

Singapore Clinical Practice Guidelines For Sarcopenia: Screening, Diagnosis, Management and Prevention

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Abstract

OBJECTIVES: To present the local evidence and final recommendations of the Clinical Practice Guidelines workgroup convened by the Chapter of Geriatricians and the Society for Geriatric Medicine Singapore. The aim is to develop contextualized evidence-based recommendations that facilitate adoption of the Asian Working Group for Sarcopenia (AWGS) 2019 consensus into current practice in Singapore.

METHODS: The workgroup drew upon the AWGS'2019 consensus, updated literature review of Singapore studies till 31 Dec 2020, and evidence from recent systematic reviews. From 40 local studies included for data extraction, we constructed evidence tables organized as: definition and epidemiology; diagnosis and evaluation; and treatment and intervention. Twenty recommendations - case-finding, diagnosis, treatment, prevention, research - were developed, and graded for strength and quality using the GRADE approach. Consensus from an expert panel (N=23) was achieved after two rounds of the modified Delphi process.

RESULTS: The local prevalence of sarcopenia among community-dwelling older adults ranged from 13.6% to 25%. Most studies adopted the AWGS'2019 and AWGS'2014 criteria. Reported case finding tools include SARC-F, calf circumference (CC) and SARC-CalF. Gender-specific AWGS cut-offs for appendicular skeletal mass were used to define low muscle mass. Different protocols and dynamometers were used to assess handgrip strength, whilst gait speed and 5-times chair stand were commonly used to assess physical performance.

RECOMMENDATIONS: We conditionally recommend a case-finding approach in at-risk older adults using validated case-finding tools. Screen-positive individuals should be assessed for 'possible sarcopenia' and underlying causes. For diagnosis, we conditionally recommend using the AWGS'2019 algorithm, and dual-energy X-ray absorptiometry when necessary to determine low lean mass for a confirmatory diagnosis of sarcopenia. For treatment, we strongly recommend resistance-based exercises and conditionally recommend a quality protein-rich diet/protein supplementation, with Vitamin D supplementation for insufficiency (<30 micrograms/L). For prevention, we recommend regular resistance-based physical activity and adequate protein intake ($\geq 1.0\text{g/kg}$ bodyweight). We encourage more research to address local evidence gaps.

Key words: Sarcopenia, guideline, screening, diagnosis, management.

Introduction

Sarcopenia is defined as the age-associated progressive and generalized skeletal muscle disorder that involves loss of muscle mass plus loss of muscle strength and/

or reduced physical performance (1). First defined in 1989 by Rosenberg, using the Greek words 'sarx' and 'penia' to denote the 'poverty of flesh', there is increasing recognition of the adverse health consequences associated with sarcopenia such as falls, functional decline, hospitalization, frailty, increased healthcare costs, and mortality (2). The prevalence of sarcopenia increases with age with a slight male predominance (3). In Asia, using the Asia Working Group for Sarcopenia (AWGS) 2014 criteria for sarcopenia diagnosis, prevalence ranges from 5.5 to 25.7 percent (4). When only larger studies >1000 in sample size are considered, the prevalence estimates become more precise, ranging from 7.3 to 12 percent (5).

Two major milestones contributed to the burgeoning interest in sarcopenia within Asia. Firstly, in 2014, the Asian Working Group for Sarcopenia (AWGS) proposed a diagnostic algorithm based on Asian data which laid the foundation for sarcopenia identification and diagnosis (4). Secondly, sarcopenia was granted an International Classification of Diseases, Tenth Revision diagnosis code (M62.84) in 2016, representing a further step forward in translating sarcopenia into clinical practice (6). Although these developments spurred clinical and research interest in sarcopenia within Asia, most clinicians remain unaware of the condition and the diagnostic tools needed to identify it. This provided the impetus for the AWGS consensus update in 2019, which proposes an algorithm for identifying and diagnosing older adults with or at-risk for sarcopenia, including case-finding and diagnostic protocols to support the management of sarcopenia across different settings of care from the hospital to primary healthcare and community-based preventative services (5). However, it is unclear how the AWGS 2019 consensus can be applied to the unique context of different Asian countries to facilitate translation into clinical practice.

Singapore has one of the most rapidly aging populations in the world, with the proportion aged 65 or older projected to almost double from the current 16% to 28% by the end of the Decade of Healthy Ageing (2020-2030). Although the life expectancy at birth ranks amongst the highest in the world (males: 82.06 years; females: 86.15 years) (7, 8), this is not matched by a similar increase in healthy life expectancy (HALE). Commensurate with the rapidly ageing population in Singapore, the local prevalence of frailty ranges from 5.7% to 6.2% among older adults (9). As an antecedent and important risk factor for physical frailty, sarcopenia is thus

a salient condition of public health concern. However, there is heterogeneity in clinical practice regarding the diagnostic criteria for sarcopenia; tests used for case finding and evaluation of muscle function; the cut-offs for these tests; and how these tests are being performed. Although there are published research studies on sarcopenia in the local population, these have not been systematically examined and summarized (10).

A workgroup was convened by the Chapter of Geriatricians and the Society for Geriatric Medicine Singapore to develop contextualized, evidence-based Clinical Practice Guidelines (CPG), which took into consideration the local evidence as well as the healthcare landscape, to facilitate the adoption of the AWGS 2019 consensus into current practice in Singapore. When developing the guidelines, the focus was to summarize available local evidence and present evidence-based recommendations which can be used by practitioners (namely clinicians and allied health professionals) to guide care in line with patient preferences and priorities. Through this process, we hope to facilitate the adoption of best practices in screening, diagnosis and management of sarcopenia into clinical practice. This paper describes the processes, results of local evidence, and final recommendations of the CPG.

Methods

Guideline development and review process

The guidelines were developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which involved a structured evaluation of the current literature base, followed by the formulation of recommendations (11). Three panels were formed to develop the guidelines:

1. A workgroup comprising geriatricians who have clinical interest and experience in the field of sarcopenia and muscle health. The purpose of the workgroup was to develop and grade the recommendations after evaluation of the evidence base. The workgroup was organized into subgroups looking at the areas of definition and epidemiology; diagnosis and evaluation; and treatment and intervention.
2. An advisory board comprising local honorary members and international experts.
3. An independent external expert panel of practising clinicians comprising Geriatric Medicine specialists (n=12), non-geriatrician specialists (n=4), family physicians (n=3); physiotherapists (n=2), and dietitians (N=2) with representation from the three local healthcare clusters, namely National Healthcare Group (NHG), National University Health System (NUHS) and Singapore Health Services (SingHealth).

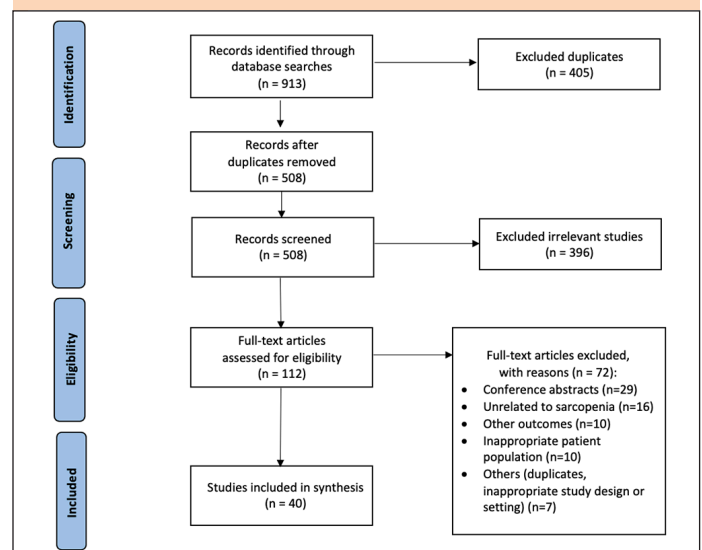
We chose the Delphi method to systematically collect and aggregate the informed judgments of the experts, as it is the most appropriate study design to develop explicit consensus-based criteria where an insufficient quantity or grade of evidence exists to develop evidence-based criteria (12). The

Delphi method maximizes the benefits of using an expert panel while minimizing potential disadvantages by implementing anonymity. It has been used extensively for program planning and the development of research priorities in various areas of medicine (13, 14).

Searching the evidence

Because the AWGS 2019 consensus included studies from East and Southeast Asia till 31 Dec 2018, the workgroup performed an updated literature review of Singapore studies till 31 Dec 2020. We adopted an inclusive approach to achieve the greatest breadth of papers, using the elementary search terms of “sarcopenia”, “muscle mass”, “muscle strength”, “muscle quality”, “physical performance”, “frailty” and “body composition” without specifying categories of research (such as epidemiology or interventional studies). Included studies were: 1) full-text articles in English language only; 2) original research articles inclusive of letters and reviews that met criteria for integrative scholarship (such as systematic, scoping or critical reviews); and 3) Singapore studies of older persons (age>60 years). We excluded editorials, expert opinion, book chapters, protocols and conference proceedings.

Figure 1. PRISMA Flow-Diagram for Study Selection



The search of five major databases (OVID Medline, OVID Embase, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Web of Science) retrieved 913 records, which were reduced to 508 abstracts after de-duplication. Two reviewers independently screened the identified articles for eligibility based on the inclusion and exclusion criteria via title/abstract followed by a full-text screen. Any conflict was resolved by discussion with adjudication by a third reviewer if required. After abstract and full-text screen, 40 studies were finally included for data extraction (Figure 1). This process was independently done by three pairs of reviewers, followed by checks for inconsistencies. Any inconsistencies were rechecked and resolved within the reviewer pair before finalization and inclusion. We organized

