JAMDA 18 (2017) 564–575

JAMDA

journal homepage: www.jamda.com

Special Article

The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty

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Keywords (MesH):
Frail elderly
Practice Guidelines as Topic*
aged
evidence-based medicine/standards*
patient care management
disease management

A B S T R A C T

Objective: To develop Clinical Practice Guidelines for the screening, assessment and management of the geriatric condition of frailty.
Methods: An adapted Grading of Recommendations, Assessment, Development, and Evaluation approach was used to develop the guidelines. This process involved detailed evaluation of the current scientific evidence paired with expert panel interpretation. Three categories of Clinical Practice Guidelines recommendations were developed: strong, conditional, and no recommendation.
Recommendations: Strong recommendations were (1) use a validated measurement tool to identify frailty; (2) prescribe physical activity with a resistance training component; and (3) address polypharmacy by reducing or deprescribing any inappropriate/superfluous medications. Conditional

ED is supported by an Australian National Health and Medical Research Council (NHMRC) grant (Grant number: 1112672).

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http://dx.doi.org/10.1016/j.jamda.2017.04.018
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recommendations were (1) screen for, and address modifiable causes of fatigue; (2) for persons exhibiting unintentional weight loss, screen for reversible causes and consider food fortification and protein/caloric supplementation; and (3) prescribe vitamin D for individuals deficient in vitamin D. No recommendation was given regarding the provision of a patient support and education plan.
Conclusions: The recommendations provided herein are intended for use by healthcare providers in their management of older adults with frailty in the Asia Pacific region. It is proposed that regional guideline support committees be formed to help provide regular updates to these evidence-based guidelines.
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Frailty is a modern geriatric giant, and a major public health problem in the older population.[1] It has been recently defined by the International Association of Gerontology and Geriatrics Frailty Consensus as a reduced strength and physiologic malfunctioning that increases an individual's susceptibility to increased dependency, vulnerability, and death.[1] Frailty can be used as a marker of adverse outcome risk in older adults[2–4] and is increasingly used to predict patient outcomes across specialties such as oncology, cardiology, and orthopedics.[5–8]

There are multiple etiologic factors leading to frailty, including physiological changes and/or diseases associated with aging, inflammation, sarcopenia, polypharmacy, endocrine disorders, protein energy malnutrition, social isolation, and poverty.[1,3,5,9] The prevalence of frailty in community-dwelling older adults in the Asia-Pacific region is approximately 3.5%-27%,[4,10–24] which is comparable to the prevalence across Europe and the Americas.[25–31] Socioeconomically disadvantaged and indigenous communities can have a frailty prevalence of over 50%.[32,33] This frailty prevalence may be underestimated in several studies because of the large number of nonresponses in population health surveys of older adults.[34]

Frailty is more common in females and increases in prevalence with age.[1,3,30] It overlaps with comorbidity, although it can and often does occur independently from the presence of any chronic disease.[3,32,35] Frailty is not synonymous with disability but is causally related.[35,36] The condition is also costly, with reported healthcare expenses around €3500 ($4000 USD) over 3 months for older adults with frailty, approximately 5 times the cost for nonfrail adults.[37] This expense is of particular concern in the Asia-Pacific region, where older adults with high healthcare needs are often those not able to access publicly funded healthcare services.[38]

Currently, no accepted reference standard exists to identify frailty, and extensive international efforts are underway to identify the means of optimal measurement. Three major approaches to defining frailty exist:

(1) The physical phenotype model of Fried et al[36] and its rapid screen: FRAIL[39]
(2) The deficit accumulation model of Rockwood and Mitnitski which captures multimorbidity[40]
(3) Mixed physical and psychosocial models, such as the Tilburg Frailty Indicator[41] and Edmonton Frailty Scale[42]

Although most of the published literature on frailty focuses on its identification, etiology, and risks, there remains a large knowledge gap: consolidating the evidence-base of scientific literature to develop Clinical Practice Guidelines (CPGs) for treating frailty once it has been identified. There is an urgent need to develop such guidelines for the Asia-Pacific region, which has the largest population of older adults worldwide combined with much heterogeneity regarding population socioeconomics, provision of healthcare services, and ethnic diversity.[11,43,44]

Developing Clinical Practice Guidelines for Frailty

Conventionally, clinicians use CPGs as the basis for their standard care.[45] CPGs are evidence-based recommendations systematically developed by expert panels who have a working clinical knowledge of respective medical conditions.[45] CPGs for frailty are urgently needed for a variety of reasons:

- For better recognition of frailty by healthcare professionals;
- For the delivery of the best available evidence for the identification and management of frailty;
- To improve health and quality of life outcomes for older individuals affected by frailty; and
- To encourage healthcare providers to focus on improving the functional ability of older adults with frailty.

