetitions will maximize performance and adaptations. • Programs should initially focus on teaching exercise execution at low, controlled speeds (approximately two weeks), especially for older individuals not familiar with exercise. Subsequently, velocity can gradually progress to maximum intentional speed, while maintaining proper exercise execution.
Maximal strength assessment for power training prescription	• After clinical assessment, 1 repetition maximum (1RM) can be safely assessed even in frail older individuals as demonstrated in previous studies. The optimal load for maximal power production should be also calculated. • Start by underestimating the initial test load. Then, carefully increase the load incrementally until the individual can only complete a single repetition with proper technique and form. • Close supervision by qualified professionals is imperative for 1RM testing to ensure safety and accuracy.
Intensity	• The load can range from 60 to 80% of 1RM, considering previous clinical assessment. • Frail individuals may benefit in terms of muscle power from intensities ranging from 60 (moderate) to 80% (high) of the 1RM but outcomes for muscle strength are greatest at the higher intensities, whether fit or frail. Therefore, the best combination of strength and power adaptations occurs at high intensity. • To maintain the same desired relative intensity over time, the loads must be progressed as the person gets stronger (as judged by perceived exertion or interim 1RM testing). The relative intensity should be assessed every session so that the loads are adjusted continuously as required by either changes in clinical status or training adaptations.
Repetitions	• Repetitions to failure should be avoided to prevent undesirable velocity loss, fatigue engagement of accessory muscles, excessive hemodynamic excursions, poor exercise technique and potential injuries.
Sets	• Perform one to three sets per exercise. Using cluster sets (i.e., 2 sets of 4 reps with a short break in between rather than one set of 8 reps) will limit fatigue, maintain proper form, and allow for the use of higher loads. This approach is particularly beneficial for novice trainers. However, cluster sets are not superior to traditional set structure if a full set can be completed in good form at the intended load.
Resting interval	• Rest intervals of 1−2 minutes between sets should be sufficient, depending on the individual's characteristics. Longer rest periods may be needed and do not impair adaptations. Performing a circuit of one set on each machine, and then repeating 3 times allows even longer rest periods for each muscle group and may be preferable except in those in whom transitioning on and off machines is more difficult/time-consuming than simply resting slightly longer between sets.
Weekly frequency	• Train 2−3 times per week. • Acutely hospitalized frail individuals can train daily during hospitalization.
Number of exercises	• Focus on lower-limb exercises, with one to three chosen. • Leg press, squats, knee extensions, and sit-to-stands are good options.
Type of exercises	• Free weights, machines, or body-weight exercises are all good modalities. • Pneumatic resistance machines can prevent momentum-assisted lifting. • While plyometrics, like box jumps, build power, they may need to be avoided in frail elders with arthritis, low bone mineral density, or balance issues. • When using isoinertial plate load leg press machine, ensure that a proper deceleration is performed before the end of concentric phase to avoid loss of contact with the push plate, especially using low-to-moderate loads (i.e., 20−50% 1RM). • With body-weight exercises, persons can start slowly with assistance, progressing to faster solo movements. • For frail individuals who have poor exercise capacity, prioritize closed kinetic chain exercises. The best and most well-tolerated exercise is the leg press for these individuals. Alternatively, exercises such as standing up from a chair exercise can be used initially.
Combination with others training modalities	• Power training can be combined with moderate aerobic or high-intensity interval training for healthy older adults. • For frail individuals, it can be included in multicomponent programs with gait training, balance, and endurance exercises if possible. It can also be performed alone or with traditional resistance training.
Tips for Improving Adherence	• Ensure that the participants understand the benefits of power training as well as the information regarding exercise execution. It may enhance treatment adherence. Special attention should be given for frail and cognitively impaired individuals. • Integrating exercises into lifestyle may improve adherence over standard approaches. • Consider personal preferences for group vs. individual training, structured vs. lifestyle PA, desired supervision level, and modality attractions/aversions to optimize behavioral change and long-term adherence. Note, if group training is used, there still has to be individualization of the training loads and

Table 2 ***(continued)***

Assessment and training variable	Recommendations
	machine settings for each person for optimal safety, progression, and adaptation. A "group exercise class" modality for PRT/power training is likely to insufficiently address individual needs. • Use behavioral and social strategies to increase motivation by emphasizing the wide-ranging benefits of an active lifestyle and enhancing self-efficacy. • For those with cognitive impairment, create a respectful, mindful, and empathetic training atmosphere to promote participation and adherence and utilize one-on-one supervision. • Make exercises enjoyable by incorporating music, variety, social interaction, and feedback on progress. Celebrate achievements. However, be aware that music may be distracting for those with cognitive or hearing impairment who need to focus on the trainer's instructions. Celebrate *after* the session is finished with high protein refreshments and conversation. • Provide exercise handouts/videos and phone/email reminders between sessions. Schedule consistent training times. Help set specific goals. Encourage family/friend involvement for social support and accountability.

monitoring techniques and controlling the velocity and range of motion. In closed chain exercises such as the leg press there is little danger even with maximal volitional velocity. However, it is possible to overextend the joint in open chain exercises such as the knee extension or chest press and cause or exacerbate underlying tendinopathy. The benefit of doing power training at moderate-to-high external loads is that even when the intended velocity is maximal, actual external velocity is limited by the load. Notably, it is the *intent* to contract at maximal velocity which optimally recruits type II fibers and therefore enhances the desired adaptations of muscle power that are required for functional mobility and independence. Conveniently, this high external load optimally enhances muscle strength, bone density and even cognitive function as well [122].

To optimize muscle adaptations, mental imagery can be used to enhance motor performance in both elite athletes and older adults, in whom it may be particularly effective, according to a recent systematic review [216]. In practical terms, this means coaching the person to imagine moving the weight as rapidly and forcefully as possible before each repetition in a power training set as they take a breath in, and then using a clap or vocal command (such as "1-2-3, GO!") to elicit maximal intended velocity for the concentric phase.

2.7. Sequencing resistance and aerobic training

A combination of resistance/power and aerobic training, known as "combined or concurrent training", is the most effective method for enhancing both neuromuscular and cardiorespiratory functions and is essential for maintaining functional capacity during aging. 'Concurrent' resistance and aerobic training involves performing both exercise modalities within the same session, either sequentially or interspersed as in circuit training. In contrast, 'combined' training refers to performing both modalities within the same training period but on separate days. Importantly, in the classical work by Hickson [217] it was observed that when resistance and aerobic training are performed concurrently, a phenomenon known as the "interference effect" can occur. This effect refers to the potential reduction in strength and hypertrophy adaptations from resistance training when preceded by, or interspersed with, aerobic exercise in the same session in comparison with a resistance-only training regimen. More recent studies showed that concurrent training (AE and PRT in the same session), performed twice weekly, resulted in similar adaptations in lower-upper body strength, power, and $\dot{V}O_2$ peak compared to PRT alone and comparable aerobic fitness to aerobic training alone [218–220] in moderately trained or untrained healthy. Thus, the clinical relevance of the interference effect is not completely clear.

By contrast, a combined training study in healthy older men (65–74 yr) compared the effects of 16 weeks of twice-weekly PRT alone (50–80% of 1RM), or twice weekly cycling aerobic training alone (HR between 70% and 90% of the maximal individual HR) or combined PRT (once weekly) and aerobic (once weekly) training on muscle mass, maximal strength and power, and cardiovascular performance [221]. The main findings of this study were that combined resistance and aerobic training in older men led to similar gains in muscle mass, maximal leg strength, and muscle power output as resistance training alone and to similar gains in maximal peak power output measured in an incremental cycling test as aerobic training alone, despite the lower volume in the combined group. Thus, during the initial 16 weeks of training a minimum weekly frequency of combined training—one session of resistance plus one session of aerobic training —might be sufficient to enhance neuromuscular and cardiovascular functions in previously untrained older adults. This comparable muscle function and morphology improvements between isolated resistance training twice weekly vs. combined training with one aerobic and one resistance day each week possibly occurred due to the lower limbs cycling stimulus, as this modality requires more strength and power output compared with other aerobic modes (i.e., jogging, walking) [221,222]. This study also supports the ability of resistance training to contribute to aerobic adaptations, as noted earlier.

Collectively, these studies demonstrate that given specific training volumes, frequencies, and training schedules (i.e., training on different days or the same day), the combined or concurrent performance of resistance and aerobic training does not impede neuromuscular and cardiorespiratory adaptations; it may not result in an interference effect in healthy older adults.

However, the sequence of exercises within the same session significantly impacts neuromuscular adaptations. Specifically, performing aerobic exercises *after* PRT within the same session does not blunt strength gains and neuromuscular adaptations [223,224]. By contrast, performing aerobic exercise *before* PRT may blunt strength and hypertrophy gains. This effect is likely due to the fact that resistance training induces specific gene expression changes in muscle fibers, enhancing neuromuscular recruitment and contractile function. This includes upregulation of genes associated with myofiber hypertrophy, mitochondrial biogenesis, and angiogenesis, which are crucial for muscle adaptation and performance improvements [225]. The interference effect between AE and PRT is largely attributed to the activation of adenosine monophosphate-activated protein kinase (AMPK), a key regulator of energy homeostasis and cellular stress responses, by aerobic exercise [226]. Aerobic exercise activates AMPK, particularly under low energy availability conditions, as it restores energy balance by increasing glucose uptake and fatty acid oxidation [226,227]. However, this activation also promotes catabolic pathways, such as mitochondrial biogenesis and autophagy, which can counteract the anabolic processes necessary for muscle hypertrophy induced by resistance training [228]. As a result, the elevated AMPK activity following aerobic exercise can interfere with the signaling pathways, like mTOR (mechanistic target of rapamycin), which are crucial for muscle protein synthesis and growth in response to PRT [229,230]. In addition, blunted adaptation to PRT may be due to the onset of neuromuscular fatigue [218,231]. This fatigue reduces the ability to generate maximal force during resistance exercises, diminishing the effectiveness of PRT in promoting muscle hypertrophy and strength gains. Consequently, performing aerobic exercise *before* resistance training in the same session may reduce the overall effectiveness of the resistance training in terms of muscle growth and strength development.

Combined training should also be progressively structured in volume and intensity to maximize benefits and avoid excessive load [232,233]. Traditional PRT may reach 80–85% of the one-repetition maximum (1RM). For optimal adaptations within a resistance training session, performing large multi-joint exercises (e.g., leg press, chest press) before smaller, single-joint exercises (e.g., biceps curls, ankle dorsiflexion) is recommended. This sequence maximizes the neuromuscular benefits of resistance training [234].

Aerobic training can target up to 95% of the anaerobic threshold (the point at which lactate begins to accumulate in the blood) using a continuous training model or HIIT [235]. Power training combined with HIIT can enhance maximal strength, muscle mass, and cardiorespiratory fitness, providing benefits comparable to traditional combined training and improve explosive power in addition [235,236]. However, in practical applications, particularly with frail older adults, attempting to integrate all exercise modalities—resistance, aerobic, balance, and gait training—into a single session may lead to suboptimal intensity and volume for each modality, even if the sequencing (PRT then aerobic) is 'optimized' as above. This dilution of exercise quality is more likely to blunt the desired adaptations than the often-cited-molecular "interference effect.

In conclusion, combined training—when performed on separate days—does not compromise the effectiveness of either resistance or aerobic exercise— making it a highly effective training structure for older adults. However, concurrent training (i.e., performing both resistance and aerobic exercise in the same session) *may* reduce the benefits of resistance training, particularly if aerobic exercise precedes it, as this can blunt neuromuscular adaptations and fatigue the muscles. This is especially relevant for frail individuals, where fatigue is a significant concern. Concurrent training may also limit the volume of each modality due to the need to shorten sessions, further diminishing strength gains.

Special consideration should be given to physically frail individuals, as fatigue is a hallmark of this population. For these individuals, resistance and aerobic training should ideally be scheduled on separate days to guarantee that both modalities can be performed effectively, thereby avoiding reduced strength gains due to either neuromuscular fatigue or blunted molecular adaptation (i.e., interference effect). However, while the potential advantages of a combined training regimen (e.g., two days of isolated aerobic training and two separate days of resistance training) may exceed those of concurrent training (e.g., two sessions per week incorporating both modalities), the increased burden—both in terms of time and cost associated with traveling for four training days versus two—must be carefully considered. A practical compromise may involve performing resistance training under supervision in a clinical setting twice weekly, while prescribing aerobic activities, such as community-based walking, on alternate days. This approach minimizes costs, transportation challenges, fatigue, and potential interference effects, while maximizing the likelihood of physiological adaptation. Thus, unless unsupervised exercise is contraindicated, separating exercise modalities across different days ensures that each can be performed with adequate intensity, optimizing the intended health benefits. Ultimately, combined or concurrent training programs must be tailored to each individual's needs, preferences, and limitations, as well as practical issues such as cost, transportation, and trainer availability to maximize health benefits in the older population.

2.8. Balance training

Balance training is an essential component of physical conditioning for older adults, especially those with medical conditions that may compromise their postural stability and increase their risk of falls. Before initiating aerobic exercise or gait retraining programs, evaluating and addressing any balance deficits through targeted balance training interventions is critical. The implementation of balance training exercises, however, presents challenges due to the inherent risk of accidental falls [110]. A cautious approach to balance training involves progressively challenging postural control and stability in a secure environment. The initial phase should concentrate on mastering basic postures or movements, such as standing on one leg without hand support, while ensuring adequate safety measures are in place. Once proficiency at this level is achieved, the individual can progress to more complex variations, such as performing the exercise with eyes closed. This progressive overload principle mirrors the well-established concept of PRT, where the load is gradually increased to continue eliciting physical adaptation and improvement. Additionally, various forms of balance training, including virtual reality systems, specific balance strategies, sensory and muscular training, cognitive dual-task training, and programs using tools like Wii Fit or activities conducted in public parks, have been shown to effectively improve balance, boost confidence, enhance function and mobility, and reduce falls in older adults [125,131,237–239]. An extensive discussion of balance training principles is beyond the scope of this article, but the fundamental principles are summarized in Table 1.

2.9. Multicomponent training

Individualized multicomponent exercise interventions, including resistance and power training, cardiovascular exercises, balance, and gait exercises, have been proven to be more effective in improving the primary indicators of frailty syndrome, such as instability, declining muscle strength, decreased walking abilities, and an increased risk of falls. It is recommended that these exercise programs be adopted to prevent frailty in older individuals and target those in the pre-frail stage [84,109,236,240–242]. For example, a multicomponent exercise program incorporating cognitive dual-tasking effectively enhances the clinical hallmarks of frailty in those with cognitive impairment (low body mass, strength, endurance, mobility, PA level, energy, and cognition) [58,142]. This exercise training modality may also be prescribed to the most vulnerable populations, including the acutely ill, hospitalized [203], or institutionalized older adults [84,109,243]. There is emerging evidence that an individualized multicomponent exercise training program for older adults can partially reverse the dependence in activities of daily living (i.e., toileting, transfers, mobility, and stair climbing) that frequently occurs during and after hospitalization [244]. Multicomponent training programs should include gradual increases in individual exercise volume, intensity, and complexity. Table 3 presents some critical points for the multicomponent exercise prescriptions.

The VIVIFRAIL multicomponent Physical Exercise Program to Prevent Frailty and the Risk of Falls is an exemplary evidence-based program recommended by the WHO in the Integrated Care Program for Older People (ICOPE) guidance for person-centered assessment and pathways in primary care [245]. The VIVIFRAIL physical exercise guide (available at http://vivifrail.com/resources/) includes lower-limb exercises, such as squats from a chair, leg presses, and bilateral knee extensions, alongside upper-body exercises like the seated bench press. It also features balance and gait retraining exercises such as semi-tandem line walking, single-leg standing, stepping practice, walking with small obstacles, and proprioceptive exercises on unstable surfaces such as foam pads. Additionally, the program facilitates weight transfer exercises from one leg to another. It includes individual prescription passports for older adults, which allows for the implementation of unsupervised sessions

Table 3
Key points for multicomponent exercise intervention prescriptions for frail older adults. From refs [8,236].

Assessment and Training variable	Recommendations
Assessment and Training considerations	• Screen for conditions common in older adults (e.g., chronic diseases, injuries) to identify special needs like balance or gait impairments.
Training Modalities	• Incorporate strength, power, gait, and balance training to improve mobility and reduce falls. Add aerobic training when possible.
Power training	• Explosive contractions optimize functional gains. Perform fast concentric (shortening) contractions followed by controlled eccentric (lengthening) movements. Intensities of 60−80% 1RM may benefit frail individuals.
Resistance training	• Builds strength and muscle mass. A suitable alternative or addition to power training. Start at lower loads (50% 1RM) progressing to heavier loads (70−80% 1RM) within 2 weeks.
Sets, Repetitions and Rest Intervals	• Perform 1−3 sets per exercise to avoid fatigue. Avoid training to repetition failure. Rest 2 min between sets.
Training Frequency	• Start with 2 sessions/week, progressing to 3 sessions/week. Hospitalized individuals can train daily
Type of resistance exercises	• Use free weights, machines, bodyweight exercises, or a combination. Unilateral exercises increase intensity and allow better muscle recruitment, maintenance of proper form, and can minimize potential for arching of lower back and pain during seated knee extension and flexion exercises
Balance exercises	• Tai Chi, yoga, standing on one leg, stepping over objects, dance. Progress from standing with support to unsupported, closing eyes, reducing proprioception, and addition of cognitive or dual physical tasks.
Gait exercises	• Walk with changes in pace, direction, and surface. Progress to tandem walking, walking on heels/toes, figure eights. Add foam, dual tasks.
Aerobic training	• Start with 5−10 min, building to 15−30 min cycling, walking, stair climbing or dancing. Consider gait ability for modality.
Cognitive Impairment Considerations	• Promote participation through a respectful, mindful, empathetic approach. Use simple instruction framework focused on demonstration over complex verbal cues.
Medication Considerations	• Use perceived exertion to monitor intensity with beta blockers. Emphasize gait and balance training if impairments from drug side effects. Monitor for orthostatic hypotension or sedation/confusion from medications, as well as hypoglycemia.
Improving Adherence	• Incorporate balance practice into lifestyle, like standing on one leg during daily tasks. Account for individual preferences when designing programs to enhance motivation and long-term commitment. Praise benefits and boost confidence to increase self-efficacy.

tailored to the person's functional capacity level, assessed using the Short Physical Performance Battery (SPPB) and walking speed test, and their risk of falling (www.vivifrail.com) [243,246,247].

The VIVIFRAIL program is effective for enhancing intrinsic capacity (IC) in older adults with conditions ranging from pre-frailty to frailty and mild cognitive impairment (MCI) or mild dementia, showing more significant benefits than usual care [248,249]. The program improves IC domains such as locomotion, cognition, and vitality [248,249]. It also increases physical performance and HGS in frail individuals and modulates circulatory miRNA expression [250]. Furthermore, integrating the VIVIFRAIL exercise program with executive function-based cognitive training has demonstrated the potential to prevent falls and fall-related negative outcomes in frail older adults [249].

Exercise is medicine, and like most medicines for chronic disease, treatment is recommended without interruption. However, older adults frequently encounter disruptions in their exercise routines due to adverse events, hospitalizations, or periods of travel and relocation, where physical activity may be reduced if social support or healthcare infrastructure is lacking. Despite these interruptions, recent evidence suggests that exercise confers a protective effect even after short and long-term cessations, which is particularly relevant for frail and institutionalized populations. For instance, a study by Courel-Ibáñez et al. [243,251]examined the impact of a tailored multicomponent exercise program (VIVIFRAIL) on the prevention of weakness and falls in older adults with sarcopenia living in nursing homes. Twenty-four residents participated in either a 24-week (long training) or a 4-week (short training) exercise intervention, followed by detraining periods of 6 or 14 weeks. The results demonstrated significant improvements in both functional capacity and strength, with 36% of participants changing scores to “robust” or “non-frail” and 59% achieving a high level of self-autonomy at 4 weeks. Participants in the long-term training group saw additional benefits, with a further 10%–20% enhancement in performance compared to the short-term group. Although detraining led to a 10%–25% decline in functional capacity, the improvements remained well above baseline levels. These findings suggest the potential of intermittent exercise strategies—such as 4-week training blocks repeated three times per year—to sustain and enhance functional capacity in frail older adults, even in the face of inevitable periods of inactivity [243,251]. This approach should be tested in future studies.