Table 1. Epidemiology

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Specific sarcopenia diagnosis used	Summary of findings (Prevalence and risk factors)	Quality (GRADE)
Chew J et al 2019 (24)	Cross-sectional study; Independent community-dwelling older adults (>50 years)	200	67.9 (7.9); Male=63 (31.5%)	NA	<ul style="list-style-type: none"> • 91 (45.5%) met criteria for low RASM • Co-existent frailty with low RASM in 63 (31.5%), 28 (14%) robust with low RASM 	++
Chew J et al 2020 (22)	Longitudinal cohort study; Independent community-dwelling older adults (>50 years)	200	67.9 (7.9); Male=63 (31.5%)	EWGSOP2, AWGS 2014	<ul style="list-style-type: none"> • Sarcopenia prevalence by AWGS: 15.5% • Sarcopenia prevalence by EWGSOP2 - Probable sarcopenia: 21% (HGS), 6.5% (5-STs>15sec), 15.5% (5-STs>12.5sec) - Confirmed sarcopenia: 14.5% (HGS), 4% (5-STs>15sec), 9% (5-STs>12.5sec) - Severe sarcopenia (gait speed<0.8m/s): 1.5% (HGS), 1.5% (5-STs>15sec), 2% (5-STs>12.5sec) - Severe sarcopenia (SPPB<10): 2% (HGS), 2.5% (5-STs>15sec), 3% (5-STs>12.5sec) 	+++
Chew J et al 2020 (77)	Cross-sectional study; Independent community-dwelling older adults (>50 years)	230	67.2 (7.4); Male=63 (27.4%)	AWGS 2019	<ul style="list-style-type: none"> • 27 (11.7%) osteo-sarcopenic (OS), 35 (15.2%) sarcopenic, 36 (15.7%) osteoporotic • Sarcopenia and osteo-sarcopenia (but not osteoporosis only) significantly associated with frailty • Sarcopenia and osteo-sarcopenia are significantly associated with all nutritional parameters (MNA, BMI, WC, CC, MAC); osteoporosis alone associated with MNA, BMI, MAC • Nutrition as mediator of the effect of osteoporosis, sarcopenia and osteo-sarcopenia on frailty, being strongest in osteo-sarcopenia 	++
Chong MS et al 2015 (23)	Cross-sectional study, Combined cohorts; Community-dwelling cohort and community-dwelling MCI and mild-moderate AD from a memory clinic	299	70.8 (8.5); Male=98 (32.8%)	AWGS 2014	<ul style="list-style-type: none"> • Prevalence: 32.2% sarcopenia, 13.4% sarcopenic obesity • Increasing prevalence of sarcopenia from health, MCI, mild AD, moderate AD (24.6%, 37.5%, 47.1%, 60.0%, $p=0.001$) • SO prevalence significantly different across cognitive stages (9.5%, 37.5%, 13.2%, 40%, $p<0.001$) 	++
Chua KY et al 2020 (31)	Prospective cohort study over 2 years; Community-dwelling 2 major Chinese dialect groups – Hokkien and Cantonese	13 789	74 (63-97); Male=5656 (41%)	NA	<ul style="list-style-type: none"> • HGS is inversely associated with a risk of mortality in a dose-dependent manner HR=2.05, 95% CI=1.44-2.90 ($p<0.001$) • TUG is positively associated with mortality in a stepwise manner HR 3.08 (2.17-4.38) ($p<0.001$) • In a Chinese population, HGS and TUG test were strong and independent predictors of short-term mortality 	+++
Fung FY et al 2019 (18)	Longitudinal cohort study over 1 yr; Cognitively intact, community-dwelling, diabetic patients from polyclinic	387	68.3 (5.66); Male=205(53%)	AWGS 2014	<ul style="list-style-type: none"> • Prevalence of sarcopenia with T2DM was 27.4% (3.9% had severe sarcopenia and 30.5% had pre-sarcopenia) • 58% of older patients with T2DM had pre-sarcopenia and sarcopenia. • Age, diabetic nephropathy, hip circumference, multi-morbidity and fewer clinic visits, but not a recent single HBA1c reading, were significantly associated with sarcopenia among patients with T2DM. 	+
Kien AKH et al 2016 (S1)	Cross-sectional study; Community-dwelling; Primary care polyclinic Diagnosed with diabetes mellitus for ≥ 1 year	56	Female: 72(5) Male: 71(4); Male=28 (50%)	NA	<ul style="list-style-type: none"> • Folate levels were significantly correlated with HGS and knee extension strength (with correction for BMI) • Vitamin D, vitamin B12 and homocysteine did not significantly predict muscle strength. Knee extension strength positively correlated with gait measures and negatively correlated with falls in the preceding year (OR=0.89, 95% CI=0.80–0.98 and OR=0.12, 95% CI=0.02–0.92, respectively) 	+
Lau S et al 2020 (27)	Cross-sectional; Cognitively intact, community-dwelling	230	67.2 (7.4); Male=63 (27.4%)	AWGS 2019 for 'possible sarcopenia'	<ul style="list-style-type: none"> • Prevalence of malnutrition risk were: 5.7% • Malnutrition risk was associated with 5-STs≥ 12s (OR=2.18, 95% CI=1.09-4.38) and SPPB≤ 11 (OR=3.00, 95%CI=1.30-6.94), but not low handgrip strength (OR=1.14, 95%CI=0.58-2.25) 	++

Table 1 (continued). Epidemiology

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Specific sarcopenia diagnosis used	Summary of findings (Prevalence and risk factors)	Quality (GRADE)
Lim JP et al 2015 (S3)	Cross-sectional; Cognitively intact and community-dwelling	143	68.0 (8.2); Male=44 (30.8%)	AWGS 2014	<ul style="list-style-type: none"> • SO groups had the lowest appendicular lean mass, highest percentage of body fat, and lowest performance scores on the SPPB and grip strength. 	++
Lim JP et al 2020 (32)	Prospective cohort; Cognitively intact, community-dwelling	200	≥50; Male=136 (68.0%)	AWGS 2014	<ul style="list-style-type: none"> • Prevalence of low HGS and sarcopenia incorporating HGSave criterion is 40% and 33% respectively, whereas that of HGSmax criterion is 21% and 19.5% respectively. 	++
Lim WS et al 2020 (34)	Cross-sectional; Cognitively intact, community-dwelling	230	67.2 (7.4); Male=63 (27.4%)	AWGS 2019	<ul style="list-style-type: none"> • Prevalence of sarcopenia: 26.9% Men: 38.1%; Women 22.8% • Prevalence of SO: 12.2% Men: 6.3%; Women: 14.4% 	++
Lu Y et al 2020 (40)	Cross-sectional; Community-dwelling	189	73.2 (5.3); Male=70 (37.0%)	AWGS 2014	<ul style="list-style-type: none"> • Malnutrition was associated with sarcopenia. • Sarcopenic elderly showed lower body mass index and high-density lipoproteins. 	++
Malhotra R et al 2020 (47)	Cross-sectional population study; Community-dwelling	Dataset 1:4446 (baseline HGS with mortality) Dataset 2:2673 (annual change in HGS)	Dataset 1: 69.6(7.4) Dataset 2: 69.1(6.9) Dataset 1: Male=1009 (45.3%) Dataset 2: Male=1212 (45.4%)	NA	<ul style="list-style-type: none"> • Baseline HGS 21.2kg (dataset1), 21.7kg (dataset 2) • HGS declined by 0.4kg (on average) annually • Baseline HGS: likelihood of mortality lower by 4% (HR=0.96 95% CI=0.94–0.97) for each kg increase in baseline HGS (adjusted model) • Annual change in HGS: likelihood of mortality lower by 13% (HR=0.87, 95% CI=0.82–0.93) for each kg increase in baseline HGS (adjusted model) 	++
Merchant RA et al 2020 (45)	Cross-sectional study; Community-dwelling	509	73(8); Male=101 (19.8%)	AWGS 2019	<ul style="list-style-type: none"> • Prevalence of sarcopenia 5% 	++
Merchant RA et al 2020 (78)	Cross-sectional Study; Primary care setting	2589	73.1(6.5); Male=1226 (47.4%)	AWGS 2019	<ul style="list-style-type: none"> • Prevalence of sarcopenia is 15.4% (n=399) overall. Prevalence amongst male participants was 9.6% (n=118), women 20.6% (n=280). • Amongst SARC-F domains: <ul style="list-style-type: none"> - Difficulty carrying 4.5 kg of weight: 25% - Difficulty walking across the room: more women (17.3%) than men (9.9%) - Difficulty transferring from a chair or bed: 33.2% - Difficulty climbing 10 flights of stairs: 31.9% 	++
Merchant RA et al 2020 (26)	Cross-sectional study; Ambulant, cognitively intact, community-dwelling Exclusion: cMMSE ≤18, history of dementia	493	73(8); Male=102 (20.7%)	AWGS 2019	<ul style="list-style-type: none"> • Prevalence of sarcopenia 6.1% overall. • Prevalence of sarcopenia amongst FOF+FAR (15.3%) was 12 times higher than no FOF (1.3%) and 4 times higher than those with FOF only (3.8%). • Significant differences between FOF, FOF+FAR and all five components of SARC-F. • Multi-variate analysis, sarcopenia is associated with OR=8.13 of FOF+FAR (95% CI= 1.52-43.41), compared to non-sarcopenia 	++
Pang BWJ et al 2020 (39)	Cross sectional; Community-dwelling	535 (>60yrs: 297)	58.5(18.8); Male=221 (41.3%)	AWGS 2019	<ul style="list-style-type: none"> • Prevalence of SO by different obesity definitions: WC – 7.6%; % body fat – 5.1%; Fat Mass Index – 2.7%; BMI – 0.4% • SO was significantly associated with SPPB only in the Fat Mass Index model (p<0.05). 	++
Pang BWJ et al 2020 (20)	Cross-sectional; Community-dwelling	535 (>60yrs: 297)	58.5(18.8); Male=221 (41.3%)	AWGS 2014, AWGS 2019	<ul style="list-style-type: none"> • Comparison between AWGS 2019 and AWGS 2014 definitions: <ul style="list-style-type: none"> - Low HGS: 9.0% vs 7.3% - Slow gait speed: 24.0% vs 4.1% • Population-adjusted sarcopenia prevalence: <ul style="list-style-type: none"> - Whole sample: 13.6% (males 13.0%, females 14.2%) - ≥60years: 32.2% (males 33.7%, females 30.9%) • Population-adjusted sarcopenia prevalence: AWGS 2019>AWGS 2014 • Age, sex, marital status, alcoholism, physical activity, body mass index, WC, and global cognition were associated with sarcopenia (P <0.05). 	+

Table 1 (continued). Epidemiology

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Specific sarcopenia diagnosis used	Summary of findings (Prevalence and risk factors)	Quality (GRADE)
Tan LF et al 2017 (19)	Cross-sectional study Patients attending medical specialist outpatient clinics	115	76.6 (6.5); Male=55 (47.8%)	SARC-F	<ul style="list-style-type: none"> • Prevalence at medical outpatient clinic: 44.3% sarcopenic, 27.0% frail; 23.5% both frail and sarcopenic • 87.1% of frail patients were sarcopenic, whereas 47.1% of sarcopenic patients were frail. • Sarcopenia and frailty were associated with a higher Charlson comorbidity index, higher likelihood of requiring a caregiver, more medical specialty follow-ups, polypharmacy, > 2 hospital admissions within a year, a higher number of falls and falls with serious consequences. • Self-rated health excellent: 50.0% robust vs 19.6% sarcopenic, 9.7% frail and 3.7% sarcopenic and frail 	+
Tan VMH et al 2020 (28)	Cross-sectional; Community-dwelling	541	58.6 (18.7); Male=227 (42.1%)	AWGS 2019	<ul style="list-style-type: none"> • Population-adjusted prevalence: nutritional risk, 18.5%; malnourished, 0.1% • 35% at nutritional risk were sarcopenic. Malnourished participants were all sarcopenic (100%, N=2); amongst those with sarcopenia, 27.0% (N=37) were at nutritional risk/malnourished. • Nutritional risk/malnourished was associated with sarcopenia (OR=2.31, 95% CI=1.22-4.37). • Favourable MNA parameter scores on food intake and BMI were positively associated with greater muscle mass and HGS (p<0.05). 	++
Tay L et al 2015 (21)	Cross-sectional; Community-dwelling	200	67.9 (7.9); Male=63 (31.5%)	AWGS 2014	<ul style="list-style-type: none"> • Prevalence of sarcopenia: 24.8 % in women and 25.4 % in men • Factors associated with sarcopenia: <ul style="list-style-type: none"> - Age in both genders; - malnutrition in women (OR=5.71, 95% CI=1.13–28.84.44); - higher serum myostatin in men (OR=1.11, 1.00–1.24), - lower IGF-1 in women (OR=0.99, 95% CI=0.98–1.00) 	++
Tey SL et al 2020 (S4)	Cross-sectional study; Community-dwelling	400	71.2(5.3); Male=183 (45.7%)	AWGS 2014	<ul style="list-style-type: none"> • Prevalence of low ASMI: 20.6% (15.5% men and 24.9% women). • Factors associated with lower ASMI were female gender, age, lower BMI and smaller calf circumference. 	++

AD: Alzheimer's dementia; ASMI: appendicular skeletal muscle mass/height²; CC: calf circumference; cMMSE: Chinese Mini Mental State Examination; EAAs: essential amino acids; FOF: fear of falling; FAR: fear-related activity restriction; HGS: hand grip strength; HGSave: hand grip strength average; HGSmax: hand grip strength maximum IGF-1: insulin-like growth factor 1; IMAT: Inter-muscular adipose tissue; MAC: mid-arm circumference; MCI: mild cognitive impairment; MCP-1: Monocyte chemoattractant protein 1; MNA: Mini Nutritional Assessment; RASM: relative appendicular skeletal muscle mass; 5-STST: 5-time sit-to-stand test; SO: sarcopenic obesity; SPPB: short physical performance battery; TUG: timed up and go; WC: waist circumference.

the evidence tables under the headings of definition and epidemiology; diagnosis and evaluation; and treatment and intervention (Tables 1 & 2, Appendix 1). Due to paucity of local evidence from intervention studies, we conducted a supplementary search of randomized controlled trials (RCTs) and systematic reviews specifically addressing sarcopenia as a diagnostic entity up to 30 June 2021 (Appendix 2).