Although best practice guidelines have been developed for frailty in community and outpatient settings by the British Geriatrics Society,[46] these guidelines fall short on providing specific clinical recommendations.

The aims of this article are to develop evidence-based, multidisciplinary CPGs for the identification and management of frailty, specifically targeting health practitioners in the Asia-Pacific region. These guidelines will incorporate principles from the World Health Organization, which has recently highlighted the need to focus on maximization of the functional independence of older adults, rather than simply using a traditional single-disease medical approach.[47] This report will also discuss the evidence-base behind the development of each CPG.

Methods

Throughout the remainder of this article, the term "guidelines" will be used when referring to CPGs. The guidelines were developed using an adapted Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.[45,48–50] The GRADE approach involved evaluating the current scientific evidence and forming consensus recommendations by a clinical expert panel comprised of multidisciplinary experts on frailty from various countries. The guidelines arose out of presentations at the Asia-Pacific Geriatrics Conference on "Geriatrics Beyond Borders: Are We Frailty Ready?" held in Singapore in 2016. Utilizing the information presented and the discussions at this conference, combined with a comprehensive literature search and review, a basic document was developed. This document was distributed to the expert panel who were encouraged to rank the strength of the guidelines and to propose changes. A modified Delphi process was used until all members of the expert panel were satisfied with the final document.

The strength of a guideline refers to its supporting evidence base, as well as the extent that its benefits outweigh any potential risks.[45,51] A strong recommendation in our manuscript is conceptualized as "we strongly recommend," and reflects that in the expert panel's judgement, there are substantial clinical benefits to the patient that distinctly outweigh the risks of undesirable effects,[45,51,52] taking into consideration patient preference.[53] A statement of "we conditionally recommend" means that although the majority of clinicians and informed patients would choose this modality, many would not because the benefits of treatment could potentially be undermined by an adverse event occurring.[45] A statement of "no recommendation" specifies that there is a low level of evidence supporting the

recommendation.[51] Recommendations are based on potentially treatable causes of frailty.

Clinical Guidelines

Table 1 summarizes guidelines for frailty; key principles outlined in this report are summarized in Table 2. Current common definitions of frailty overlap considerably with sarcopenia in relation to both muscle strength and physical function,[54–56] with sarcopenia defined as the progressive loss of skeletal muscle mass and strength that occurs with aging.[57] Sarcopenia may even be a component of frailty.[58] Thus, the clinical management of both frailty and sarcopenia can follow along similar lines. This document does not cover the overlap of frailty with other major systems, for instance, cognitive frailty.

There is a spectrum of frailty ranging from fit to frail,[59] from which 3 categories are often distinguished: "frail," "prefrail," and "robust." It is possible for older adults to dynamically transition between these frailty categories.[10] For instance, individualized treatment or natural resolution of acute conditions in an older adult may result in an improvement of frailty status from a frail to prefrail state. The lower on the frailty spectrum an older adult is, the less likely they will move up the spectrum to the highest functioning levels.[60,61] An intervention that may benefit an older adult in the early stages of frailty might not be beneficial, or may even be harmful to, an older adult with severe frailty. Thus, frailty should be identified and managed as early as possible, with healthcare professionals advised to carefully weigh any benefits of treatments against harm to patients, particularly in those who are most frail and in whom treatments are less likely to show any benefit to the patient. Shared decision making between healthcare professionals, older adults, and their families is recommended when developing a management plan for an older adult with frailty.[62]

Recommendation 1: We Strongly Recommend that a Validated Measurement Tool Be Used to Identify Frailty

Frailty should be identified with a validated measurement tool. There are many such tools in existence (Table 3), with much heterogeneity in their classification and predictive abilities.[86–88] When choosing a frailty measurement to use, it is essential to select one, which not only accurately identifies frailty and predicts patient outcomes, but is also simple to use, well validated, and accounts for the priorities, resources, and objectives of the specific clinical setting.[3,5] The 2 most common frailty measurements are Fried's Frailty Phenotype[36] and Rockwood and Mitnitski's Frailty Index (FI).[40]

Table 1
Clinical Practice Guidelines for the Management of Frailty

Clinical Practice Guidelines for the Management of Frailty
Strong Recommendations
1. We strongly recommend that frailty be identified using a validated measurement tool.
2. We strongly recommend that older adults with frailty be referred to a progressive, individualized physical activity program that contains a resistance training component.
3. We strongly recommend that polypharmacy be addressed by reducing or deprescribing any inappropriate/superfluous medications.
Conditional Recommendations
4. We conditionally recommend that persons with frailty are screened for causes of fatigue.
5. We conditionally recommend that older adults with frailty who exhibit unintentional weight loss should be screened for reversible causes and considered for food fortification/protein and caloric supplementation.
6. We conditionally recommend that vitamin D be prescribed for persons found to be deficient in Vitamin D.
No Recommendation
7. We have no recommendation for the provision of an individualized support and education plan for older adults with frailty.

