**Appendix 2: Interventions – Summary of Evidence**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author (year)** | **Study design and setting** | **Sample size** | **Mean age, gender** | **Assessment of sarcopenia using established diagnostic criteria** | **Intervention(s)** | **Outcome Measures and Effects** | **Quality (GRADE)** |
| Esriche-Escuder A et al  2021 [98] | Systematic review and meta-analyses of randomized and non-randomized studies  Any setting | 4 RCTs and 3 non-randomized studies, N=235 | Restricted to older adults >60 years | Yes (EWGSOP and EWGSOP2) | Exercise | Muscle mass  Muscle strength**↑**  Physical performance (SPPB, 5-STS, gait speed)**↑** | +++ |
| Matrinez-Arnau FM et al  2019 [107] | Systematic review - RCTs, placebo-controlled and observational studies  Community-dwelling and nursing homes | 23 studies | 57.6 to 86.6+4.8  3 studies women only, 7 studies men only; rest 29.4% to 89.4% women | Yes/No  14 studies used specific criteria (12 EWGSOP, 1 AWGS, 1 FNIH) | Leucine | Muscle mass**↑** in 10/ 16 studies  Muscle strength**↑** in 6/ 16 studies  Physical performace (gait speed)**↑** in 3/6 studies | + |
| Oktaviana J et al 2019 [106] | Systematic review of RCTs  Community-dwelling and rehabilitation facilities | 3 RCTs (N=203) | 67.1+1.7 to 85.4+6.3  63.6% women | No  Only 1 study used EWGSOP | HMB | Muscle mass**↑** in 1 study; preserved (vs loss) 1 study  Muscle strength in 1 study; **↑** in 1 study | + |
| Rooks D et al  2020 [113] | RCT, community-dwelling older adults | 180 | 79.1+3  60.6% women | No  Does not follow diagnostic algorithm of AWGS/ EWGSOP, but all participants had slow gait + low muscle mass | Bimagrumab | Muscle mass (DXA)**↑** with Bimagrumab  Muscle strength between Bimargumab vs placebo  Physical performance (SPPB, 6MWD, gait speed) | +++ |
| Wu PY et al  2021 [99] | Systematic review and network meta-analysis of RCTs  Any setting | 28 RCTs (N=2561) | Restricted to studies with older adults >65 years  Studies including both gender (14), men only (2), women only (10) | No  But studies had to include at least one indicator: low muscle mass, low muscle strength or poor physical performance | Exercise only  Nutrition only  Combined exercise + nutrition | Muscle mass  Muscle strength**↑** with exercise alone, nutrition alone, combined exercise and nutrition  Physical performance (gait speed, dynamic balance)**↑** with exercise alone, combined exercise and nutrition | +++  (sensitivity analyses performed for studies using muscle mass AND muscle strength or physical performance for diagnosis of sarcopenia) |
| Yamada M et al  2019 [110] | RCT, community-dwelling older adults | 112 | 84.2+5.5  65.2% women | Yes (AWGS) | Combined resistance exercise + nutrition  Exercise only  Nutrition only  (versus control) | Muscle mass (BIA)**↑** with combined exercise + nutrition  Muscle strength**↑** with combined exercise and nutrition  Physical performance (walk time)**↑** with exercise alone, combined exercise and nutrition | +++ |
| Yoshimura Y et al  2017 [97] | Systematic review and meta-analysis of RCTs  Community-dwelling | Exercise: 4 RCTs (N=448)  Nutrition: 5 RCTs (N=501)  Drug: 1 RCT (N=170)  Combined: 4 RCTs (N=501) | Restricted to older adults >60 years across studies | No  But all trials included measure of muscle mass | Exercise only  Nutrition only  Drug therapy only  Combined exercise + nutrition | Muscle mass (DXA/BIA)**↑** with exercise  Muscle strength**↑** with exercise, combined exercise and nutrition  Physical performance (gait speed)**↑** with exercise, combined exercise and nutrition | ++ |

BIA: Bioelectrical impedance analysis; DXA: Dual-energy X-ray absorptiometry; 6MWT: 6-minute walk test; RCT: randomized controlled trials; 5-STS: 5-time sit-to-stand test; SPPB: Short Physical Performance Battery.