The Otago Exercise Program (OEP) is also a multicomponent, evidence-based program that is effective in reducing fear of falling, falls, and mortality in community-dwelling older adults [252–254]. The OEP is a comprehensive home-based exercise program that encompasses warm-up exercises (5 movements), progressive muscle strength training (5 movements), balance training (12 movements), and walking aerobic sessions [255,256]. The program offers four levels of difficulty for strength training and balance training [156]. The OEP is currently customized to suit frail nursing home residents' physical conditions and abilities by adjusting the difficulty level. Research has demonstrated [157–161] that the OEP can effectively improve physical function in older community groups through balance and strength training, thereby reducing the incidence of falls and fall-related injuries by 35%. Additionally, it can delay or reverse the frailty status, bolster cognitive function, and promote the overall health status of residents [254,257]. The OEP has also been shown to reduce the self-reported number of falls over 12 months among community-dwelling older adults who have already experienced a fall [253].

2.10. Deconditioning and retraining effects on strength and functional capacity

Deconditioning in older adults refers either not engaging in appropriate levels of PA *per se* or to the cessation of established exercise routines and their impact on various health indicators. Older individuals often face interruptions in PA and exercise due to illness, injury, or other factors, leading to a reduction in or complete cessation of their usual PA levels [258–262]. The impact of deconditioning depends on its duration [263,264] and an individual's prior training levels [265]. Deconditioning is also relevant when older adults are hospitalized, ill, or temporarily immobilized, thereby disrupting their PA [266,267].

Stopping training and reducing usual daily PA can negatively affect muscle mass, strength, cognitive performance, and functional capacity [268,269]. The degree of muscle mass and strength loss varies with the duration of the detraining period, with significant decreases occurring over extended periods. For instance, stopping training for merely 3–4 weeks led to only minor changes in muscle power and strength loss [262,270]. However, reductions of approximately 5% in maximal strength are seen after six weeks, and more substantial decreases (~15%) occur after 12–20 weeks [271,272]. Conversely, cognitive performance, executive function, and mobility can continue to improve or retain improvements even after training stops, as noted above in the study by Courel-Ibáñez et al. [243,251] and others [273–275].

A two-year longitudinal study [276,277] showed that the benefits of 16 weeks of PRT on functional capacity, maximal muscle strength, and power output partially persisted and were maintained above baseline values in pre-frail and frail older adults aged >70 years with T2D, even after 38 weeks of detraining [276]. This study demonstrated that intermittent multimodal interventions could partially maintain improvements in functional capacity and muscle power in frail older adults with T2D who are at increased risk of adverse events such as falls, hospitalization, disability, and mortality. This maintenance may have occurred due to the increased level of activities of daily living following training-induced improvements. Although there might be a brief period after training cessation, during which some functional reserves are retained, the long-term benefits of exercise are best maintained through ongoing activity [276]. This is particularly true for T2D, where the insulin sensitivity benefits are primarily present in the first 48 h after an exercise bout, apart from any benefits attributable to changes in body composition. Thus, healthcare professionals and policymakers should encourage older adults to exercise regularly to maintain functional independence.

Following a period of deconditioning, retraining in older adults has been shown to quickly restore neuromuscular function and the cardiometabolic health benefits that were initially achieved. This recovery has been observed in the general older population [262,270,274,278] and frail individuals [276], highlighting the adaptability of the aging neuromuscular system and its ability to regain strength and overall PA levels after a break in training. This suggests that retraining can be a powerful tool to reinstate and enhance the health benefits initially obtained from exercise regimens.

2.11. Exercise safety and tolerance in older adults

Guidelines from the American College of Sports Medicine (ACSM) [17,279] and the American Heart Association (AHA) emphasize the importance of pre-exercise screening to detect cardiovascular and musculoskeletal conditions that could pose risks during exercise. This allows programs to be tailored to match individual capabilities and health status [17,279,280]. Before starting an exercise program, comprehensive screening and assessment are essential to identify potential risks requiring specific modifications [17]. This process may involve obtaining a detailed medical history, performing a physical examination, and reviewing relevant diagnostic tests and laboratory findings. Healthy older adults who plan to increase PA gradually do not need to be seen by a health care professional. However, according to ACSM and AHA guidelines, those with CV or renal or metabolic disease or signs or symptoms of them need medical clearance. This ensures that any undiagnosed symptoms are identified, preventive care is in place, and any existing medical conditions are stable before making changes to their physical activity levels.

Proper preparation to engage in PA is vital. Older adults should be educated about appropriate exercise attire, including well-fitting, comfortable clothing and adequate footwear, to minimize the risk of trips, falls, or skin irritation [17,279]. Maintaining adequate hydration before, during, and after exercise sessions is also crucial, particularly in warm or humid environments, to prevent dehydration and its associated complications [281]. Avoiding the Valsalva maneuver and breath-holding can also help to minimize hemodynamic excursions during exercise sessions or abdominal/inguinal hernia occurrence or exacerbation. These steps and a safe exercise environment help reduce the likelihood of accidents and injuries. Monitoring signs of exercise intolerance is critical. This includes checking vital signs before and during exercise sessions (such as heart rate and orthostatic blood pressure), with individualized target ranges established based on an individual's age, physical function including frailty status, health status, and exercise capacity [282]. It is also essential that older adults and their caregivers receive education on recognizing symptoms such as angina, claudication, undue shortness of breath, dizziness, or excessive fatigue that may require modifying exercise, or termination of the exercise session [279].

Exercise programs should begin slowly with low-intensity activities. Exercise can then progressively increase intensity and duration to allow physiological adaptations and minimize injury risk [124]. Incorporating warm-up and cool-down periods can also prevent injuries and support cardiovascular health [283]. Long-term (> one year) physical exercise interventions [284,285] have been shown to reduce the risk of falls and improve muscle strength, balance, physical function, and cognition [285] without increasing the risk of health-related dropouts, mortality, or fractures compared to usual care [284,285]. Epidemiological data show that although the risk of myocardial infarction (MI) is more significant during exercise than at rest, the overall risk of MI is 50% lower in those who are regularly active compared to sedentary adults and nearly 50-fold lower following an acute bout of exercise in highly active adults [286]. Therefore, long-term physical exercise is safe and effective in older adults, and its benefits accrue regardless of age, physical function, or cognitive status at baseline [285].

The type and frequency of exercise (PRT, aerobic MICT, or HIIT) and the individual's age, as well as cognitive and physical function levels, do not affect attrition rates owing to medical problems or mortality [285]. Despite the proven safety of PRT for older adults [108,285,287], including those who are frail [288,289], or have multiple chronic conditions [108], clinicians often hesitate to prescribe this exercise modality [108,285,287–289]. High-intensity interval training is now recommended as a beneficial aerobic exercise option [290], offering efficiency and better tolerance for some individuals with chronic conditions. However, its efficacy and safety [120] in older adults with frailty and multimorbidity [75] need further study [175,176].

2.12. Effectiveness of mobile applications for prescribing physical exercise in older adults

Traditional exercise prescription methods for older adults have several disadvantages, including a lack of adaptability to changing needs [291], limited personalization to individual health conditions, reduced accessibility for those with mobility limitations [292], and lower engagement without interactive features [291]. These limitations can be overcome by using mobile applications [293,294]. The use of apps makes exercise prescriptions more accessible and enjoyable to older adults, who can access personalized exercise programs directly on their mobile devices. Additionally, many apps are dynamic and can adapt to users' needs anytime, conduct self-assessments, and promote intergenerational usage. The increasing popularity of health apps can facilitate the scaling up of exercise prescriptions to reach a larger population of frail older adults. Moreover, apps enable the prescription of tailored exercise programs according to individual needs, preferences, and health status. They can also incorporate reminders, progress tracking, and social elements to help motivate and engage older adults in their exercise routines.

Despite certain benefits, mobile applications prescribing physical exercise to older individuals present certain restrictions. A recent review revealed that out of 15 exercise apps analyzed, only one was based on scientific evidence, which underscores a gap in catering to the needs of older adults [293]. This study emphasizes the importance of adapting apps to older users' cognitive and physical requirements, suggesting that involving older individuals in the 'co-design' of the app creation process is crucial for effectiveness. In addition, although most older adults have access to smart phones, there are still a substantial proportion who have low computer and/or health literacy, visual impairments, motor coordination difficulties, language limitations, low self-efficacy, or financial limitations which preclude use of such technology. Such social inequity needs to be considered in PA promotion efforts.

Based on research findings, the most widely used mobile application for physical exercise prescription in frail older adults is VIVIFRAIL [251]. This evidence-based app fulfills the needs of frail older adults by providing adaptable, accessible, and progressive exercise programs that provide both written and audiovisual information. In addition, an integrated system based on VIVIFRAIL multicomponent training was developed to monitor frailty within a community-dwelling environment and provide a multimodal tailored intervention. This technological solution enabled older users to engage with the intervention over a six-month period. Older users and their healthcare professionals also perceived it as a usable, user-friendly, and satisfactory solution [295,296]. In summary, while mobile apps show potential for prescribing exercise for older adults, further development and customization are urgently needed to address this population's specific needs better and to assure access is equitable in lower-income and culturally diverse settings.

3. Role of exercise and physical activity in bone health, adipose tissue, muscle mass, maximal strength, and power

Many studies suggest that habitual engagement in PA/exercise can markedly attenuate most decreases in exercise capacity that would otherwise occur with aging. In the last few years, evidence from well-designed studies has been accumulating, supporting the benefits of PA for bone health, increase in muscle mass and strength/power, and reduction in adipose tissue (Table 4).

3.1. Bone health, physical exercise, and fracture risk

Bone mass begins to decrease well before menopause in women (as early as the 20s in the femur of sedentary women). It accelerates in perimenopausal years, with a continuous decline through age. Similar patterns are observed in men, although with no acceleration related to the loss of ovarian function during menopause seen in women. As with the loss of muscle tissue, strength, and function (sarcopenia), many factors related to genetics, lifestyle, nutrition, disease, and medications may predict bone density at a given age. Epidemiological studies suggest that a 10% increase in peak bone mass (PBM) at the population level would be predicted to reduce the risk of fracture later in life by 50%. Thus, the accretion of PBM and bone strength among young people is essential for attenuating bone mass loss and osteoporosis risk later in life [297].

Mechanical loading of the skeleton generally leads to favorable site-specific changes in bone density, morphology, and strength, whereas unloading (in the form of bed rest, immobilization, casting, spinal cord injury, or low gravity) produces rapid and sometimes dramatic resorption of bone, increased biochemical markers of bone turnover, and therefore changes in morphology, such as increased osteoclast surfaces and susceptibility to fracture.

A significantly greater bone density has been observed in athletic cohorts, with effects depending on the type, intensity, and duration of exercise training and the characteristics of the athletes [298]. Exceptions include non-weight-bearing activities (e.g., swimming, cycling) and competitive distance runners, whose bone density appears similar to, or lower than the non-exercising controls.

The incidence of hip fractures is 30–50% lower in older adults with a history of higher PA levels than in age-matched, less active individuals. In the prospective Epidemiology of Osteoporosis (EPIDOS) study of 6901 white women aged $\geq$ 75 years who were followed for 3.6 years [299], low PA levels increased the risk of proximal humerus fracture by more than two-fold.

Significant changes in bone health of the femur, lumbar spine, and radius have been observed following high-impact aerobic training, PRT, and combined aerobic and resistive exercise programs. The effectiveness of isolated high-impact training (jumping, skipping, and heel drops) documented in young women has yet to be replicated in studies of postmenopausal women [300], which may be due to the lower ground reaction forces generated in older women with lower muscle power attempting to jump, or simply doing heel drops.

Table 4
Exercise recommendations for optimal body composition for older adults.

Exercise recommendations	Decreased adipose tissue mass and visceral deposition	Increased muscle mass and strength	Increased bone mass and density and reduced fracture risk
Modality	Aerobic or resistance training	Resistance training	• Resistance training • High-impact activities (jumping using weighted vest during exercise) if tolerated by joints. Not recommended for people with vertebral osteoporosis • Balance training
Frequency	Aerobic: 3–7 days/week Resistance: 3 days/week	3 days/week	Resistance training: 3 days/week Balance training: up to 7 days/week
Volume	Aerobic: 30–60 min of continuous exercise using large muscle groups / session Resistance: 2–3 sets of 8–10 repetitions of 6–8 muscle groups	2–3 sets of 8–10 repetitions of 6–8 muscle groups	2–3 sets of 8–10 repetitions of 6–8 muscle groups 50 jumps per session for high impact[a] 2–3 repetitions of 5–10 different static and dynamic balance postures
Intensity	Aerobic: 60–75% of maximum exercise capacity (VO_2 max or maximum heart rate) or 13–14 on the Borg Scale of perceived exertion Resistance: 70–80% of maximum strength (one repetition maximum) exertion	70–80% of maximum capacity (one repetition maximum)	70–80% of maximum capacity (one repetition maximum) as load 5–10% of body weight in vest during jumps; jumps or steps of progressive height Practice the most difficult balance posture not yet mastered

[a] Thus far, proven only in premenopausal women and adolescents or when combined with resistance training/multi-modality exercise in older adults.

3.1.1. Optimal exercise modality and intensity for bone health

The predominant exercise training factors that influence bone adaptation are the intensity and novelty of the load. Studies on the effects of mechanical loading in animals show that the bone is most sensitive to short loading periods, characterized by unusual strain distribution, high strain magnitudes, and a rapid loading rate [301].

Kohrt et al. [302] found that in older women, aerobic activities with high ground-reaction forces (walking, jogging, stair climbing) and exercises with high joint reaction forces (weightlifting, rowing) significantly increased whole-body bone mineral density (BMD), lumbar spine, and Ward's triangle. In contrast, only the ground-reaction group showed increased femoral neck BMD [302]. At the same time, lean mass and muscle strength increased only in the weight-lifting group, which is necessary for gait improvement and fall reduction. These findings suggest that both types of exercise are equally important for fall and fracture prevention. In another study, in postmenopausal women, PRT significantly increased total and intertrochanteric BMD after two years [303]. Compared with aerobic exercise, PRT in older adults is more favorable because of its broader benefits for muscle, bone, balance, and fall risk. However, if aerobic training is used, activities that are weight-bearing and have a higher impact have greater efficacy for bone health than non-weight-bearing or low-impact aerobic activities [304].

It is essential to choose the optimal exercise modality and the relative intensity, as skeletal adaptation is critically linked to the loading intensity (whether due to increased weight lifted during PRT or higher ground-reaction forces during aerobic/jumping activities). A multimodal exercise program over 12 months (high-intensity PRT and a weight-bearing circuit of moderate-impact activities, including walking/jogging, skipping, hopping, and stair climbing/stepping with weighted vests) resulted in significant BMD improvements at the femoral trochanter [305]. These results were linearly related to the total weight lifted and exercise-specific weight lifted (e.g., leg press, squat, and military press exercises) but not to the volume or quality of the non-resistance training components of the program [305]. Moreover, multicomponent exercise training that included PRT of moderate-to-vigorous intensity prevented the increase in bone turnover and attenuated the decrease in hip BMD in frail older adults with obesity engaged in a weight loss intervention [306].

Overall, most studies demonstrating the efficacy of exercise on BMD have been conducted in women between 50 and 70 years of age, and it is not yet known whether the efficacy is similar in women over 80 years of age with multiple comorbidities, who have often been excluded from such trials [114,307,308]. A randomized clinical trial (RCT) of 90 men and 90 women aged 65–74 comparing Tai Chi, resistance exercise, and a control intervention three times a week for 12 months on BMD, muscle strength, balance, and flexibility in community-dwelling people showed modest effects, which may not translate into better clinical outcomes, although the adherence rate was high [128]. However, recent studies suggest optimal adaptations continue to accrue with high-intensity resistance and power training in older adults [309].

Importantly, while BMD may be considered a surrogate outcome for bone health, a recent meta-analysis of 20 randomized controlled trials found that exercise intervention was even more importantly associated with a 26 percent reduction of fall-related fractures in older adults [310]. The meta-analysis concluded, however, that more large-scale trials are needed on different types of exercise. Simple walking exercise has been shown to increase fall-related fractures in 2 studies [311], indicating such a prescription is contraindicated in recurrent or high-risk fallers. Notably, in a 5-country European healthy longevity trial, DO-HEALTH, testing a simple low intensity, home-based, body weight/elastic band exercise program in 2157 generally healthy and active adults age 70 and older compared with a control exercise of seated stretching, found no benefit of the exercise program on fracture reduction [312] or BMD [313] over a 3-year follow-up. A close inspection of the methodology indicates that although the intervention was described as "strength training", it did not conform to the principles of overload and progression that are critical to this modality of exercise since initially described by deLorme in 1951 [314]. In addition, 83% of participants in DO-HEALTH were at least moderately physically active at baseline, yet were prescribed exercise that did not challenge their capacities sufficiently to induce adaptation [312]. It is worth noting that none of the clinical outcomes in this large study improved with exercise, in contrast to decades of data from RCTs of robust, evidence-based exercise programs which do show clinically relevant benefits for bone health and fracture risk, as well as all the other outcomes in DO-HEALTH.

3.2. Adipose tissue and physical exercise

Aging is associated with changes in body composition, including increased visceral adipose tissue, redistribution of adipose tissue from the subcutaneous to internal organs, appendicular to central deposition, infiltration of skeletal muscle tissue with fat, increases in intracellular adiposity, and deposition of ectopic adipose tissue. All of these are risk factors for diseases, including osteoarthritis, cardiovascular disease, gall bladder disease, T2D, breast, colon, and endometrial cancer, hypertension, peripheral artery disease, stroke, reduction in vascularization and hypoxia, increased fibrosis, and senescent cell accumulation [315]. Reduced visceral fat has been shown to improve glucose tolerance and insulin sensitivity in individuals with and without diabetes. Reductions in trunk fat correlate with improved glycemic control in T2D [316,317]. Therefore, exercise has the potential of favourably affect the accretion and distribution of adipose tissue. In this section, we review the significance of exercise's effects on reducing the disease burden associated with reducing adipose tissue in older adults.

3.2.1. Experimental studies of the influence of physical activity on abdominal fat

Evidence from well-designed studies supports the benefits of PA in reducing total abdominal fat. Most studies have included middle-aged to older populations with higher abdominal and visceral fat accumulations than younger adults. These studies were more likely to demonstrate a greater magnitude of change in these individuals than in those with lower abdominal fat mass at baseline [318]. Furthermore, the potential for PA to attenuate the gain in visceral fat is evident in obese individuals as early as childhood.

Decreases in total adipose tissue accumulation and abdominal (visceral) deposition are achievable by both aerobic exercise and PRT. However, reductions in total body weight are more rapid when combined with energy-restricted diets or when performing substantial volumes of exercise (i.e., 7 h per week resulting in high energy expenditure), both of which support a negative energy balance. However, these exercise dosages are not always attainable, especially in older adults. Preferential visceral fat mobilization is often observed in response to exercise and dietary intervention, which means a slight reduction in total body weight or fat mass (5%) may be associated with substantial changes in visceral fat (25% or more). These changes in adipose tissue have important metabolic implications for preventing and treating insulin resistance syndrome [319].

Combining exercise and diet is the most effective nonsurgical treatment for obesity and metabolic health. All international consensus panels advocate this approach. One of the most common undesired effects of the hypocaloric diets to lose weight in older people is an impairment in functioning due to the loss of skeletal muscle, with the highest impact in older people with sarcopenia and frailty [320,321]. The advantages of adding anabolic exercise to the diet attenuates this side effect [322], whereas aerobic exercise does not. Other benefits include more significant weight loss, preservation of fat-free mass (both muscle and bone) preservation of resting metabolic rate (when PRT is included), improved fitness levels, correction of metabolic abnormalities associated with visceral obesity, and better long-term adherence to dietary modifications, resulting in sustained weight maintenance. Therefore, exercise including PRT plus diet appears to be an optimal evidence-based treatment for obesity in individuals of all ages.