Table 2
Key Principles

1. Frailty is a defined as an age-related state characterized by a reduced strength and physiologic malfunctioning that increases an individual's susceptibility to increased dependency, vulnerability, and death.[1,3]
2. Frailty identification and management should be incorporated into a Comprehensive Geriatric Assessment (CGA) where possible.
3. Frailty should be identified with a validated frailty measurement tool, such as Fried's Frailty Phenotype, Rockwood and Mitnitski's Frailty Index, the Tilburg Frailty Index, or the FRAIL scale. The measurement tool should be chosen to match the clinical goal. Blood investigations are not required in the identification of frailty.
4. Frailty overlaps with sarcopenia, therefore, management principles may be similar between the 2 conditions.
5. Shared decision making between healthcare professionals, older adults, and their families should be facilitated when developing a management plan for older adults with frailty.
6. Practical recommendations for lifestyle modification should be provided for older persons with frailty, paying special attention to the incorporation of resistance training and adequate protein intake.
7. Identifying the treatable risk factors of frailty may prevent its progression— polypharmacy, weight loss, physical activity (resistance training), among others.
8. Education and support should be provided to older people and their caregivers. This training can be community based.

Frailty screening in the clinical setting

Frailty should be routinely screened for in adults aged 70 years and older, or those who have unintentionally lost >5% of their body weight in the previous year.[1] It is advised that frailty not be subjectively identified by superficial visual appearance of an older patient, because of large variations in clinical judgement across specialties, reproducibility of assessment, and the heterogeneity in frailty presentation.[89,90] Although there have been studies finding that initial clinical impression of frailty can predict patient outcomes,[91] a superficial visual inspection of an older adult is likely to only identify severe frailty.

Frailty identification as part of a Comprehensive Geriatric Assessment

Frailty can be measured as part of a Comprehensive Geriatric Assessment (CGA), which is the current reference standard for identifying and managing frailty,[46] or by practicing clinicians using the shorter-duration Rapid Geriatric Assessment.[78] A CGA determines the medical, functional, and psychosocial aspects of a frail older person using a thorough, multidimensional assessment process, and then uses this information to guide a person-centered support and care plan.[46,92] CGA and subsequent interventions have been demonstrated to be effective in reducing mortality and admission to higher level care in numerous randomized controlled trials (RCTs).[92] However, despite the many successes of CGAs, they can be labor-intensive and expensive to perform,[93] and in the Asia-Pacific region, the majority of practitioners may not have the resources to perform a full CGA. Thus, frailty screening should be performed in these cases to identify older adults for referral to full CGAs.

Frailty screening using Fried's Frailty Phenotype

Fried's phenotype classifies frailty as 3 or more physical setbacks out of a list of 5: slowness (slow walking speed), weakness (low grip strength), weight loss (≥4.5 kg in the previous year), exhaustion (self-reported), and low physical activity.[36] Conceptually, Fried's Frailty Phenotype captures the presence and severity of a distinct clinical syndrome of dysregulation in both energy and complex

Table 3
Frailty Measurements for Use in Clinical Practice

Frailty Measurements
Screening
Rapid screening
- FRAIL Scale[39]
- PRISMA-7[63]
- Tilburg Frailty Index (TFI)[41]
- Vulnerable Elders Survey (VES)[64]
- Self-Rated Health Deficits Index (HDI)[65]
- Sherbrooke Postal Questionnaire (SPQ)[66]
- The G8 Questionnaire[67]—for oncology patients
- Easy Care—short version[68]
- Study of Osteoporotic Fractures (SOF) Index[69]
- Identification of Seniors at Risk (ISAR)[70]
Detailed Screening
- Fried's Frailty Phenotype[36]
- Groningen Frailty Indicator (GFI)[71]
- Frailty Trait Scale (FTS)
Measurements (incorporates screening and assessment)
- Grip Strength[72–74]
- Gait Speed[75]
- Timed Up and Go (TUG)[76]
- Short Physical Performance Battery (SPPB)[77]
Assessment
Rapid Assessment
- Rapid Geriatric Assessment (RGA)[78]
- Edmonton Frailty Scale (EFS)[42]
Comprehensive Assessment
- Comprehensive Geriatric Assessment (CGA)[79]
- Easy-Care[80]
Metrics-Computed Assessment
- Frailty Index (FI)[40]
- Kihon Checklist[81]
- Multidimensional Prognostic Index (MPI)[82]
- Frailty Risk Score (FRS)[83]
Synthesis Assessment
- Clinical Frailty Scale (CFS)[84]
- Gérontopôle Frailty Screening Tool (GFST)[85]

