

亚太地区临床实践指南： 衰弱的管理（翻译）



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译者: 广西壮族自治区江滨医院 (广西第三人民医院)

老年康复科 林卫 linweidr@hotmail.com

Elsa Dent PhD^{a,*}, Christopher Lien MBBS, MPA^b, Wee Shiong Lim MBBS, MRCP, MHPEd^c, Wei ChinWong MBBS^c, Chek HooiWong MBBS, MPH^d, Tze Pin Ng MD^e, JeanWoo MD^f, Birong Dong MD^g, Shelley de la Vega MD, MSc^h, Philip Jun Hua Poⁱ MB, ChBⁱ, Shahrul Bahyah Binti Kamaruzzaman MD^j, ChangWon MD, PhD^j, Liang-Kung Chen MD, PhD^k, Kenneth Rockwood MD^l, Hidenori Arai MD, PhD^m, Leocadio Rodriguez-Mañas MD, PhDⁿ, Li Cao MDo, Matteo Cesari MD, PhD^p, Piu Chan MD, PhD^q, Edward Leung FRCP^r, Francesco Landi MD^s, Linda P. Fried MD^t, John E. Morley MB, MCh^u, Bruno Vellas MD, PhD^v, Leon Flicker PhD, MBBS^w

^a 老年医学研究中心, 医学院, 昆士兰大学, 布里斯班, 澳大利亚

^b 老年医学科, 樟宜总医院, 新加坡城, 新加坡

^c 老年医学科, 老年医学与主动老化研究所, 陈笃生医院, 新加坡城, 新加坡

^d 老年教育与研究机构, 新加坡城, 新加坡

^e 林永禄医学院, 新加坡国立大学, 新加坡城, 新加坡

^f 何善衡老年学及老年病学研究中心, 香港中文大学, 香港, 中国

^g 华西医院老年医学中心, 四川大学, 成都, 中国

^h 菲律宾大学医学院, 马尼拉, 菲律宾; 老龄化研究所, 国立卫生研究院, 菲律宾大学, 马尼拉, 菲律宾

ⁱ 老年医学科, 马来亚大学医学中心, 吉隆坡, 马来西亚

^j 家庭医学部, 京熙大学医学院, 首尔, 韩国

^k 老年学及老年病学中心, 台北荣民总医院; 老化与健康研究中心, 国立阳明大学, 台北, 台湾地区

^l 达尔豪西大学, 哈利法克斯, 新斯科舍省, 加拿大

^m 国家老年医学和老年病学中心, 大府市, 日本

ⁿ 老年科, 赫塔菲大学医院, 马德里, 西班牙

^o 老年医学和老年病学中心, 华西医院, 四川大学, 成都, 中国

^p 图卢兹大学中心医院, 图卢兹, 法国

^q 老年医学科、神经病学科、神经生物学教研室, 宣武医院, 首都医科大学, 北京, 中国

^r 香港养和医院, 欢乐谷, 香港

^s 圣心天主教大学, 罗马, 意大利

^t 梅尔曼公共卫生学院, 哥伦比亚大学医学中心, 纽约, 美国

^u 老年医学与内分泌学系, 圣路易斯大学, 圣路易斯, 密苏里州

^v 健康与老化西澳大利亚中心, 西澳大利亚大学, 珀斯, 澳大利亚

通讯作者: Elsa Dent, PhD, 老年医学研究中心, 亚历山德拉公主医院, 昆士兰大学, 伍隆加巴, 布里斯班, 昆士兰 4102, 澳大利亚。E-mail 地址: elsa.dent@adelaide.edu.au (E. Dent)。

摘要

目的: 为老年人衰弱状态的筛查、评估和管理提供临床实践指导。

方法: 采用推荐分级的评估、制定与评价方法来制定指南。这一过程包括对现有科学证据的详细评估, 并辅以专家小组的解释。三类临床实践指南建议被制定: 强推荐, 有条件推荐, 没有推荐建议。建议: 强推荐: (1) 使用有效的测量工具来识别脆弱; (2) 使用抗阻力训练组分进行体育锻炼; 以及 (3) 通过减少或停用任何不适当/多余的药物来解决多重用药问题。有条件的推荐: (1) 筛选和解决可改变的疲劳原因; (2) 对于表现为非故意减肥者, 筛选可逆原因, 并考虑饮食强化和蛋白质/热量补充; 和 (3) 为缺乏维生素 D 的个人开具维生素 D 处方。没有就提供患者支持和教育计划提出建议。

结论: 本文提供的建议, 适用于亚太地区的医疗保健提供者在老年人衰弱的管理中使用。建议成立区域指南支援委员会, 协助定期更新这些循证指南。

关键词: 衰弱老人, 作为主题的时间指南, 老年, 循证医学/标准, 患者护理管理, 疾病管理。

衰弱是现代老年医学的巨人，也是老年人口中的主要公共健康卫生问题之一¹。国际老年病学和老年医学协会最近一致定义：虚弱是一种力量下降和生理功能紊乱状态，增加了个体易损性，导致依赖性、脆弱性和死亡的增加¹。在老年人中，衰弱可作为不良结局风险的一个标志²⁻⁴，并越来越多地用于预测肿瘤、心脏病和骨科等专业的患者结局⁵⁻⁸。

有多种病因导致衰弱，包括生理变化和/或与疾病相关的衰老、炎症、肌肉减少症、多重用药、内分泌紊乱、蛋白质能量营养不良、社会隔离和贫困^{1,3,5,9}。亚太地区社区老年人的衰弱患病率约为 3.5%~27%^{4, 10-24}；与欧洲和美洲的患病率相当。社会经济弱势群体和土著社区的衰弱患病率可能超过 50%^{32, 33}。因为在一些对老年人的人口健康调查中存在大量的无反应现象，衰弱的患病率在一些研究中可能被低估³⁴。

衰弱更常见于女性，发病率随年龄增加而增加^{1,3,30}。衰弱与共病重叠，尽管它可以而且经常独立于任何慢性病的存在而发生^{3,32,35}。衰弱不是残疾的同义词，而是因果关系^{35,36}。这种病也很昂贵，据报道，老年人衰弱的医疗费用约为 3500 欧元（4000 美元）超过 3 个月，其费用是不患有衰弱的老年人的 5 倍³⁷。这项开支在亚太地区尤为值得关注，在有高医疗需求的老年人中，往往是那些不能获得公共资助医疗服务的人³⁸。目前，没有公认的参考标准来定义衰弱，并且国际社会正在进行广泛的努力来确定最佳测量方法。定义衰弱有三种主要方法：

- (1) Fried 等³⁶的身体表型模型及其快速筛查工具：FRAIL³⁹量表
- (2) Rockwood 和 Mitnitski 的健康缺陷累积模型，其内容紧抓共病评价
- (3) 身体与心理社会的混合评估模式，如 Tilburg 衰弱量表⁴¹ 和埃德蒙顿衰弱量表 Edmonton Frailty Scale⁴²

尽管大多数关于衰弱的文献都集中在辨识、病因和风险评估，衰弱的认识仍然存在很大的知识差距：加强循证医学的科学文献以发展临床实践指南（Clinical Practice Guidelines, CPGs），一旦识别为衰弱，就要对其进行治疗。亚太地区是世界上老年人口最多的地区，再加上人口社会经济学的异质性，提供医疗服务和种族多样性，迫切需要为亚太地区制定这样的指南^{11,43,44}。

制定衰弱临床实践指南

传统意义上，临床医生应该使用临床实践指南作为标准治疗的基础。临床实践指南是基于循证医学的系统性推荐，由具有各自医疗临床知识的专家小组制定。衰弱的临床实践指南是急需的，由于以下的原因：

- 让医护人员更好地认识到衰弱；
- 为辨识和管理衰弱提供最佳的可用证据；
- 为受到衰弱影响的老年人，改善健康和生活质量；和
- 鼓励医疗保健服务提供者专注于改善衰弱老人功能性的能力。