3.2.2. Relationship between exercise intensity and changes in body fat

In general, weight loss parallels energy expenditure via exercise, whether achieved by a more significant volume, intensity, or duration of the exercise prescription. There is no evidence from well-designed studies that low-intensity exercise effectively reduces abdominal fat. Most robustly designed studies used moderate- to high-intensity aerobic interventions. A higher-intensity stimulus can be delivered via intermittent intensities with resistance or interval training. This exercise prescription may be more effective and better tolerated by 'at-risk' populations than sustained, moderate, or intense exercises.

Furthermore, a recent meta-analysis of studies comparing body composition changes between HIIT and MICT suggested that the intensity of effort during endurance exercise minimally influences longitudinal changes in fat mass and lean mass [323]. These changes underscore the importance of exercise volume (resulting in higher energy expenditure) to facilitate fat mass loss. However, the amount of exercise required to achieve practically meaningful changes in fat mass (∼100 min/day) is not feasible for most of the general public and thus has limited practical relevance. Dietary energy restriction thus plays a vital role in creating an energy deficit and facilitating fat mass loss [324]. However, exercise may help preserve lean mass and functional performance during periods of energy restriction [325]. It should be considered an essential complement to nutritional approaches for those who attempt to alter their body composition.

There is some evidence that aerobic training may be better than PRT at reducing abdominal fat [326]. However, at doses resulting in a sustained negative energy balance for several months, resistance and aerobic exercises generally result in significant reductions in fat mass when sensitive measurement techniques (generally not anthropometrics) are used. Resistance exercise may be more suitable as a fat-reduction strategy for obese older individuals with cardiovascular disease, osteoarthritis, osteoporosis, or mobility limitations, who may not tolerate moderate- to high-intensity aerobic training or may need the added benefits of PRT for maintaining muscle and bone mass. Importantly, energy restriction results in significant loss of muscle and bone [320,321]. The addition of PRT to hypocaloric dieting has been shown to prevent such adverse changes in body composition [327], which are not attained with aerobic exercise alone. The combination of aerobic and PRT has demonstrated superiority in reducing trunk fat in older men compared to aerobic training alone [320,328,329]. Further well-designed studies are needed, particularly in overweight older adults, to explore the relative benefits of these exercise modes in optimizing body composition.

3.3. Role of exercise in preserving muscle mass with age

In contrast to the changes in fat and bone, a significant increase in muscle mass is achievable only with progressive PRT or weight gain from extra energy and protein consumption. The accretion of lean tissue with exercise has a potentially beneficial effect in preventing diabetes and metabolic syndrome [330], functional dependency, falls, and fractures as well as in the treatment of chronic diseases and disabilities that are often accompanied by disuse, catabolism, and sarcopenia. For persons with T2D, there are potential advantages to minimizing fat and maximizing muscle tissue because these compartments have opposite and likely independent effects on insulin resistance. Resistance exercise coupled with leucine-enriched essential amino acid supplements (when the diet is inadequate in energy and protein provision) is recommended to treat sarcopenia [331]. Various epidemiological and experimental studies have shown that muscle weakness, decreased muscle mass, reduced activation of glycogen synthase, and alterations in the numbers of glycolytic skeletal muscle fibers are related to, and may precede, insulin resistance, glucose intolerance, and T2D [332,333].

3.3.1. Exercise to maintain or increase muscle mass and strength

A properly designed PRT program can counteract age-related changes in contractile function, atrophy, and morphology of the aging human skeletal muscles [17,35,36]. Appropriate progressive PRT programs of 3–6 months duration can increase muscle strength by an average of 40–150%, depending on the person's characteristics and intensity of the program, and increase total body lean mass by 1–3 kg or muscle fiber area by 10–30% [334,335]. Exercise training reduces frailty in older adults by suppressing muscle inflammation and promoting anabolism, thereby increasing muscle protein synthesis rate [148,336,337]. Thus, even if some of the neural control of muscles and the absolute number of motor units are not affected by exercise, the adaptation to muscle loading, even in advanced age, causes neural, metabolic, and structural changes in muscles, which can compensate for strength losses and, in some cases, age-related atrophy [338]. Generally, strength gains after exercise far exceed and are not directly correlated with muscle size changes due to the importance of neural adaptation in this process, particularly in the early phases of training.

High-load PRT is also more beneficial than low-intensity training for maximizing muscle and bone mass/strength and treating gait disorders, functional impairments, and disability. It is ideal as a multiple-risk factor intervention strategy for injurious fall prevention in osteopenic adults. A key question in research into the adaptability of the older muscle remains whether there is the equivalent potential for growth as in younger muscle

3.3.2. Predictors of muscle hypertrophy after exercise

There is mixed evidence regarding whether there are significant sex differences in the functional or hypertrophic response to PRT in older adults, heavily influenced by the presentation of the results in absolute or relative contexts [339]. Some studies have found that women have smaller gains in muscle strength, power, or hypertrophic response to training, whereas others have found no differences or even more significant gains. Differences in training regimens (mainly related to intensity) and measurement techniques used to assess muscle mass, cross-sectional area, or volume may explain some of these discrepant results. Malnutrition, impaired protein synthesis rates, inflammatory cytokines, and depression are other factors identified as detrimental to robust anabolic and functional adaptations to PRT. However, the roles of genetic and epigenetic factors remain under investigation [622].

3.4. Skeletal muscle energetics, muscle mass and exercise

Mitochondria are intracellular organelles that play a crucial role in cellular redox balance, calcium handling, cellular metabolism, and the production of ATP by oxidative phosphorylation. Declining mitochondrial function is frequently described as a characteristic of skeletal muscle aging [340–344]. However, there is ongoing debate on the nature of age-associated mitochondrial dysfunction, and several studies found no effect of age on mitochondrial oxidative capacity [345–349] and in some cases older athletes have presented with "healthier" mitochondria compared to young non-exercisers [350]. Studies that have observed an age effect have often not considered covariates impacting mitochondria [351–354], such as participant PA/sedentary behaviors [343], cardiovascular fitness, and adiposity [344]. Regardless of its cause, recent studies have shown that loss of mitochondrial energetics in sub-optimal aging contributes to slower walking speed [355–358], fatigability [359], multimorbidity [360], frailty [361] and sarcopenia [345,362]. Despite the critical role that mitochondrial function plays in aging muscle, practical strategies to achieve improvements in mitochondria function still need to be developed. Endurance and resistance exercises are the only proven measures to improve muscle health and mitochondrial bioenergetics in older adults.

Resistance training remains the most effective way to counteract the progression of sarcopenia. In 1990, Fiatarone et al. [35] showed that an 8-week high-intensity PRT program in frail institutionalized nonagenarians led to a 9% increase in mid-thigh muscle area determined by computer tomography. The efficacy of PRT in stimulating protein synthesis, lean mass accrual, and increases in strength is well- documented [334]. Although aerobic training can improve myofiber size and strength as well as whole muscle size and strength [363], studies in older adults have shown that PRT is more effective for increasing muscle size and muscle fiber cross-sectional area [364–366]. Many studies in older adults examine varying lengths and intensities of PRT and the impact of various nutritional supplements. Balachandran et al. [367] compared muscle mass gains in older adults after 15 weeks of high-intensity PRT as measured either by Dual-energy X-ray Absorptiometry (DXA)-assessed appendicular lean mass or by a D3-creatine (D_3Cr) dilution method, which directly measures skeletal muscle mass. Significant mass gains were seen using both methods, but the correlation between mass changes between the two methods was low (r = 0.19). The combination of whey protein supplementation and PRT achieves more significant increases in muscle mass compared to PRT alone; the effect appears larger in low-functioning older adults [368,369]. Resistance training is also effective for reducing the amount of muscle mass lost during hypocaloric weight loss in obese and overweight older adults, while aerobic exercise is not [320,370].

Resistance training had long been thought to have little or no effect on mitochondrial content or function. More recently, strong evidence shows that PRT increases mitochondrial protein fractional synthesis rates [119,371] and improves mitochondrial function [119,372]. Progressive resistance training-induced improvements in mitochondrial respiration are modest compared with those elicited by endurance exercise. However, in older adults, improvements in phosphocreatine (PCr) recovery rates assessed in vivo and oxidative capacity appear comparable between the two training modalities [373]. Similarly, resistance exercise training increased state III of mitochondrial respiration and maximal oxidative phosphorylation capacity in muscle biopsies from older adults, concurrent with improvements in adenosine diphosphate (ADP) sensitivity [374].

In contrast to PRT, the impact of endurance exercise on mitochondrial function is more widely appreciated. Holloszy [375] was the first to demonstrate that endurance exercise induces mitochondrial biogenesis. Since then, studies have consistently documented that endurance exercise improves mitochondrial content and function [376–378]. This is achieved through increased mitochondrial turnover since endurance exercise increases mitochondrial biogenesis (protein synthesis) [371,379] and mitophagy (mitochondrial-specific autophagy) [380]. In addition, improvements in mitochondrial efficiency and antioxidant capacity imply less oxidative stress and damage, which would improve the quality of the proteome. Overall, endurance exercise-mediated improvements in mitochondrial content and function which could theoretically protect against sarcopenia [381]. Enhanced mitochondrial content and function can sustain greater energetic flux and oxidation of substrates, decreasing the accumulation of lipotoxic intermediates that promote inflammation and oxidative stress [382]. Exercise-induced improvements in substrate flux thus reduce inflammation and oxidatively modified proteins [383]. Therefore, aerobic exercise improves the ability to maintain cellular integrity and adapt to stress [384]. Notably, endurance exercise improves the ability of the muscle to provide energy on demand for muscle contraction to facilitate mobility in older adults. However, as Klitgaard showed in 1990 [385], recreationally strength-trained men (mean age 68 years), who had been training for 12–17 years, exhibited maximal isometric torque, movement speed, cross-sectional muscle areas, specific tension, and levels of myosin and tropomyosin isoforms in the biceps and quadriceps muscles comparable to those of much younger controls (mean age 28 years), whereas older habitual runners and swimmers had muscle morphology and function similar to older sedentary men. This study, along with other epidemiological and empirical evidence, convincingly shows that aerobic exercise alone cannot prevent sarcopenia.

4. Role of exercise in primary, secondary and tertiary disease prevention

Physical activity, particularly exercise, can reduce the burden of comorbidity, disability, and premature death caused by incident disease and is valuable for primary, secondary, and tertiary prevention. Exercise patterns may vary with age and genotype, influencing physiological capacity, psychological health, dietary intake, adverse behaviors, and risk factors. These are the potential pathways through which exercise can affect the prevalence of chronic diseases in a population.

Although optimal levels of PA can ameliorate risk profiles, the presence of risk factors may lead to reduced PA, thereby increasing disease risk. For example, inactivity can lower muscle mass, followed by muscle weakness and further reduction of activity levels, subsequently contributing to osteoporosis, gait abnormalities, and, ultimately, a high risk of falls and hip fractures.

Preventive exercise prescriptions for middle-aged sedentary adults with low fitness markedly reduce cardiovascular mortality, suggesting that exercise in middle age can be as effective as activities started at a younger age to reduce mortality. Empirical data have shown that exercise can prevent some diseases (e.g., secondary cardiovascular events, diabetes mellitus, and osteoporotic fractures). In addition, evidence confirms epidemiological risk reduction for other conditions (renal failure, stroke, dementia, and depression). Based on findings from the Finnish Diabetes Study [330], the Diabetes Prevention Program (DPP), and other similar trials, diabetes can be prevented in high-risk obese adults with impaired glucose tolerance through diet and exercise interventions [692,693]. In the DPP, participants randomly assigned to an intensive lifestyle intervention including diet and exercise reduced their risk of incident T2D by 58% at three years compared to the control group (lifestyle advice only), and this intervention was significantly better than metformin prescription [386]. Notably, those older than 60 years showed the best response, with a 71% reduction in incident diabetes during this timeframe. By contrast, metformin was no more effective than the control condition in older adults. It is noteworthy that although metformin is often subsidized by some governments and health insurance plans for diabetes prevention in older adults (despite its lack of efficacy in this cohort for this purpose), proven long-term lifestyle interventions are *not* covered.

Table 5 lists the major diseases and syndromes for which exercise could serve as a preventive strategy or aid in disease prevention (secondary and tertiary prevention). The table outlines the likely mechanisms of exercise benefit and the specific modality of exercise that is most relevant for these outcomes (Fig. 4).

4.1. Role of exercise in the secondary and tertiary disease prevention

Exercise is particularly effective in targeting syndromes of disuse and decelerating the trajectory of decline, notably in conditions such as Parkinson's disease, chronic obstructive pulmonary disease, and cardiometabolic disorders. Some disease-related pathophysiological abnormalities are specifically addressed by exercise, making it a valuable adjunct to pharmacological treatment. Muscle-derived myokines are known for their beneficial effects of promoting a healthy anti-inflammatory and anabolic environment [107,387]. Excess adipose tissue is associated with inflammation [388]. Loss of visceral fat through resistance or aerobic training improves insulin resistance and complements dietary and pharmacological management in older adults with T2D and central obesity [108]. Regular exercise fosters anti-atherogenic changes in vascular function and structure independent of traditional CVD risk factors [107]. Exercises that stimulate skeletal muscle hypertrophy in congestive heart failure counteract the catabolic effects of circulating cytokines, which cannot be achieved by available medications [389]. Lower extremity exercises in individuals with osteoarthritis improve joint stability.

It is not feasible to discuss every disease for which exercise has beneficial effects. Type 2 diabetes, cancer, cognitive impairment, dementia, and mental health are prototypical examples of the disorders outlined in Table 5. We additionally review the role of exercise interventions in geriatric syndromes (frailty, falls, and sarcopenia) in the prevention and treatment of disability to counteract iatrogenic diseases and for acute hospitalized older persons.

Table 5
Role of Exercise in Primary, Secondary and Tertiary Disease Prevention.

Disease	Postulated mechanisms of exercise effect on disease prevention	Considerations for the prescription for secondary and tertiary prevention (disease expression and progression)	Recommended exercise modality
Arthritis (osteoarthritis for prevention; all arthritis for treatment)	• Decreased body weight • Maintenance of cartilage integrity • Maintenance of muscle and tendon strength	• Low impact • Sufficient volume to achieve a healthy weight if obese • Sufficient intensity to maintain muscle and tendon strength	• Aerobic exercise • Resistance exercise
Cancer (breast, colon, prostate)	• Decreased body fat • Decreased oestrogen levels • Decrease in gastrointestinal transit time • Increased prostaglandin F2 • Improved immune function and reduced inflammation	• Resistance training with dietary intervention may offset myopathy and reduce prevalence of cancer cachexia	• Aerobic exercise • Resistance exercise
Chronic obstructive pulmonary disease	• Increased adherence to smoking cessation, dietary behaviours • Increased muscle mass • Improved lung function	• Resistance training may be more tolerable in severe disease, and addresses cachexia or COPD • Combined effects complementary if feasible • Time exercise sessions to coincide with bronchodilator medication peak. • Use oxygen during aerobic exercise as needed	• Aerobic exercise • Resistance exercise
Chronic renal failure	• Reduced risk of hypertension • Reduced risk of type 2 diabetes mellitus	• Exercise reduces cardiovascular and metabolic risk factors, improves depression • Resistance training offsets myopathy of chronic renal failure	• Aerobic exercise • Resistance exercise
Congestive heart failure	• Decreased risk of ischaemic heart disease • Decreased risk of hypertension • Decreased risk of type 2 diabetes mellitus • Decreased risk of visceral obesity	• Improves cardiovascular function and contractility, morphology • Improves hypertension and lipid profile, inflammation, visceral obesity, risk of secondary ischemic events • Resistance training addresses cardiac cachexia • Exercise improves psychological health	• Aerobic exercise • Resistance exercise[a]
Coronary artery disease	• Decreased blood pressure • Decreased LDL cholesterol • Increased HDL cholesterol • Decreased fibrinogen • Decreased total body fat, visceral fat • Decreased insulin resistance, hyperinsulinemia • Decreased cortisol levels, inflammatory cytokines • Increased adherence to smoking cessation, dietary behaviours • Decreased depression, anxiety • Improved endothelial cell function • Increased aerobic capacity	• Exercise improves all risk factors to prevent recurrent events • Exercise improves aerobic capacity which is linked to lower mortality • Complementary effects on exercise capacity and metabolic profile from combined exercise modalities • Resistance training may be more tolerable if the ischaemic threshold is very low due to lower heart rate response to training	• Aerobic exercise • Resistance exercise
Dementia	• Improved cerebral blood flow • Increased neurotrophic factors in CNS • Hippocampal neurogenesis • Anabolic hormones • Prevention of diabetes/insulin resistance • Prevention of stroke • Prevention of hypertension • Prevention and treatment of depression, anxiety and insomnia	• Exercise under supervision if cognition is moderately to severely impaired • Attenuation of cardiometabolic risk factors for progression • Improved functional independence • Reduced falls risk with resistance and balance exercise	• Aerobic • exercise • Balance/gait/functional exercise • Resistance exercise

(continued on next page)

Table 5 ***(continued)***

Disease	Postulated mechanisms of exercise effect on disease prevention	Considerations for the prescription for secondary and tertiary prevention (disease expression and progression)	Recommended exercise modality
	• Avoidance of head trauma during exercise is critical		
Depression	• Increased self-efficacy, mastery • Internalised locus of control • Decreased anxiety • Improved sleep • Increased self-esteem • Increased social engagement, decreased isolation • Decreased need for drugs associated with depression (beta blockers, alpha blockers, sedative hypnotics) • Decreased body fat, improved body image	• High-intensity resistance training and adequate volumes of aerobic exercise are more efficacious than low-intensity/low-volume exercise in major depression	• Aerobic exercise • Resistance exercise • Yoga/other mind-body exercise
Osteoporosis / Osteoporotic fracture	• Increased bone density • Increased tensile strength • Increased muscle mass • Improved gait stability and balance • Improved nutritional intake (energy, protein, calcium, vitamin D) • Reduced fear of falling, improved self-efficacy • Increased overall activity levels, mobility • Decreased need for drugs associated with postural hypotension, falls, hip fractures (antidepressants, antihypertensives, sedative-hypnotics)	• High-impact, high-velocity activity (e.g., jumping) is potent if tolerable; avoid if osteoarthritis is present. • Resistance training effects are local to muscles contracted. • Balance training should be added to prevent falls and must be challenging	• High-impact exercise • Progressive resistance training • Balance training
Peripheral vascular disease	• Prevention of hypertension • Prevention of diabetes • Improved lipid profile • Assistance in smoking cessation • Reduction in adiposity/visceral adiposity	• Vascular effect is systemic; upper limb ergometry may be substituted for leg exercise if necessary • Resistance training has a similar effect on claudication as aerobic exercise • Low-intensity resistance training is ineffective. • Exercise only to the onset /early phase of claudication; rest and repeat	• Aerobic exercise • Resistance exercise
Stroke	• Decreased obesity • Decreased cholesterol • Prevention of diabetes • Prevention of hypertension • Prevention of atrial fibrillation	• Start with resistance and balance training until ambulation is safe • Cognitive impairment may require close supervision • Avoid Valsalva and breath holding to minimise hemodynamic excursions	• Aerobic exercise • Resistance exercise • Balance and functional training
Type 2 diabetes mellitus	• Improved insulin sensitivity • Increased GLUT-4 protein and translocation to membrane sites • Reduced visceral fat mass • Decreased cortisol response to stress • Improved lipid profile • Decreased blood pressure • Increased muscle mass	• Exercise at least every 48 h to optimise glucose regulation • May need to avoid impact exercises if peripheral neuropathy present • Monitor blood glucose before and after exercise if not well-controlled	• Aerobic exercise • Resistance exercise
Venous insufficiency	• Increased muscle mass/strength lower limbs • Decreased adiposity	• Local muscle contractions in calf stimulate the return of fluid via the lymphatic system • Utilise lower body training; elevate legs when possible	• Aerobic exercise • Resistance exercise

[a] Indicates that the modality of exercise has been shown to affect the postulated mechanistic factors but has not yet been shown to prevent distal disease outcomes in epidemiological/clinical studies.