PRISMA-7, The Program of Research to Integrate Services for the Maintenance of Autonomy. The categorization of frailty measurements is subject to change, and frailty measurements can belong in more than 1 category

adaptive systems essential to homeostasis, which in turn, offers a physiological basis for sarcopenia and fatigue.[36,94] Because of this physiological basis, Fried's Frailty Phenotype is well suited for identifying frailty in the clinical setting,[3,95] although it can sometimes be time-consuming to measure patient grip strength and walking speed in clinical settings.[96] Fried's Frailty Phenotype is regularly used in clinical settings in the Asia-Pacific region, where it is predictive of mortality, disability, falls, hospitalization, and risk of surgery.[17,18,20,21,87,97–100]

Frailty Index (FI) of cumulative deficits

The FI considers frailty as an age-related, dynamic state. It is expressed as a ratio between the number of health deficits an older person has from a predetermined list of 30 or more variables.[40,101,102] FI scores range from 0 to 1, with an upper limit of around 0.67.[103] For example, in a list of 50 health deficits, if an individual scores "yes" to 10 of these deficits, then their FI score is 0.2 (=10/50).

The FI has a multidimensional nature, incorporating domains such as physical function, multimorbidities, cognition, and psychosocial factors. Interventions to manage frailty can focus on these domains, thereby adding to the utility of the FI in clinical practice. Like Fried's Frailty Phenotype, the FI is frequently applied in the Asia-Pacific region.[11,12,19,100,104–112] The FI is also indicative of an older adult's biological age,[104] captures risk of mortality,[3] and is predictive of disability, admission to nursing homes, functional decline, surgery risk, and hospitalization.[98,113,114]

Despite the advantages of the FI, it can be time-consuming to undertake if collecting the data at the clinical level from scratch.[79] However, a major advantage of the FI is that it can be obtained from data already collected from a CGA.[115] Moreover, an electronic FI can be automatically derived from routinely collected electronic medical records, which was recently demonstrated by Clegg et al[115] in their study of 900,000 older adults using primary care records.

Other frailty measurements and screening tools

Recently, a hybrid measure containing elements from both the Frailty Index and Fried's Frailty Phenotype was developed: the FRAIL scale.[39] The FRAIL scale shows similar predictive accuracy to both the FI and Fried's Frailty Phenotype,[116] and is recommended by the International Academy on Nutrition and Aging (IANA) for use in clinical practice.[117] The FRAIL scale is being increasingly used in the Asia-Pacific region.[15,33,99,116,118–120]

Also emerging in the Asia-Pacific region is the Clinical Frailty Scale (CFS),[121,122] which is a well-validated 9-point global assessment tool[84] that predicts adverse outcomes in older adults.[121–123] The CFS allows frailty to be defined and graded using simple clinical descriptors available from routine clinical assessment.[122] However, the tool requires some clinical judgement and trained assessors are required for accurate classification.[124]

Other frailty measurements regularly applied in the Asia-Pacific region include the Study of Osteoporotic Fractures (SOF) index,[16,87] the Reported Edmonton Frailty Scale,[6,21,86] the Timed-Up-and-Go (TUG),[125–127] the Short Physical Performance Battery (SPPB),[128–131] and the Kihon checklist.[81]

For frailty measurement tools requiring physical assessments, using locally defined cut-off points is advised. For instance, populations in the Asia-Pacific region may have lower grip strength,[72,73] with Wu et al[74] reporting a ≥25% lower grip strength in Taiwanese older adults than in European adults. It is, thus, suggested that for Asian populations, the lowest 20th quintile of grip strength be used to define low muscle strength, or <26 kg for men and <18 kg for women.[43]

Recommendation 2: We Strongly Recommend that Older Adults with Frailty be Referred to a Progressive, Individualized Physical Activity Program that Contains a Resistance Training Component

The adage "move it, or lose it" is of fundamental importance for frailty management and prevention. Several recent systematic reviews and meta-analyses have concluded that physical activity is a crucial way to maintain and improve the physical strength, function and mobility of older adults with frailty.[55,132–135] Physical activity programs for older adults with frailty and/or the oldest old should contain targeted exercises to address sarcopenia-related muscle wastage and mobility loss.[55,136] Resistance training (strength training) is strongly recommended, with multiple RCTs demonstrating benefits for even the oldest old.[137–144] Benefits of resistance training include enhanced strength and power,[135,143,145,146] reductions in disability,[135,142,144] reduced fatigue,[147,148] and a decreased likelihood of admission to a hospital or nursing home.[144]