尽管英国老年医学会制定了社区和门诊部的衰弱最佳实践指南⁴⁶，

但该指南没有提供具体的临床建议。

本文的目的是开发基于循证医学的多学科的，用于识别和管理衰弱的临床实践指南，特别针对亚太地区的卫生从业人员。世界卫生组织最近强调了需要专注于最大化老年人的功能独立性，而不是简单地使用传统的单一疾病医疗方法⁴⁷，本指南将纳入世界卫生组织的这一原则。本报告还将讨论每项临床实践指南背后的证据基础。

方法

在本文的其余部分中，当提到临床实践指南时，将统一使用术语“指南”。这些指南是采用指南推荐分级的评估、制定与评价方法（Grading of Recommendations, Assessment, Development and Evaluation, GRADE）来制定的^{45, 48-50}。GRADE 方法涉及评估当前的科学证据，并由来自各个国家的衰弱研究多学科专家组成的临床专家小组形成共识。该指南源自 2016 年在新加坡举行的亚太老年医学会发表的演讲《超越国界的老年医学：衰弱，我们准备好了么？》。利用会议提供的信息和讨论意见，结合全面的文献检索和审查，编写了一份基本文件。该文件已分发给专家小组，鼓励他们对指南的强度进行排名并提出更改建议。使用改进的德尔菲流程进行修改，直到所有的专家成员对最终文件都满意。

指南的强度是指其支持的证据基础，以及其收益超过任何潜在风险的程度^{45, 51}。在我们的原稿中，强推荐的概念是“我们强烈的推荐”，并反映出专家组的判断，对患者而言有很大的临床受益明显大于不良

反应的风险^{45,51,52}，而且考虑了患者的偏好⁵³。“我们有条件的推荐”的陈述意味着，尽管大多数临床医生和知情患者会选择这种方式，但许多人不会这样做，因为发生的不良事件可能会损害治疗的益处⁴⁵。“无推荐”的陈述说明支持该建议的证据不足。建议是基于潜在可治疗的衰弱的原因。

临床指南

表1总结了衰弱的指南；本报告概述的主要原则见表2。就肌肉强度和身体机能而言，当前衰弱的通用定义与肌肉减少症有很大重叠⁵⁴⁻⁵⁶，肌肉减少症的定义为与增龄相关的肌肉功能和质量的下降⁵⁷。肌肉减少症甚至可能是虚弱的一部分⁵⁸。因此，衰弱和肌肉减少的临床治疗可以遵循类似的路线。本文件不包括其他主要系统的衰弱，例如认知衰弱。

表1
治疗衰弱的临床实践指南

强推荐

1. 我们强烈推荐使用经过验证的测量方法来识别衰弱。
2. 我们强烈推荐衰弱老人转诊进行循序渐进的，个性化的体育锻炼计划，其中应包括抗阻力训练的内容。
3. 我们强烈推荐通过减少或停用任何不合适/多余的药物来解决多重用药问题。

有条件的推荐

4. 我们有条件推荐对衰弱患者进行疲乏原因的筛查。
5. 我们有条件推荐对衰弱老人，表现为非故意减轻体重者，应筛查其可逆的原因，并考虑给予食品强化/蛋白质和能量补充。
6. 我们有条件推荐给缺乏维生素D人群开具维生素D的处方。

无推荐

7. 对于为衰弱老人制定个性化支持和教育计划，我们无推荐意见。
-

由强壮到衰弱有一系列的变化过程，经常将其分为3类：“衰弱”、“衰弱前期”、“健壮”。老年人可能在三种类别的衰弱状态中动态过渡。例如，个性化治疗或自然治疗老年人急性病，可能导致衰弱状态中改变，由“衰弱”状态改善到“衰弱前期”状态。老年人的衰弱程度越严重，就越不可能将衰弱程度提升到最高的功能水平^{60,61}。一项可能有助于老年人衰弱早期的干预措施也可能没有益处，甚至可能对严重衰弱的老年人有害。因此，应尽早识别和管理衰弱，建议医疗专业人员仔细权衡治疗的任何益处和对患者的伤害，特别是那些最衰弱和治疗不太可能给患者带来任何益处的患者。在为年老体弱者制定管

理计划时，建议由医护人员、老年人及其家人共同进行决策。

表2
主要原则

1. 衰弱是一种与增龄相关状态，其特征是力量下降和生理功能紊乱，增加了个体易损性，导致依赖性、脆弱性和死亡的增加^{1,3}。
 2. 衰弱的识别和管理应尽可能纳入全面的老年综合评估技术(CGA)。
 3. 应该使用有效的衰弱测量工具来识别衰弱，例如Fried的脆弱表型、Rockwood和Mitnitski的脆弱指数、Tilburg的衰弱指数和FRAIL量表。选择测量工具应符合临床目标。识别衰弱不需要进行血液检查。
 4. 衰弱与肌肉减少症有所重叠，因此，二者的治疗原则可能相似。
 5. 当为衰弱老人制定管理计划时，医疗专业人员、老年人及他们的家人应共同参与决策。
 6. 对于衰弱老人，应提供改变生活方式的实用建议，并特别注意抗阻力训练和足够的蛋白质摄入量。
 7. 识别衰弱的可治疗因素可阻止其进展—包括多重用药、体重下降、体力活动（抗阻力训练）。
 8. 应该向老年人和他们的照顾者提供教育和支持。培训可以基于社区进行。
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推荐1：我们强烈推荐使用经过验证的测量方法来识别衰弱。

应使用经验证的测量方法来识别脆弱性。存在许多这样的工具（表3），在分类和预测能力方面，具有很大的异质性⁸⁶⁻⁸⁸。当选择使用工具的来测量衰弱，必须选择一样方法，它不仅能准确地识别衰弱并能预测病人的预后，也简单易用，经过充分验证，并说明了特定临床环境的优先级、资源和目标^{3,5}。最常见的两个衰弱测量工具是弗里

德 (Fried) 的衰弱表型³⁶ 以及 Rockwood 和 Mitnitski 的脆弱指数 (Frailty Index, FI)⁴⁰。

衰弱筛查的临床环境

对于 70 岁及以上的成年人，或那些在过去一年中非预期减轻体重 5%以上的人，应定期进行衰弱筛查。建议不要通过老年患者表面的主观表现来识别衰弱，这是因为各个专业的临床判断、评估的可重复性以及衰弱表型的异质性差距很大^{89,90}。尽管有研究发现，对衰弱患者的最初临床印象可以预测患者的预后⁹¹，但对老年人进行表面的目视检查很可能只能识别出严重的衰弱。

衰弱评估可作为老年综合评估的一部分

衰弱评估可以作为老年综合评估的一部分 (Comprehensive Geriatric Assessment, CGA)，这是目前识别和管理衰弱的参考标准⁴⁶，或由临床医生使用短期的快速老年评估方法进行评估⁷⁸。老年综合评估通过全面的、多维度的评估来确定衰弱老人的医疗、功能和心理社会方面的状态，然后利用这些信息来指导以人为主的治疗和支持计划^{46,92}。在许多随机对照试验 (randomized controlled trials, RCTs) 中，CGA 和随后的干预措施被证明在降低死亡率和接受更高水平的护理方面是有效的⁹²。然而，尽管 CGAs 取得了许多成功，但它们可能耗费大量人力，且执行成本高昂⁹³，而在亚太地区，大多数健康从业人员可能没有医疗资源来执行完整的 CGA。在这些情况下，应进

行衰弱筛查，以确定老年人是否需要转诊进行完整的 CGAs。

利用 Fried 衰弱表型进行衰弱筛查

Fried 衰弱表型将衰弱分为 3 种或 3 种以上的身体障碍（5 项清单列表）：迟缓（行走速度减慢）、虚弱（握力下降）、体重减轻（较前一年下降 ≥ 4.5 公斤），筋疲（自我报告）和低体力活动³⁶。从概念上讲，Fried 的衰弱表型反映了能量调节失调的临床综合征，以及复杂的适应系统对体内平衡至关重要性，这反过来又为肌肉减少症和疲劳提供了生理基础^{36,94}。因为这一生理基础，Fried 的衰弱表型非常适合在临床环境中识别衰弱^{3,95}，尽管在临床环境中测量患者的握力和步行速度有时很耗时⁹⁶。Fried 的衰弱表型在亚太地区的临床环境中经常使用，它可以预测死亡率、残疾、跌倒、住院和手术风险^{17, 18, 20, 21}。