Grading the Evidence

Next, the workgroup developed twenty recommendations for case detection, diagnosis, treatment and prevention; and research of sarcopenia in older persons. The workgroup graded the strength and quality of each recommendation. In line with the GRADE Evidence to Decision (EtD) framework, the strength of evidence was graded as 'strong', 'conditional' or 'no recommendation' (15). A strong recommendation indicated that the desirable clinical benefits of the intervention strongly outweighed the risk of undesirable outcomes (16).

For a conditional (weak) recommendation, the treatment had considerable undesirable outcomes (such as patient burden, unwanted side effects, and risk of adverse clinical outcomes), which undermined the health benefits, such that health practitioners may or may not choose this treatment modality. When insufficient evidence existed to support any recommendation, a statement of "no recommendation" was reported. Quality refers to the overall certainty of the evidence for the effect. Based on the factors of imprecision, risk of bias, inconsistency, publication bias and indirectness (11, 15), the workgroup graded evidence certainty as follows: 1) High: Further research is very unlikely to change confidence in the estimate of effect; 2) Moderate: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; 3) Low: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate; and 4) Very Low: Any estimate of effect is very uncertain.

Table 2. Diagnosis and evaluation of sarcopenia and sarcopenia-associated conditions

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Sarcopenia diagnosis criteria & Muscle mass measurement	Summary of findings (Measures used and outcomes)	Quality (GRADE)
Chew J et al 2020 (22)	Longitudinal cohort study; Independent community-dwelling older adults	200	67.9 (7.9); Male =63 (31.5%)	EWGSOP2, AWGS 2014 DXA (Discovery™, APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> Only 5-STs >12.5sec independently predicted incident frailty at 2-year HGS, 5-STs>15sec and 5-STs >12.5sec all predict poor physical performance HGS: hydraulic hand dynamometer (North Coast™). Two trials of HGS for each hand were obtained and the highest value was used. 	+++
Chong MS et al 2015 (23)	Cross-sectional study Combined cohorts: community-dwelling cohort and community-dwelling MCI and mild-moderate AD from a specialty memory clinic	299	70.8 (8.5); Male =98 (32.8%)	AWGS 2014 DXA (Discovery™, APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> SO independently increased odds for frailty (OR=4.80, 95% CI 1.78-12.94) in the overall cohort and among cognitively healthy older adults (OR=15.55, 95% CI=1.63-148.42) 	++
Keng BMH et al 2019 (41)	Cross-sectional study; Community-dwelling participants from existing cohort study (cardiac aging study who were from the Singapore Chinese health study).	378	72 (4.4); Male=244 (64.6%)	AWGS 2014 BIA (InBody 370, Biospace), ASM/ht ²	<ul style="list-style-type: none"> Sarcopenic participants without clinical cardiovascular disease had smaller LV sizes, lower posterior wall end-diastole, lower LV wall end-systole, lower LV mass, lower LA volume Skeletal muscle is associated with LV diameter, LA diameter, LA volume, LV outflow tract size, aortic diameter, LA diameter, LA volume (After adjusting for age and DM) A positive linear relationship was observed between LV mass and HGS 	+
Khor EQE et al 2020 (43)	Cross-sectional study; Cognitively intact, community-dwelling, functionally independent older adults >50 years	200	67.9 (7.9); Male=63 (31.5%)	AWGS 2014 DXA (Discovery™, APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> Inter-definitional agreement lowest between BMI and WC ($\kappa=0.364$), and at best moderate between FM% and WC ($\kappa=0.583$). Only SO defined by WC performed the worst amongst body composition phenotypes in handgrip strength, gait speed and SPPB (all $p<0.01$) SO was associated with decreased SPPB scores ($\beta=-0.261$, $p=0.001$) only for the WC definition 	+++
Lim JY et al 2020 (42)	Nested cross-sectional study (prefrail participants recruited for interventional study); Cognitively intact, pre-frail, community-dwelling, fit adults (ambulant > 100m independently)	75	73 (6); Male=42 (56%)	AWGS 2019 BIA (Inbody S10), ASM/ht ²	<ul style="list-style-type: none"> Using SARC-F for case finding reduced the overall prevalence of sarcopenia to 4.0%, possible sarcopenia to 12.0% and severe sarcopenia to 4.0%. Using SARC-F for case finding underestimated prevalence in this group by 75% The addition of CC to SARC-F (SARC-CalF) did improve the positive agreement percentage from 33% to 42%. Positive percentage agreement of case finding criteria of SARC-F, SARC-CalF and CC for sarcopenia was 33%, 42% and 58% respectively CC had the highest positive percentage agreement of 58%, which was in keeping with previous studies that CC is a good estimate of appendicular skeletal muscle mass, functional status and a good indicator for sarcopenia 	+
Lim JP et al 2020 (32)	Prospective cohort; Cognitively intact, community-dwelling	200	≥ 50 ; Male=136 (68.0%)	AWGS 2014 DXA (Discovery™, APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> HGS was measured using a hydraulic hand dynamometer (North Coast Medical, Inc, Gilroy, CA, USA). Two trials were obtained for each hand, and the average and maximal values were recorded. Moderate agreement between the 2 HGS criteria for sarcopenia diagnosis ($\kappa=0.604$) and poorer agreement for low HGS ($\kappa=0.570$). At 2 years, only low HGSmax was significantly associated with low SPPB (adjusted OR=3.91, 95% CI=1.24 – 12.33). 	++
Lim WS et al 2019 (35)	Cross-sectional; Cognitively intact, community-dwelling	193	67.9 (7.9); Male=60 (31.1%)	AWGS 2014 DXA (Discovery™, APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> Adding CC to SARC-F (SARC-CalF) improves diagnostic performance by increasing sensitivity (and not specificity) 	+++

Table 2 (continued). Diagnosis and evaluation of sarcopenia and sarcopenia-associated conditions

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Sarcopenia diagnosis criteria & Muscle mass measurement	Summary of findings (Measures used and outcomes)	Quality (GRADE)
Lim WS et al 2020 (33)	Cross-sectional; Cognitively intact, community-dwelling	230	67.2 (7.4); Male=63 (27.4%)	AWGS 2019 DXA (Discovery™ APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> • SARC-CalF had better diagnostic accuracy than SARC-F for overall sarcopenia diagnosis. • When stratified by obesity status, SARC-F had poor diagnostic accuracy (AUC<0.7) in both sarcopenic non-obese and SO, whereas SARC-CalF had moderate diagnostic accuracy (AUC<0.7) in sarcopenic non-obese, albeit remained poor in SO. 	++
Lim WS et al 2020 (34)	Cross-sectional; Cognitively intact, community-dwelling	230	67.2 (7.4); Male=63 (27.4%)	AWGS 2019 DXA (Discovery™ APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> • Compared with SARC-F, CC had better diagnostic performance for sarcopenia diagnosis - Better diagnostic performance in sarcopenic non-obese (AUC: 0.799 vs 0.539, P < 0.001) compared with SO (AUC: 0.657 vs 0.610, p=0.527). • In sex stratified analyses, CC performed worse in female participants (AUC: 0.699 vs 0.853, p=0.023), especially in the SO subgroup (AUC: 0.621 vs 0.804, p=0.059). 	+++
Lim WS et al 2018 (36)	Cross-sectional; Cognitively intact, community-dwelling	200	67.8 (2.2); Male=137 (31.5%)	AWGS 2014 DXA (Discovery™ APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> • Factor analysis yielded an optimal 2-factor structure comprising “muscle function” and “muscle performance,” accounting for 50.35% and 52.67% of total variance of SARCF-strength and SARCF-slowness, respectively • The “falls” item (loading <0.3) did not load onto either of the factors for both SARC-F versions. • Both scales had poor internal consistency (Cronbach alpha: SARCF-strength: 0.093, SARCF-slowness: 0.244), which correspondingly improved if the “falls” item were deleted. 	+++
Lu Y et al 2020 (40)	Cross-sectional population study; Community-dwelling	189	73.2 (5.3); Male=70 (37.0%)	AWGS 2014 DXA (not specified), ASM/ht ²	<ul style="list-style-type: none"> • Knee extension strength was used to measure muscle strength. • Cutoff values for low lower limb strength were ≤18 kg for men and ≤16 kg for women. 	++
Malhotra R et al 2020 (47)	Cross-sectional population study; Community-dwelling	Dataset 1:4446 (baseline HGS with mortality) Dataset 2:2673 (annual change in HGS)	Dataset 1: 69.6(7.4) Dataset 2: 69.1(6.9) Male=1009 (45.3%) Dataset 2: Male=1212 (45.4%)	NA	<ul style="list-style-type: none"> • HGS was measured using a Smedley spring-type dynamometer [Hand Grip Meter, No. 6103 (75 kg); TANITA, Tokyo, Japan]; standing with arms hanging by side, elbows fully extended; average of the 2 HGS measurements for each hand was assigned as the HGS value for that hand 	++
Malhotra R et al 2016 (48)	Cross-sectional observational study; Community-dwelling	2664	60 to 89 years; Male=184 (11.1%)	NA	<ul style="list-style-type: none"> • Mean HGS stratified by sex/hand dominance decreased with age • Mean HGS higher for men vs women and dominant vs non-dominant hand • Specific elderly characteristics influencing normative HGS values -Height had a consistent positive association with the higher (20th and 50th) percentile values of HGS for both men and women -Influence of ethnicity largely observed in the higher percentile values for men. Indian ethnicity lowered these values • Mean HGS for elderly Singaporeans is lower than Western counterpart and lower than counterparts in other Asian populations (Japan/Taiwan) -Weight was positively associated with HGS at the 5th percentile for men but not women; but had positive association with HGS at the 50th percentile for women 	++

Table 2 (continued). Diagnosis and evaluation of sarcopenia and sarcopenia-associated conditions

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Sarcopenia diagnosis criteria & Muscle mass measurement	Summary of findings (Measures used and outcomes)	Quality (GRADE)
Merchant RA et al 2020 (46)	Cross-sectional population study; Community-dwelling	722	71(5); Male=325 (45%)	NA	<ul style="list-style-type: none"> • HGS measured using measured three times in a seated position with each arm flexed at a 90° angle using a digital dynamometer (A5401, Takei Scientific Instruments Co., Ltd, Japan) • Maximum HGS reading for the dominant hand was used in analyses • Mean HGS: 22.5 (6.9) total cohort; 22.8(6.7) no MetS; 22.1(2.1) with MetS • No significant difference in HGS between the MetS and no-MetS -Significant differences between the 2 groups when HGS was adjusted for BMI and BWT, respectively -HGS adjusted for BMI or BWT was a better predictor for MetS and its components than HGS alone -HGS adjusted for BMI or BWT revealed a significantly better dose–response relationship with adverse outcomes including ADL assistance and cognition -Adjusting muscle strength for BWT or BMI was a better predictor of functional performance, MetS, dyslipidemia, cardiovascular risks, or prediabetes 	++
Merchant RA et al 2020 (45)	Cross-sectional study; community-dwelling	509	73(8); Male=101 (19.8%)	NA	<ul style="list-style-type: none"> • HGS determined using hand-held dynamometer (Jamar) and maximum HGS was taken from two trials participant's dominant hand • GS was assessed over 10m with 1m each for acceleration and deceleration on levelled ground 	++
Merchant RA et al 2016 (52)	Cross-sectional study; Community-dwelling Exclusion: Chronic obstructive pulmonary disease, presence of cardiac pacemakers, on steroid or growth hormones Reference group: 20 male adults between 21 to 50 years	90	66-70 years;Male=41 (45.6%)	NA	<ul style="list-style-type: none"> • GS: based on 6-minute walk test (cut off <1.0m/s), using walking speed • HGS: using hand dynamometer (<26kg) (Using AWGS cut-offs) • Mean GS in patients -CSHA1-2: 1.42 (SD0.25) m/s, -CSHA3: 1.43 (0.23) m/s, -CSHA4 1.27(0.33) m/s. -Mean hand grip strength for -CSHA 1-2: 28.9(SD 5.93)kg, -CSHA3: 29.88(SD 5.11)kg, -CSHA4: 29.62(SD 4.85)kg 	+
Merchant RA et al 2020 (26)	Cross-sectional study; Ambulant, cognitively intact, community-dwelling Exclusion: cMMSE ≤18, history of dementia	493	73(8); Male=102 (20.7%)	AWGS 2019 (SARC-F) No muscle mass measurements	<ul style="list-style-type: none"> • GS: Usual walking speed, 10m gait speed, with 1m at both ends of the course for initial acceleration and terminal deceleration. Maximum GS of two trials used. Cut-off: <1.0m/s. • HGS: Jamar hand-held dynamometer. Maximum HGS taken from 2 trials of dominant hand. Low HGS: <28kg for men and <18kg for women 	++
Ong HL et al 2017 (49)	Cross-sectional study; Right-handed, cognitively intact, community-dwelling Disproportionate stratified sampling design used with over-sampling of older adults and Malay and Indian ethnic groups	2043	68.8;Male=934 (45.7%)	NA	<ul style="list-style-type: none"> • HGS -measured with Jamar Plus Digital Hand Dynamometer-Average of 2 handgrip attempts over dominant hand-As per American Society of Hand Therapist's (ASHT) recommendation-taken seated, shoulder adducted and neutrally rotated, elbow flexed at 90deg with forearm in neutral position HGS in 60-64 age group: Males 31.1 kg, females 18.2kg; 85years+: Males 18.5kg, females 12.4kg • HGS in Malay and Indian participants were significantly lower than in Chinese after adjustment for other sociodemographic attributes. • Mean HGS amongst Singapore older adults were relatively lower compared to Western and other Asian countries except for Taiwan. • US and UK had the highest mean HGS followed by Japan, Malaysia, Hong Kong, Singapore and Taiwan. (NB. Type of dynamometer, handgrip protocols widely varied across studies) 	++