Multijoint resistance exercises should be performed in the first few weeks of physical activity prescription, with the gradual progression to more single-joint exercises.[149] Exercises mimicking daily activities are encouraged.[143,150] Higher intensities of resistance training appear to have more benefits than low intensity exercise for older adults,[55,135,145,151] although the optimal volume (number of sets and repetitions) of resistance training is not yet clear.[55,134] From a physiological point of view, muscle cells adapt the same way to physical activity regardless of age,[146] even though older adults may take longer to improve to the same level as younger adults.[136]

Balance and aerobic training are also recommended for older adults with frailty, even if these modes of exercise may not directly influence muscle strength.[55] Ongoing participation in a balance program can reduce fear of falling, and improve mobility and balance, according to a recent meta-analysis of 88 trials in older adults.[55] Balance training can also reduce falls risk[55,152] and major mobility disability[153] when combined with a resistance training program. It is, therefore, proposed that balance exercises accompany resistance training once an older adult with frailty is able to stand.[55] Prescription of walking for older adults with frailty is also advocated, ideally when an individual's balance, strength, and cognition are adequate to perform walking safely[55] given the close association between unstable walking and falls risk.[154] Reducing sedentary time may also be a first step in promoting older adults with frailty to be more physically active.[155]

Multimodal physical activity programs may also be beneficial for older adults with frailty. For instance, the recent large-scale Lifestyle Interventions and Independence for Elders (LIFE) Phase III RCT[153,156,157] found that multimodal exercise (resistance training, aerobic exercise (walking), balance, and flexibility exercises) reduced major mobility disability in older adults.[153] Most surprising was that the effects of this multimodal training on preventing mobility disability were highest among those who were frail (SPPB <8).[153] In the Asia-Pacific region, the recent Steps to Avoid Falls in the Elderly (SAFE) Study demonstrated that a combination of resistance, balance, and gait training reduced falls risk in older adults (with and without frailty) discharged from an emergency department[131]; however, this finding was only observed in those with low comorbidity. Future large-scale intervention studies should investigate the impact of multimodal exercise programs in older adults with frailty in the Asia-Pacific region.

Health practitioners should be aware that community-based programs for older people with frailty often fall very short of evidence-based recommendations.[55] Furthermore, adherence to physical activity programs is poor in older adults for a variety of reasons, including a fear of falling[158]; a lack of self-belief and coping strategies[142,159,160]; attitude[160,161]; and adverse social and environmental influences.[142] Essentially, older adults are more likely to adhere to a physical activity program if the program is supervised,[151] individually tailored,[55,131] contains self-efficacy training,[142] and the referring clinician encourages patient participation.[161]

Recommendation 3: We Strongly Recommend that Polypharmacy Be Addressed by Reducing or De-prescribing Any Inappropriate/Superfluous Medications

Much research has linked frailty development with polypharmacy.[1,162–166] We recommend that medications prescribed by frail older people be reviewed regularly. Medications, which are no longer needed can be deprescribed, regulating the dose in accordance with kidney function.[167,168] Withdrawal of inappropriate medications should be conducted under the supervision of a healthcare professional, with the aim to improve the outcomes of patients.[168] A recent systematic review reported that deprescription is most effective when implemented earlier, and that older adults can tolerate the withdrawal of certain medications without harmful circumstances.[169] Deprescribing is unlikely to lead to any significant adverse clinical outcomes, at least based on a recent RCT of older adults residing in residential aged care facilities.[170]

Regrettably, there exists a distinct lack of well-designed clinical trials on reducing inappropriate/superfluous medications in older adults with frailty, based on the findings of a systematic review by Tija et al.[171] In general, it is advised that deprescribing of inappropriate medications for older adults with frailty should occur using guidelines provided by: the Screening Tool of Older Person's Prescriptions (STOPP) criteria and Screening Tool to Alert doctors to Right Treatment (START) criteria[172–174]; the Beers criteria; and the McLeod criteria.[175] These deprescription guidelines focus on specific medications that should not be prescribed. General deprescription guidelines also exist, which do not solely focus on specific medications, and instead rely on evidence-based medicine and the older adult themselves: the Medication Appropriateness Index (MAI),[176] and the Inappropriate Medication Use and Prescribing Indicators tool.[177]

To implement a deprescription program for older adults with frailty, it is recommended that clinicians and pharmacists openly discuss the projected benefits of deprescription against potential harms with both the patient and their carer.[178] Health practitioners should also be aware of barriers to deprescription for older adults with frailty, including: incentives to over-prescribe[178]; a lack of agreement as to what medications to deprescribe[179]; and a lack of awareness of deprescription benefits.[178] Of note, in rural and/or lower socioeconomic areas, there may be the opposite problem: older adults with frailty may have unknown and untreated diseases.