87、97-100
◦

表3
应用于临床实践的衰弱测量方法

筛查

快速筛查

- FRAIL 量表³⁹
- PRISMA-7⁶³
- Tilburg 衰弱指数 (TFI)⁴¹
- 衰弱长者调查 (VES)⁶⁴
- 自评健康缺陷指数 (HDI)⁶⁵
- Sherbrooke邮寄问卷(SPQ)⁶⁶
- 肿瘤患者G8问卷⁶⁷
- 简易护理短问卷⁶⁸
- 骨质疏松症骨折研究 (SOF) 索引⁶⁹
- 老年人风险识别 (ISAR)⁷⁰

详细筛查

- Fried衰弱表型³⁶
- 格罗宁根虚弱指数⁷¹
- 衰弱特质量表 (FTS)
- 测量 (包括筛选和评估)
 - 握力⁷²⁻⁷⁴
 - 步行速度⁷⁵
 - 起立步行试验 (TUG)⁷⁶
 - 简易机体功能评估法 (SPPB)⁷⁷

评估

快速评估

- 快速老年评估 (RGA)⁷⁸
- Edmonton衰弱量表 (EFS)⁴²

综合评估

- 老年综合评估 (CGA)⁷⁹
- 简易护理问卷⁸⁰

计算度量评估

- 衰弱指数 (FI)⁴⁰
- Kihon检查清单⁸¹
- 多维预后指数 (MPI)⁸²
- 衰弱风险评分 (FRS)⁸³

综合评估

- 临床虚弱量表 (CFS)⁸⁴
- Gérontopôle衰弱筛查工具 (GFST)⁸⁵

PRISMA-7, 维护自主性而整合服务的研究计划。衰弱测量的类别可能会发生变化，并且衰弱测量可以属于多个类别。

缺陷累积的衰弱指数(Frality Index, FI)

衰弱指数将衰弱看做与年龄动态相关状态。衰弱指数表现为老年人由预设的 30 个或更多变量列表中得出的健康缺陷累积数量之间的比例^{40, 110, 102}。FI 从 0 到 1，上限约为 0.67¹⁰³。例如，在 50 个项目的健康缺陷列表中，一名患者在这些缺陷中的 10 项得分为“是”，那么他的 FI 得分为 0.2 (=10/50)。

FI 具有多维性，包含了作为身体机能、多种疾病、认知和社会心理因素。衰弱管理的干预措施可以集中在这些领域，从而增加 FI 在临床实践中的应用。如同 Fried 衰弱表型一样，FI 在亚太地区也经常使用^{11, 12, 19, 100, 104-112}。FI 也可以显示老年人的生理年龄¹⁰⁴，捕捉死亡风险³，并预测残疾、入住养老机构、功能下降、手术风险和入院治疗^{98, 113, 114}。

尽管 FI 具有优势，但如果临床层面从零开始收集数据，此项工作可能会非常耗时。但是，FI 的一个主要优点是它可以从已经收集的 CGA 数据中提取。此外，基于 Clegg 等¹¹⁵ 使用初级保健记录的研究结果，电子化的 FI 可以自动从常规的电子病历中提取信息。

其他衰弱测量和筛选工具

最近，一种包含衰弱指数和 Fried 衰弱表型的混合指标测量方法被开发：FRAIL 量表³⁹。FRAIL 量表显示出与 FI 和 Fried 衰弱表型相类似的预测精度¹¹⁶，并且被国际营养与衰老学会(the International Academy on Nutrition and Aging, IANA) 推荐用于临床实践。FRAIL 量表越来越多的应用于亚太地区^{15, 33, 99, 116, 1181-120}。

同样出现在亚太地区的临床衰弱量表 (Clinical Frailty Scale, CFS)^{121, 122}, 是一个经过充分验证的九分法的全球化评估工具⁸⁴, 可预测老年人的不良后果¹²¹⁻¹²³。CFS 允许在常规临床评估中, 使用可用的简单临床描述来定义和分级衰弱¹²²。然而, 该工具需要一些具有临床判断和训练有素的评估人员进行准确分类¹²⁴。

亚太地区的其他常规使用的衰弱测量方法包括骨质疏松骨折 (Osteoporotic Fractures, SOF) 指数^{16, 87}、埃德蒙顿虚弱量表^{6, 21, 86}、起立行走试验 (Timed-Up-and-Go, TUG)¹²⁵⁻¹²⁷、简易机体功能评估法 (short physical performance battery, SPPB)¹²⁸⁻¹³¹ 和 Kihon 清单⁸¹。

对于需要进行身体评估的衰弱测量工具, 建议采用当地规定的截断值。例如, 亚太地区的人群的握力可能较低^{72, 73}, Wu 等⁷⁴ 报告台湾地区老年人的握力比欧洲成年人低 25%。因此, 建议对亚洲人群使用握力最低值的第一个五分位数的握力强度来定义低肌肉强度, 或男性 <26 kg, 女性 <18kg⁴³。

建议 2: 我们强烈建议衰弱老人参加渐进性的、个性化的体育活动项目, 该项目应包含抗阻力训练。

格言“运动起来或衰弱下去”对于管理和预防衰弱至关重要。最近的一些系统回顾和荟萃分析得出结论, 体育活动是维持和提高衰弱老人的体力、功能和活动能力的关键途径^{55, 132-135}。针对身体衰弱和/或高龄老人的体育活动计划, 应包含有针对肌肉减少症相关的肌肉损耗

和活动能力丧失的锻炼^{55,136}。强烈建议进行抗阻力训练(力量训练)，多个随机对照试验显示，抗阻力训练即使是对最老的老人也有好处。抗阻力训练的好处包括增强力量^{135,143,145,146}，减少残疾^{135,142,144}，减轻疲劳^{147,148}，以及降低了入住医院或疗养院的可能性¹⁴⁴。

在首次执行运动处方的前几周，应进行多关节阻力训练，逐渐发展到更多的单关节运动¹⁴⁹。鼓励进行模拟日常活动的运动^{143,150}。对老年人来说，高强度的抗阻训练似乎比低强度训练更有益处^{55,135,145,151}，尽管尚不清楚抗阻力训练的最佳剂量(组数和重复次数)^{55,134}。从生理学的角度来看，肌肉细胞适应体力活动的方式与年龄无关¹⁴⁶，尽管老年人可能需要更长的时间才能达到与年轻人相同的水平¹³⁶。

对于衰弱老人，也建议进行平衡和有氧运动，即使这样的运动方式不能直接影响肌肉力量⁵⁵。根据最近对88位老年人试验的荟萃分析，持续参与平衡计划可以减少跌倒的恐惧、改善行动能力和平衡能力⁵⁵。平衡训练与抗阻力训练相结合，还可以降低跌倒风险^{55,152}和严重的行动不便¹⁵³。因此，有人提议，一旦衰弱老人能站立起来，就要进行平衡与抗阻力相结合的训练。理想情况下，当一个人的平衡、力量和认知能力足以安全行走⁵⁵，并考虑到不稳定步行和跌倒风险¹⁵⁴，还提倡衰弱老人步行的处方。减少久坐时间可能是促进衰弱老人进行更多体育运动的第一步¹⁵⁵。

多种形式的体育活动项目也可能有益于衰弱老人。例如，最近的大规模老年人生活方式干预和独立性随机对照试验(Lifestyle Interventions and Independence for Elders, LIFE)^{153,156,157}第III

阶段，发现多种形式的运动（抗阻力训练、有氧运动（步行）、平衡训练、柔韧性训练）可减少老年人主要的运动障碍¹⁵³。最令人惊讶的是，这种多形式训练对于预防行动不便的效果，在那些身体虚弱程度最高的人群中最显著（SPPB<8）¹⁵³。在亚太地区，最近一项“避免老年人跌倒的步骤（Steps to Avoid Falls in the Elderly,SAFE）”研究表明，抗阻力、平衡、步态训练降低了从急诊出院的老年人跌倒的风险（伴有或不伴有衰弱）¹³¹；然而，这一发现仅在低程度共病的人群中观察到。未来的大规模干预研究应调查在亚太地区老年衰弱者的多形式训练的影响。