Table 2 (continued). Diagnosis and evaluation of sarcopenia and sarcopenia-associated conditions

Author (year)	Study design and study setting	Sample size	Age (SD) & gender	Sarcopenia diagnosis criteria & Muscle mass measurement	Summary of findings (Measures used and outcomes)	Quality (GRADE)
Pang BWJ et al 2020 (20)	Cross-sectional; Community-dwelling	535	58.5(18.8); Male=221 (41.3%)	AWGS 2014, AWGS 2019 DXA (Discovery WI, Hologic) ASM/Ht ²	<ul style="list-style-type: none"> Cutoffs using young adult reference: <ol style="list-style-type: none"> Low appendicular lean mass index - Men: 5.28 kg/m²; Women: 3.69 kg/m² (lower than AWGS 2019 cut-off) Low handgrip strength - Men: 27.9 kg/m²; Women: 16.7 kg/m² (close to AWGS 2019 cutoff) Slow gait speed - 0.82 m/s (lower than AWGS 2019 cut-off) 	++
Pang BWJ et al 2021 (39)	Cross sectional; Community-dwelling	535	58.5 (18.8); Male=221 (41.3%)	AWGS 2019 DXA (Discovery WI, Hologic) ASM/Ht ²	<ul style="list-style-type: none"> SO was significantly associated with SPPB only in the Fat Mass Index model (p<0.05), and total variance explained by different regression models was highest for Fat Mass Index model. 	++
Woo J et al 2017 (44)	Cross-sectional study; Community-dwelling Not physically or mentally incapacitated Predominantly Chinese (89.6%); Malay & Indians (10.4%)	1002	3 age groups: 65–74, 75–84, 85+ Male=393 (39.3%)	NA	<ul style="list-style-type: none"> There was considerable variation in BMI, appendicular skeletal mass index, HGS, and GS between different Asian ethnic groups, and between same ethnic groups living in different geographic locations. Differences in mean values were greater between the Asian groups compared with Caucasians Comparison of ASM/ht² between Asian groups was limited by the use of different instruments A universal definition of sarcopenia that depends on absolute measurements may not be applicable to all ethnic groups and different geographic locations. 	++
Yang YX et al 2017 (37)	Cross-sectional study; Cognitively intact, community-dwelling	196	67.9(7.9); Male=58 (32.7%)	AWGS 2014 DXA (Discovery™ APEX 13.3; Hologic), ASM/ht ²	<ul style="list-style-type: none"> Correlation between CSA and volume were significantly high (p<0.001) for all components of muscle (0.907), SF (0.963), and IMF (0.939). Thigh CSA and volume both correlated significantly with a clinical diagnosis of normal, obesity, sarcopenia, and SO (p<0.03) 	++

ASM/ht²: Appendicular skeletal muscle mass/height²; BIA: Bioelectrical Impedance Analysis; BMI: body mass index; BWT: body weight; CC: calf circumference; CHSA-CFS: Canadian Study for Health and Ageing Clinical Frailty Scale; CSA: cross-sectional area; DXA: dual-energy X-ray absorptiometry; FM%: fat mass percentage; GS: gait speed; IMF: intermuscular fat; HGS: Hand grip strength; LA: left atrium; LV: left ventricle; MetS: metabolic syndrome; SF: subcutaneous fat; 5-STs: 5-time sit-to-stand test; SO: sarcopenic obesity; SPPB: short physical performance battery; WC: waist circumference.

Modified Delphi Process

The workgroup adopted a modified Delphi methodology to achieve expert consensus on the recommendations. The survey was electronically administered to the panel members, and recommendations were rated on a 5-point Likert scale, with 1 being “strongly disagree” to 5 being “strongly agree”. Panel members could additionally furnish comments for each recommendation if necessary. The minimal response rate for each round was defined as >70% and the consensus threshold was defined a priori as ≥75% ‘agree’ or ‘strongly agree’ responses (4 or 5 on the Likert Scale) for all recommendations (12, 17). In Round 1, the response rate was 95.7% (n=22). Nineteen (95%) recommendations fulfilled the consensus threshold level of 75% or more. The single recommendation which failed to achieve consensus had 54.6% “agree” or “strongly agree” responses. In Round 2, we presented three recommendations which were modified based on the comments gathered from Round 1. One did not achieve consensus, whereas the remaining two which achieved consensus were modified for clarity. The response rate was 100% (n=23). All three recommendations met the threshold for consensus (range: 78.3 to 100%). In summary, all twenty recommendations achieved consensus after two rounds of the modified Delphi process.

Local Evidence (Singapore)

Epidemiology

Prevalence of sarcopenia in local studies

The local prevalence of sarcopenia ranged from 6.1% to 44.3%, reflecting differences in study setting, sarcopenia criteria, and cut-offs. The prevalence of sarcopenia in primary care and specialist outpatient clinics was 27.4% (18) and 44.3% (19), respectively. Among healthy community-dwelling older adults, the reported prevalence ranged from 13.6% (20) to 25% (21).

Most studies adopted AWGS 2019 (N=9) and AWGS 2014 (N=10), with one study referencing the EWGSOP2 criteria. The Yishun study observed higher sarcopenia prevalence when applying AWGS 2019 compared to AWGS 2014 [4] and EWGSOP2 in adults >60 years old. Separately, different muscle strength definitions and cut-offs within the EWGSOP2 algorithm affected sarcopenia prevalence - 14.5% for low handgrip strength, 4% for 5-time sit-to-stand test (5-STs) >15s, and 9% for 5-STs >12s (22).

Factors associated with sarcopenia and sarcopenia-related conditions

Factors significantly associated with sarcopenia include female gender, older age (18) and medical co-morbidities (19) – specifically diabetes mellitus, diabetic nephropathy, stroke disease, and cognitive impairment (23). Sarcopenia was also associated with physical frailty (24), social frailty (25), low physical activity (20), and falls. A bi-directional relationship between falls and sarcopenia was suggested, with patients who had fallen and developed a fear of falling (FOF) and fall-associated activity restriction (FAR) being 12 times more likely to be sarcopenic than those without FOF and FAR (26). Risk of malnutrition (identified using the Mini Nutritional Assessment and Simplified Nutritional Appetite Questionnaire) was another risk factor amongst community-dwelling older adults (27, 28). The local prevalence of being at-risk of malnutrition or malnourished as assessed using the Mini Nutrition Assessment-Short Form (MNA-SF) ranged from 18-28% among community-dwelling older Singaporeans (21, 29, 30). Taken together, these results highlight a high-risk group in which case-finding and early intervention for sarcopenia may be beneficial.

Adverse outcomes associated with sarcopenia and sarcopenia-related conditions

One study found that handgrip strength (HGS) predicted mortality risk at 2 years in a dose-dependent manner (HR 2.05, 95%CI 1.44-2.90) (31). Another study reported that low HGS predicted poor physical performance measured by Short Physical Performance Battery (SPPB) at 2 years (32).

Diagnosis and Evaluation

Case-finding

SARC-F has low-moderate sensitivity and moderate-high specificity for case detection in the community setting (33). When stratified by obesity status, SARC-F had poor diagnostic accuracy (AUC<0.7) in both non-obese sarcopenia and sarcopenic obesity (34). A small study suggested that calf circumference (CC) could provide a reasonable estimate of muscle mass for case finding in the community (35). Similarly, another local study affirmed that CC performed better for sarcopenia diagnosis than SARC-F, particularly in non-obese sarcopenia (34). When CC was added to SARC-F (SARC-CalF), the overall sarcopenia diagnostic performance improved with increased sensitivity but not specificity (35).

Muscle Mass Measurement

Muscle mass is assessed by summing fat-free lean mass in the four limbs to derive the appendicular skeletal mass (ASM). Most studies measured ASM using whole-body dual-energy X-ray absorptiometry (DXA) (DiscoveryTM APEX 13.3 (22,

23, 32–37); Discovery WI (38, 39); not specified (40)), while only two studies used multi-frequency bioelectrical impedance analyzer (BIA) (InBody 370 (41); InBody S10 (42)). In all studies, ASM was standardized using height square (ASM/ht²) (22, 23, 32–36, 38–43) to derive the relative appendicular skeletal mass index (ASMI). Magnetic resonance imaging was used in only one study, which reported that the cross-sectional area and volume of thigh muscle was significantly lower in sarcopenia and sarcopenic obesity (37).

Most studies adopted gender-specific AWGS DXA cut-offs (males <7.0 kg/m², female <5.4kg/m²) to define low muscle mass (32–34, 39, 40). There is a lack of locally validated norms for ASMI. A report which compared ethnic and geographic variations in muscle mass for different Asian populations did not report any corresponding figures for Singapore (44). Although the Yishun Study proposed DXA cut-offs for ASMI (males <5.28 kg/m², females <3.69 kg/m²) by subtracting two standard deviations from the reference group mean, the use of young adults (21-40 years of age) as a reference may limit its generalizability (38).

Muscle Strength

While HGS was most commonly used as a measure of muscle strength, the measurement protocols were variable across local studies. Reported methods included the highest reading of two (26, 45) or three trials (46) of the dominant hand, the highest value of two trials for each hand (22, 38, 39), average of two measurements of each hand (23, 47–50) or the average of the highest readings of both hands (41). The devices used most often to measure HGS are the hydraulic hand dynamometer (Jamar, North Coast), followed by spring type (Smedley) and digital dynamometer (Takei). Only one study reported the use of knee extension strength (KES) to measure quadriceps strength in the working diagnosis of sarcopenia (40). KES was measured using the Lord's strap and strain gauge with the cut-off values of ≤18 kg for men and ≤16 kg for women based on a Thai study (51).

Physical Performance

A wide range of physical performance tests were used, with usual gait speed being the most frequently used test. Although AWGS 2019 recommends 6-m walk, gait speed in the local studies were measured with different protocols, including 10-m walk (45) with 1m each for acceleration and deceleration on level ground and the 6-m walk test (52) (cut off <1.0m/s). Other tests included the 5-STs (22) and SPPB (32, 39, 43). 5-STs >12.5s predicted poor physical performance and frailty incidence at 2 years (22).