Recommendation 4: We Conditionally Recommend that Persons with Frailty Are Screened for Reversible Causes of Fatigue

There are a number of treatable causes of fatigue including sleep apnea,[180,181] depression,[182,183] anemia,[182] hypotension,[183] hypothyroidism,[184] and B_{12} deficiency.[185] Fatigue is a key component of both Fried's Frailty Phenotype and the FRAIL scale.[36,39] Research reports have indicated that screening for reversible causes of fatigue, combined with targeted interventions, can improve the outcomes of older adults with frailty.[1,186] Nevertheless, very little rigorous research has addressed modifiable causes of fatigue in older adults with frailty. Although there are clinical trials showing that fatigue can be treated by addressing sleep apnea[180,187] and depression,[183] good quality clinical trials on other reversible causes of fatigue are required. Of note, Selective Serotonin Reuptake Inhibitors (SSRIs), which are widely prescribed to treat depression, may actually worsen frailty.[188]

Recommendation 5: We Conditionally Recommend that Older Adults with Frailty Who Exhibit Unintentional Weight Loss Should Be Screened for Reversible Causes and Considered for Protein and Caloric Supplementation/Food Fortification

Weight loss is a key feature of frailty[36,189,190] and should be managed by screening for and addressing identified reversible causes. Potentially reversible causes of weight loss can be identified using the comprehensive Meals on Wheels mnemonic[191] (Table 4) and include illness, dementia, medications, swallowing problems, and other such factors that contribute to weight loss and malnutrition.

Protein and caloric supplementation

Caloric and protein supplementation in frail persons with weight loss is conditionally recommended.[192–195] Food fortification (energy dense meals) is recommended foremost, with supplements as a complementary aspect.[196] Notwithstanding this, previous meta-analyses have been unable to ascribe benefits to protein calorie supplementation un-confounded with other treatments.[193,195,197] If nutritional supplementation does improve nutritional status, this improvement may not translate into functional improvement or mortality reduction.[197,198] Unfortunately a major concern of protein supplementation trials in older adults with frailty is that the control group is either nonexistent or significantly more nourished at baseline than the intervention group.[193,195,197,198] Future intervention studies should devise methodology to address this limitation to increase the evidence base behind protein supplementation in older adults with frailty.

Table 4
The Meals on Wheels Mnemonic of Reversible Causes of Weight Loss

Medications
Emotional (depression)
Alcoholism, anorexia tardive, abuse (elder)
Late life paranoia
Swallowing problems
Oral problems
Nosocomial infections, no money (poverty)
Wandering/dementia
Hyperthyroidism, hypercalcemia, hypoadrenalism
Enteric problems (malabsorption)
Eating problems (eg, tremor)
Low salt, low cholesterol diet
Shopping and meal preparation problems, stones (cholecystitis)

Supplementation with Essential Amino Acids (EAAs) is suggested for older people with frailty. EAAs are proteins the body cannot manufacture itself and are, therefore, essential to obtain from dietary intake. They include valine, leucine, isoleucine, lysine, threonine, tryptophan, methionine, phenylalanine, and histidine.[199] Several studies have found that older adults improve in their physical function when supplemented with leucine enriched EAAs.[199,200] For instance, Bauer et al reported that leucine-enriched whey protein increased muscle mass and leg function in older adults with sarcopenia.[200] Leucine is metabolized to β-hydroxy-β-methyl butyrate (HMB) in cells, and it appears that an HMB enriched protein mixture enhances muscle mass and function.[201]

Recommended daily intake for protein

Older adults are likely to need more protein intake than younger adults.[202,203] Current Recommended Daily Intakes (RDIs) for protein intake in older adults varies from 0.8 g/kg body weight (BW) per day[199,203] to 1.0 to 1.2 g/kg BW/day by the Protein needs with Ageing (PROT-AGE) study group,[204] and up to at least 1.2 g/kg BW/d as proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN).[196] ESPEN also recommend that protein intake be increased to 1.2 to 1.5 g/kg BW/d for those with malnutrition. The current upper limit of protein supplementation for older adults is not yet clear due to insufficient studies.[199] When supplementing older adults with high levels of protein, renal function should be monitored,[196,203] and the ESPEN suggest that a protein intake of 0.8 to 1 g/kg body weight per day for patients with acute or chronic kidney failure who are not receiving renal replacement therapy.[196] Also of consideration is that Asia-Pacific populations may show differing responses to protein supplementation compared with European or North American populations, thus, additional clinical trials in this region are encouraged.