卫生从业人员应意识到，针对衰弱老人的社区方案往往缺乏循证建议⁵⁵。此外，由于各种原因，老年人对体育锻炼项目的坚持程度很低，包括害怕摔倒¹⁵⁸、缺乏自信和应对策略^{142,159,160}、态度^{160,161}；以及不利的社会和环境影响¹⁴²。基本上，如果体育锻炼计划是受监督的¹⁵¹、单独定制^{55,131}、包含自我效能训练¹⁴²和转诊医生鼓励患者参与¹⁶¹，老年人更可能坚持体育锻炼计划。

建议 3：我们强烈建议通过减少或取消任何不适当/多余药物的处方来解决多重用药。

许多研究已经将衰弱的发展与多重用药联系起来^{1,162-166}。我们建议对衰弱老人处方药物定期复查。不再需要的药物可以取消处方，根据肾功能调整剂量^{167,168}。旨在改善患者的预后，不适当药物的取消应在医疗专业人员的监督下进行¹⁶⁸。最近的一项系统评价报告表明，取

消处方在更早时间实施较为有效，老年人可以忍受取消某些药物的服用而不会造成有害情况¹⁶⁹。至少基于一项最近的随机对照试验，居住在老年护理设施中老年人¹⁷⁰，取消处方药不太可能导致任何重大的不良临床结局。

根据 Tija 等¹⁷¹的一项系统回顾研究结果，令人遗憾的是，针对衰弱老人，明显缺乏减少不适当/多余药物的精心设计的临床试验。一般而言，建议对衰弱老人停止使用不适当药物，应使用以下标准：老年人处方筛查工具（the Screening Tool of Older Person's Prescriptions, STOPP）和提醒医生注意正确治疗的标准（Screening Tool to Alert doctors to Right Treatment, START）、Beers 标准、McLeod 标准¹⁷⁵。这些取消处方的指南，关注的是不应该开具的特殊药物。还存在通用的取消处方的指南，不仅仅关注特定药物，而是依靠询问医学和老年人自身：药物适宜指数（the Medication Appropriateness Index, MAI）¹⁷⁶，以及不恰当的药物使用和处方指标工具¹⁷⁷。

为了实施针对衰弱老人的取消处方计划，建议临床医生和药剂师公开与患者及照顾者讨论停用处方药方案预期益处和潜在的伤害¹⁷⁸。健康从业者还应意识到衰弱老人拒绝取消处方药的障碍，包括：过度处方的激励措施¹⁷⁸、对取消处方的药物缺乏一致意见¹⁷⁹；缺乏对取消处方好处的认识¹⁷⁸。值得注意的是，在农村和/或社会经济水平较低的地区，可能存在相反的问题：衰弱老人可能患有未知和未经治疗的疾病。

建议 4：我们有条件地建议对衰弱患者进行筛查，以确定是否有可逆疲劳原因。

疲劳有很多可治疗的原因，包括睡眠呼吸暂停^{180,181}、抑郁^{182,183}、贫血¹⁸²、低血压¹⁸³、甲状腺功能减退¹⁸⁴和B12缺乏¹⁸⁵。疲劳是 Fried 衰弱表型和 FRAIL 量表的关键组成部分。研究报告表明，筛选可逆转的疲劳原因，结合有针对性的干预措施，可以改善老年人衰弱的结局^{1,186}。然而，很少有严谨的研究解决了衰弱老人可改变的疲劳原因。尽管有临床试验表明疲劳是可以治疗的，通过解决睡眠呼吸暂停^{180,187}、抑郁¹⁸³，针对其他可逆疲劳原因进行高质量的临床试验是必须的。值得注意的是，选择性 5-羟色胺再摄取抑制剂（Selective Serotonin Reuptake Inhibitors, SSRIs）是广泛用于治疗抑郁症的处方药物，实际上可能会使疲劳加重¹⁸⁸。

建议 5：我们有条件地建议，对于衰弱老人，如果出现意外的体重下降，应进行可逆原因的筛查，并考虑补充蛋白质和热量/食物强化。

体重下降是衰弱的关键特征^{36,189,190}，应该通过筛选和解决已确定的可逆原因进行管理。可以使用“送餐上门”助记符¹⁹¹（首字母简写 Meals on Wheels，译者注）（表 4）来帮助记忆，包括疾病、痴呆、药物、吞咽问题和导致体重减轻和营养不良的因素。

表 4

关于可逆体重下降的“送餐上门 (Meals on Wheels)” 助记符

Medications 药物

Emotional (depression) 情绪 (抑郁)

Alcoholism, anorexia tardive, abuse (elder) 酗酒、厌食症、虐待 (长者)

Late life paranoia 老年妄想症

Swallowing problems 吞咽问题

Oral problems 口腔问题

Nosocomial infections, no money (poverty) 医院感染, 经济困难 (贫穷)

Wandering/dementia 流浪/痴呆

Hyperthyroidism, hypercalcemia, hypoadrenalism 甲状腺、高钙血症、肾上腺皮质功能减退

Enteric problems (malabsorption) 肠道问题 (吸收不良)

Eating problems (eg, tremor) 饮食问题 (如震颤)

Low salt, low cholesterol diet 低盐、低胆固醇饮食

Shopping and meal preparation problems, stones (cholecystitis) 购物和用餐准备问题, 结石 (胆囊炎)

蛋白质和热量补充

有条件的建议对身体衰弱的减肥者补充热量和蛋白质¹⁹²⁻¹⁹⁵。首先建议强化食物 (高能量餐), 并辅以补充剂¹⁹⁶。尽管如此, 以前的荟萃分析未能将蛋白质热量补充的益处归因于其他疗法^{193, 195, 197}。如果营养补充确实改善了营养状况, 这种改进可能不会转化为功能上的改进, 或者降低死亡率^{197, 198}。不幸的是, 在衰弱老人中蛋白质补充试验的一个主要问题是对照组在基线水平不存在, 或营养水平更高^{193, 195, 197, 198}。未来的干预研究应设计出解决这一局限性的方法, 以增加衰弱老人补充蛋白质的证据基础。

建议每日蛋白质摄入量

老年人可能比年轻人需要更多的蛋白质摄入^{202,203}。目前老年人的蛋白质每日推荐摄入量 (Recommended Daily Intakes, RDI) 各不相同, 从 0.8g/kg 体重 (body weight, BW) 每天^{199,203} 到 1.0 到 1.2g/kg BW/天, 根据年龄需要蛋白 (Protein needs with Ageing, PROT-AGE) 研究功能组报道²⁰⁴, 而欧洲临床营养与代谢学会 (the European Society for Clinical Nutrition and Metabolism, ESPEN) 建议至少 1.2g/kg BW/天。ESPEN 还建议对于营养不良者, 蛋白质的摄入增加到 1.2 到 1.5g/kg BW/天。由于研究不足, 目前对老年人补充蛋白质的上限尚不清楚。

当给老年人补充高蛋白时, 应监测肾功能^{196,203}, 且 ESPEN 建议急性或慢性肾衰患者每天摄入 0.8 至 1g/kg 体重的蛋白质可不接受肾脏替代治疗¹⁹⁶。还应考虑的是, 与欧洲或北美人群相比, 亚太地区人群对蛋白质补充的反应可能不同, 因此, 鼓励在该地区开展更多的临床试验。

多成分干预

在亚太地区, 虽然需要更大规模的研究, 但新出现的临床试验显示, 综合干预 (物理、营养和认知干预)²⁰⁵ 对治疗衰弱有益。例如, 当与抗阻力训练相结合时, 补充蛋白质的益处可能会增强¹⁹⁹。Tieland 等人²⁰⁶ 最近的研究发现, 衰弱老人补充蛋白质, 接受抵抗力训练, 可以增强身体功能。同样地, 肌肉减少症的老年妇女在补充 3g 蛋白和

进行体力活动（这一组仅体力活动不影响的力量）后，其身体功能和力量也得到改善²⁰⁷。目前尚不清楚体力活动/蛋白质补充是否会对肌肉质量产生影响，研究报告的结果不一^{199, 206, 207}。