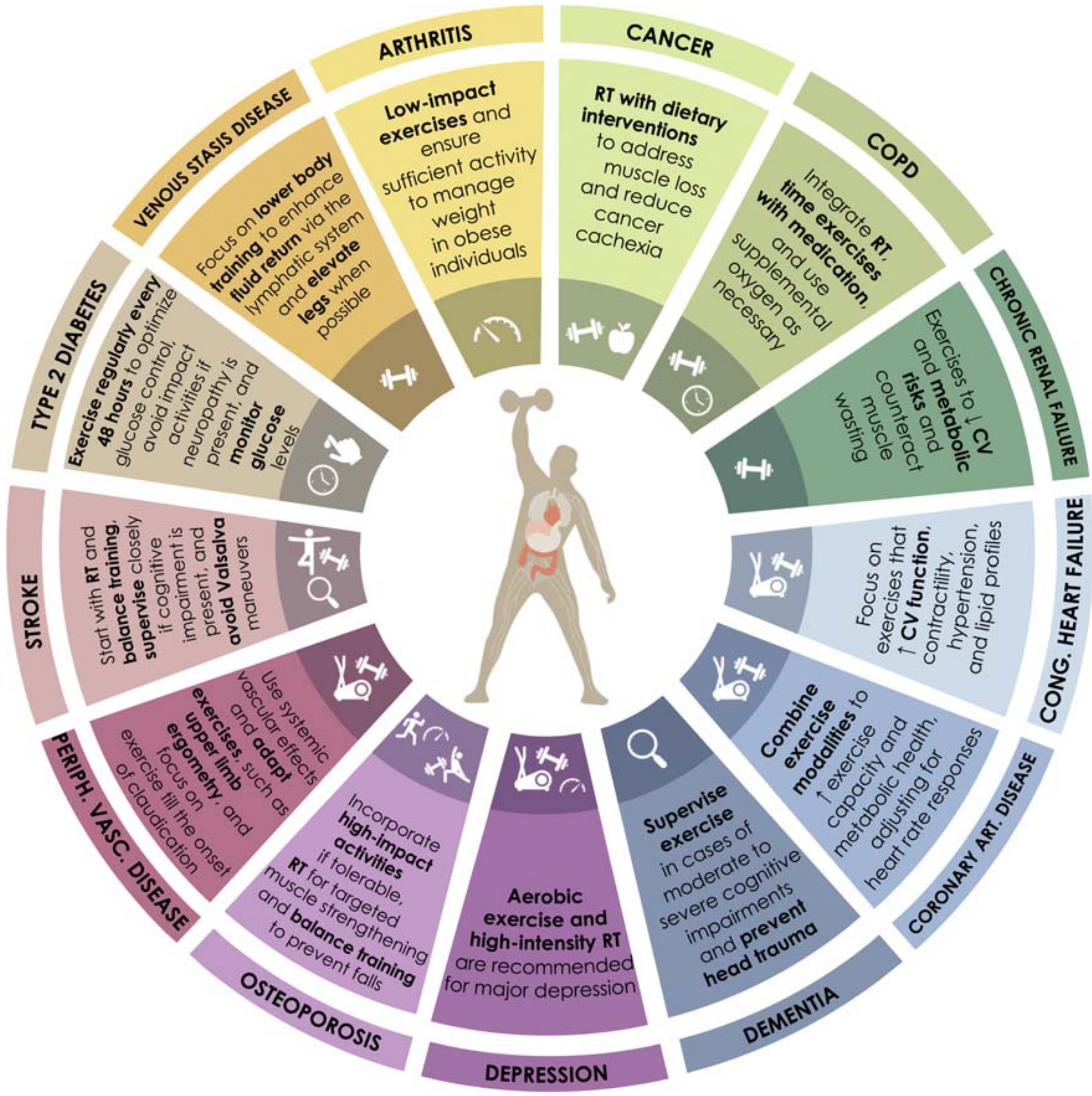

Fig. 4. Graphical illustration of the considerations for the prescription for secondary and tertiary prevention (disease expression and progression).

4.1.1. *Exercise in type 2 diabetes*

Targeting glycemic control without simultaneously addressing central obesity and a sedentary lifestyle may hasten the emergence of disease complications and add to the burden of polypharmacy in individuals with insulin resistance. Weight loss due to diet alone in older adults with obesity leads to loss of lean tissue (muscle and bone), exacerbating age-related sarcopenia and osteopenia [390].

Many consensus [98,391] and position statements [392] recommend moderate- to high-intensity aerobic exercise for 3–4 h per week to improve insulin sensitivity and glucose homeostasis, assist in maintaining lower body weight, reduce visceral fat, modestly improve blood pressure and lipids, and lower the risk of cardiovascular morbidity and mortality in individuals with T2D. However, the clinical management of obese individuals with T2D is often complicated by multiple comorbid conditions, such as cognitive impairment, osteoarthritis, ischemic heart disease, peripheral vascular disease, renal failure, peripheral neuropathy, and hypertension, which may impede adherence to dietary and aerobic exercise recommendations [108]. This clustering makes implementation of consensus statements and clinical guidelines challenging because performing aerobic exercise at the volumes and/or intensities shown to produce metabolic benefits is unrealistic for these individuals.

An alternative approach in adults with diabetes is PRT. The specific benefits for older adults include combating age- and diabetes-related sarcopenia, preventing loss of muscle and bone mass, reduced resting metabolic rate accompanying hypocaloric dieting, increased glucose uptake and storage in skeletal muscle, reduced visceral fat, lowered C-reactive protein, and improved resting blood pressure, functional status, mobility, sleep, and depressive symptoms [393–395]. The effects on muscle mass are distinct from those of aerobic exercise and are essential for preventing dementia in older adults with diabetes, although more evidence is needed [396]. Current recommendations include aerobic and PRT and dietary modifications for T2D.

In older adults with coexisting frailty, diabetes, and functional decline, evidence from a large RCT shows functional benefits with a combined approach of PRT, nutritional education, and readaptation of the clinical targets for glycosylated hemoglobin and blood pressure. In this study, the benefits were evident early (week 8) and continued long-term (12–24 months) [277]. A multicomponent exercise program consisting of resistance, endurance, balance, and gait training is also recommended to increase functional capacity and quality of life and to avoid falls, institutionalization, and disability [97]. Strategies to develop skeletal muscle power in this population are essential to prevent or delay functional limitations and subsequent disability [84,397].

4.1.2. Exercise in cancer patients

Cancer is a group of diseases characterized by an abnormal growth and spread of cells due to multiple genetic mutations. Cancer cells often accumulate and adhere together to form a tumor or neoplasm at the site of initial carcinogenesis. These primary tumors, in turn, can shed cancer cells that spread or metastasize throughout the body via the lymph system and blood vessels and form colonies at distant sites. Once widely disseminated, these cancer cells can invade and destroy vital organs and tissues, ultimately resulting in death.

In 2020, over 19 million people were diagnosed with cancer, and this is expected to reach 28 million by 2040 [398]. Furthermore, cancer fatalities have also followed this upward trend, with more than 9 million deaths in 2020 and over 16 million projected by 2040 [398]. Cancer is a disease of older adults, with approximately 80% of all cancer diagnoses worldwide in people over 50 years of age and 60% in highly developed countries in those over 65 years of age [399].

Cancer is one of the most extensively treated chronic diseases worldwide. The most common cancer treatment modalities include surgery, radiation therapy, chemotherapy, endocrine (hormone) therapy, immunotherapy, and targeted therapy. Modern cancer treatment approaches often consist of multiple lines of multimodal treatment combined concurrently and sequentially to treat a disease that can progress or recur numerous times. Consequently, patients with cancer may receive many different treatments for many months or even years.

Cancer and its treatments affect all organ systems and tissues [400]. The side effects may include nausea, vomiting, diarrhea, mucositis, peripheral neuropathy, hand-foot syndrome, pain, fatigue, depression, hair loss, lymphedema, poor sleep quality, cardiotoxicity, cognitive dysfunction, and urinary issues [400]. Additionally, cancer and its treatment can accelerate aging and functional decline, adversely affecting cardiorespiratory fitness, muscle strength, balance, body composition, and physical function and potentially leading to sarcopenia and frailty [400–402]. Frailty and sarcopenia in older adults with cancer increase the risk of treatment complications, which in turn result in postoperative complications, longer hospital stays, greater chemotherapy toxicity, treatment reductions, and decreased survival [401,402]. Older adults and those with advanced cancer are particularly vulnerable to adverse effects.

Exercise has been shown to assist cancer patients in preparing for treatments, managing treatments, recovering after treatments, and improving long-term outcomes [400,403–405]. It offers benefits across health-related fitness parameters, physical functioning, some cancer treatment side effects, psychosocial functioning, treatment tolerance, treatment response, and possibly even survival [400,403–405]. Additionally, exercise can prevent and reverse sarcopenia and sarcopenic obesity in patients with cancer [401], demonstrating positive effects even in frail cancer patients [402]. In particular, counteracting the catabolic effects of steroids or androgen deprivation therapy requires specific attention to anabolic exercise (PRT) to prevent body composition changes (increased visceral fat, decreased muscle and bone) which will otherwise lead to clinical sequelae such as diabetes, osteoporotic fracture and sarcopenia.

Based on solid evidence of benefits with minimal harms, many countries and organizations worldwide have issued exercise guidelines for exercise prescription in patients with cancer and survivors. The American Society for Clinical Oncology (ASCO) recommends that oncology providers provide both aerobic and resistance exercises to patients with cancer during curative treatment to help mitigate the side effects of treatment [403]. While ASCO supports exercise for cancer patients, it does not specify the volume or intensity of aerobic or resistance exercise. Conversely, the ACSM advises that all cancer patients and survivors should avoid inactivity and perform at least 150 min/week of aerobic exercise and at least two days/week of strength exercise at a moderate or high intensity [400]. Moreover, the ACSM offers more detailed exercise prescriptions to address specific symptoms and side effects (Table 6).

Although the benefits of exercise outweigh the harms for most cancer patients, some risks and contraindications must be considered [400]. One significant concern is the risk of fracture related to primary or metastatic bone cancer [406]. Exercise prescriptions for these patients should avoid high-intensity or high-impact exercise. Patients with cancer may also be at a higher risk of falls due to side effects of chemotherapy, such as peripheral neuropathy, ataxia, fatigue, and cognitive dysfunction. Providing safe and stable exercises and balance training when indicated is essential [400].

Table 6
Recommended exercise prescriptions for managing specific symptoms and side effects in cancer patients.

Symptom/ Side Effect	Aerobic Exercise Only	Resistance Exercise Only	Combined Aerobic and Resistance Exercise
Fatigue	3×/week for 30 min/ session at moderate intensity	2×/week of 2 sets of 12–15 repetitions for major muscle groups at moderate intensity	3×/week for 30 min/session of moderate aerobic exercise plus 2×/ week of 2 sets of 12–15 repetitions of strength exercise for major muscle groups at moderate intensity
Sleep quality	3–4×/week for 30–40 minutes/ session at moderate intensity	Insufficient evidence	Insufficient evidence
Anxiety	3×/week for 30–60 minutes/ session at moderate to vigorous intensity	Insufficient evidence	2–3×/week for 20–40 minutes/session of ≥ moderate aerobic exercise plus 2×/week of 2 sets of 8–12 repetitions of strength exercise for major muscle groups at ≥ moderate intensity
Depression	3×/week for 30–60 minutes/ session at moderate to vigorous intensity	Insufficient evidence	2–3×/week for 20–40 minutes/session of ≥ moderate aerobic exercise plus 2/week of 2 sets of 8–12 repetitions of strength exercise for major muscle groups at ≥ moderate intensity
Quality of life	2–3×/week for 30–60 minutes/ session at moderate to vigorous intensity	2×/week of 2 sets of 8–15 repetitions for major muscle groups at moderate to vigorous intensity	2–3×/week for 20–30 minutes/session of moderate aerobic exercise plus 2/week of 2 sets of 8–15 repetitions of strength exercise for major muscle groups at ≥ moderate intensity
Lymphedema	Insufficient evidence	2–3×/week of progressive, supervised exercise for major muscle groups (will not exacerbate lymphedema)	Insufficient evidence
Bone health	Insufficient evidence	2–3×/week of moderate to vigorous resistance training plus high impact training (ground reaction force of 3–4 time body weight) for ≥12 months	Insufficient evidence
Physical function	3×/week for 30–60 minutes/ session at moderate to vigorous intensity	2–3×/week of 2 sets of 8–12 repetitions for major muscle groups at moderate to vigorous intensity	3×/week for 20–40 minutes/session of ≥ moderate aerobic exercise plus 2–3×/week of 2 sets of 8–12 repetitions of strength exercise for major muscle groups at ≥ moderate intensity

[1]Adapted from Campbell et al. [400].

Additionally, exercise might worsen some symptoms and side effects such as fatigue, diarrhea, and hand-foot syndrome. Therefore, exercise specialists must be careful in advancing exercise prescriptions, particularly during treatments with cumulative toxicities. Heeding these guidelines and precautions will aid exercise professionals in achieving precision exercise oncology and tailoring the proper exercise prescription to the right cancer patient at the right time.

4.1.3. Cognitive impairment and dementia

Both observational and experimental studies show PA and exercise can positively impact a broad range of cognitive functions [122,407–411] in older individuals with and without cognitive impairment [412]. Age-related cognitive dysfunction may be influenced by suboptimal PA participation across the life course lifespan. Reduced PA and sedentary behavior are precursors of cardiometabolic diseases and systemic inflammation that contribute to cognitive decline [413]. Evidence also suggests a link between sarcopenia and various neurocognitive disorders [414].

Cross-sectional and longitudinal studies consistently demonstrate that higher lifetime PA levels are associated with a lower likelihood of cognitive impairment and a reduced risk of dementia [415]. For instance, in a prospective cohort study, walking reduced the risk of dementia in a dose-dependent manner, with walking less than 0.25 miles per day compared to walking $>$ 2 miles per day, controlling for other risk factors [356]. Evidence further supports a dose-dependent inverse relationship between PA levels and the risk of mild cognitive impairment (MCI) and dementia [416].

Multidomain interventions that incorporate physical exercise have emerged as promising non-pharmacological strategies for dementia prevention [417,418]. These interventions integrate exercise with other lifestyle factors, including cognitive training, nutritional guidance (e.g., vitamin B, vitamin D, omega-3 supplementation), socioemotional support, and cardiovascular risk factor management [418]. By addressing multiple modifiable risk factors simultaneously, these programs have shown modest but meaningful benefits in mitigating cognitive decline among older adults at high risk for dementia [418–420]. For instance, the FINGER trial, a two-year multidomain lifestyle intervention involving 1,190 at-risk community-dwelling older adults, demonstrated significant improvements in global cognitive function, executive function, and processing speed compared to a control group receiving general health advice [410].

A meta-analysis evaluated the long-term effects of sustained physical exercise and multidomain interventions on global cognitive function and the incidence of MCI and dementia in community-dwelling older adults. The analysis revealed inconclusive results regarding the impact of long-term physical exercise as a single intervention on cognitive function, though a small benefit was suggested. In contrast, multidomain interventions that incorporate physical exercise showed a small but significant positive effect on global cognitive function, underscoring their potential as valuable tools in population-level dementia prevention strategies [418]. When all available studies were combined, a trend toward a protective effect of physical exercise on dementia risk was observed in random-effects models, reaching significance in fixed-effects models for low-heterogeneity trials. However, the role of exercise in preventing MCI remains uncertain.

Effects of exercise on cognition are partially mediated by structural and functional adaptations in the brain, including changes in gray matter volumes and white matter microstructural integrity [412]. Exercise attenuates cognitive decline, potentially through myokines and brain-muscle crosstalk. Potential mechanisms include increased cerebral blood flow, higher levels of neurotrophic factors such as BDNF, insulin-like growth factor-1 (IGF-1), reduced levels of neurotoxic factors [C-reactive protein, cortisol, and interleukin-6 (IL-6)], and modulation of other inflammatory cytokines. Additionally, exercise contributes to better control of chronic diseases such as stroke, diabetes, cardiovascular disease, and prevention of depression [421]. Progressive resistance training leads to beneficial long-term structural brain changes in older adults, as assessed by MRI and fMRI [422,423].

While aerobic and endurance training has traditionally recommended to improve cognition, research highlights the importance of resistance and mind-body exercises, such as Tai Chi [411,424–426]. Progressive resistance training has been linked to improvements in reasoning and executive functions. In the SMART study [427], six-month high-intensity PRT improved global and cognitive function in older adults with MCI compared with sham exercise (calisthenics), with more than 18 months of benefits, including increased thickness of the posterior cingulate cortex and functional connectivity [422], as well as long-term attenuation of hippocampal atrophy [423]. Changes in lower extremity strength mediated 64% of the benefit in executive function in the training group [122]. Tai Chi has shown benefits in attention and processing speed. Baduanjin (movement exercise) improved general memory and its subdomains (i.e., immediate and delayed memory), executive function, and processing speed [409,425,428].

Exercise also decelerates cognitive decline in patients with Alzheimer's disease, reducing the behavioral and psychological symptoms of dementia [429]. Although many studies of older adults with dementia have shown improvements in physical function, cognitive gains are less consistent [430]. Exercise programs that address falls, frailty, sarcopenia, depression, osteoporosis, and cardiometabolic diseases are recommended in aged care settings or in cohorts with established dementia.

4.1.4. Considerations regarding exercise for frail individuals with cognitive impairment

The cognitive frailty construct is characterized by both physical frailty and potentially reversible cognitive impairment in the absence of dementia [431]. Four months of low-intensity high-speed PRT (i.e., based on the use of elastic bands) improves cognitive function and physical performance [432] in older adults with MCI. Other exercises that benefit this group include multicomponent and dual-task exercises [86,419,433].

The potential beneficial benefits of exercise should not be overlooked, even in patients with advanced dementia receiving residential care. After long-term use of restraints in patients with coexisting frailty and dementia, multicomponent exercise training comprising high-speed PRT combined with walking and balance exercises improved gait ability, balance, and muscle strength and reduced the incidence of falls [76]. Tailored multicomponent exercise training with a particular emphasis on lower load (30–50% of 1RM) and high-speed PRT may be a cornerstone for enhancing both physical and cognitive functions [109]. Direct comparisons of various intensities of PRT for these outcomes are required to refine the prescription for this cohort.

4.1.5. Multicomponent training in dementia

Research studies in older adults with cognitive impairment have demonstrated the feasibility and efficacy of multicomponent exercise interventions that combine cognitive training, nutritional strategies, and social enrichment for older adults with cognitive impairment [433–436]. However, the effectiveness of these multicomponent interventions compared to single-exercise protocols remains uncertain [407,427,437]. It is crucial to ensure proper supervision during intervention, as there is no evidence that low-intensity, minimally progressive, multimodal exercise improves cognitive outcomes in patients with mild [438] to moderate dementia [439,440]. Additional recommendations include addressing dementia-related behavioral issues and communication challenges. Simplified instructions, constant reassurance, and mirror techniques can aid patients in making meaningful progress during training sessions. Creating a respectful, mindful, and empathetic training atmosphere for individuals with cognitive impairment can promote participation and adherence [84,109,243]. Examples of evidence-based guidelines for mindful caregiving combined with home-based, progressively intense resistance and balance training for the dementia dyad (caregiver and loved one with dementia) are available at (www.strongmindshomecare.org) [441].

4.1.6. Role of exercise in mental health

The risk of incident depression is estimated to be 21% lower in older adults who engage in PA, especially at moderate to vigorous intensities [442,443]. Indeed, a dose-response relationship has been observed, where an activity volume equivalent to 2.5 h of brisk walking per week is associated with a 25% lower risk of depression, and half that dose yields an 18% lower risk than no activity. Most benefits are achieved when moving from no activity to at least one activity [444]. Similar effects are observed in older adults with other mental health symptoms, such as anxiety [445]. PA is linked to positive psychological attributes and a reduced prevalence and incidence of depressive symptoms, which are most significant in those with comorbid illnesses such as CVD, pulmonary disease, and major depression [445–448].