Local interventional studies for Sarcopenia

We found four interventional studies for sarcopenia – nutritional intervention only (N=1) (53), exercise only (N=1) (54), and multi-domain lifestyle interventions (N=2). Only one study used specific criteria for sarcopenia diagnosis (AWGS 2014) (55). In this study, amongst community-dwelling prefrail

or frail older persons with sarcopenia, multi-domain lifestyle interventions (physical exercise, nutritional enhancement, cognitive training, combined treatment, and standard care) were shown to be associated with 27.2% and 26.1% reduction in sarcopenia prevalence at 3 months and 6 months respectively. The other study with multi-domain intervention found beneficial effects of the combined intervention in the physical frailty domain of energy (56). In the study with nutritional intervention only, participants who consumed the oral nutritional supplement containing beta-hydroxy-beta-methylbutyrate (HMB) had higher HGS and greater calf and mid-arm circumference at Day 90 or 180, compared to placebo (53). Similarly, in the study with exercise intervention only, HGS, knee extension strength, and fall risk scores improved in the intervention group (55).

Recommendations

The final recommendations are summarized in Table 3.

Case Finding

1. We recommend a case-finding instead of a universal screening approach for sarcopenia. (Grade: conditional recommendation, low certainty of evidence)

Although sarcopenia often remains unrecognized, universal screening at the population level is not recommended because screening tools have diagnostic limitations and the effect of such screening on relevant outcomes is unproven (57). The cost-effectiveness of a screening program at the population level has also not been established, and issues such as resources and patient accessibility to screening services also need to be considered (1). Therefore, the workgroup conditionally recommends a case-finding approach for at-risk cases. This approach involves looking for sarcopenia when relevant symptoms such as difficulties or decline in carrying out daily life activities, unintentional weight loss, low mood, cognitive impairment, and repeated falls are reported, or in the presence of relevant co-morbidities. Case finding is particularly relevant in care settings where a higher prevalence of sarcopenia might be expected, such as admission to hospital, rehabilitation settings, or nursing homes (2).

2. We recommend case-finding for sarcopenia in older adults aged 65 years and above, especially in high-risk populations with relevant co-morbidities (for instance, chronic lung, kidney, liver or heart disease; diabetes mellitus; stroke and Parkinson's disease; osteoporosis; and central obesity), history of falls, functional decline or limitation, and malnourished or at risk of malnourishment. (Grade: conditional recommendation, low certainty of evidence)

In line with the AWGS 2019 algorithm for case finding of older adults with or at-risk for sarcopenia (5), the workgroup conditionally recommends case-finding for sarcopenia in older adults aged 65 years and above, especially in at-risk populations with relevant co-morbidities (such as chronic lung, kidney, liver or heart disease; metabolic diseases such as diabetes mellitus and osteoporosis; neurological diseases

such as stroke or Parkinson's disease; and central obesity) or risk factors such as history of falls, functional decline or limitation, poor nutritional and dental status, dysphagia, and physical inactivity. The likelihood of developing sarcopenia is significantly correlated with the number of cardiometabolic risk factors, notably diabetes, hypertension, and dyslipidaemia. With the rising prevalence of diabetes in Singapore, it is important to screen for sarcopenia in older adults with Type 2 diabetes, which can lead to accelerated decline in leg lean mass and muscle strength (58). Similarly, with the rising trend of obesity across most age groups and amongst men in Singapore, in older adults with high waist circumference indicating central adiposity, it is important to screen for sarcopenia to rule out concomitant sarcopenic obesity (58).

Case-finding should be opportunistic, for instance, at annual health check-ups or flu vaccination appointments; during clinical consultation for related symptoms; or after the occurrence of major health events such as functional decline after a recent hospitalization. Unlike the ICFSR guidelines, the workgroup did not recommend regular screening annually for sarcopenia. There is currently no direct evidence supporting a specific frequency for sarcopenia screening, and pragmatic cost-effectiveness modelling studies are needed to evaluate the benefits of incorporating regular screening at the primary care setting (1).

3. Case-finding for sarcopenia can be performed using either the SARC-F questionnaire, calf circumference or SARC-CalF. (Grade: conditional recommendation, low certainty of evidence)

Screening tests used for case-finding should be easy to use and feasible. In line with the AWGS 2019 algorithm, the workgroup conditionally recommends three case-finding tools: SARC-F, CC or the combination of the two (SARC-CalF). The SARC-F is a self-reported 5-item questionnaire that assesses symptoms in strength, assistance in walking, rising from a chair, climbing stairs, and falls (59, 60). Local studies affirmed the low-moderate sensitivity and moderate-high specificity of SARC-F (using the recommended cut-off ≥ 4) for sarcopenia diagnosis in the community and outpatient clinic setting (26, 36, 42). With evidence from local and international community studies supporting increased sensitivity of SARC-F using the lower ≥ 2 cut-off, further assessment for sarcopenia would be warranted if there is clinical suspicion, even though the SARC-F score may be < 4 (36, 61). CC has moderate-to-high sensitivity and specificity in predicting sarcopenia or low skeletal muscle mass. The recommended cut-offs are CC < 34 cm for men and < 33 cm for women (5). The importance of accurate measurement for CC cannot be over-emphasized. As there is systematic overestimation of sitting over standing measurements by 0.7 cm leading to under-detection in the sitting position (62), CC should be measured in the standing position using a nonelastic tape. Notably, the diagnostic performance of CC is attenuated in sarcopenic obesity due to decreased sensitivity with under-detection in women (34). The SARC-CalF gives equal weightage to SARC-F (surrogate of muscle function, 10 points) and calf circumference (surrogate of muscle mass, 10 points) in the 20-point scale (63), with a score of ≥ 11

Table 3. Final recommendations with strength and certainty of evidence

	Recommendation	Strength of Evidence*	Certainty of Evidence †
A. Case finding	1. We recommend case-finding instead of a universal screening approach for sarcopenia.	Conditional	++
	2. We recommend case-finding for sarcopenia in older adults aged 60 years and above, especially in high-risk populations with relevant co-morbidities (for instance, chronic lung, kidney, liver or heart disease; diabetes mellitus; stroke and Parkinson's disease; knee osteoarthritis; osteoporosis; and central obesity), history of falls, functional decline or limitation, and malnourished or at risk of malnourishment.	Conditional	++
	3. Case-finding for sarcopenia can be performed using the SARC-F questionnaire, calf circumference or SARC-CalF.	Conditional	++
	4. Individuals screened as positive should be evaluated for 'possible sarcopenia' via the assessment of handgrip strength or the 5-time chair stand.	Conditional	++
	Individuals with 'possible sarcopenia' should be evaluated for the presence of reversible causes and counselled on lifestyle modifications in diet and exercise.	Conditional	++
B. Diagnosis	1. We recommend using the Asian Working Group for Sarcopenia (AWGS) 2019 algorithm for the diagnosis and grading of severity of sarcopenia.	Conditional	+++
	2. We recommend the use of the Asia Working Group for Sarcopenia (AWGS) 2019 cutoffs to ascertain low lean mass and low levels of muscle strength and physical performance.	Conditional	++
	3. When it is necessary to determine low lean mass for a confirmatory diagnosis of sarcopenia, we recommend the use of dual-energy X-ray absorptiometry (DXA) as the imaging modality.	Conditional	++
	4. Muscle strength should be assessed using the standard protocol for Jamar or Smedley hand dynamometers.	Strong	+++
	5. To measure handgrip strength, it is recommended to take the maximum reading (rather than the average reading) of at least two trials using the dominant hand.	Strong	+++
	6. Physical performance should be assessed using the 5-time chair stand, 6-m usual gait speed, or Short Physical Performance Battery.	Strong	+++
C. Treatment	1. Older persons with sarcopenia should be encouraged to participate in resistance-based exercises to improve muscle strength and physical performance.	Strong	+++
	2. Clinicians should advise older persons with sarcopenia on the importance of a quality diet with adequate caloric and protein intake.	Conditional	++
	3. Clinicians should consider nutritional intervention with protein supplementation for older persons with sarcopenia	Conditional	++
	4. Nutritional intervention should be combined with physical exercise to improve muscle strength and physical performance in older persons with sarcopenia	Conditional	++
	5. We do not recommend prescription of pharmacotherapy for the specific management of sarcopenia in older adults	Conditional	++
	6. Clinicians should consider Vitamin D supplementation for sarcopenic older adults with Vitamin D insufficiency (<30 micrograms/L).	Conditional	++
D. Prevention	1. Regular physical activity and resistance-based exercise should be recommended to prevent sarcopenia in older adults.	Strong	+++
	2. Older adults should be encouraged to have adequate protein intake of at least 1.0g/kg bodyweight/day to prevent sarcopenia	Conditional	++
E. Research	We encourage more local research in sarcopenia focusing specifically on local cutoffs by sex and ethnicity; community prevention programmes and interventional studies; impact on quality of life, cost-effectiveness and patient acceptability; and overlap syndromes such as sarcopenic obesity, osteosarcopenia, and osteosarcopenic obesity.	n/a	n/a

* Strength of evidence considers the benefit-harm balance, patient preferences/values, cost-effectiveness, as well as the certainty of evidence. Strong means that benefits clearly outweigh any risks; Conditional means that clinicians would only refer the intervention under specific conditions because there is a fine balance between risks and burdens; Insufficient evidence (No recommendation) – there is insufficient evidence to determine net benefits or risks. † Certainty of Evidence (categories): ++++ High: Further research is very unlikely to change confidence in the estimate of effect; +++ Moderate: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; ++ Low: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate; + Very Low: Any estimate of effect is very uncertain

indicating sarcopenia. Local studies affirmed the improved sensitivity (albeit not specificity) of SARC-CalF over SARC-F for case-finding in the community (33). Similar to CC, the diagnostic performance of SARC-CalF is attenuated by obesity with under-detection of sarcopenic obesity in both older men and women (33).

Other candidate screening tools not mentioned in the AWGS algorithm were also considered (57). The workgroup decided that the Mini Sarcopenia Risk Assessment (MSRA), anthropometric predictive equations, and combination of arm circumference and SARC-F required further studies to establish their validity in the local context (64–68). The workgroup also excluded performance tests such as HGS, 5-STS and gait speed as these were considered diagnostic rather than screening assessments in the AWGS 2019 algorithm (69, 70).

4. Individuals screened as positive should be assessed for 'possible sarcopenia' either via handgrip strength or 5-time chair stand. (Grade: conditional recommendation, low certainty of evidence)

The AWGS algorithm considers the challenges of early identification of older adults with or at-risk for sarcopenia in settings without advanced diagnostic equipment (5). Specifically, the AWGS 2019 introduces the category “possible sarcopenia,” defined by low muscle strength (handgrip strength <28kg in men, <18kg in women) or reduced physical performance (5-STS ≥12s), which is recommended for use in primary health care and preventive services, but not in the hospital or research settings. Thus, older adults with relevant symptoms or chronic conditions, or are positive on the case-finding tools, should be further assessed for ‘possible sarcopenia’ with either HGS or 5-STS. Both HGS and 5-STS have been shown in local studies to predict outcomes such as physical performance, quality of life, frailty and mortality (22, 31, 32).

5. Individuals with 'possible sarcopenia' should be assessed for reversible causes and counselled on lifestyle modifications in diet and exercise. (Grade: conditional recommendation, - low certainty of evidence)

Management of ‘possible sarcopenia’ in clinical practice comprises two key components: 1) Assess and treat underlying causes, and 2) Intervention, with mainstay being non-pharmacological modalities of exercise and diet (2). This can usually be performed in the primary care setting. Where relevant, suitable cases can be referred for further specialist medical evaluation of underlying causes and to community or hospital-based services for provision of appropriate personalized intervention programs by the multidisciplinary team.