在欧洲，老年人的肌肉减少症和身体衰弱多组分治疗策略（Sarcopenia and Physical frailty IN older people multicomponent Treatment strategies, SPRINTT）项目，目前正在调查多因素干预的效果，包括体育活动、营养咨询/饮食干预，以及以及信息通讯技术的干预。SPRINTT 研究是一项多中心的 III 的随机对照试验，其目的是在 36 个月的试验期内，防止 1500 例老年人衰弱和肌肉减少症进展^{208, 209}。在亚太地区，很少有关衰弱老人的多成分干预的临床研究。

非故意减肥和营养不良的筛查

附加的有条件的建议是：体重丧失和营养不良者应使用公认的营养筛查工具进行筛查，其中包括迷你营养评估 (Mini Nutritional Assessment, MNA)²¹⁰，是简短版本的 MNA-SF²¹¹，或营养不良综合筛查工具²¹²。这些营养筛查工具在亚太地区经常使用，通常针对不同人群人体测量有特点截止点²¹³⁻²¹⁷。营养筛查也可以有助于确定不易发现的但可以导致衰弱情况；例如，肌肉减少性肥胖（低肌肉质量和高体脂）。对食欲不振的老年人进行筛查也可能有益于衰弱。

建议 6：我们有条件地建议对缺乏维生素 D 的老年人，开具维生素 D

处方补充。

维生素 D 是一种对肌肉和骨骼至关重要功能的脂溶性维生素，有许多生理功能作用，如炎症、新陈代谢和血糖调节²¹⁹⁻²²²。它主要是由胆固醇在皮肤中合成的，尽管饮食来源如油性鱼类可以贡献高达 10% 的维生素 D 摄入量^{220,223}。维生素 D 缺乏与身体机能减退^{224,225}、衰弱进展²²⁶⁻²²⁸、跌倒和死亡²²⁶⁻²²⁸有关。维生素 D 缺乏在衰弱老人中很常见^{226,229-233}，居住在亚太地区的老年人也常见^{221,228,234-238}，尽管并非所有的研究都发现了高比例的维生素 D 缺乏^{239,240}。

阳光照射与维生素 D

尽管有可能仅通过阳光照射摄入足够的维生素 D，因为避免阳光暴晒²²¹ 或残疾限制了户外暴露（如居住在住宅区）²²⁷，和皮肤中合成维生素 D 的能力降低了 75%²⁴¹，这可能不会发生在老年人身上。为了在不被太阳有害紫外线灼伤的情况下优化维生素 D 的摄入，建议在冬季，老年人在紫外线指数较低（UV index is low, UV index I<3）的中午外出；在夏天，当紫外线指数较低时，只需在早晨或下午几分钟的时间里将前臂和手暴露在阳光下^{242,243}。重要的是，维生素 D 需要与一种维生素 D 结合蛋白结合，这种结合蛋白在肤色较深的个体中含量较低^{244,245}，因此，这些人可能需要更高剂量的阳光照射才能获得足够的维生素 D²²²。

衰弱老人补充维生素 D

有几个临床试验发现在缺乏维生素 D 的老年人中补充维生素 D 可降低死亡、跌倒和骨折¹。然而，这些试验关注的是不伴有衰弱的老年人²³³。为衰弱老人补充维生素 D 仍然是文献中争论不休的话题^{3, 246, 247}。如果开具补充处方，建议剂量为每天 800 至 1000 国际单位的维生素 D²⁴⁸，尽管这一剂量也取决于个人的状况、饮食和阳光照射²⁴⁷。然而，有人担心高剂量的维生素 D 补充的风险，尤其是在没有维生素 D 缺乏的人群，因为这可能增加了跌倒和骨折的风险²⁴⁹⁻²⁵¹。

一般老年人补充维生素 D

当考虑到一般的老年人时，有很多 meta-分析以及关于补充维生素 D 有效性的系统综述，与对照研究结果进行比较^{246, 248, 252-254}。例如，Rosendahl Riise 等²⁵² 和 Rejnmark 等²⁵³ 都分别报告了在老年人中补充维生素 D 并没有改善肌肉力量或死亡风险，尽管 2012 年 Rejnmark 等²⁵³ 报道确实观察到当维生素 D 与钙补充剂相结合时的死亡率降低的效果。另一方面，Muir 等²⁴⁸ 发现每天补充 800 到 1000 个 IU 维生素 D 确实改善了老年人的力量和平衡。此外，最近的一项 Cochrane 评价报告称，维生素 D 的补充降低了居住在护理机构的老年人跌倒的风险²⁵⁵。相关的临床试验仍然很少，特别是在特定种族中，尽管最近来自中国的一项试验发现，至少对在基线时维生素 D 缺乏的老年男性而言，长期维生素 D 补充并没有改善肌肉质量或功能²⁵⁶。

维生素 D 的筛查

不推荐在所有衰弱老人中进行常规测量 25(OH) 维生素 D 水平。肤色较深的人维生素 D 结合蛋白含量较低^{244,245}，因此，确定亚洲裔或非洲裔人正常维生素 D 水平的能力值得怀疑。

建议 7：我们没有相关建议：为衰弱老人提供个性化的支持和教育计划。

目前，只有一个有限的证据基础，为衰弱老人和他们的照顾者提供了个性化的支持和教育计划。尽管在传闻中和小规模研究中，这样的计划似乎是有效的²²⁹，确实需要大规模的、精心设计的随机对照试验来支持这一建议。尽管如此，最近有几份报告强调了支助和教育计划的重要性^{257,258}。这种支持/培训可以来自社区、家庭护理恢复性服务、联合健康专业人员、护理人员、全科医生和老年医师²⁵⁹⁻²⁶¹，并且应该以物理功能最大化为目标²⁶⁰。还应包括老年人本身的特殊需要，以促进独立性和以人为本的护理^{258,261}。

可以雇用医护人员作为卫生系统导航员，促进医疗服务之间的有效整合²⁶²。对于身体衰弱的老年人而言，对医疗保健服务有更高的要求，以及他们获得这些服务面临的障碍更多，因此医疗保健集成很有价值^{259,263}。多学科干预计划，包括由管理医生、护士和相关卫生专业人员进行的病例管理/病例会议，可以改善衰弱老人的护理提供的协调性，反过来，这可以帮助成功地治疗衰弱²⁶³。尽管这是一个积极的发现，最近的研究报告说，多学科干预老年人衰弱的依从性低，不过

那些坚持干预的人可能会经历体验到衰弱和行动能力的改善²⁶⁴。目前几乎没有证据显示，为衰弱老人整合护理服务确实可以改善个人结果²⁶⁵⁻²⁶⁸，尽管这可能只有在拥有充足的初级保健服务资源的国家才是正确的²⁶⁸。

讨论

本报告基于当前的科学证据，结合国际临床专家对衰弱的评估，为衰弱老人的管理提供临床指南。本指南意见旨在为医疗保健服务提供者使用，以支持他们对衰弱老人的日常管理。指南意见并不单独使用。相反，建议卫生专业人员与患者及其护理人员讨论关于个体化治疗的最佳决策。卫生专业人员还必须认识到，任何干预措施的预期益处应大于对年老虚弱患者的任何潜在危害。

本指南文件经过精心设计，简洁明了，以确保医疗保健提供者的理解和遵守²⁶⁹。此外，对于衰弱的患者来说，参考本报告中概述的所有治疗策略可能不可行、不实用，甚至不有益。也就是说，在衰弱的早期阶段对老年人有益的干预可能对严重虚弱的老年人不利，甚至有害。

个体从业者应选择最合适的干预措施，以符合患者的喜好、可获得的资源并最大程度地降低患者的伤害^{58,270}。指南还需要根据当地情况进行调整。例如，在亚太地区，大多数卫生从业人员可能没有资源来执行完整的CGA，因此使用快速老年评估可能是有益的⁷。