Despite numerous trials documenting the benefits of physical exercise for older adults, the integration of PA and exercise programs into routine medical treatment remains ad hoc. Evidence of exercise as an isolated intervention for treating clinical depression across age groups is robust and consistent. Both aerobic and PRT exercises have produced clinically meaningful improvements in depression in such patients, with response rates ranging from 25 to 88% [449,450]. In studies addressing exercise modalities, aerobic, resistance, and mind-body exercises, including yoga, are equivalent in mitigating the symptoms of depression in older adults. In addition, PRT was comparable to aerobic training in young adults with depression, and yoga was as effective as aerobic exercise [451]. Blumenthal et al. [448] compared high-intensity aerobic exercise with antidepressant medications in older adults with major depression and found that the two approaches were equipotent with no added benefit from combining exercise and medication [448] and reduced remission rate in the aerobic exercise only group. Singh et al. [447] compared high-intensity PRT versus low-intensity PRT in those individuals with significant depression and found that a clinical response (50% reduction in Hamilton Rating Scale for depression) was achieved in 61% with high-intensity training, 29% with low-intensity training, and 21% as compared with a control group receiving usual general practitioner care who responded similarly to placebo [447].

Low-intensity aerobic training in older adults with depression is similar in efficacy to social contact controls, reducing depression scores by only 30%, equivalent to a placebo effect [449]. Considering the exercise dose, a single exposure to exercise can ameliorate the mood of individuals who are depressed. When a person experiences heightened symptoms, exercise can be a therapeutic strategy for short-term symptom relief [452]. Thus, the literature on exercise and depression suggests that it is effective in younger and older adults and is as effective as antidepressants in clinical cohorts. Aerobic and resistance modalities appear equally beneficial, and optimal responses are observed with higher training intensities. Future trials should determine whether the exercise program duration influences the severity or duration of depressive symptom improvement following physical exercise in individuals with depression.

Evidence supports the anxiety-reducing effects of physical exercise in older adults and those with multiple comorbidities. Previous trials have primarily focused on the efficacy of moderate-intensity exercise for anxiety, particularly continuous aerobic training (i.e., walking and cycling). Progressive resistance training has also been shown to reduce anxiety symptoms in older adults. For example, Tsutsumi et al. [453] found that high and moderate-intensity PRT induced potential benefits in anxiety state after 12-week training period in previously sedentary older adults compared to a non-exercising control group. There is a critical need to examine dose-response relationships in older adults with anxiety and to provide more consistent findings regarding understudied exercise modes, such as multicomponent exercise training.

Non-adherence to exercise prescriptions, specifically non-compliance with the prescribed exercise dose, remains a significant challenge for older adults with anxiety. Health practitioners prescribing exercise should be prepared to identify risk factors for low adherence to exercise prescriptions, helping individuals take personal responsibility in exercise program implementation, monitoring compliance with exercise dosage, identifying modifiable barriers, and developing strategies to overcome the obstacles to promote self-efficacy and self-motivation during exercise interventions [454].

Overall, the literature on exercise and depression suggests that it is effective in both younger and older adults and is as effective as antidepressants in clinical cohorts, including those with major depression. Aerobic and resistance modalities appear equally beneficial, and with higher resistance training intensities, optimal responses are observed. The mechanism of the antidepressant effect of exercise is not precisely known, and is likely multi-factorial, with alterations in neurotransmitters, inflammatory cytokines, neuroendocrine pathways, dopamine processing, oxidative stress, neuroplasticity, reward processing, body image, self-efficacy, functional independence, and many other pathways likely operative [455] The dose-response characteristics, such as adequate doses for aerobic exercise [193] and appropriate intensity for PRT [447], indicate that its benefits stem from biological mechanisms rather than merely the effects of attention or socialization. This highlights exercise as a potent biological agent, where the specific parameters of training, including intensity and volume, play crucial roles in eliciting health benefits across various systems

Ultimately, the choice of exercise modality for depression often rests on consideration of the other co-morbidities present in the older adult, and those exercise requirements. For example, in contrast to the increased risk of falls and fractures and confusion often associated with antidepressant medications in older adults, PRT is not only at least as effective for the depressive symptoms, but it also reduces the risks of injurious falls. improves bone density and cognition in such individuals. Therefore, if frailty, sarcopenia, mobility impairment, osteoporosis or recurrent falls are present, in addition to depression, the evidence-based prescription for the depression would naturally focus on PRT rather than aerobic exercise.

4.2. Effects of exercise interventions on geriatric syndromes

Geriatric diseases and syndromes such as frailty, sarcopenia, and falls significantly affect the health and well-being of older adults. Recent studies have indicated that exercise interventions can be an effective non-pharmacological strategy for addressing complex, multifactorial conditions that cannot be framed in the conventional disease paradigm. Table 7 lists the major geriatric syndromes for which exercise may be beneficial as a preventive or therapeutic measure, along with the proposed mechanisms of exercise benefit and the types of exercise most relevant to achieving these outcomes.

4.2.1. Frailty

Frailty is a state of reduced physiological reserve that leaves individuals vulnerable to stress, leading to disability and increased mortality. Its multisystem and multidimensional aspects include the cognitive, social, and physical domains. Resistance training programs or multicomponent exercise interventions with robust PRT have enhanced muscle strength in older adults with frailty and sarcopenia [35,84,241,456–459]. Several intervention studies have shown that exercise as a single component or part of a multicomponent intervention can prevent/reverse frailty [460]. These studies included either PRT alone or combined aerobic training with resistance and balance training, and the intensity of exercise (both aerobic and resistance-based) was low to moderate.

Multicomponent exercise interventions are effective in improving most, if not all, components of frailty, such as poor balance, reduced

Table 7
Exercise and geriatric syndromes.

Geriatric syndromes	Considerations for the prescription	Recommended exercise modality
Frailty and Sarcopenia	• Resistance and power training: 2–3 sessions per week, combining slower and faster (power training) muscle actions at intensities of 40–80% of 1RM. • Functional exercises e.g., standing from a chair. • Balance and gait exercises progressing in complexity: line walking, tandem foot standing, standing on one leg, heel-toe walking.	• Resistance training • Balance exercises • Gait retraining • Multicomponent exercise
Falls	• Resistance training aimed to improve muscle strength and power. • Balance and gait exercises progressing in complexity: line walking, tandem foot standing, standing on one leg, heel-toe walking. • Dual task exercises including dual task gait and resistance exercises (counting numbers, naming animals, etc.). • Adapted Tai Chi exercises progressing in complexity. • Dance interventions may improve adherence.	• Resistance training • Balance exercises • Gait retraining • (uncertain evidence) • Multicomponent exercise • Dance interventions (uncertain evidence) • Tai Chi exercises
Cognitive impairment	• High intensity resistance training combined to power training aimed to improve functional abilities. • Walking may reduce the risk of dementia. • Dual task exercises may be beneficial to cognitive function. • Use of mirror techniques rather than complex oral instructions. Use of haptic support. • Considerations of emotional aspects such as reassurance, respect and empathy.	• Walking • Aerobic exercise • Resistance training • Multicomponent training
Mobility limitations	• Resistance training aimed to improve muscle strength and power. • Functional exercises e.g., standing from a chair. • Balance and gait exercises progressing in complexity: line walking, tandem foot standing, standing on one leg, heel-toe walking. • Aerobic training using a seated recumbent cycle ergometer.	• Aerobic exercise • Resistance training • Balance exercises • Gait retraining • Multicomponent exercise

muscle strength, poor gait ability, and increased incidence of falls. Therefore, such interventions are recommended for this condition. These interventions, including PRT, gait retraining, and balance exercises, can be prescribed to prevent the onset of frailty in older adults and those with pre-frailty or to manage them once they have been developed [84,88,461,462]. The VIVIFRAIL Project, an EU-funded part of the Erasmus + program, recently focused on providing training and educational materials to promote and prescribe physical exercise in older adults [246,247,463] (www.vivifrail.com).

Additionally, owing to the strong associations between functional capacity test performance, muscle power output, and rate of force development in healthy older adults [199,202,397,464], explosive resistance training (power training) has become an essential intervention to improve functional capacity in older adults, including those who are frail [85,88]. In a 12-week multicomponent exercise intervention involving institutionalized frail nonagenarians, explosive resistance training improved the muscle cross-sectional area, muscle fat infiltration, maximal strength and power, balance, gait, and sit-to-stand ability, and reduced fall incidence [84,109]. Therefore, explosive resistance training should be considered in exercise interventions to improve frailty and reduce functional capacity in older adults.

Programs consisting of home-based exercises, weight-bearing exercises, or very low workloads are less effective in achieving strength gains [130,465,466]. The use of scales of perceived exertion instead of strength testing to guide the progression of loads during PRT in older adults with frailty is another factor that may result in insufficient muscle overload and, consequently, reduce the magnitude of physical adaptations [461].

4.2.2. Sarcopenia

Sarcopenia is a condition characterized by a progressive loss of muscle mass, strength, and function, which often leads to physical frailty [58,59,467]. When accompanied by frailty, has been linked to several negative outcomes, such as falls, disability, cognitive decline, and mortality [58,102,468]. However, it is important to note that some of these outcomes may be attributed to the coexistence of frailty [469].

International Clinical Practice Guidelines for Sarcopenia recommend PRT as the primary treatment for managing sarcopenia [58,59,102]. As mentioned in previous sections, existing evidence-based medicine has shown that PRT can positively impact strength, power, gait speed, functional capacity, and the skeletal muscle index in older adults with sarcopenia, regardless of whether they are living in the community, hospitalized, or institutionalized [58,112,146,203,367,458,470–472], while no drug has yet translated clinically relevant improvements on physical performance [473]. Additionally, PRT can prevent and ameliorate sarcopenia in patients with T2D [393–395], sarcopenic obesity [474] and cancer [401,402]. When combined with whey protein supplementation, PRT (when the diet is inadequate in energy and protein provision) has been shown to result in greater increases in muscle mass compared to PRT alone, with a more significant effect observed in low-functioning older adults [368,369]. Detailed PRT and muscle power training recommendations to enhance muscle mass and performance have been provided in previous sections.

4.2.3. Falls

As noted by Cameron et al. [475], "Exercise is the key intervention to prevent falls and fall injuries", as detailed in the *World guidelines for falls prevention and management for older adults: a global initiative* [476] - a comprehensive document that provides extensive recommendations with additional background materials available on an accompanying website. Much effort in the past has gone into complex algorithms to identify and classify risk, with far less effort spent developing ways to deliver what is already known to be the most effective preventive strategy: robust, challenging balance and strength training. Multicomponent exercise programs that combine PRT, balance plus functional exercises such as transferring from a chair and using steps [84,123,130,131], programs involving balance and functional exercises [123], or an alternative exercise intervention such as Tai Chi [127–129] have been shown to reduce falls compared with control in older adults by 20−40%. The effects of programs primarily involving resistance exercise (without balance and functional exercises) [123,149], dance programs [477–480] or gait retraining [84,130,131] remain uncertain [110,123,126]. The efficacy of programs is reduced when walking is included in falls prevention programs [110], and walking by itself has been shown to *increase* the risk of fractures in osteoporotic women compared to controls [311]. This stands in contrast to the significant 25% reduction in fractures achieved with other exercise modalities [481].

The US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the effectiveness and harms of primary care-relevant interventions to prevent falls and fall-related morbidity and mortality in community-dwelling adults 65 years or older [482]. The authors concluded with moderate certainty that exercise interventions provide a moderate net benefit in preventing falls and fall-related morbidity in older adults at an increased risk of falls. In addition, they concluded with moderate certainty that multifactorial interventions provide a small net benefit in preventing falls and fall-related morbidity in older adults at increased risk of falls [482]. Programs incorporating a higher dose of exercise—categorized at three hours per week—and targeting balance or function have demonstrated a significant 42% reduction in the rate of falls [123]. This underscores the critical importance of both the type and dose of exercise [482]. Unfortunately, many community-based falls prevention programs fail to utilise these principles.

In addition to exercise-related deficits in strength and balance and motor coordination, there are many other factors which may increase fall risk, including obesity, degenerative neurological conditions, osteoarthritis, peripheral neuropathy, visual impairment, use of multifocal lenses, vertigo, orthostatic hypotension, cognitive impairment, fear of falling/low self-efficacy for other tasks, malnutrition, and polypharmacy, as well as environmental hazards and inappropriate/insufficient assistive devices. Therefore, in addition to appropriate evidence-based exercise, assessment and targeting of these additional risk factors, if present, seems logical. However, even when such multifactorial interventions are designed, their effectiveness will depend on the robustness of the interventions delivered as well as the fidelity and adherence achieved. For example, the largest multifactorial falls prevention program ever published, the STRIDE Trial [483] did not reduce fall rates at all compared to usual care in 5451 adults of mean age 80, followed up to 44 months. A close look at the STRIDE exercises recommended to be delivered in various community settings (at which attendance was not even monitored) included only very low-level body weight "strengthening" such as a quarter squat with diminishing hand support. Compared to the high-challenge balance and strength training protocols shown to be effective in other clinical trials [123], it is not surprising that this strategy was ineffective. Similarly the DO-HEALTH study [312] of low intensity exercises, which had no benefit for bone health or other clinical outcomes, was also ineffective for falls prevention.

The clear gap is how to deliver evidence-based exercise programs that are successful in supervised clinical trial settings in a broader community context with no exercise professionals to guide the implementation. This is potentially possible for challenging balance interventions delivered remotely with digital technology including web-, App-, or tablet-based protocols, such as the Standing Tall RCT [484]. In this study of 503 older adults, implementing a remotely-delivered balance training protocol via a tablet, the intervention group did not reduce falls at 12 months (the primary outcome) but showed a significant 16% lower rate of falls and a 20% lower rate of injurious falls over 24 months compared with the control group (incidence rate ratio 0.80, P = 0.031). This is about one-half of the risk reduction achievable with programs such as the Otago Exercise Program of strength and balance training [485], and almost one-half of participants were not using the remote balance program at 24 months. Therefore, the challenge is no longer to define the effective exercise modalities for falls prevention, but rather to develop strategies to achieve and sustain long-term adherence to evidence-based interventions, as falls prevention exercise must be continued life-long in high-risk individuals.

4.3. Exercise in nursing home residents

Nursing home residents are typically frail and multimorbid and often suffer from dementia and several disabilities, making their physical exercise needs and risks complex. They frequently experience mobility impairment [486], thereby emphasizing the significant potential benefits of exercise on their well-being. While individual attitudes and needs vary, exploring residents' motivation and preferences is crucial when promoting PA [486].

Frailty and advanced dementia are prevalent among the majority of nursing home residents, underscoring the precise indications for PA [487]. However, a systematic review reveals that only 60%–67% of these residents receive physiotherapy services [488]. Chair-based exercises are commonly utilized to mitigate adverse events, with a systematic review noting task-specific improvements in physical and cognitive outcomes and enhanced well-being [489] may accrue.

Physical exercise has been rigorously tested in numerous RCTs. A systematic review of 10 RCTs focusing on residents with dementia in long-term care facilities found that nine trials reported improvements or a slower decline in mobility, functional limitations, or physical functioning, although many trials were of poor quality [490]. A more recent systematic review and meta-analysis of randomized controlled trials (including 105 studies, n = 7759 participants) demonstrated that exercise interventions significantly improve overall physical function in older adults living in care facilities. These improvements were observed regardless of the individuals' baseline functional or cognitive status. Key benefits included enhanced functional independence in activities of daily living (as reflected by higher Barthel Index scores) and notable gains in muscle strength, physical performance, balance, and flexibility. Notably, the most consistent improvements were achieved with approximately three hours of exercise per week, with no significant differences observed across various types of exercise [491]. A high-quality French trial involved twice-weekly, one-hour exercise sessions over a year and demonstrated a slower decline in Activities of Daily Living (ADL) in the intervention group compared to the control group [492]. Another recent systematic review identified 30 trials that investigated either multicomponent training (19 studies) or PRT (12 studies) among nursing home residents [493], of which17 were included in a meta-analysis. The studies provided evidence that both multicomponent exercise and PRT could effectively enhance the physical performance of institutionalized older adults, as measured by the Short Physical Performance Battery, 30-second Chair-Stand, Timed Up and Go tests, and gait ability [84,109,493], and potentially ameliorate frailty and reduce falls [84,109,240].

The OEP described earlier has been implemented in nine nursing home studies, indicating that it effectively supports residents' postural control, lower limb muscle strength, and short-distance functional mobility [485]. A meta-analysis incorporating 14 trials suggested that exercise, particularly balance training, plays a crucial role in falls reduction in the nursing home [494]. The VIVIFRAIL multicomponent program has shown potential as an effective intervention for maintaining and ameliorate physical frailty in vulnerable institutionalized older adults [243,251]. However, not all trials have observed the effects of exercise on fall prevention [495].

Nutritional supplements combined with PA have also been examined. The VIVE2 trial demonstrated that six months of exercise alone improved gait speed, while adding whey protein and vitamin D supplements did not yield further enhancements [496] although they did improve muscle density [497]. Similarly, two other trials found that dietary supplements did not provide additional benefits when combined with PA [498,499].

Research also indicates that PA benefits cognitive functions, mental health [109], and overall well-being [488], supporting its broad utility in improving the quality of life for nursing home residents. The major barrier to the implementation of robust exercise in this setting, as shown since 1990 [35], is the lack of financial reimbursement, trained professionals and the necessary equipment to conduct these programs with fidelity. The recently-completed FRIEND study (Frailty Reduction via the Implementation of Exercise, Nutrition and Deprescribing) [500] was designed to implement the Asia-Pacific Frailty Management Guidelines [501] in residential aged care for the first time. These guidelines recommend anabolic exercise along with the optimization of medications and nutrition. This required setting up an exercise gym with PRT equipment, hiring an Accredited Exercise Physiologist to deliver the PRT and balance training, creating a café and new menus, as well as training staff in polypharmacy, nutritional assessment and support, and anabolic exercise. Improvements in function, fall rate, drug burden, and body weight were demonstrated, indicating the vast potential for improved outcomes in this vulnerable cohort with such an approach.

4.4. Role of exercise in the prevention and treatment of disability

Physical activity is known to influence the development of disabilities in old age [502]. Studies from the Established Populations for Epidemiological Studies of the Elderly (EPESE) were more likely to survive to age 80 or above and have about half the risk of dying with disability than their sedentary counterparts [503]. Additionally, data from the Longitudinal Study of Aging showed that PA was associated with slower progression of functional limitations and, thereby, slower progression to ADL/instrumental activity of daily living (IADL) disability [504]. There was a significant overlap between the risk factors for disability and correlates of chronic inactivity, including advanced age, female sex, non-Caucasian ethnicity, and lower educational level, and income. The standard psychosocial features in EPESE and Longitudinal Study of Aging cohorts included social isolation, low self-esteem, low self-efficacy, depressive symptoms, and anxiety. Lifestyle factors prevalent among disabled and inactive adults include smoking and excessive alcohol consumption. Body composition changes associated with functional decline and inactivity include sarcopenia, obesity, visceral obesity, and bone loss, which contribute to gait instability, slowness, impaired lower-extremity function, and mobility. Exercise capacity, including aerobic capacity, muscle strength, endurance, power, flexibility, and balance, is reduced under these conditions. As most studies did not assess the whole range of factors known to be associated with disability, and many were cross-sectional observations, it is not possible to establish how all these complex relationships fit together, which relationships are causal, and which risk factors are independent of each other.

Chronic diseases linked to inactivity, such as obesity, osteoarthritis, cardiovascular disease, stroke, osteoporosis, T2D, hypertension, and depression are risk factors for disability. In some cases, data linking inactivity to disability-related diseases are available from cross-sectional prospective cohort studies, experimental trials, and epidemiological data [505]. Disability is complex and not fully explained by deficits in physical capacity such as strength and balance. Other mechanistic pathways, including sensory function, glycemic control, psychological constructs, and other aspects of health-related, also play a role.