Multicomponent interventions

In the Asia-Pacific region, there are emerging clinical trials showing the benefit of combining interventions (physical, nutritional, and cognitive interventions)[205] to manage frailty, although larger scale studies are needed. For example, the benefits of protein supplementation may be enhanced when combined with resistance training.[199] A recent study by Tieland et al[206] found that protein supplementation increased the physical function in older adults with frailty undergoing resistance training. Similarly, physical function and strength improved in older women with sarcopenia after they were supplemented with 3 g protein combined with physical activity (with physical activity alone not affecting strength in this cohort).[207] It is not yet clear whether a combination of physical activity/protein supplementation impacts on muscle mass, with studies reporting different results.[199,206,207]

In Europe, the Sarcopenia and Physical fRailty IN older people multicomponenT Treatment strategies (SPRINTT) project is currently investigating the effect of a multicomponent intervention including structured physical activity, nutritional counselling/dietary intervention, and an information and communication technology intervention. The SPRINTT study is a multicenter, Phase III RCT designed to prevent mobility disability in 1500 older adults with frailty and sarcopenia for 36 months.[208,209] In the Asia-Pacific region, there are very few clinical trials investigating multicomponent interventions in older adults with frailty.

Screening for unintentional weight loss and malnutrition

An adjunct conditional recommendation is that weight loss and malnutrition should be screened for using an accepted nutritional screening tool, such as the Mini Nutritional Assessment (MNA),[210] its short form version (MNA-SF),[211] or the Malnutrition Universal Screening Tool (MUST),[212] among others. These nutritional screening tools are regularly used in the Asia-Pacific region, often with population-specific cut-off points for anthropometric measures.[213–217] Nutritional screening may also identify conditions that can contribute to frailty but which may be not be easily spotted; for instance, sarcopenic obesity (low muscle mass and high body fat). Screening for low appetite may also be beneficial in older adults with frailty.[218]

Recommendation 6: We Conditionally Recommend that Vitamin D Be Prescribed for Older Adults Found to Be Deficient in Vitamin D

Vitamin D is a fat-soluble vitamin crucial for muscle and bone function, among many other physiological roles such as inflammation, metabolism, and blood glucose regulation.[219–222] It is predominantly synthesized in the skin from cholesterol, although dietary sources such as oily fish can contribute up to 10% of vitamin D intake.[220,223] Deficiencies in vitamin D are linked with reduced physical functioning[224,225] frailty development,[226–228] as well as falls and mortality.[226–228] Vitamin D deficiencies are common both in older adults with frailty[226,229–233] and in older populations residing in the Asia Pacific region,[221,228,234–238] although not all studies have found high rates of deficiencies.[239,240]

Sun exposure and vitamin D

Although it is possible to obtain an adequate vitamin D intake via sun exposure alone, this may not occur in older adults because of sun avoidance,[221] disability that limits outdoor exposure (such as residing in residential care),[227] and an ~75% reduced ability to synthesize vitamin D in the skin.[241] To optimize vitamin D intake without being burnt by the sun's harmful ultra violet (UV) rays, it is advised that in winter, older adults go outside in the middle of the day when the UV index is low (UV index l < 3); and in summer, to uncover arms and hands to the sunlight for only a few minutes in the morning or afternoon when the UV index is lower.[242,243] Importantly, vitamin D is bound to a vitamin D binding protein which is lower in darker skinned individuals,[244,245] so sunlight exposure may need to be higher in these individuals to gain adequate levels of vitamin D.[222]

Vitamin D supplementation for older adults with frailty

There are several clinical trials finding that vitamin D supplementation in older adults with vitamin D deficiency reduces likelihood of mortality, falls, and fractures.[1] However, these trials tend to focus on older adults without frailty.[233] Vitamin D supplementation for older adults with frailty remains a topic of much debate in the literature.[3,246,247] If supplements are prescribed, the suggested dosage is between 800 and 1000 IU of vitamin D daily,[248] although this dosage does also depend on an individual's condition, diet, and sunlight exposure.[247] However, there is concern regarding high dosages of vitamin D supplementation, especially in people without vitamin D deficiency, as this may *increase* the risk of falls and fractures.[249–251]

Vitamin D supplementation for older adults in general

When considering older adults in general, there are many meta-analyses and systematic reviews regarding the effectiveness of vitamin D supplementation, with contrasting findings.[246,248,252–254] For instance, Rosendahl-Riise et al[252] and Rejnmark et al[253] both reported that vitamin D supplementation in older adults did not improve muscle strength or mortality risk, respectively, although Rejnmark et al (2012) did observe a mortality reduction effect when vitamin D was combined with calcium supplementation.[253] On the other hand, Muir et al[248] found that supplementation with 800 to 1000 IU vitamin D daily did improve strength and balance in older adults. In addition, a recent Cochrane review reported that vitamin D supplementation decreased the risk of falls in older adults residing in care facilities.[255] There remains a paucity of clinical trials particularly in specific ethnic groups, although one recent trial from China found that long- term vitamin D supplementation did not improve muscle mass or function, at least in older men not deficient in vitamin D at baseline.[256]

Screening for vitamin D

Routine measurement of 25(OH) vitamin D levels cannot be recommended for all populations of older adults with frailty. Darker skinned individuals have lower vitamin D binding protein,[244,245] and, thus, the ability to determine normal vitamin D levels is questionable in persons of Asian or African descent.