总体而言，解决衰弱的治疗方式缺乏精心设计的临床试验。患有

衰弱的老年人通常被排除在临床试验之外²⁵⁸，限制了制定临床指南的证据基础。需要对衰弱的老年人进行更可靠、质量更好的临床试验，特别是那些受关注的结果对老年人本身有价值，例如功能独立、生活质量和留在家里²⁶⁰。亚太地区尤其需要进行此类试验，因为支持衰弱管理的大多数证据基础来自欧洲和北美，而欧洲和北美可能无法直接应用于亚太地区的人群。

该报告的主要局限性在于，没有对每项建议进行全面的系统审查。专家小组成员也未采用将证据合成为准则的标准化方法。此外，由于涉及衰弱老人的临床试验证据有限，因此，根据本文提供的指南为衰弱管理过程制定临床质量指标时，应谨慎行事。

重要的是，随着新的评估技术、治疗方式和定期开发的技术，老年医学的知识不断进步。因此，基于循证的衰弱临床指南需要定期更新和修订。建议成立指南区域支持委员会帮助定期更新循证指南。这些区域委员会还可以针对衰弱管理制定针对具体环境的指南，包括急诊科、初级保健、肿瘤科、心脏病科和骨科。定期更新临床指南将确保从业者可根据最新的循证证据基础来指导衰弱老人的管理。此外，衰弱指南应与临床病例相联系，以传播其管理知识。

总体而言，随着全球老年人数量的快速增长，迫切需要必须辨别衰弱并加以适当管理。预期这些临床指南将改善医疗保健专业人员对衰弱的认识，并改善对衰弱老人的护理质量和结果。

参考文献：

1. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: A call to action. *J Am Med Dir Assoc* 2013;14:392e397.
2. Hartley P, Adamson J, Cunningham C, et al. Clinical frailty and functional trajectories in hospitalized older adults: A retrospective observational study. *Geriatr Gerontol Int* 2016; <http://dx.doi.org/10.1111/ggi.12827>.
3. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381:752e762.
4. Lee Y, Kim J, Han ES, et al. Frailty and body mass index as predictors of 3-year mortality in older adults living in the community. *Gerontology* 2014;60:475e482.
5. Dent E, Kowal P, Hoogendoorn EO. Frailty measurement in research and clinical practice: A review. *Eur J Intern Med* 2016;31:3e10.
6. Kua J, Ramason R, Rajamoney G, Chong MS. Which frailty measure is a good predictor of early post-operative complications in elderly hip fracture patients? *Archives of orthopaedic and trauma surgery* 2016;136:639e647.
7. von Haehling S, Anker SD, Doehner W, et al. Frailty and heart disease. *International journal of cardiology* 2013;168:1745e1747.
8. Hamaker ME, Jonker JM, de Rooij SE, et al. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: A systematic review. *Lancet Oncol* 2012;13:e437ee444.
9. Lu Y, Tan CT, Nyunt MS, et al. Inflammatory and immune markers associated with physical frailty syndrome: Findings from Singapore longitudinal aging studies. *Oncotarget* 2016;7:28783e28795.
10. Lee JS, Auyeung TW, Leung J, et al. Transitions in frailty states among community-living older adults and their associated factors. *J Am Med Dir Assoc* 2014;15:281e286.
11. Woo J, Zheng Z, Leung J, Chan P. Prevalence of frailty and contributory factors in three Chinese populations with different socioeconomic and healthcare characteristics. *BMC Geriatr* 2015;15:163.
12. Noguchi N, Blyth FM, Waite LM, et al. Prevalence of the geriatric syndromes and frailty in older men living in the community: The Concord Health and Ageing in Men Project. *Australas J Ageing* 2016;35:255e261.

13. Zeng P, Wu S, Han Y, et al. Differences in body composition and physical functions associated with sarcopenia in Chinese elderly: Reference values and prevalence. *Arch Gerontol Geriatr* 2015;60:118e123.
14. Vaingankar JA, Chong SA, Abdin E, et al. Prevalence of frailty and its association with sociodemographic and clinical characteristics, and resource utilization in a population of Singaporean older adults. *Geriatr Gerontol Int* 2016 Aug 31 [Epub ahead of print].
15. Woo J, Yu R, Wong M, et al. Frailty Screening in the Community Using the FRAIL Scale. *J Am Med Dir Assoc* 2015;16:412e419.
16. Jung HW, Kim SW, Ahn S, et al. Prevalence and outcomes of frailty in Korean elderly population: Comparisons of a multidimensional frailty index with two phenotype models. *PLoS One* 2014;9:e87958.
17. Liu LK, Lee WJ, Chen LY, et al. Association between Frailty, Osteoporosis, Falls and Hip Fractures among Community-Dwelling People Aged 50 Years and Older in Taiwan: Results from I-Lan Longitudinal Aging Study. *PLoS One* 2015;10:e0136968.
18. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults: A prospective cohort study. *BMJ open* 2015;5:e008462.
19. Sathasivam J, Kamaruzzaman SB, Hairi F, et al. Frail Elders in an Urban District Setting in Malaysia: Multidimensional Frailty and Its Correlates. *Asia-Pacific journal of public health* 2015;27:52se61s.
20. Chen S, Honda T, Chen T, et al. Screening for frailty phenotype with objectively-measured physical activity in a west Japanese suburban community: Evidence from the Sasaguri Genkimon Study. *BMC Geriatr* 2015;15:36.
21. Chang CI, Chan DC, Kuo KN, et al. Prevalence and correlates of geriatric frailty in a northern Taiwan community. *J Formos Med Assoc* 2011;110:247e257.
22. Ng TP, Feng L, Nyunt MS, et al. Frailty in older persons: Multisystem risk factors and the Frailty Risk Index (FRI). *J Am Med Dir Assoc* 2014;15:635e642.
23. Chong MS, Tay L, Ismail NH, et al. The case for stage-specific frailty interventions spanning community aging to cognitive impairment. *J Am Med Dir Assoc* 2015;16:1003.e13e1003.e19.

24. Zheng Z, Guan S, Ding H, et al. Prevalence and incidence of frailty in community-dwelling older people: Beijing Longitudinal Study of Aging II. *J Am Geriatr Soc* 2016;64:1281e1286.
25. Moreira VG, Lourenco RA. Prevalence and factors associated with frailty in an older population from the city of Rio de Janeiro, Brazil: The FIBRA-RJ Study. *Clinics (Sao Paulo, Brazil)* 2013;68:979e985.
26. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc* 2010;58:681e687.
27. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009;64:675e681.
28. Garcia-Pena C, Avila-Funes JA, Dent E, et al. Frailty prevalence and associated factors in the Mexican health and aging study: A comparison of the frailty index and the phenotype. *Exp Gerontol* 2016;79:55e60.
29. Cawthon PM, Marshall LM, Michael Y, et al. Frailty in older men: Prevalence, progression, and relationship with mortality. *J Am Geriatr Soc* 2007;55:1216e1223.
30. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: A systematic review. *J Am Geriatr Soc* 2012;60:1487e1492.
31. Xue QL, Bandeen-Roche K, Varadhan R, et al. Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. *J Gerontol A Biol Sci Med Sci* 2008;63:984e990.
32. Biritwum RB, Minicuci N, Yawson AE, et al. Prevalence of and factors associated with frailty and disability in older adults from China, Ghana, India, Mexico, Russia and South Africa. *Maturitas* 2016;91:8e18.
33. Hyde Z, Flicker L, Smith K, et al. Prevalence and incidence of frailty in Aboriginal Australians, and associations with mortality and disability. *Maturitas* 2016;87:89e94.
34. McCaul KA, Almeida OP, Norman PE, et al. How many older people are frail? Using multiple imputation to investigate frailty in the population. *J Am Med Dir Assoc* 2015;16:439.e1e439.e7.
35. Theou O, Rockwood MR, Mitnitski A, Rockwood K. Disability and comorbidity in relation