Exercise has been shown to alter the trajectory of disability in older adults with frailty, as evidenced by one of the most extensively reported RCTs of exercise and disability in older adults with frailty, where 704 residents of nine different nursing homes were randomized into resistance, balance, and aerobic exercise, nursing rehabilitation, or a control condition. After 17 months, residents in both types of intervention homes had significantly less decline in ADL functioning than those in control homes [506]. The Lifestyle Interventions and Independence for Elders (LIFE) multicenter randomized clinical trial in 1635 older persons at risk of disability showed a significant reduction in the risk of major mobility disability after an average of 2.6 years of follow-up in those randomized to PA compared to a health education program [507]. Similar findings were reported by the Sarcopenia and Physical Frailty in Older People: Multicomponent Treatment Strategies (SPRINTT) randomized trial that enrolled 1519 older adults with frailty and sarcopenia in 11 European countries [458]. This risk reduction was most evident in study participants with the greatest degree of mobility limitations at baseline (Short Physical Performance Battery Score < or equal to 7).

A review of studies targeting disability in disease-specific populations, such as patients with depression, cardiovascular disease, stroke, chronic lung disease, or osteoarthritis, is beyond the scope of this review. However, there is evidence that exercise is beneficial as a primary or adjunctive treatment in all these conditions. The largest body of data exists for older adults with osteoarthritis of the knee, which is one of the most common conditions leading to disability in advanced age [508]. These studies have used various weight-bearing functional exercises, walking, and PRT combinations. There is no clear indication of the superiority of any modality over another in reducing pain or disability due to osteoarthritis. Notably, land-based exercise is superior to stretching and aquatic exercise despite the common perception that these less robust exercises are more productive or feasible in this patient population. The reduction in disability observed in patients with osteoarthritis is likely due to the impact of exercise on various factors, including muscle strength, gait and balance, body weight, pain, comorbid disease expression, self-efficacy, and depressive symptoms. There is no simple link between improvements in function, pain, and fitness adaptations [508]. WHO also recognizes the global burden of disease associated with low back pain and other musculoskeletal conditions [509], the need for rehabilitation services [510], and the need to respond with global guidelines to improve outcomes on health and well-being and health system performance, especially in primary and community care settings [511].

4.5. Exercise to counteract iatrogenic disease

Exercises to mitigate the adverse effects of standard medical care are gaining increasing attention. Examples include PRT for patients receiving corticosteroid treatment to counteract the associated proximal myopathy and osteopenia not fully addressed by bisphosphonates or to neutralize the adverse effects of energy-restricted diets in obesity or protein-restricted diets in chronic renal failure [512].

An excellent target group in which both resistance and aerobic exercises can offer significant benefits would be older men with steroid-dependent chronic lung disease, in whom the harmful combination of pulmonary cachexia, malnutrition, tobacco use, steroid myopathy, and osteoporosis produces profound wasting, osteoporotic fractures, and impaired exercise tolerance. Aerobic training improves functional status in this clinical cohort but is insufficient to address musculoskeletal wasting [513].

4.6. Exercise for acutely hospitalized older patients

Older adults are especially susceptible to hospitalization hazards, such as immobility, delirium, and functional decline, which are often linked to an increased likelihood of prolonged hospital stay, institutionalization, and mortality. Even after resolving acute medical illnesses or complications necessitating admission, hospitalization can pose risks to older patients [514]. Exercise and in-hospital early rehabilitation protocols are vital for preventing functional decline in hospitalized older adults [474,515–519].

Healthcare systems often need help to meet the needs of older adults adequately. Reduced PA levels in hospitals are directly linked to functional decline at discharge and post-discharge [520]. Exercise is essential in preventing functional and cognitive decline associated with hospitalization in older adults. The advantages of exercise have been clinically, biologically, and economically confirmed [203,521], establishing it as a vital component of the therapeutic arsenal. Numerous recent RCTs have explored the benefits of exercise on multiple health-related outcomes. These include functional capacity, cognition, mood, and muscle function (i.e., muscle strength and power), all of which commonly deteriorate during hospital stays, especially among the oldest old [203,518,521,522]. Martínez-Velilla et al. [203] and Saez de Asteasu et al. [522] showed that individualized multicomponent exercise training programs can significantly enhance the functional capacity and cognition in older patients with frailty during acute hospitalization compared to usual care. The latter group received "usual" hospital care, which included physical rehabilitation when needed. The intervention group participated in exercise training scheduled for twice-daily sessions, morning and evening, each lasting 20 min over five to seven consecutive days, including weekends, all under the supervision of a qualified fitness specialist. Sessions occurred in a specially equipped room in an acute care for the elderly (ACE) unit. The exercises were adapted from the VIVIFRAIL multicomponent physical exercise program to prevent weakness and falls (www.vivifrail.com) [246,247]. Resistance exercises were tailored to the functional capacity of each participant. This involved using variable PRT machines for 2–3 sets of 8–10 repetitions with a load equivalent to 30–60% of the 1-RM. The program focused on three exercises primarily involving the lower-limb muscles (squats rising from a chair, leg press, and bilateral knee extension) and one for the upper-body musculature. Similar results were obtained in a multicenter trial after three to five days of in-hospital multicomponent exercise intervention [523]. This finding contrasts with an earlier RCT that did not report significant benefits of a single in-hospital mobility program and behavioral strategy designed to promote mobility in older patients, particularly in their ability to perform ADLs following acute hospitalization [524]. These observations indicate that multifaceted interventions extending beyond simple walking exercises are required to preserve or enhance the functional capacity of older patients during acute hospitalization. This necessity arises from the tendency of muscle mass to decline rapidly in hospitalized older adults, with consequent losses in muscle strength and mass linked to increased rates of disability, morbidity, and mortality [525]. Similarly, basal functional status can predict the ameliorated response rate among frail and pre-frail older persons [526,527]. Specifically, individuals with lower baseline functional status are more likely to exhibit a diminished response to exercise interventions, as they have less functional reserve to draw from during rehabilitation or training efforts, which may limit the potential for improvement

An individualized multicomponent physical exercise intervention incorporating moderate-intensity PRT represents an effective therapeutic measure to counteract muscle strength/power and mass losses frequently observed during hospitalization [203,522,526]. Upon discharge, it is advisable to escalate to moderate to high-intensity PRT to attain the benefits documented in numerous RCTs [17,140,309,447,528,529]. This recommendation is based on the well-established dose-response relationship between exercise intensity and anabolic body adaptations to exercise. Kitzman et al. [518] found that in a diverse group of older patients hospitalized for acute decompensated heart failure, an early, transitional, and tailored progressive rehabilitation intervention encompassing multiple physical function domains led to a greater improvement in physical function than usual care.

Beyond functional enhancements, recent meta-analyses have underscored the significance of in-hospital physical exercise in improving cognitive function in acutely hospitalized older patients [530]. Notably, amelioration of physical function following an in-hospital exercise program seems to be mediated by cognitive improvement [515]. Exercise benefits physical function and cognition concurrently, suggesting overlapping physiological pathways. However, the mechanisms underlying these improvements remain unclear. Acute hospitalization often triggers an inflammatory response in the older population, resulting in a catabolic effect on skeletal muscle metabolism. Additionally, persistent low-grade inflammation inherent to aging exacerbates the vulnerability of older adults to the adverse effects of hospitalization, as evidenced by alterations in body composition and declining physical function [531]. Resistance and multicomponent in-hospital exercise may exert an anti-inflammatory effect, potentially accounting for observed enhancements in functional capacity, cognition, and other health-related outcomes [532]. Moreover, neural adaptations may serve as initial positive responses to exercise, contributing to improvements in muscle function, such as strength and power output [472], during hospitalization. This early stage of neuro-adaptation, often beginning shortly after the commencement of training, could lead to improved functional capacity at discharge and during the post-discharge follow-up. Nevertheless, only a few trials have investigated neuromuscular changes following individualized exercise programs. Additional research is needed to ascertain whether structured exercise induces changes in muscle mass, as evaluated by alterations in muscle structure and architecture, in acutely hospitalized older patients.

Given the propensity of acutely ill hospitalized patients to be confined to bed rest, exercise and PRT are of heightened importance for mitigating deconditioning. Such activities should be conducted daily, as tolerated by the patient's medical condition, until hospital discharge. Training sessions may be divided into two shorter periods (morning and afternoon) [246,247] to improve patient tolerability. Additionally, it is imperative to carefully monitor vital signs before and after exercise sessions to prevent adverse events.

Despite its numerous advantages, exercise is only rarely incorporated into geriatric acute care protocols. It is crucial to begin integrating exercise as a standard element of care for acutely hospitalized older adults, irrespective of their level of frailty [9]. Similar to other treatments, such as nutritional support, behavioral counseling, and pharmaceutical co-treatments, in-hospital physical exercise must match unique characteristics to ensure proper adoption, adherence, and treatment adaptation, optimizing health-related clinical outcomes.

When considering the optimal exercise prescription for acutely hospitalized older patients, it is important to recognize individual responsiveness. Physiological responses and adaptations to in-hospital physical exercise exhibit interindividual variability, and the extent of responsive also varies depending on the specific clinical outcome assessed [526]. Notably, adverse responses to physical exercise or usual care during hospitalization, in terms of functional capacity in older medical patients, are linked to increased mortality one year post-discharge [526].

A recent dose-response meta-analysis reported effective ranges of PA doses for improving functional capacity and reducing adverse events in acutely hospitalized older patients [533]. These findings suggest that brief daily sessions of multicomponent exercise interventions, for instance, approximately 15 min per day of resistance band exercises and about 10 min per day of aerobic training, can yield functional improvements. It was also highlighted that extended sessions of multicomponent training, such as approximately 20 min/day of resistance band exercises and approximately 20 min/day of aerobic activities, could offer additional benefits [533]. Nonetheless, the optimal exercise dosages may differ according to the specific clinical outcomes being measured. More recently, researchers identified a dose-response relationship between the duration of the exercise program and change in physical and cognitive functions, with four consecutive days of exercise being the optimal dosage for enhancing functional capacity in hospitalized older patients [534].These data and other new findings regarding exercise dosage should be considered in developing clinical guidelines for periods of acute hospitalization.

Incorporating patient education and self-management strategies into in-hospital exercise programs is vital for creating a sustainable approach to maintaining physical and cognitive gains after discharge. This integration could bridge the gap between hospital-based programs and long-term community-based support, encouraging continuous participation in health-promoting behaviors. In addition, the establishment of habitual PA and the integration of lifestyle interventions are essential for the maintenance of health benefits post-discharge. Comprehensive follow-up programs and access to community resources are required to ensure long-term benefits. This continuity is crucial for extending the lifespan and quality of health enhancements initiated during the hospital stay [534]. For example, the VIVIFRAIL Clinical Guide for exercise prescription could help promote an active lifestyle after discharge in older adults (www.vivifrail.com) [246,247].

4.6.1. Managing delirium among acutely hospitalized older adults

When specific clinical conditions permit, exercise should be prescribed to acutely hospitalized older adults. Before initiating an exercise program in Acute Care of the Older (ACE) units, it is essential to ensure that the patient's hemodynamic state is stable and that there are no relative or absolute contraindications related to exercise such as unstable ischemia, arrhythmias, or sepsis [17,279]. Moreover, cooperation and willingness to engage with healthcare professionals are essential for successfully prescribing exercises.

A recent systematic review with meta-analysis explored the feasibility and effectiveness of in-hospital exercise in managing delirium in acutely hospitalized older patients, although the results remained inconclusive [530]. Delirium, a significant neuropsychiatric condition characterized by acute and fluctuating disturbances in attention, perception, awareness, and cognition, is associated with higher risks of functional decline, cognitive impairment, prolonged hospital stay, institutionalization, and mortality [535,536]. An in-hospital RCT recently indicated that individualized multicomponent exercise intervention is a safe and effective method for improving physical function in older patients hospitalized with delirium [536]. However, functional improvements were noted using a subjective self-reported functional scale, with no parallel trends observed in objective outcomes such as the SPPB test or HGS. Moreover, the critical health status of participants contributed to a high dropout rate. Therefore, further research is needed to assess the feasibility and impact of in-hospital physical exercise on delirium. Future studies should explore alternative exercise approaches and determine the most appropriate time for introducing such interventions during the fluctuating course of delirium.

5. Integrative pharmacotherapy and exercise in geriatric care: strategies for optimizing physical function in older adults

In an aging population, polypharmacy and chronic disease management are critical concerns that significantly impact health outcomes. The intersection of medication use and PA/exercise offers a promising approach to enhancing the well-being of older adults. An integrated strategy that combines exercise prescriptions with pharmacotherapy can optimize the vitality and functionality of older people while minimizing adverse drug reactions [537]. This approach addresses the physical and cognitive decline associated with aging and mitigates the risks posed by multiple medications. The following section explores the benefits of incorporating exercise into the care, interactions between drugs and exercise, and specific management strategies to ensure safe and effective treatment plans.

5.1. Polypharmacy concerns and exercise benefits

Strategies to manage polypharmacy and potentially inappropriate medications (PIMs) in older adults often overlook the role of exercise prescription [538,539]. Current exercise prescription guidelines seldom consider the potential consequences of concurrent medication use, which constitutes significant oversight [17,137]. A holistic drug review should consider how medications affect exercise engagement [8]. Certain drugs, such as psychotropic and anticholinergic medications, can impair exercise through their effects on cognition, sedation, orthostasis, and mobility [540–543]. These medications might reduce a patient's ability or willingness to engage in PA, thereby exacerbating the health decline. Furthermore, some pharmacological side effects may be more effectively managed with exercise interventions rather than adding further medications to the patient’s regimen, potentially initiating a harmful “prescription cascade” [544–547].

Exercise can serve as a better alternative for managing the side effects of medications, as PA often provides benefits beyond the targeted condition and shifts the risk-benefit in favor of exercise [8]. For example, constipation from calcium supplements, insomnia from selective serotonin reuptake inhibitors (SSRIs), and depression from beta-blockers can all be managed through tailored exercise [548–552]. Incorporating exercise into treatment plans may also reduce medication dosage [537]. Other common examples are: metformin can diminish the improvement in aerobic capacity, corticosteroids may lead to osteoporosis and muscle wasting, and chemotherapy agents can affect gait and balance through peripheral neuropathy [553–558]. Patients taking such medications may require more intensive or higher doses of exercise and enhanced strategies for behavioral changes or protein supplementation to achieve optimal health benefits. Drug-nutrient interactions, such as vitamin B12 deficiency from metformin or proton-pump inhibitors, can negatively affect gait, balance, peripheral neuropathy, and cognition. Addressing these deficiencies through appropriate supplementation and exercise, such as balance, PRT, and appropriate supplementation, can mitigate these risks [559–562].

Exercise should substitute for potentially hazardous drugs whenever possible, as it often offers broader benefits beyond the target condition, enhancing the risk-benefit ratio [537]. For instance, in patients with chronic pain such as those with osteoarthritis, exercise can reduce drug dosages [e.g., opioids, gabapentin, non-steroidal anti-infammatory drugs (NSAIDs)] and improve overall health [563–568]. This substitution is crucial because exercise addresses the primary condition and enhances physical resilience, reducing the likelihood of adverse drug reactions and additional health issues.

A holistic drug review should consider how medications affect exercise engagement. A comprehensive assessment should begin by documenting all current health conditions and risk factors for future diseases or geriatric syndromes in conjunction with a complete list of all medications and nutritional supplements/nutraceuticals being consumed [537]. This integration is essential for enhancing the vitality and functionality of older adults while reducing the likelihood of adverse drug reactions. Table 8 presents a comprehensive framework for integrated management of these elements. It outlines specific examples of drug-related challenges expected in the geriatric population and provides targeted management strategies (Fig. 5). This table is a pivotal reference for clinicians to harmonize medication regimens with individualized exercise protocols and dietary considerations, ensuring a holistic approach to enhancing older adults' overall well-being and functional independence [8].

5.2. Interactions between medications and exercise response

Clinicians should address exercise-drug interactions to improve the care of older patients. Some drugs can impair exercise engagement and adaptation, necessitating adjustments in exercise prescriptions, behavioral support, and monitoring. For example, psychotropics that cause sedation, fatigue, cognitive deficits, mobility impairment, depression, and anorexia may be replaced by aerobic or PRT [569–572]. If withdrawal is not feasible, specific exercises (balance, resistance, or aerobic training) should be prescribed to counteract the side effects.

Table 8
Integrated Management of Exercise, Pharmacotherapy, and Nutritional Interventions in Older Adults Care. Adapted from [8,537].

Interaction Category	Examples	Management Strategies
Adverse Drug Reactions	Gait disturbances, orthostatic hypotension, constipation, fatigue, depressive and [543] impairments, anorexia	Implement balance and resistance exercises for neuromotor control, aerobic activities for constipation, and targeted exercises to alleviate depressive symptoms and cognitive decline. Consider exercise as an alternative to certain medications.
Drug-Drug Interactions	Reduced blood pressure from multiple antihypertensives, bleeding risks from NSAIDs and anticoagulants	Prescribe appropriate aerobic or resistance exercises to manage blood pressure and cardiovascular health, and as non-pharmacological alternatives for pain management in musculoskeletal conditions.
Drug-Nutrient Interactions	B12 deficiency from metformin, decreased calcium and vitamin D absorption from corticosteroids	Offer balance exercises for neuropathy due to B12 deficiency and incorporate resistance and power training to promote bone health and counteract corticosteroid effects.
Drug-Disease Interactions	Hypoglycemia in diabetes, osteoporosis in androgen deprivation therapy	Adjust drug dosages in tandem with exercise, ensure safe timing of exercise post-meal, and provide resistance exercises for osteoporosis management.
Drug-Aging Interactions	Increased fall risk from polypharmacy, constipation from various medications, autonomic neuropathy exacerbation	Substitute exercises where possible for medications causing systemic effects, encourage aerobic exercises for gastrointestinal mobility, and incorporate balance training to mitigate fall risks.
Impaired Exercise Engagement	Sedation, fatigue, cognitive and mobility impairment from various medications	Substitute exercise where feasible, enhance balance and resistance training for improved mobility and strength, and encourage cognitive engagement through exercise. Exercise at most alert time of day.
Altered Exercise Prescription/ Monitoring	Beta-blockers affecting heart rate response and exercise tolerance, masking symptoms of angina	Utilize perceived exertion for intensity monitoring, stay vigilant for non-cardiac signs of cardiac distress, and ensure hydration and appropriate clothing for thermoregulation.
Impaired Exercise Adaptation	Metformin and corticosteroids affecting aerobic capacity and muscle-bone anabolism	Emphasize higher-intensity aerobic or interval training to maximize capacity gains and resistance training to support anabolic adaptations in musculoskeletal tissues.

The table provides a brief overview of the common interactions among exercise, medications, and nutrients affecting older adults, along with tailored management strategies. It categorizes interactions into adverse drug reactions, drug-drug, drug-nutrient, drug-disease, drug-aging, drugs impairing exercise engagement, drugs requiring alteration of exercise prescription/monitoring, and drugs impairing exercise adaptation. Specific examples such as gait and balance impairment, hypotension, and hypoglycemia are detailed for each category. The management column suggests practical interventions, including exercise timing relative to medication dosing, the type of exercise recommended (aerobic, resistance, or balance), and considerations for modifying exercise prescriptions in the presence of certain drugs. This information is crucial for healthcare providers to optimize older people's health and functional independence through personalized exercise plans that consider their unique pharmacological profiles. NSAIDs = non-steroidal anti-inflammatory drugs.

Fig. 5. Integrated Management of Exercise, Pharmacotherapy, and Nutritional Interventions in Older adults Care. Adapted from [537].

Certain medications, such as psychotropics and anticholinergics, can interference with exercise participation and physiological adaptation, necessitating adjustments to exercise prescriptions, behavioral interventions, and careful monitoring to ensure treatment efficacy [540–542]. When medications cannot be discontinued despite their effects on mobility, sedation [543], impairment, or weight loss, specific exercise modalities are recommended to counteract these effects (balance, resistance, or aerobic training) [573–575]. For patients taking beta-blockers, exercise intensity should be monitored through perceived exertion rather than by the heart rate, and hydration is crucial because of potential heat intolerance and orthostasis [570]. High-intensity training may be required for those on metformin to optimize aerobic capacity gains [576–578]. Progressive resistance training should be performed at the highest feasible intensity for chronic glucocorticoid users or during androgen deprivation therapy, with power training added to promote muscle and bone adaptations [579,580]. These tailored approaches help ensure that the benefits of exercise are maximized despite medication-induced limitations.