Recommendation 7: We Have No Recommendation for the Provision of an Individualized Support and Education Plan for Older Adults with Frailty

Currently, there exists only a limited evidence-base regarding the provision of an individualized support and education plan for older adults with frailty and their caregivers. Although anecdotally and in small-scale studies such programs appear effective,[229] there is a definite need for large-scale, well-designed RCTs to support this recommendation. Notwithstanding this, there are several recent reports highlighting the importance of support and educational plans.[257,258] This support/training can come from communities, home care restorative services, allied health professionals, nursing staff, general practitioners, and geriatricians,[259–261] and should aim to maximize physical function.[260] The specific needs of the older person themselves should also be included in order to promote independence and person-centered care.[258,261]

A healthcare worker can be employed as a health system navigator to facilitate effective integration among healthcare services.[262] Healthcare integration is valuable given the higher need for healthcare services by older adults with frailty, and the barriers they face accessing these healthcare services.[259,262] Multidisciplinary intervention planning involving case management/case conferencing by managing physicians, nurses, and allied health professionals may improve the coordination of care delivery for older adults with frailty, which in turn, may assist in successfully treating frailty.[263] In spite of this positive finding, recent research has reported that compliance to multidisciplinary intervention is low for older people with frailty; although those that do adhere to the intervention may experience improved frailty status and mobility.[264] There is currently little evidence that integrating care services for older adults with frailty does improve individual outcomes,[265–268] although this may be true only in countries with already well-resourced primary care services.[268]

Discussion

This report provides clinical guidelines for the management of frailty in older adults and is based on current scientific evidence combined with an appraisal by international clinical experts in frailty. These guidelines are intended for use by healthcare providers to support their everyday management of older adults with frailty. They are not intended for use in isolation. Rather, it is advised that health professionals discuss with patients and their carers as to the best decisions regarding individualized treatment. It is also imperative for the health professional to recognize that the perceived benefit of any intervention should outweigh any potential harm for the older patient with frailty.

This guidelines document has deliberately been designed to be concise and condensed to ensure uptake and adherence by healthcare providers.[269] In addition, it may not be feasible, practical, or even beneficial for a frail patient to be referred to all treatment strategies outlined in this report. That is, an intervention that may benefit an older adult in the early stages of frailty might not beneficial, or may even be harmful to, an older adult with severe frailty.

Individual practitioners should select the most appropriate interventions consistent with patient preference, accessible resources, and minimization of patient harm.[58,270] The guidelines will also need to be adapted to the local context. For instance, in the Asia-Pacific region, the majority of practitioners may not have the resources to perform a full CGA, and, thus, use of a Rapid Geriatric Assessment may be beneficial.[78]

As a whole, there exists a lack of well-designed clinical trials addressing treatment modalities for frailty. Older adults with frailty are often excluded from clinical trials,[258] which limits the evidence base that clinical guidelines can be developed from. More robust clinical trials of adequate quality for older people with frailty are needed, particularly those focusing on outcomes that are valuable to the older adult themselves, such as functional independence, quality of life, and remaining at home.[260] Such trials are especially needed in the Asia-Pacific region given that most of the evidence-base underpinning frailty management comes from Europe and North America, which may not directly extrapolate to Asia-Pacific populations.

A major limitation of this report is that full systematic reviews were not undertaken for each recommendation. Standardized methods for synthesizing evidence into guidelines were also not adopted by expert panel members. Furthermore, because of the limited-evidence base of clinical trials involving older adults with frailty, caution is advised when developing clinical quality indicators for frailty management processes from the guidelines provided in this article.

Importantly, knowledge in geriatric medicine is constantly progressing, with new assessment techniques, treatment modalities, and technologies developed regularly. As such, evidence-based clinical guidelines for frailty need to be kept regularly updated and revised. It is proposed that regional guideline support committees be formed to help provide regular updates to evidence-based guidelines. These regional committees can also devise setting-specific guidelines for frailty management, including for emergency departments, primary care, oncology, cardiology, and orthopedics. Regular updating of clinical guidelines will ensure that practitioners have the latest evidence-base to guide the management of older adults with frailty. In addition, guidelines for frailty should be linked with clinical case scenarios to disseminate knowledge of its management.

Overall, with the rapid rise in the number of older people globally, it is imperative that frailty be identified and appropriately managed. It is anticipated that these clinical guidelines will improve the recognition of frailty by healthcare professionals and improve the quality of care and outcomes for older persons with frailty.

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