In line with other consensus recommendations (1, 2, 5), individuals assessed with ‘possible sarcopenia’ should be evaluated for underlying causes which may be potentially reversible. This includes the 4Ds of drugs (medications such as statins, fibrates and steroids can cause myalgia and proximal weakness); diabetes mellitus; other diseases (chronic lung, kidney, liver or heart disease, osteoporosis, knee osteoarthritis and neurological conditions); and deficiency (poor dentition or oral health, swallowing difficulties, vitamin D deficiency, conditions/medications causing anorexia or malabsorption, or socioeconomic factors affecting access to food) (71) (Table 4). In addition, they should be offered advice on lifestyle modifications in diet, namely a good quality diet with an adequate caloric and protein intake, and regular physical activity, which includes resistance-based muscle strengthening activities (>2 days/ week) and multi-component physical activity (>3 days/ week) for maintaining muscle strength (72).

Table 4. Underlying causes of Sarcopenia - 4Ds Mnemonic

1) Drugs
<i>Common</i>
<input type="checkbox"/> Statins
<input type="checkbox"/> Fibrates
<input type="checkbox"/> Steroids
<input type="checkbox"/> Alcohol
<i>Less common</i>
<input type="checkbox"/> Chloroquine
<input type="checkbox"/> Colchicine
<input type="checkbox"/> Antiretroviral drugs e.g. lamivudine, zidovudine
<input type="checkbox"/> Chemotherapy medications
2) Diabetes Mellitus
3) Other Diseases
<input type="checkbox"/> Chronic lung, kidney, liver or heart disease
<input type="checkbox"/> Osteoporosis
<input type="checkbox"/> Knee Osteoarthritis
<input type="checkbox"/> Neurological diseases e.g. stroke, Parkinson’s disease
<input type="checkbox"/> Cancer
4) Deficiency
<input type="checkbox"/> Poor dentition or oral health
<input type="checkbox"/> Swallowing difficulties
<input type="checkbox"/> Vitamin D deficiency
<input type="checkbox"/> Conditions/medications causing anorexia or malabsorption
<input type="checkbox"/> Socioeconomic factors affecting access to food

Diagnosis

1. We recommend using the Asian Working Group for Sarcopenia (AWGS) 2019 algorithm for the diagnosis and grading of severity of sarcopenia. (Grade: conditional recommendation, moderate certainty of evidence)

Based on the AWGS 2019 algorithm, the diagnosis of sarcopenia requires the presence of both low muscle mass and impaired muscle function (muscle strength or physical performance), with specified cut-offs for each diagnostic component. The presence of low muscle mass, low muscle strength, and low physical performance would constitute “severe sarcopenia.”

Amongst the different international consensus definitions for sarcopenia diagnosis which exist (5, 73–76), the workgroup recommends the AWGS 2019 consensus criteria for the following reasons: 1) the AWGS consensus considers the special considerations of Asian populations in terms of anthropometric, cultural and lifestyle-related differences, such as the relatively smaller body habitus, higher adiposity, and more physically active lifestyle compared with their Western counterparts (5); 2) local evidence supports the validity of the AWGS diagnostic algorithm, showing the association of sarcopenia diagnosis using AWGS 2019 with outcomes such as physical performance, frailty, nutritional parameters, fear of falling, and fear-related activity restriction (39, 77, 78); and 3) AWGS 2019 proposes specific updated cut-offs which have been validated in Asian populations, including contribution from Singapore studies (79, 80). In comparison to the revised European Working Group on Sarcopenia in Older People (EWGSOP2) criteria, the cut-offs proposed by AWGS 2019 are lower for ASMI in women (<5.4 kg/m² vs <5.5 kg/m²) and more stringent for 5-STs (≥12s vs ≥15s) and usual gait speed (<1m/s vs <0.8m/s).

The workgroup graded the level of certainty as moderate, with the important caveat that the AWGS 2019 algorithm for sarcopenia is applicable only for older adults aged ≥60 years. This is in line with the definition of sarcopenia as age-associated by AWGS 2019, and the recommended age cut-off at either age 60 or 65, depending on how each country defines “older people” (5). Although sarcopenic features may occur in younger adults, the underlying pathophysiology should be investigated rather than simply pursuing a diagnosis of sarcopenia (5). Moreover, the evidence base for younger adults is less well defined, and results from East Asian studies suggest that the young adult cut-offs for ASMI (especially in young adult women) may differ from older adults (81, 82).

2. We recommend the use of the Asian Working Group for Sarcopenia (AWGS) 2019 cut-offs to ascertain low lean mass and low levels of muscle strength and physical performance. (Grade: conditional recommendation, low certainty of evidence)

The workgroup conditionally recommends the use of AWGS 2019 cut-offs for sarcopenia diagnosis, namely: 1) low appendicular skeletal mass index (ASMI) (<7.0 kg/m² for men and <5.4 kg/m² for women) as measured using DXA; 2) low HGS (<28.0 kg in men and <18.0 kg in women) as measured using the Smedley or Jamar dynamometers; and 3) impaired physical performance defined in one of three ways: a) 5-STs ≥12s; b) usual gait speed <1.0m/s on the 6-metre walk test; or c) SPPB ≤9.

The DXA-cutoffs for low ASMI were retained from

AWGS 2014 (4), and has been validated for blood biomarkers (myostatin in men and IGF-1 in women), magnetic resonance muscle imaging, HGS and physical performance in local studies (21, 32, 37). Similarly, the cut-offs for 5-STS and SPPB have also been validated in local studies (22, 32, 83). Compared with AWGS 2014, the AWGS 2019 cutoffs were higher for HGS in men (<28kg vs <26kg) and usual gait speed (<1.0m/s vs <0.8m/s). The higher HGS cut-offs were derived using the lowest quintile from pooled data of eight Asian cohorts (including the GeriLABS study from Singapore) comprising 21,984 participants aged >65 years (24, 49, 79), and were comparable to the mean HGS values in the 60-64 age group in a local population study. Consistent with higher gait speed reported in Asian populations, the <1m/s cut-off to define slow gait speed likewise corresponds to the mean gait speed in older adults with low HGS reported in one local study (32).

Overall, the workgroup graded the level of certainty for cut-offs as low, noting the lack of good quality local data for cut-offs of ASMI. For instance, the AWGS 2016 report pointed out that using two standard deviations below the mean of a young reference group ("T-score") in Asian populations would lead to low prevalence of inadequate muscle mass and proposed that the lowest 20th percentile ("Z-score") is a more suitable threshold for diagnosing sarcopenia (82, 84). Thus, the lower cut-offs for ASMI (<5.28 kg/m² for men and 3.69 kg/m² for women), gait speed (<0.82 m/s), and HGS in women (<16.7 kg/m²) reported in the Yishun Study may have been influenced by the choice of the young adult reference group, and may not reflect the true local population norms. In addition, only one study reported the use of KES for sarcopenia diagnosis using cut-offs from a Thai study (40, 51). Thus, more population studies are required to establish local norms for ASMI, HGS, KES and physical performance measures using the Z-score approach. A promising recent development is the reporting of subgroup-specific local reference ranges for gait speed and 5-STS in older adults with no self-reported mobility limitations (85).

3. When it is necessary to determine low lean mass for a confirmatory diagnosis of sarcopenia, we recommended the use of dual-energy X-ray absorptiometry (DXA) as the imaging modality. (Grade: conditional recommendation, low certainty of evidence)

The workgroup conditionally recommends the use of dual-energy X-ray absorptiometry (DXA) for a confirmatory diagnosis of sarcopenia. The certainty of evidence was ranked low for the following reasons: (i) the distinct lack of local DXA studies in the clinical context, especially in the primary care setting; (ii) the limitations of DXA imaging, whereby lean mass is measured rather than muscle mass per se, and can misclassify body composition in individuals with high levels of water and fibrous tissue; and (iii) the weak association with adverse health outcomes and inability to provide information about muscle quality (1, 86). Despite these limitations, DXA remains a useful modality with the capacity for rapid clinical implementation (87). The workgroup recommends that DXA is performed only when it is necessary to determine low lean mass for a

confirmatory diagnosis of sarcopenia, for instance, in complex cases with diagnostic and/or management conundrums. As per the recommendations of AWGS 2019, the diagnosis of 'possible sarcopenia' without the need for confirmatory DXA imaging would suffice in the primary care or community preventive services settings (5). The guidelines of the International Conference on Sarcopenia and Frailty Research (ICSFR) adopted a similar approach, on the justification that older adults with sarcopenia often did not want expensive scans or testing to determine muscle loss (noting unnecessary costs and time), preferring instead to rely on their primary care provider's clinical judgement for a diagnosis of sarcopenia (1). From the health economics standpoint, the added value of DXA for diagnosis may not justify additional costs (1).

The workgroup did not recommend bioelectrical impedance analysis (BIA) for clinical practice at this juncture although it is relatively easy to use and is endorsed by AWGS 2019. BIA equations and cut-off points are population specific and device-specific. Hence its routine use in clinical care is not recommended in the absence of well-conducted local validation studies (88). It is recommended to use a multi-frequency device, which correlated more closely with DXA-measured ASM than did BIA measured with other devices (89). BIA devices designed for home use are not recommended because of suboptimal diagnostic accuracy (90). It is also important to note that BIA readings can be affected by other factors such as hydration status and is contraindicated in those with pacemakers or cardiac devices. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are currently considered gold standards for body composition measurement; however, they are costly and less readily available than DXA, hence they are mostly used in research and when needed for follow-up of another condition – for example, in patients with cancer (91). Ultrasound has been proposed as a simple alternative to measure muscle quantity and quality in clinical practice; however, it is user-dependent, and studies are currently underway to standardize the measurement protocols and to develop validated cut-offs (92). D3 creatine is a recently developed non-invasive isotope dilution test that shows a better correlation with outcome measures than DXA lean mass (93); its applicability and potential for scalability in the clinical setting remain to be established.

4. Muscle strength should be assessed using the standard protocol for either Jamar or Smedley hand dynamometers. (Grade: strong recommendation, moderate certainty of evidence)

The workgroup strongly recommends HGS as a feasible and valid assessment of muscle strength in clinical practice, on the basis of the evidence and endorsement by AWGS 2019 and international working groups for sarcopenia (1, 5, 73, 91). The devices used most often in Asia are the spring-type dynamometer (Smedley) and the hydraulic-type (Jamar). It is important to note that there are different measurement protocols available and that results of dynamometers are not interchangeable. For instance, the recommended positions for measuring HGS are sitting with 90-degree elbow flexion for

the Jamar dynamometer and standing with full elbow extension for the Smedley dynamometer (94); the protocol for Smedley dynamometer also permits sitting for those who are unable to stand unassisted (95). In one study, HGS readings measured using the Smedley were consistently lower than the Jamar by 3.1kg in men and 2.6kg in women, leading to higher prevalence rates of weakness across different diagnostic criteria (96).

The workgroup does not recommend the use of hand dynamometers other than the Jamar or Smedley. Where possible, local validation studies of other hand dynamometers should be carried out in order to ascertain whether there is systematic or proportional bias relative to the Jamar or Smedley. At this juncture, dynamometer-specific cut-off values are not recommended because of insufficient comparative data (5). If HGS is below the gender-specific reference value, it is important to exclude differential diagnoses that can impede handgrip performance (such as hand osteoarthritis, depression, dementia, Parkinson's disease and other neurological disorders) before ascribing the diagnosis of 'possible sarcopenia' (71).

5. To measure handgrip strength, it is recommended to take the maximum reading (rather than average reading) of at least two trials using the dominant hand. (Grade: conditional recommendation, moderate certainty of evidence)

We recommend taking the maximum reading of at least two trials of HGS using the dominant hand in a maximum-effort isometric contraction, rather than using a fixed acquisition time, as per the measurement protocol of AWGS 2019. The maximum reading (instead of average reading) should be used, in view of better agreement with sarcopenia diagnosis and better predictive validity for poor physical performance at 2 years (32).