Many medications, such as benzodiazepines, opioids, and anticholinergics, can cause side effects at the central nervous system, including sedation and cognitive impairment, which may exacerbate sarcopenia and compromise coordination and dual-task performance. These cognitive deficits can lead to diminished physical capabilities, impaired balance, and an increased risk of falls, potentially deterring patients from participating in progressive balance exercises [581–584]. Other common adverse drug interaction-related adverse events include neuropsychological symptoms (delirium), acute renal failure, and hypotension [585]. Healthcare practitioners can implement strategies to address these complications. For example, scheduling therapy sessions when medication effects are minimized can enhance cognitive responsiveness [586,587].

Medications such as statins may provoke symptoms such as muscle pain or weakness, which can be confused with normal post-exercise soreness, especially in individuals not accustomed to PRT [588–590]. It is essential to carefully monitor symptom onset relative to medication initiation to distinguish between pharmacological myopathy and exercise-induced discomfort, particularly in patients with diabetes who require close metabolic monitoring during PA.

A practical framework for modifying exercise regimens in the context of optimizing health outcomes for older populations, taking into consideration common medication classes is presented in Fig. 6. It offers modifications that can accommodate sedation, the risk of falls, muscle function, and cardiovascular response, which may be affected by various medications (Fig. 6). By making these modifications, physical engagement and physiological adaptations can be maintained, enhancing the therapeutic benefits of exercise while considering the pharmacological factors that may influence these outcomes [537].

5.3. Customized exercise prescriptions amidst pharmacotherapy

Customized exercise prescriptions should be designed to address specific drug interactions and enhance overall health. Balance and resistance exercises can compensate for orthostatic hypotension, peripheral neuropathy, and gait and balance impairments. Aerobic exercise can alleviate constipation, whereas aerobic and resistance exercises benefit depression, fatigue, and cognitive impairment. Where feasible, aerobic or resistance exercise should substitute for psychotropics or analgesics [8] [537].

Aerobic or resistance exercises can help manage blood pressure and cardiovascular health for patients taking multiple antihypertensives, beta-blockers, and nitrates. For individuals with diabetes, it is critical to adjust for insulin and other glycemic agents in conjunction with PA [591]. Proper exercise timing after meals is crucial for maintaining glycemic balance, enhancing glucose utilization, and preventing hyperglycemia or post-activity hypoglycemia. Exercise can also reduce the need for NSAIDs in the treatment of osteoarthritis and chronic pain syndrome. Addressing drug-nutrient interactions, such as vitamin B12 deficiency from metformin or proton-pump inhibitors and reduced calcium and vitamin D absorption from corticosteroids through balance and power training, can mitigate these adverse effects [559–562].

Importantly, exercise can substitute for medications that impair cognitive function and mobility. Psychotropic medications (antipsychotics, anxiolytics, insomniacs, antidepressants), which can cause confusion, sedation and fatigue, may be replaced with aerobic or PRT, significantly enhancing a patient's physical and cognitive health. Similarly, for patients who cannot to cease medications that impair mobility or mental function, exercises such as balance, resistance, or aerobic training should be prescribed to offset these side effects [540–543].

5.4. Nutritional considerations in exercise and drug regimens

Nutritional considerations are also crucial for managing drug-exercise interactions, yet this three-way framework is not commonly appreciated. For example, to prevent falls and cognitive decline, potential vitamin B12 deficiency due to medications should be screened for in those with peripheral neuropathy taking metformin or proton-pump inhibitors (PPIs), addressed with balance training and supplementation if needed [559–562], and consideration given to alternatives to PPIs. Resistance and power training should be used to counteract anabolic deficits in bones and muscles due to protein-calorie undernutrition and/or catabolic drugs [537]. Drug-induced hypoglycemia in diabetes should be managed by adjusting exercise timing and intensity, adjusting dosages of insulin on exercise days when needed to ensure safe glucose levels, and using snacks

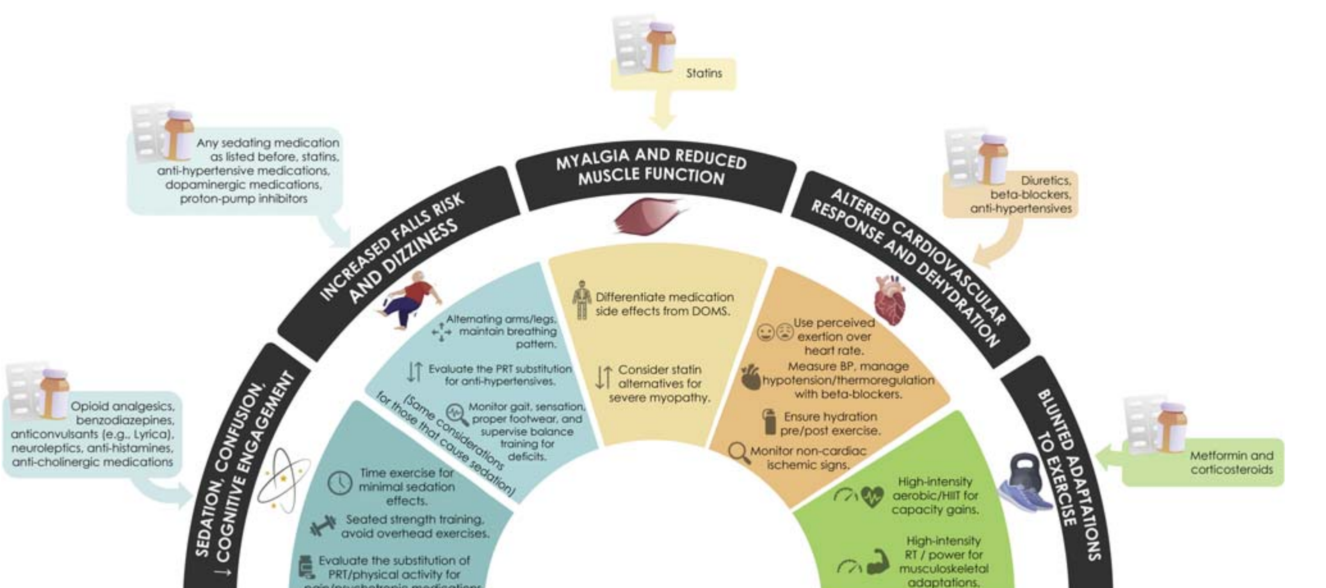

Fig. 6. Strategies for Modifying Exercise Regimens in Response to Medication-Related Impacts on Patient Engagement and Physiological Adaptations. Adapted from [537].

and available monitoring tools [553–558]. Exercising about one hour after a meal is ideal for management of post-prandial hyperglycemia with no risk of hypoglycemia. Resistance exercise is essential for preventing and treating chronic conditions such as osteoporosis in COPD or rheumatic diseases, and where catabolic drugs are often used, complicating the anorexia, cachexia and inflammation of the diseases themselves, protein supplementation may be needed as well [592,593]. Balance training, aerobic exercise, and increased hydration and fiber intake can help manage side effects of anticholinergic and other drugs causing constipation. Incorporating nutritional support may further improve the benefits of exercise in malnourished individuals, those with catabolic or inflammatory diseases or those taking medications adversely affecting muscle mass/function, such as androgen deprivation therapy. Ensuring adequate protein intake, vitamin D supplementation when needed, adequate calcium intake, high-intensity resistance and power training can help mitigate catabolic effects on muscle and bone [579,580]. The complexity of age-related nutritional needs, multiple co-morbidities, polypharmacy, and exercise specificity require this holistic oversight, as summarized in Table 8 and Figs 5, 6 and 7.

5.5. Prioritizing exercise in treatment plans

Exercise as a central component of treatment plans addresses primary health concerns and enhances overall resilience and well-being. For example, aerobic exercise can reduce the severity of depression and anxiety, often managed with psychotropics, while improving cardiovascular health. Resistance training can mitigate the muscle-wasting effects of corticosteroids and enhance bone density while simultaneously addressing primary and secondary health concerns [537].

Fig. 7 examines the diverse effects of medication on physical ability. It highlights particular side effects, such as sarcopenia and osteoporosis, which are prevalent in the older population and presents evidence-based modifications for exercise regimens. This figure illustrates how PRT and other forms of exercise can effectively alleviate these effects, improve physical outcomes, and promote general health and well-being.

6. Interindividual variability and dose-response heterogeneity to exercise

Dose-response heterogeneity is not exclusive to pharmaceutical treatments; it is also applies to the physiological decline associated with aging [594]. Similarly, there is significant variability in the physiological, performance, and health-related adaptations of individuals undergoing the same exercise training program [595]. Various factors, such as intensity, duration, frequency, mode of exercise, functional status, adherence, and age, determine the effectiveness of exercise training interventions. Other responses to exercise training can be influenced by factors such as macronutrient intake and genetics [596]. The concept of heterogeneity in response to exercise training gained attention in the 1980s [597], with studies focusing on the trainability of sedentary adults. Understanding the causes and potential strategies to manage interindividual variability and dose-response heterogeneity during exercise is essential. This knowledge has profound implications for public health.

6.1. Understanding variability in exercise response

Physiological adaptations to chronic exercise have been shown to enhance several age-related health outcomes, demonstrating a positive impact of exercise on the fundamental biology of aging [598,599]. Interindividual variability and dose-response heterogeneity to exercise can be influenced by various factors, both intrinsic (e.g., sex, race, ethnicity, age, genotype) and extrinsic (e.g., comorbidities, functional capacity, diet, medications, recovery sleep, stochastic factors) [600]. Exercise has benefits for many clinically important outcomes in older adults, such as reducing fall risk, cardiovascular disease, and death. However, despite engaging in exercise at the same relative intensity, not only young but also older populations exhibit significant variations in acute physiological responses to exercise and the time to task failure [601]. Understanding the threshold and optimal levels of activity necessary for health promotion and disease management has become increasingly important in recent years [602].

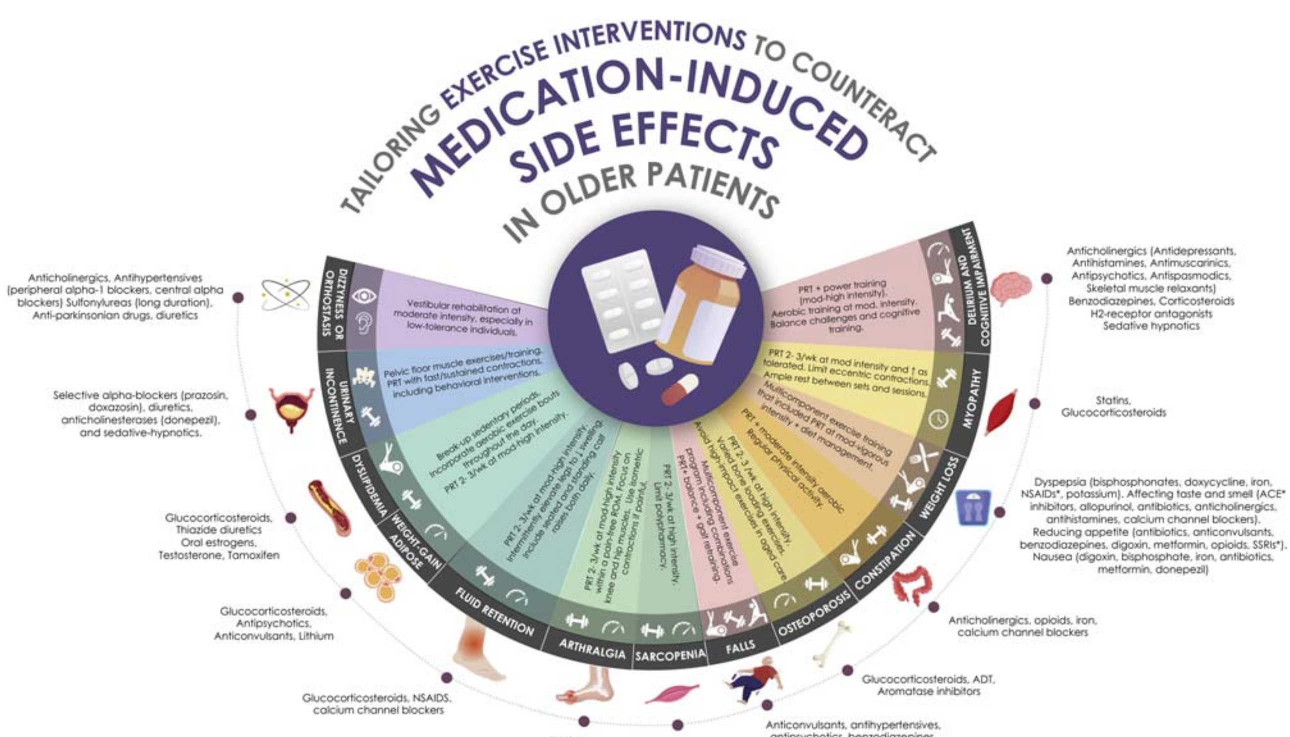

Fig. 7. Tailoring Exercise Interventions to Counteract Medication-Induced Side Effects in Older Patients. Adapted from [537].

A significant hurdle in understanding training response variability is the need for a standardized definition for classifying individuals as responders or non-responders. This challenge is compounded by technical difficulties in accurately measuring the physiological responses to many exercise protocols. To determine the impact of exercise on overall disease risk, disease pathobiology, health status, and outcomes, some studies have classified a fixed proportion of the lowest training response, absolute changes in pre- to post-intervention values, and changes of more than one standard deviation [603,604]. More recently, it has been suggested that technical error, minimal clinically important differences, and the combination of day-to-day biological variability and measurement error should be considered when categorizing response rates [600].

Consensus is yet to be reached on the ideal analytical approach for studying exercise response variation, which is a critical unmet need that must be addressed. Significant efforts have been made to explain variations in training response variability by assessing intrinsic (non-modifiable) and extrinsic (modifiable) factors [605]. Meyer et al. [606] systematically explored the impact of biological factors on the variability of cardiorespiratory fitness ($\dot{V}$O2 max) responses, finding that sex and age collectively account for less than 10–16% of the $\dot{V}O_2$ peak response [607]. Furthermore, cardiac autonomic recovery, as measured by heart rate variability, provides a practical assessment of physical recovery, although it does not reflect all physiological systems affected by exercise. Precisely, baseline cardiovascular autonomic function, characterized by high-frequency power (indicating high vagal activity) [608], has emerged as one of the strongest predictors of $\dot{V}O_2$ peak response, accounting for 27% of the response after eight weeks of aerobic training and 34% after 12 weeks of interval training [609].

Another possible reason for non-response is insufficient training stimuli, such as intensity or specificity to intervention, sex-related differences in response to exercise, and baseline physical fitness levels. The literature has shown age-related declines in physical function, muscle mass, and metabolic efficiency and wide heterogeneity in exercise response among older adults [90]. It is essential to note that a physiological non-response to exercise in one outcome does not equate to a non-response in other outcomes. It is well recognized that physiological and phenotypic responses to exercise are highly variable and depend significantly on the outcome of interest. An individual may benefit from an exercise intervention that differs from the chosen response variable. For instance, a person may experience an improvement in $\dot{V}O_2$ peak, without a corresponding reduction in fasting glucose levels, despite showing significant improvements in HbA1c, waist circumference, and body fat percentage across all subjects [610]. Which outcome is most important depends on an individual's current health status and health-related goals. However, no study has comprehensively assessed all possible parameters determining exercise response variability in older adults, including extrinsic and intrinsic factors. Therefore, while response heterogeneity poses a challenge for investigators, it also allows one to explore its mechanistic basis, highlighting the importance of continued research in clinical settings when studying non-responsiveness to exercise [611].

6.2. Genetic predisposition and personalized exercise regimens

Understanding the benefits of exercise in older adults is mainly based on typical standardized responses from small sample sizes with restricted or prescribed exercise regimens and considering a limited number of outcomes [90]. Furthermore, researchers have examined the individual interactions of physiological and molecular factors (such as genetics, epigenetics, transcriptomics, and metabolic factors) and environmental factors as potential mediators of the lack of response to exercise in certain participants [612]. From a public health viewpoint, a high $\dot{V}O_2$ peak is a proven negative predictor of CVD and overall mortality, and thus a major target of global exercise recommendations, yet $\dot{V}O_2$ peak varies more than twofold among sedentary individuals, supporting the existence of significant genetic or other contributions to $\dot{V}O_2$ peak in addition to the influence of PA patterns. Additionally, studies designed to investigate the response variability in aerobic training adaptation have reported significant differences across cohorts, supporting the heritability of $\dot{V}O_2$ peak. For example, investigating the genetic contributions to changes in cardiorespiratory fitness in response to a 20-week standardized exercise program, Bouchard et al. [93] estimated that 47% of the variation of $\dot{V}O_2$ peak response was genetically determined. In a subsequent report, a genome-wide association study (GWAS) suggested that multiple genes influence $\dot{V}O_2$ peak trainability, each with minor effects; however, much remains to be discovered regarding this variability in the response [613]. Recent data show that the variation in $\dot{V}O_2$ peak changes among individuals ranges from -4.7 to 47.8% [614].

Similarly, other clinical outcomes in older adults exhibit heterogeneity in the magnitude of their exercise response. For instance, in the HEalth, RIsk factors, exercise Training And GEnetics (HERITAGE) Family Study involving 316 women and 280 men (173 black and 423 white) and healthy sedentary individuals, approximately 42% of the participants showed no change in glycemic control indices after completing a 20-week exercise program on cycle ergometers three times a week for 60 sessions [615]. Similarly, a secondary analysis of the Functional Improvement from Aerobic Training in Alzheimer's Disease (FIT-AD trial), which aimed to evaluate the effects of aerobic exercise on community-dwelling older adults with mild-to-moderate dementia due to Alzheimer's disease, revealed interindividual differences in aerobic fitness and cognitive responses to aerobic exercise [616]. Whipple et al. [617] reported a high prevalence of non-responders among individuals with peripheral artery disease, with or without T2D, who completed at least two-thirds of their prescribed exercise sessions. When non-response was defined as a negative or no change in the 6-minute walk test distance, its prevalence was 35%. However, when defined as a lack of clinically meaningful change (20 meters), non-response prevalence was as high as 56% [618]. Despite these varying responses, all participants improved in at least one outcome, and only one individual improved across all measures.

Physiological, performance, and health-related adaptations to PRT also display considerable heterogeneity. Previous studies have shown either no responsiveness or substantial gains in the whole-muscle cross-sectional area (ranging from -2% to +59%) and maximal dynamic strength (ranging from 0% to +250%) [91,92]. Heritability estimates for general muscle strength range from 30% to 60%, with the overall heritability of strength-related phenotypes estimated at approximately 50% [91,92,619]. More than 200 polymorphisms have been linked to strength/power phenotypes, particularly in athletic performance [620]. At baseline, individuals with the CC genotype of the PPARGC1A Gly482Ser (rs8192678) had lower 1-RM values compared to T-allele carriers. However, after eight weeks of maximal strength training, C-allele carriers showed a greater improvement in 1-RM compared to those with the TT genotype [621]. A systematic review of genetic influences on functional adaptations to aerobic or PRT in older adults identified seven studies that measured ten single-nucleotide polymorphisms and nine different functional performance test outcomes. The ACE (D), ACTN3 (RR), UCP2 (GG), IL-6-174 (GG), TNF-α-308 (GG), and IL-10-1082 (GG) genotypes all predicted significantly superior adaptations in at least one functional outcome in older men and women after prescribed exercise or in those with higher levels of PA [622].