6. Physical performance should be assessed using either the 5-time chair stand, 6-m usual gait speed, or Short Physical Performance Battery. (Grade: strong recommendation, moderate certainty of evidence)

The workgroup strongly recommends 5-STS, 6-m usual gait speed, or SPPB as feasible and valid measurements of physical performance in clinical practice, based on the evidence, and endorsement by AWGS 2019 and international working groups for sarcopenia (1, 5, 73, 91). Timed-up-and-go is not recommended, because the results may reflect multiple complex patho-etologies (5). The 5-STS involves asking the participant to stand up from a chair and to sit back down as quickly as possible five times. Either the stand or sit stop can be used, as long as the same protocol is consistently used (83). AWGS 2019 recommends ≥ 12 s as the cut-off for low physical performance to correspond to a walking speed of 1.0 m/s. As per AWGS 2019 recommendation, the 6-m usual gait speed test involves measuring the time taken to walk 6 m at a normal pace from a moving start, without deceleration, and taking the average result of at least 2 trials as the recorded speed. The SPPB assesses lower limb function in the 3 domains of balance, gait speed, and 5-STS. Each of the 3 subtests is scored from 0 to 4, and summing the 3 subtests yields the total score (range: 0-12). It should be noted that compared with the EWGSOP2

criteria, AWGS 2019 recommends higher cut-offs for gait speed (<1 m/s vs ≤ 0.8 m/s) and SPPB (≤ 9 vs ≤ 8), respectively (5).

Treatment

1. Older persons with sarcopenia should be encouraged to participate in resistance-based exercises to improve muscle strength and physical performance. (Grade: strong recommendation, moderate certainty of evidence)

The workgroup strongly recommends physical exercise focusing on progressive resistance-based (strength) training as first-line therapy to manage sarcopenia in older persons. Evidence from systematic reviews and meta-analyses of exercise interventions specifically targeting sarcopenia as a diagnostic entity supports the positive effects of resistance-based training on muscle strength and physical performance, with limited benefits on muscle mass. There were benefits in muscle strength for both HGS and KES, with one meta-analysis supporting a medium effect size for HGS (97, 98). Benefits in physical performance measures were reported for gait speed, 5-STS, and SPPB, with large effect sizes for SPPB and 5-STS and the observed improvements in usual gait speed fulfilling the minimal clinically important difference of at least 0.1m/s (99).

While training protocols of exercise varied across retrieved studies with respect to the type of exercise, frequency and duration, the cardinal feature was the incorporation of resistance-based training, either in isolation or as part of a multi-component exercise intervention. Resistance exercise requires muscles to hold or work against an applied force or weight through resistance machines, free weights, resistance bands or bodyweight. Resistance training should be progressive and involve sufficient exercise dose to induce a training stimulus. A proposed resistance exercise prescription for older adults with sarcopenia considered the variables of: (i) training frequency (2 sessions per week); (ii) exercise selection (targeting lower body muscle strength with squat/ leg press, knee extension, leg curl, calf raise and upper body muscle strength through chest press, seated row or pull down); (iii) exercise intensity (e.g. repetition continuum based prescription progressing from 40-60% of 1 Repetition Maximum to 70-85% of 1RM); (iv) volume as represented by number of sets and repetitions of each exercise (e.g. 1-3 sets of 6-12 repetitions) and (v) rest periods within and between sessions (6–120s between sets and 3-5mins between exercises; at least 48 hours between sessions).

Supplementing exercise programmes with simple exercises that can be performed at home without equipment (e.g. multiple sets of sit-to-stands or wall press) may improve overall exercise dose and adherence. The incorporation of functional strength movements or "task specific" exercise such as repeated sit-to-stands may also transfer more closely into improvements in functional ability. In parallel, an upper extremity functional exercise may involve lifting and carrying household items (e.g. bag of groceries) and placing it on a shelf. The principles of overload and resistance progression can be conceptually applied to functional tasks. With regards to exercise intensity, it is notable that older adults with severe sarcopenia may commence

at lower intensity (e.g. 30-60% 1RM) compared to those with higher baseline strength, with repeated assessment of muscle strength and physical performance used to guide progression of training dose (100, 101).

2. Clinicians should advise older persons with sarcopenia on the importance of a quality diet with adequate caloric and protein intake. (Grade: conditional recommendation, low certainty of evidence)

The workgroup conditionally recommends a quality diet with adequate caloric and protein intake as first-line therapy for older persons with sarcopenia. Malnutrition and sarcopenia are common and frequently co-exist in older adults. We advocate a diet-first whole food approach, which is based on the premise that whole foods, unlike single nutrients, provide benefits that are greater than the sum of their constituents (102). Moreover, employing a food-first approach may resonate better with older adults who understand foods better than isolated nutrients for healthy nutrition. Relevant myo-protective food groups are meats, fruits and vegetables, dairy products and other whole foods such as cereals and fish.

The term “diet quality” has been widely applied to describe how well an individual’s diet conforms to dietary recommendations and to describe how “healthy” the diet is. While still lacking in longitudinal evidence, a small body of cross-sectional data highlighted the possible benefit of healthier diets to reduce sarcopenia in older people, typically characterized by greater consumption of fruit and vegetables, wholemeal cereal and oily fish, indicating higher intakes of a range of nutrients such as Vitamin D, n-3 long-chain polyunsaturated fatty acids, antioxidant and protein intakes that could be important for muscle function (103). The ICFSR task force also highlighted the need to address full dietary patterns beyond protein intake, including healthy fat/ Omega 3, hydration, quality of calories (processed vs non-processed foods), and impact of medications on nutritional intake [1].

3. Clinicians should consider nutritional intervention with protein supplementation for older persons with sarcopenia. (Grade: conditional recommendation, low certainty of evidence)

The anabolic resistance of aging muscle results in blunted response to nutrients and hormones such that older adults have higher daily protein requirements than younger people to prevent sarcopenia. The PROT-AGE and AWGS guidelines recommend a daily protein intake of 1.0–1.2 g/kg bodyweight (BW), which is higher than the 0.8 g/kg BW of general guidelines (104, 105). Thus, the workgroup conditionally recommends protein supplementation in older persons with sarcopenia who are unable to meet the recommended protein intake through diet.

A systematic review of 5 RCTs reported that essential amino acid supplementation for 3 months in older adults with sarcopenia was associated with significant improvement in KES but not physical performance or muscle mass (97). A more recent systematic review using network meta-analysis of nutritional interventions that included amino acid or protein

supplementation, vitamin D or high-protein foods over various durations (the mode period being 12 weeks) reported significant improvements in HGS and KES, with no effect of nutritional intervention alone on physical performance and muscle mass (99). Notably, while both systematic reviews sought to focus on sarcopenia, none adopted established diagnostic criteria although characteristic features in the definition of sarcopenia such as low muscle mass, low muscle strength or poor physical performance were incorporated. Additionally, studies including older adults with specific health conditions such as diabetes, stroke, chronic obstructive pulmonary disease, chronic kidney disease, liver cirrhosis or other critical illness were excluded from both meta-analyses, limiting the generalizability of findings to all older persons with sarcopenia.

We reviewed evidence for both leucine and its active metabolite, beta-hydroxy beta-methylbutyrate (HMB). A systematic review of 3 RCTs of HMB (2-3g daily) focused on older adults with sarcopenia or frailty reported muscle mass improvement, maintenance or reduced loss, but inconsistent effects for muscle strength and physical performance, with maintenance (versus loss in control group) seen in only 1 of 3 studies (106). Studies included in the systematic review of leucine supplementation (1.2-6g daily) were not specific to sarcopenia at baseline, with inconsistent effects on muscle mass, strength and gait speed (107). The evidence-base for both leucine and HMB thus remains insufficient for a recommendation for either leucine or HMB in the management of sarcopenia.

It is noteworthy that more recent RCTs of nutritional interventions adopted established sarcopenia criteria and included quality of life outcomes beyond conventional sarcopenia parameters. In one RCT comparing a combined supplement of whey protein, Vitamin D and Vitamin E among older adults with AWGS-defined sarcopenia, supplementation was associated with improved muscle mass, HGS and self-reported quality of life (108). Yet another RCT adopting AWGS criteria for sarcopenia comparing once-daily fortified yoghurt (3g HMB, Vit D (1000IU) and Vit C) with placebo reported significant improvements in HGS, gait speed and quality of life, but with no effect on muscle mass (109). However, both RCTs were performed on a small scale with only 60 participants, and it is not possible to ascertain the nutritional component driving the positive outcomes.

4. Nutritional intervention should be combined with physical exercise to improve muscle strength and physical performance in older persons with sarcopenia. (Grade: conditional recommendation, low certainty of evidence)

We conditionally recommend that nutritional interventions should be combined with physical exercise in older adults with sarcopenia, as this may confer additional benefit over either intervention in isolation. A meta-analysis reported that the combination of exercise and nutritional intervention was more effective in improving KES compared with nutritional intervention alone, and achieved greater improvement in gait speed compared with exercise alone, without additional benefit on muscle mass (97). A more recent systematic review further

supported the benefits of combined exercise and nutritional intervention on muscle strength and physical performance, with relative ranking probabilities showing combined intervention being most effective for improving HGS and KES, followed by exercise intervention alone and nutritional intervention alone, although the additional gains were not statistically significant in network meta-analysis of pairwise comparisons (99). The failure to demonstrate significant gains with combined as opposed to exercise intervention alone was attributed to protocol heterogeneity of nutritional interventions, including possible suboptimal protein doses as total protein intake was not reported. Applying the AWGS criteria to target sarcopenic older adults and those with dynapenia, a combination of resistance exercise and protein supplementation yielded significantly greater improvement in knee extension torque compared with either intervention in isolation, with no change to muscle mass (110). In another study targeting AWGS-defined sarcopenic older adults, combined and exercise-only interventions improved KES and physical performance without additive benefit from supplementation over exercise alone, despite improvement in muscle mass observed only in the combination intervention group (111).

5. We do not recommend the prescription of pharmacotherapy for the specific management of sarcopenia in older adults (Grade: conditional recommendation, low certainty of evidence)

No specific drugs have been approved for the treatment of sarcopenia [2]. In terms of anabolic hormones, the evidence to date does not support testosterone supplementation for the management of older adults with sarcopenia. A meta-analysis of RCTs of testosterone supplementation in middle-aged and older men found significant gains in lean body mass and muscle strength but not physical performance. It should be noted that participants were not selected for sarcopenia at baseline, and sub-group analyses by age were not performed (112). Another systematic review of RCTs examining the therapeutic effects of pharmacotherapy for sarcopenia identified only one relevant article involving selective androgen receptor modulator (SARM), in which supplementation with 50mg SARM (MK-0773) in sarcopenic older women was not effective in improving muscle strength or physical performance despite improvement in lean body mass (97). Bimagrumab, a monoclonal antibody targeting myostatin through blockade of ActRIIA and ActRIIB to promote myoblast differentiation, was evaluated in a recent RCT of older adults with sarcopenia. All participants were subjected to optimized nutrition, Vitamin D and a home exercise programme. Bimagrumab (700mg intravenously every 4 weeks for 24 weeks) was not more effective than placebo in improving muscle strength and physical performance, despite significant changes in body composition with increased lean body mass and decreased fat mass (113). These findings suggest that monotherapy with pharmacological agents focused exclusively on promoting skeletal muscle hypertrophy does not effectively improve muscle function, and emphasis should still be accorded to ensuring adequate nutritional intake and physical exercise for sarcopenia management.

Based on the current evidence, the workgroup does not recommend pharmacologic interventions for the specific management of sarcopenia. However, the field of pharmacotherapy is a rapidly evolving one with clinical trials underway to develop new drugs which target different mechanistic pathways in sarcopenia (114).

6. Clinicians should consider Vitamin D supplementation for sarcopenic older adults with Vitamin D insufficiency (<30 micrograms/L). (Grade: conditional recommendation, low certainty of evidence)

Low or deficient levels of serum 25-hydroxyvitamin D (25(OH)D) have been frequently associated with lower muscle mass, reduced muscle function, and adverse consequences such as falls and fractures. An umbrella review of systematic reviews and meta-analyses undertaken by the Sarcopenia Guidelines Development Group of the Belgian Society of Gerontology and Geriatrics recommended vitamin D supplementation to improve muscle strength and physical performance in older people, especially in older women with very low baseline levels (<25nmol/L) (115). However, the recommendations could not be differentiated for sarcopenic versus non-sarcopenic older people due to the lack of specific characterization of sarcopenia status in most studies. In the PROVIDE study, a combined Vitamin D and leucine-enriched protein supplement in sarcopenic older adults significantly improved muscle mass and lower extremity function (116). Subsequent subgroup analysis suggested that the gain in muscle mass but not lower extremity function was influenced by baseline 25(OH)D levels (117). Nonetheless, the administration of combined supplementation limits further assessment of whether the benefits could be attributed to Vitamin D alone. In a more recent network meta-analysis of randomized controlled trials evaluating Vitamin D in the treatment of sarcopenia, while no trial provided therapeutic-dose Vitamin D as an isolated intervention, Vitamin D supplementation in combination with exercise and protein supplementation significantly increased HGS, while the combination of Vitamin D with protein supplementation improved performance on the 5-STS. While the available evidence for Vitamin D supplementation as a stand-alone intervention for sarcopenia is not strong, its delivery may be considered holistically with exercise and nutritional interventions.

Prevention

1. Regular physical activity and exercise should be recommended to prevent sarcopenia in older adults. (Grade: strong recommendation, moderate certainty of evidence)

Physical activity has been commonly advocated as a preventive strategy to slow the onset of both frailty and sarcopenia. In a recent systematic review, the only interventional trial did not show benefit of physical activity on sarcopenia outcomes; however, all 3 observational studies suggested a positive association between physical activity and prevention of sarcopenia in older adults (118). The wide variation in study design and measures of physical activity

limited conclusions on specific recommendations about the modality or dose of physical activity required, although studies with positive impact involved resistance training, combinations of resistance, balance and endurance exercises, as well as overall physical activity. Despite the relative paucity of studies specifying sarcopenia as an outcome to be prevented, past physiological studies had clearly demonstrated the impact of exercise and active lifestyles on maintaining muscle strength and muscle mass. The Singapore Physical Activity Guidelines (SPAG) for older adults specifies a target of 150 to 300 minutes of moderate-intensity aerobic physical activity per week, with recommendations for muscle strengthening activities (>2 days/week) as well as multi-component physical activity (>3 days/week) for maintaining muscle strength (72).

2. Older adults should be encouraged to have adequate protein intake of at least 1.0g/kg bodyweight/day to prevent sarcopenia (Grade: conditional recommendation, low certainty of evidence)

Dietary protein is key to the provision of amino acids necessary for muscle synthesis. The evidence for ‘anabolic resistance’ in older adults arising from blunted synthetic response to amino acids, especially at low intakes, has justified the need to raise recommended protein intake in older adults to prevent muscle loss (119). The Health, Aging and Body Composition Study reported greater loss of lean mass over 3 years in older adults with low energy-adjusted protein intakes at baseline (120). The Japanese guidelines for the prevention of sarcopenia recommends proper nutritional intake with an emphasis on adequate daily protein intake >1.0g/kg BW. The recommendation was supported by higher muscle mass index among older women with sarcopenic obesity who received high (1.2g/kg BW) compared with normal (0.8g/kg BW) daily protein intake over 3 months (121). The evidence linking nutrition to muscle mass, strength and function of older adults corroborates the importance of nutrition in sarcopenia prevention. Thus, beyond protein intake, dietary diversity should be considered as dietary components are often highly correlated with each other. Dietary patterns of adequate quality should ensure sufficient intakes of protein, vitamin D, antioxidant nutrients and long-chain polyunsaturated fatty acids (122).

Research

We encourage more local research in sarcopenia focusing specifically on local cutoffs by sex and ethnicity; community prevention programmes and interventional studies; impact on quality of life, cost-effectiveness and patient acceptability; and overlap syndromes such as sarcopenic obesity, osteosarcopenia, and osteosarcopenic obesity. (Grade: N/A)

The workgroup encourages more local research into sarcopenia using the AWGS 2019 diagnostic criteria as a common framework to move the body of evidence and translation into practice forwards. For instance, a recent scoping review of research studies of sarcopenia in distal radius fractures identified the lack of clear definition and

diagnostic criteria for sarcopenia as a major limitation (123). One identified area for further research is the need for well-conducted population studies to derive local cut-off values for muscle mass, muscle strength (HGS and KES) and physical performance which can be stratified by sex and ethnicity. Validation studies of multi-frequency BIA would also facilitate the measurement of muscle mass in community settings. Another area of pressing need would be the conduct of robust, large-scale studies of community prevention programmes or interventional studies with adequate follow-up to inform treatment options for sarcopenia which are appropriate for the local context (124, 125). The outcome measures should incorporate patient reported outcome measures (PROMs) such as quality of life, as well as outcomes relevant to healthcare policy makers such as cost-effectiveness analysis (9). Using a mixed-methods approach, the results of qualitative research can complement the quantitative findings by explicating issues of adherence and acceptability of interventions, including the importance of the social environment. Lastly, we echo the AWGS 2019 consensus in advocating more research into related overlap syndromes such as sarcopenic obesity, osteosarcopenia, and osteosarcopenic obesity, in order to build up the body of evidence regarding the potential synergistic adverse effects, specific diagnostic criteria and treatment (39, 43, 77, 126).

Discussion

This CPG builds upon the earlier work in Singapore arising from the National Frailty Consensus Discussion in 2019 to translate the Asia Pacific guidelines for frailty management into clinical practice (9). Despite sarcopenia being accorded a formal diagnosis code in 2016, most clinicians remain unaware of the condition and the diagnostic tools needed to identify it. Furthermore, there is great heterogeneity in clinical practice with regard to the diagnostic criteria, assessment methods and cut-offs, which is compounded by the lack of a systematic review of the local evidence (10). The AWGS 2019 consensus with updated Asian-centric cut-offs and protocols for case-finding and diagnosis, presented a golden opportunity by providing a ‘common language’ to facilitate adoption of evidence-based recommendations into local practice (5). This provided the impetus for this CPG to bridge the gaps in both the knowledge and practice of sarcopenia in Singapore, and portends recent trends towards region-specific guidelines (127).

Uniqueness of this CPG

To the best of our knowledge, this is the first country-specific CPG to be developed for sarcopenia. In formulating the recommendations, the workgroup was mindful to follow closely the principles of the seminal work by the ICFSR 2018 guidelines on screening, diagnosis and management of sarcopenia (1). Importantly, these recommendations were developed from the lenses of use-inspired Pasteur’s quadrant, which combines both rigor (i.e. underpinned in evidence through literature review and modified Delphi process) and

relevance (i.e. person-centered perspective to support health practitioners in managing older adults with sarcopenia in their daily practice) (128). Where gaps exist in the evidence-base, the workgroup supplemented with consensus-based best practice recommendations.

These guidelines have been designed to support practitioners (namely clinicians and allied health professionals) in their evaluation and management of older adults with sarcopenia in their daily practice. They are meant to guide care in line with patient preferences and priorities, and are not designed for use in isolation. Similar to the approach adopted by the ICFSR 2018 guidelines, we emphasize the importance of healthcare practitioners exercising their clinical judgement for patient management to take into account patient co-morbidities, medications, as well as preferences and values of care. Healthcare practitioners should also discuss the harms and benefits of appropriate management options for sarcopenia with the patient and their caregiver (1). Several key differences are worth highlighting. Unlike the more generic ICFSR 2018 guidelines which did not endorse any specific international consensus criteria, this CPG was specific in the choice of adopting the AWGS 2019 consensus diagnostic algorithm and cut-offs. In addition, we considered both the local evidence as well as salient contextual factors (such as resource constraints, current practice and healthcare delivery in the local setting) which can impact on the translation of the recommendations.

Key findings

The workgroup developed twenty recommendations which covered the areas of case finding, diagnosis, treatment, prevention and future research. There are important distinctions from the ICFSR 2018 guidelines. Firstly, we uphold the AWGS 2019 definition of sarcopenia as an age-associated condition, and therefore, recommend that the AWGS 2019 algorithm be applied only to older adults aged 60 years and above (5). Secondly, we recommend opportunistic case finding without a specific interval, unlike the recommendation for annual screening (for instance, during annual health check-ups or flu vaccination appointments) in the ICFSR 2018 guideline. Thirdly, in line with the AWGS 2019 consensus, there is a diagnostic category of “possible sarcopenia,” defined by low muscle strength with or without reduced physical performance, to facilitate early identification and intervention in primary care and preventive services settings which may not have access to advanced diagnostic equipment. Next, we provide clear details of the choice of tests and attendant cut-offs for muscle strength and physical performance as per the AWGS 2019 algorithm. Lastly, in terms of treatment, we recommend considering vitamin D supplementation for vitamin D insufficiency in older adults with sarcopenia.

Notwithstanding these differences, there are similarities from the standpoint of person-centric perspectives in the recommendations. Commensurate with the ICFSR 2018 guidelines, the measurement of muscle mass is not mandated except in instances where it is necessary to determine low lean mass for a confirmatory diagnosis of sarcopenia. This is

consistent with the preferences of older adults for a clinical diagnosis of sarcopenia by their primary care provider, as well as the lack of cost-effectiveness data to support a strict DXA-based approach for sarcopenia diagnosis (1). Similarly, our CPG did not endorse BIA for routine clinical use due to concerns about the heterogeneity of BIA machines which are available, possible lack of accuracy in obesity and frail older women, low concordance between BIA and DXA at the individual level, and the lack of local validation data (129, 130). In addition, we also recommend exercise and nutrition as the mainstay of treatment and prevention, taking care to emphasize the importance of combining both exercise and nutrition, and to advocate a diet-first approach for adequate caloric and protein intake. Recognizing the dynamic nature of evidence-based practice, our CPG also suggested areas of priority for future local research into sarcopenia.

Limitations

The CPG were developed for the unique context of Singapore and may not be applicable to other contexts with different considerations such as current level of awareness of sarcopenia in clinical practice; system of healthcare delivery; funding for healthcare; and socioeconomic factors. Notably, the guidelines focused on sarcopenia management in community-dwelling older adults. It is likely that frailer older adults in different settings (for instance, in long-term care facilities) may require different case identification and management approaches. Consistent with the AWGS 2019 definition of sarcopenia as an age associated condition, the recommendations apply only to adults >60 years of age. In parallel, this guideline does not specifically address secondary sarcopenia resulting from underlying medical conditions (such as malignancy or end-stage chronic diseases of the lung, heart, kidney or liver). Nonetheless, we recommend the evaluation for underlying causes, while a recent review suggested exercise remains beneficial in secondary sarcopenia (such as malignancy or end-stage chronic diseases of the lung, heart, kidney or liver) (131). Although the guidelines were largely developed from the perspectives of experts without specific consultation with patients or caregivers, the workgroup was mindful to incorporate patient-centered perspectives culled from literature or clinical experience. Nonetheless, it is encouraged that future updates of the CPG for sarcopenia should involve patients and caregivers. Lastly, the workgroup recognizes that the CPG represent a time-limited document which should be updated to keep pace with advances in medical treatments, technologies, and future modifications in diagnostic criteria for sarcopenia. To this end, the workgroup recommends a review between 2025-2027 to ascertain the need for a full or partial update of the guidelines.

Conclusions

We present the final recommendations of the workgroup, which was convened by the Chapter of Geriatricians and the Society for Geriatric Medicine Singapore to develop

contextualized, evidence-based CPG incorporating local evidence, to facilitate the adoption of the AWGS 2019 consensus into current practice in Singapore. We believe our experience in drafting the country-specific guidelines would be helpful to others who may be considering embarking on a similar initiative. Building upon the ICFSR 2018 guidelines, we adopted use-inspired Pasteur's quadrant processes combining both rigor and relevance to develop twenty recommendations which spanned the areas of case finding, diagnosis, treatment, prevention and future research. These guidelines pave the way for the adoption of the AWGS 2019 consensus to bridge the knowledge and practice gap in Singapore, and also set the stage for future guidelines which are specialty-specific (such as endocrinology; surgery; cardiology; oncology; and rehabilitative medicine).

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Conflicts of interest: None declared by all authors.

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