Although genetics have been shown to play a significant role in this variability, research utilizing candidate gene or GWAS approaches has yet to conclusively identify genetic predictors that fully explain the intrinsic biological mechanisms driving individual variability in response to exercise. While specific genetic variants and the proteins they code for have been identified, it remains unclear whether these proteins are solely responsible for the variability in exercise response. These findings suggest that other factors, such as environmental or epigenetic influences, may counteract any genetic 'handicap'. Therefore, overemphasizing genetics when tailoring exercise prescriptions may be counterproductive [623]. Identifying the genetic predictors of blunted adaptations to exercise may enhance our ability to target individuals at risk of poor outcomes by recommending advanced training techniques, better behavioral strategies, or physiological augmentation via nutritional or pharmacological co-interventions. An important research direction involves the identification of the genetic factors contributing to variations in responsiveness to exercise across clinically relevant endpoints, which could lead to more precise and effective exercise prescriptions to optimize the clinical benefits of exercise training in older adults.

7. Exercise and geroscience: toward recommendations

Physical activity and exercise are associated with a reduced risk of developing most several chronic diseases, geriatric syndromes, and disabilities during aging [41,284,502,624–628]. Physical activity and exercise benefits apply to conditions characterized by very distinct pathophysiology, such as Alzheimer's disease [629], cancer [628], heart disease [630], and pneumonia/other infections [631,632]. One possible explanation for such pleiotropic effects is that PA and exercise positively affect resilience mechanisms that oppose aging and exert positive effects by decelerating the pace of aging. This would prevent or delay the onset of different clinical conditions (e.g., several diseases, frailty, and disability) and reduce their severity. Thus, PA and exercise may be considered central geriatric care interventions, that is, interventions that act on the cellular and molecular drivers of biological aging to decelerate the rates of aging, which constitute the basics of the geroscience field [633,634].

Several reviews have discussed the biological mechanisms through which PA and exercise may modify the pace of aging [635–638], including their benefits for immune function [639,640] (in particular, adaptive immune function), low-grade chronic inflammation, their effects on mitochondrial biogenesis and mitophagy [641,642], and as regulators of multiple metabolic cascades important to aging, such as insulin/IGF1, Akt-mTOR, AMPK [638], sirtuins, and PGC1α. A seminal work by Contrepois et al. [643] found that a simple amount of acute exercise (and up to 1 -h recovery after the training in individulas aged 40–75 years) induced substantial changes in more than half (n = 9,816 analytes) of the 17,662 analytes evaluated through a multi-omics approach. Interestingly, several of these analyses and pathways are known to be involved in the central biological cascades driving the pace of aging, such as mitochondrial stress markers (e.g., GDF-15), immune function (e.g., the natural killer signaling pathway, Th1 and Th2 activation pathways, B- and T-cell receptors), inflammatory markers (e.g., interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), oxidative stress (e.g., myeloperoxidase, a marker of neutrophil degranulation [644]), and mTOR signaling.

Epidemiological data and biological investigations converge, indicating PA and exercise as major geriatric care interventions. However, most data linking exercise to the main drivers of biological aging have been obtained from animal experiments or human studies on young adults. Only a few investigations employed a sample with a significant age range covering adulthood or recruited older people, challenging the generalizability of findings to the aging process. While the magnitude of the response of the biological mechanisms of aging to PA and exercise depending on age range is unknown, knowledge of human physiology suggests that adaptive and resilience mechanisms tend to decrease over time during aging. The specificity and age dependency of the response to exercise could have important consequences for prevention strategies. The prescription of exercise in gerotherapeutic counseling may need to be different for a specific range of ages. In other words, specific PA programs might be more appropriate at certain times later in life. This underscores the need for continued investment in translational research on exercise interventions for older adults. Second, most investigations used one bout of acute exercise or an observational design, which makes it challenging to establish the best exercise regimen for decelerating the pace of aging, which may depend heavily on how gradually the intensity of exercise increases over time. Non-pharmacological prevention strategies in the field of aging can only be considered in the long term, especially because exercise in very old individuals may not be without risks. This involves thinking about strategies that consider acceptability, adherence, and implementation of safety procedures to minimize the chances of adverse effects. These factors can also vary depending on the age group. No previous investigation has gathered evidence on how exercise affects the main determinants of aging using prospective experimental exercise trial designs. Therefore, to provide initial pragmatic guidance on exercise regimen (in terms of exercise type, frequency, intensity, session duration, and intervention length) as a gerotherapeutic intervention, we searched for trials that tested the effects of any exercise training on one or several biological drivers of aging [7].

Meta-analyses on both modalities [645,646] or either aerobic exercise [647,648] or PRT alone [649,650] found that exercise was able to reduce the levels of traditional biomarkers of conventional chronic inflammation, such as C-reactive protein (CRP), IL-6, and TNF-a, including in the context of specific age-related diseases, such as T2D [651], heart failure [652] and mild cognitive impairment and dementia [653]. Exercise training involving aerobic plus strength exercises ("multicomponent training") appeared to be the best choice, although other elements of the exercise regimen need further investigation. An overview of these meta-analyses suggests that 3–5 times a week of moderate-to-vigorous exercises (some data also support the effectiveness of mild intensity exercises), for at least 25 min/session, and an intervention length of 12 weeks or more, preferentially, can reduce inflammatory biomarkers of aging/disease.

Evidence of the effects of exercise training regimens on other biological determinants of aging is less abundant than that for chronic inflammation. However, there is emerging evidence that exercise increases mitochondrial biogenesis (PRT) [654], oxidative metabolism (cycling-aerobic exercise [655]), cellular senescence [72,73], and muscle oxidative capacity [656] (as measured by phosphocreatine recovery rate constant (kPCr) using 31 P Magnetic Resonance Spectroscopy). In a well-designed RCT, Colleluori et al. [148,336,337] showed that 6-month multicomponent training among obese older adults was more effective than aerobic or PRT alone for improving muscle protein synthesis and myocellular quality, even though mitochondrial biogenesis increased the most in the aerobic exercise group. A recent meta-analysis (small-scale, n = 164) concluded that exercise training improved mitochondrial quality, density, dynamics, and oxidative and antioxidant capacities [657], although the strength of evidence is still weak. Multicomponent training also resulted in the best response in IGF1 levels compared to PRT or aerobic exercises alone. Multicomponent training also resulted in the best response in IGF1 levels compared to PRT or aerobic exercises alone [474] in older people with sarcopenic obesity. However, PRT is known to increase IGF1 levels in the plasma of older people [658,659], mainly when performed at least three times a week [660].

Furthermore, improvements in several autophagy markers were found in older adults engaging in either aerobic exercise [661] (25–30 min/session) or PRT [662] (three sets [8−12 repetitions/set] of three exercises) twice a week for eight weeks, including changes in the expression of regulatory proteins such as phosphorylated ULK-1, beclin-1, Atg12, and Atg16. Resistance training (6-week, 2−3 days/week at a low-to-moderate intensity) also led to a reduction in the cell counts of the most differentiated CD8 T-cells [663], which, according to the authors, are senescence-prone cells, while aerobic exercise (12-week – goal of 12,000 steps/day) and HIIT reduced p16INK4a levels in young adults [664], including those with obesity [665], supporting the senescence-targeting effect of exercise. Aerobic exercise (45 min/session, thrice a week for six months) also increased telomerase activity [666]. Finally, multicomponent training improved the composition of gut microbiota (modulation of the relative abundance of gut microbiota associated with cardiovascular disease) [667].

Although the high heterogeneity of the exercise interventions implemented across the original trials renders it challenging to establish the best exercise regimen for decelerating the pace of biological aging, multicomponent training is probably the exercise type that brings the most benefits for decreasing aging rates. Current evidence does not allow establishment of solid recommendations for the other elements of the exercise regimen for attenuation of aging rate (as opposed to the specific disease management strategies outlined in previous sections). However, it is plausible that 3–5 times a week of moderate-to-vigorous exercise, for at least 25 min/session and at least 8−12 weeks, could be a good compromise between effectiveness and feasibility of the intervention from a long-term perspective to slow the biological processes underpinning aging. Nevertheless, a key message care professionals should insist on is that any PA/exercise is better than no PA, and the more a person does, the more benefits s/he will achieve. Indeed, observational evidence shows that PA levels lower than recommended threshold are already associated with reduced mortality [65,628,668], and benefits exhibit a curvilinear dose-dependency [628,668].

Some gaps must be addressed in future investigations in this domain. The best exercise protocol from a life course perspective remains to be established, and the potential benefits acquired through short-term exercise intervention may disappear during the detraining period, but maintaining an exercise routine throughout adult life is very difficult to achieve. Protocols testing short-to medium-term exercise interventions with intervals characterized by no supervised training (e.g., 12-week/year training in a 3-year study) should be tested to understand the feasibility of such an approach and its effectiveness in decelerating the pace of aging on a durable basis. Determining whether exercise should be boosted at critical moments in an individual's life is also essential. For instance, several age-related diseases start their pathogenesis at mid-life, even if overt clinical expressions appear only decades later; this makes middle-aged people a target population for intensive exercise protocols.

8. Cost-effectiveness: analyzing economic benefits of exercise over medical treatments in older adults

The global healthcare system incurs over $50 billion in costs due to physical inactivity, underscoring the critical importance of PA programs in reducing health-related expenses [669–671]. These economic effects encompass direct healthcare expenditures and indirect financial impacts such as reduced productivity, costs of informal caregiving, and losses in human capital due to early mortality. Aging is associated with increased healthcare costs, which increase with declining health and functional ability [672–674]. Research has shown that very old individuals with lower functional capacities face greater healthcare costs than their more physically capable peers [659], with these expenses being notably higher for those in care facilities [672]. Therefore, improving functional capacity and health in institutionalized older adults could significantly impact healthcare spending. Conditions common in geriatrics, such as sarcopenia, frailty, cognitive impairment, and falls, escalate healthcare costs. For example, older adults with cognitive deficits are more frequently hospitalized [675] and admitted to care facilities [676], and dementia patients require more complex, prolonged, and expensive care [677,678].

Falls result in a substantial economic burden owing to hospitalization and long-term rehabilitation costs [679,680]. Consequently, the cost-effectiveness of exercise interventions designed to prevent falls in older adults has been extensively studied [681]. It was shown that the OEP, when delivered to individuals over 80 years and targeted at high-risk groups, can prevent the most significant number of falls at the lowest incremental costs [681]. Hewitt et al. [682] found that an exercise program emcompassing strength and balance exercises is cost-effective in preventing falls in institutionalized older adults aged 65–100 years. This aligns with earlier findings that reported reduced healthcare costs in community-dwelling older adults participating in outdoor PA interventions aimed at fall prevention, which resulted in fewer acute care and rehabilitation admissions and lower expenditures on allied health and community services [683]. Recently, Bays-Moneo et al. [684] evaluated the economic impact of two exercise interventions versus usual care among nonagenarian nursing home residents. This study revealed that a tailored multicomponent exercise program emphasizing power training remarkably reduced monthly healthcare costs for institutionalized oldest-old individuals (mean change = -€330.43). In contrast, costs in the usual care group significantly increased (mean change = +300.00 over a 12-month follow-up). The third group engaged in daily calisthenics exercises maintained the monthly mean cost during the intervention and had lower healthcare costs after 12 months than usual care. These findings suggest that both exercise interventions are beneficial in reducing healthcare costs among institutionalized oldest-old individuals, with the tailored multicomponent exercise group showing a more significant reduction. Associated care needs, such as bathing, dressing, walking, medications, and physiotherapy assistance, were also reduced. Notably, both exercise groups had reduced hospital stays during the intervention year [684]. In this study, the multicomponent group incurred higher estimated implementation costs (€672.00 per year) compared to the calisthenics group (€134.4 per year), mainly due to the personalized nature of the intervention, whereas the calisthenics group included 25 residents.

In a comprehensive German study involving over 1.5 million individuals aged 70 and older, Dams et al. [685] compared two exercise interventions targeting at fall prevention: a tailored individual program ("LIFE") and a group-based program ("gLIFE"). Over five years, both programs prevented 2,692 deaths and 618,060 falls. The tailored individual intervention, however, incurred substantially higher costs (€510 million) than the group-based approach (€186 million), and neither intervention achieved cost savings compared to standard care. However, cost savings were more pronounced among participants with higher care needs, particularly in formal care, outpatient treatment, and inpatient rehabilitation [685]. This highlights that while national programs broadly target fall prevention, the risk varies across populations, suggesting that more targeted interventions could be more cost-effective for high-risk groups.

Several studies underscore the economic benefits of diverse PA programs for older adults [682,686,687]. Multicomponent exercise regimens and supervised initiatives often prove to be more economically viable than those limited to a single exercise type. Additionally, combining exercise with other interventions, such as PRT, within a multimodal approach (exercise, nutrition, and education) has shown economic benefits. A study led by Rodriguez-Mañas et al. [277] demonstrated a significant reduction in healthcare costs, primarily through decreased hospitalization expenses, resulting in a decrease of €420 per patient over a year compared to a control group.

The development and implementation of cost-effective exercise programs are not just desirable but essential public policy objectives, especially given the increasing attention paid to the economic impact of such interventions on healthcare costs in older populations. However, data on the cost efficiency of tailored exercise programs still needs to be improved, highlighting the urgent need for more extensive research. Preliminary findings suggest that these programs could be prudent investments to improve health outcomes later in life. To manage expenses and enhance health outcomes for older patients, healthcare systems and long-term care facilities must take immediate action to integrate structured PA into their services.

9. Implementation science: barriers and facilitators to physical activity participation

Older adults, a diverse group with varying physiological capacities, frequently lead sedentary and inactive lifestyles despite the well-documented advantages of physical activity for health. Understanding the culturally specific factors influencing exercise adherence across different societies and socioeconomic backgrounds is essential to promote regular physical activity. This understanding is particularly critical in the fields of geriatrics and public health. Implementation science, which examines how evidence-based interventions can be integrated into routine practice and policy, is crucial in addressing barriers and enhancing facilitators to exercise adherence among older adults [688].

The Consolidated Framework for Implementation Research (CFIR) presents a comprehensive and structured approach, encompassing intervention characteristics such as the strength of evidence, adaptability, and complexity, as well as the inner setting (e.g., culture, readiness, resources), outer setting (e.g., patient needs, incentives, public health policy), characteristics of individuals involved (e.g., knowledge, attitudes, beliefs, perceptions), and the implementation process (e.g., planning, engagement, evaluation [689]. Researchers and practitioners can employ CFIR principles to systematically identify barriers and facilitators in exercise interventions for older adults, allowing for the development of targeted strategies to enhance the uptake, sustainability, and effectiveness of exercise programs tailored for older populations.

The application of behavior change theory is crucial in encouraging physical activity among older adults. The Capabilities, Opportunities, Motivations, Behavior (COM-B) model, which considers an individual's capability, opportunity, and motivation, helps to understand the determinants that influence exercise behavior in this population [690]. This model emphasizes the interplay between physical ability, social support, and personal motivation in shaping exercise habits among older adults.

Both participants and healthcare professionals encounter facilitators and barriers that impact exercise adherence. Older adults' barriers to exercise adherence include low self-confidence, competing priorities, perceived risks, and limited perceived benefits. Healthcare providers, on the other hand, face challenges such as time constraints, uncertainty in the referral process, and reimbursement issues, which can hinder their ability to prescribe effective exercise regimens [691]. Additionally, external factors such as community resources, social support availability, and policy frameworks significantly influence the uptake of exercise recommendations among frail older adults.

Older adults often face challenges in engaging in regular physical activity due to intervention-specific factors such as the need for tailored interventions based on individual profiles and health conditions, the importance of intensity, dosage (considering factors like pain, cognition, frailty, and falls), and social support. These challenges can be addressed by implementing comprehensive strategies that include tailored interventions, enhancing social support, educating participants, and empowering them to maintain exercise engagement [690].

In summary, promoting exercise adherence in older adults requires a multifaceted approach that considers both individual and systemic factors. By addressing barriers and leveraging facilitators through the integration of implementation science and behavior change theory, healthcare professionals and policymakers can help promote healthier aging through regular physical activity.

10. Conclusions

Given the increasing prevalence of older adults worldwide, effective interventions that promote functional capacity and prolong the number of years lived without disabilities are vital when evaluating the impact of life-extending interventions on the health span of older adults. Insufficient PA and sedentary behaviors are potent risk factors for a range of age-related health issues, including all-cause and cardiovascular mortality, obesity, sarcopenia, frailty, and disability, as well as other chronic illnesses. On the other hand, adopting a healthy diet, engaging in regular physical activity, avoiding smoking, consuming alcohol in moderation, and maintaining an appropriate body mass index can significantly contribute to overall health and well-being across all age groups. Regular physical activity and structured exercise can help counteract age-related declines in physical, cognitive, and psychological health, extending health span and improving quality of life. Exercise participation influences various biological mechanisms, such as chronic inflammation, mitochondrial dysfunction, myokine release, autophagy, oxidative damage, and insulin-like growth factor signaling. Engaging in physical activity and exercise can improve physical function and reduce the burden of non-communicable diseases and premature mortality, including cause-specific mortality from cardiovascular disease, cancer, and chronic lower respiratory tract diseases.

Exercise should be viewed as a form of treatment, with prescriptions tailored to specific outcomes, such as primary prevention, enhanced fitness or functional status, or disease treatment. Just like any other medical intervention, it is crucial to personalize, adjust, and manage these prescriptions, considering external (exercise variables) and internal (acute response to exercise) factors influenced by personal, genetic, functional, psychosocial, and environmental factors. Exercise recommendations for achieving health-related outcomes must consider the relationship between dose and response, volume, intensity, and the specific adaptations necessary for the desired outcomes. For instance, resistance, aerobic, balance, and mobility training can specifically target age-related deficits. Multicomponent exercise programs that integrate cognitive tasks effectively improve frailty characteristics, such as low muscle mass, strength, endurance, mobility, PA level, and energy, while also enhancing cognition to optimize functional capacity during aging.

The development of wearable technology has facilitated personalized exercise regimens by monitoring physiological responses in real time. Omic technologies, which encompass fields in biology such as phenomics, metagenomics, metabolomics, proteomics, and genomics, enable multi-omic approaches. These methods are crucial for identifying molecular transducers of exercise, revealing substantial interindividual variability, and suggesting evidence-based doses when treating healthy and unhealthy populations. Future research should explore how response diversity varies across population groups within older adults and develop personalized lifestyle medicine tailored to optimize clinical outcomes.

Polypharmacy and potentially inappropriate medications (PIMs) in older adults often overlook the importance of exercise prescription. The connection between medication use and PA/exercise offers a promising approach to enhancing the well-being of older adults. By combining exercise prescriptions with pharmacotherapy, a comprehensive strategy can optimize the vitality and functionality of older individuals while minimizing adverse pharmaceutical reactions. Exercise can serve as a better alternative for managing the side effects of medications, as it often provides benefits beyond the targeted condition and shifts the risk-benefit in favor of exercise. Exercise can lead to a decrease in doses or substitute some potentially hazardous drugs whenever possible, as it often offers broader benefits beyond the target condition, enhancing the risk-benefit ratio in favor of exercise.

Despite the numerous advantages of exercise, its integration into medical practice for older people remains limited. Many healthcare professionals, including geriatricians, need more training to incorporate exercise directly into patient care. Although progress has been made in this area, the approach to exercise counseling within healthcare settings is often reserved for those without significant physical or mental limitations and includes mild activities such as walking at dosages and intensities not supported by the current evidence. This cautious approach to exercise counseling appears to stem from an unfounded fear of exercise-related injuries or the perceived risks of more vigorous activities for older adults, whereas, in reality, the greater danger lies in sedentariness. Integrating evidence-based exercise programs that are comprehensive and adaptable to individual health conditions is crucial across all healthcare settings, including community and institutional settings. By doing so, healthy aging can be promoted, and the growing burden of non-communicable diseases associated with inactivity can be addressed.

Promoting PA in older adults is a multifaceted societal issue that involves not only geriatricians but also family doctors, health fitness trainers/physiotherapies, policymakers, health agencies, insurance companies, and urban planners. The effective promotion of PA requires a collaborative approach and the development of environments and policies that encourage active lifestyles among older adults. Thus, this consensus calls for evidence-based exercise programs tailored to the needs and capabilities of older adults, ensuring that these programs are comprehensive and adaptable to individual health conditions. The ultimate goal is enhanced quality of life, regardless of age or initial state of fitness or frailty.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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