- to frailty: How much do they overlap? Arch Gerontol Geriatr 2012;55:e1ee8.
36. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146eM156.
37. Bock JO, Konig HH, Brenner H, et al. Associations of frailty with healthcare costsdResults of the ESTHER cohort study. BMC Health Serv Res 2016;16:128.
38. Reddy SR, Ross-Degnan D, Zaslavsky AM, et al. Health care payments in the Asia Pacific: Validation of five survey measures of economic burden. Int J Equity Health 2013;12:49.
39. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601e608.
40. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. Sci World J 2001;1:323e336.
41. Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator:Psychometric properties. J Am Med Dir Assoc 2010;11:344e355.
42. Rolfsen DB, Majumdar SR, Tsuyuki RT, et al. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006;35:526e529.
43. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: Consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc 2014;15:95e101.
44. Chen L-K, Rockwood K. Planning for frailty. J Clin Gerontol Geriatr 2012;3:3e4.
45. Woolf S, Schunemann HJ, Eccles MP, et al. Developing clinical practice guidelines: Types of evidence and outcomes; values and economics, synthesis, grading, and presentation and deriving recommendations. IS 2012;7:61.
46. Turner G, Clegg A. Best practice guidelines for the management of frailty: A British Geriatrics Society, Age UK and Royal College of General Practitioners report. Age Ageing 2014;43:744e747.
47. Maurice J. WHO puts healthy ageing on the front burner. Lancet 2016;387:109e110.
48. Brozek JL, Akl EA, Alonso-Coello P, et al. Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. Allergy 2009;64:669e677.
49. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of

- recommendations. BMJ (Clinical research ed) 2004;328:1490.
50. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol 2013;66:726e735.
51. Cruz JE, Fahim G, Moore K. Practice Guideline Development, Grading, and Assessment. P T 2015;40:854e857.
52. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 2012; 64:465e474.
53. Dirksen CD. The use of research evidence on patient preferences in healthcare decision-making: Issues, controversies and moving forward. Exp Rev Pharmacoeconomics Outcomes Res 2014;14:785e794.
54. Landi F, Calvani R, Cesari M, et al. Sarcopenia as the Biological Substrate of Physical Frailty. Clin Geriat Med 2015;31:367e374.
55. Bauman A, Merom D, Bull FC, et al. Updating the evidence for physical activity: Summative reviews of the epidemiological evidence, prevalence, and interventions to promote "active aging". Gerontologist 2016;56: S268eS280.
56. Cesari M, Landi F, Vellas B, et al. Sarcopenia and physical frailty: Two sides of the same coin. Frontiers Aging Neurosci 2014;6:192.
57. Morley JE. Sarcopenia in the elderly. Fam Pract 2012;29:i44ei48.
58. Cesari M, Nobili A, Vitale G. Frailty and sarcopenia: From theory to clinical implementation and public health relevance. Eur J Intern Med 2016;35:1e9.
59. Romero-Ortuno R, O'Shea D. Fitness and frailty: Opposite ends of a challenging continuum! Will the end of age discrimination make frailty assessments an imperative? Age Ageing 2013;42:279e280.
60. Espinoza SE, Jung I, Hazuda H. Frailty transitions in the San Antonio Longitudinal Study of Aging. J Am Geriatr Soc 2012;60:652e660.
61. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. Arch Intern Med 2006;166:418e423.

62. van de Pol MH, Fluit CR, Lagro J, et al. Expert and patient consensus on a dynamic model for shared decision-making in frail older patients. *Patient Educ Counsel* 2016;99:1069e1077.
63. Raiche M, Hebert R, Dubois MF. PRISMA-7: A case-finding tool to identify older adults with moderate to severe disabilities. *Arch Gerontol Geriatr* 2008;47:9e18.
64. Chapman MD, Le BH, Gorelik A. The Vulnerable Elders Survey and its prognostic relationship to survival in an older community-based palliative population. *BMJ Support Palliat Care* 2013;3:335e342.
65. Lucicesare A, Hubbard RE, Searle SD, Rockwood K. An index of self-rated health deficits in relation to frailty and adverse outcomes in older adults. *Aging Clin Exp Res* 2010;22:255e260.
66. Hebert R, Bravo G, Korner-Bitensky N, Voyer L. Predictive validity of a postal questionnaire for screening community-dwelling elderly individuals at risk of functional decline. *Age Ageing* 1996;25:159e167.
67. Baitar A, Van Fraeyenhove F, Vandebroek A, et al. Evaluation of the Groningen Frailty Indicator and the G8 questionnaire as screening tools for frailty in older patients with cancer. *J Geriatr Oncol* 2013;4:32e38.
68. Melis RJ, van Eijken MI, Borm GF, et al. The design of the Dutch EASYcare study: A randomised controlled trial on the effectiveness of a problem-based community intervention model for frail elderly people [NCT00105378]. *BMC Health Serv Res* 2005;5:65.
69. Ensrud KE, Ewing SK, Taylor BC, et al. Frailty and risk of falls, fracture, and mortality in older women: The study of osteoporotic fractures. *J Gerontol A Biol Sci Med Sci* 2007;62:744e751.
70. McCusker J, Bellavance F, Cardin S, et al. Detection of older people at increased risk of adverse health outcomes after an emergency visit: The ISAR screening tool. *J Am Geriatr Soc* 1999;47:1229e1237.
71. Steverink N, Slaets JP, Schuurmans H, van Lis M. Measuring Frailty: Developing and testing of the Groningen Frailty Indicator (GFI). *Gerontologist* 2001;41:236e237.

72. Lam NW, Goh HT, Kamaruzzaman SB, et al. Normative data for hand grip strength and key pinch strength, stratified by age and gender for a multiethnic Asian population. Singapore Med J 2016;57:578e584.
73. Malhotra R, Ang S, Allen JC, et al. Normative Values of Hand Grip Strength for Elderly Singaporeans Aged 60 to 89 Years: A Cross-Sectional Study. J Am Med Dir Assoc 2016;17:864.e1e864.e7.
74. Wu SW, Wu SF, Liang HW, et al. Measuring factors affecting grip strength in a Taiwan Chinese population and a comparison with consolidated norms. Appl Ergonomics 2009;40:811e815.
75. Stanaway FF, Gnjidic D, Blyth FM, et al. How fast does the Grim Reaper walk? Receiver operating characteristics curve analysis in healthy men aged 70 and over. BMJ (Clinical research ed) 2011;343:d7679.
76. Podsiadlo D, Richardson S. The timed "Up & Go": A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142e148.
77. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85eM94.
78. Morley JE, Adams EV. Rapid Geriatric Assessment. J Am Med Dir Assoc 2015;16:808e812.
79. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: Different instruments for different purposes. Age Ageing 2014;43:10e12.
80. Craig C, Chadborn N, Sands G, et al. Systematic review of EASY-care needs assessment for community-dwelling older people. Age Ageing 2015;44:559e565.
81. Satake S, Senda K, Hong YJ, et al. Validity of the Kihon Checklist for assessing frailty status. Geriatr Gerontol Int 2016;16:709e715.
82. Pilotto A, Ferrucci L, Franceschi M, et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res 2008;11:151e161.
83. Pijpers E, Ferreira I, van de Laar RJ, et al. Predicting mortality of psychogeriatric patients: A simple prognostic frailty risk score. Postgraduate Med J 2009;85:464e469.

84. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173:489e495.
85. Vellas B, Balardy L, Gillette-Guyonnet S, et al. Looking for frailty in community-dwelling older persons: The Gerontopole Frailty Screening Tool(GFST). *J Nutri Health Aging* 2013;17:629e631.
86. Hii TB, Lainchbury JG, Bridgman PG. Frailty in acute cardiology: Comparison of a quick clinical assessment against a validated frailty assessment tool. *Heart Lung Circ* 2015;24:551e556.
87. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised older people. *Age Ageing* 2014;43:477e484.
88. Hoogendoijk EO, van der Horst HE, Deeg DJ, et al. The identification of frail older adults in primary care: Comparing the accuracy of five simple instruments. *Age Ageing* 2013;42:262e265.
89. Mack M. Frailty and aortic valve disease. *J Thorac Cardiovasc Surg* 2013;145:S7eS10.
90. Rodes-Cabau J, Mok M. Working toward a frailty index in transcatheter aortic valve replacement: A major move away from the “eyeball test”. *JACC Cardiovasc Intervent* 2012;5:982e983.
91. O'Neill BR, Batterham AM, Hollingsworth AC, et al. Do first impressions count?Frailty judged by initial clinical impression predicts medium-term mortality in vascular surgical patients. *Anaesthesia* 2016;71:684e691.
92. Ellis G, Whitehead MA, Robinson D, et al. Comprehensive geriatric assessment for older adults admitted to hospital: Meta-analysis of randomised controlled trials. *BMJ (Clinical research ed)* 2011;343:d6553.
93. Romero-Ortuno R. Frailty in primary care. *Interdisciplinary topics in gerontology and geriatrics* 2015;41:85e94.
94. Fried LP. Interventions for human frailty: Physical activity as a model. *Cold Spring Harbor Perspect Med* 2016;6:6.
95. Chen X, Mao G, Leng SX. Frailty syndrome: An overview. *Clin Intervent Aging* 2014;9:433e441.

96. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: A systematic review. *Age Ageing* 2015;44:148e152.
97. Dent E, Hoogendoijk EO. Psychosocial factors modify the association of frailty with adverse outcomes: A prospective study of hospitalised older people. *BMC Geriatr* 2014;14:108.
98. Ensrud KE, Ewing SK, Cawthon PM, et al. A comparison of frailty indexes for the prediction of falls, disability, fractures, and mortality in older men. *J Am Geriatr Soc* 2009;57:492e498.
99. Jung HW, Jang IY, Lee YS, et al. Prevalence of frailty and aging-related health conditions in older Koreans in rural communities: A cross-sectional analysis of the aging Study of Pyeongchang Rural Area. *J Korean Med Sci* 2016;31:345e352.
100. Zhu Y, Liu Z, Wang Y, et al. Agreement between the frailty index and phenotype and their associations with falls and overnight hospitalizations. *Arch Gerontol Geriatr* 2016;66:161e165.
101. Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. *BMC Geriatr* 2008;8:24.
102. Cesari M, Costa N, Hoogendoijk EO, et al. How the Frailty Index may support the allocation of health care resources: An example from the INCUR Study. *J Am Med Dir Assoc* 2016;17:448e450.
103. Bennett S, Song X, Mitnitski A, Rockwood K. A limit to frailty in very old, community-dwelling people: A secondary analysis of the Chinese longitudinal health and longevity study. *Age Ageing* 2013;42:372e377.
104. Goggins WB, Woo J, Sham A, Ho SC. Frailty index as a measure of biological age in a Chinese population. *J Gerontol A Biol Sci Med Sci* 2005;60:1046e1051.
105. Yu P, Song X, Shi J, et al. Frailty and survival of older Chinese adults in urban and rural areas: Results from the Beijing Longitudinal Study of Aging. *Arch Gerontol Geriatr* 2012;54:3e8.
106. Ma L, Zhang L, Tang Z, et al. Use of the frailty index in evaluating the prognosis of older people in Beijing: A cohort study with an 8-year follow-up. *Arch Gerontol Geriatr* 2016;64:172e177.

107. Yang F, Gu D. Predictability of frailty index and its components on mortality in older adults in China. *BMC Geriatr* 2016;16:145.
108. Hao Q, Song X, Yang M, et al. Understanding risk in the oldest old: Frailty and the metabolic syndrome in a Chinese community sample aged 90þ years. *J Nutr Health Aging* 2016;20:82e88.
109. Liu Z, Wang Q, Zhi T, et al. Frailty Index and its relation to falls and overnight hospitalizations in elderly Chinese people: A population-based study. *J Nutr Health Aging* 2016;20:561e568.
110. Zeng A, Song X, Dong J, et al. Mortality in relation to frailty in patients admitted to a specialized geriatric intensive care unit. *J Gerontol A Biol Sci Med Sci* 2015;70:1586e1594.
111. Armstrong JJ, Mitnitski A, Launer LJ, et al. Frailty in the Honolulu-Asia Aging Study: Deficit accumulation in a male cohort followed to 90% mortality. *J Gerontol A Biol Sci Med Sci* 2015;70:125e131.
112. Almeida OP, Hankey GJ, Yeap BB, et al. Depression, frailty, and all-cause mortality: A cohort study of men older than 75 years. *J Am Med Dir Assoc* 2015;16:296e300.
113. Dent E, Hoon E, Karonn J, et al. Frailty and health service use in rural South Australia. *Arch Gerontol Geriatr* 2016;62:53e58.
114. Rochat S, Cumming RG, Blyth F, et al. Frailty and use of health and community services by community-dwelling older men: The Concord Health and Ageing in Men Project. *Age Ageing* 2010;39:228e233.
115. Rockwood K, Rockwood MR, Mitnitski A. Physiological redundancy in older adults in relation to the change with age in the slope of a frailty index. *J Am Geriatr Soc* 2010;58:318e323.
116. Woo J, Leung J, Morley JE. Comparison of frailty indicators based on clinical phenotype and the multiple deficit approach in predicting mortality and physical limitation. *J Am Geriatr Soc* 2012;60:1478e1486.
117. Abellan van Kan G, Rolland Y, Bergman H, et al. The I.A.N.A Task Force on frailty assessment of older people in clinical practice. *J Nutr Health Aging* 2008;12:29e37.
118. Chao CT, Hsu YH, Chang PY, et al. Simple self-report FRAIL scale might be more closely

- associated with dialysis complications than other frailty screening instruments in rural chronic dialysis patients. *Nephrology* (Carlton,Vic) 2015;20:321e328.
119. Lopez D, Flicker L, Dobson A. Validation of the frail scale in a cohort of older Australian women. *J Am Geriatr Soc* 2012;60:171e173.
120. Li Y, Zou Y, Wang S, et al. A Pilot Study of the FRAIL Scale on Predicting Outcomes in Chinese Elderly People With Type 2 Diabetes. *J Am Med Dir Assoc* 2015;16:714.e7e714.e12.
121. Basic D, Shanley C. Frailty in an older inpatient population: Using the clinical frailty scale to predict patient outcomes. *J Aging Health* 2015;27:670e685.
122. Gregorevic KJ, Hubbard RE, Lim WK, Katz B. The clinical frailty scale predicts functional decline and mortality when used by junior medical staff: A prospective cohort study. *BMC Geriatr* 2016;16:117.
123. Bagshaw SM, Stelfox HT, McDermid RC, et al. Association between frailty and short- and long-term outcomes among critically ill patients: A multicentre prospective cohort study. *CMAJ* 2014;186:E95eE102.
124. Rockwood K, Abeysundara MJ, Mitnitski A. How should we grade frailty in nursing home patients? *J Am Med Dir Assoc* 2007;8:595e603.
125. Fang WH, Huang GS, Chang HF, et al. Gender differences between WOMAC index scores, health-related quality of life and physical performance in an elderly Taiwanese population with knee osteoarthritis. *BMJ Open* 2015;5:e008542.
126. Li CI, Li TC, Lin WY, et al. Combined association of chronic disease and low skeletal muscle mass with physical performance in older adults in the Sarcopenia and Translational Aging Research in Taiwan (START) study. *BMC Geriatr* 2015;15:11.
127. Kim H, Suzuki T, Kim M, et al. Incidence and predictors of sarcopenia onset in community-dwelling elderly Japanese women: 4-year follow-up study. *J Am Med Dir Assoc* 2015;16:85.e1e85.e8.
128. Fukui S, Kawakami M, Otaka Y, et al. Physical frailty in older people with severe aortic stenosis. *Aging Clin Exp Res* 2016;28:1081e1087.
129. Kim YH, Kim KI, Paik NJ, et al. Muscle strength: A better index of low physical performance

- than muscle mass in older adults. *Geriatr Gerontol Int* 2016;16:577e585.
130. Oh B, Cho B, Choi HC, et al. The influence of lower-extremity function in elderly individuals' quality of life (QOL): An analysis of the correlation between SPPB and EQ-5D. *Arch Gerontol Geriatr* 2014;58:278e282.
131. Matchar DB, Duncan PW, Lien CT, et al. Randomized Controlled Trial of Screening, Risk Modification, and Physical Therapy to Prevent Falls Among the Elderly Recently Discharged From the Emergency Department to the Community: The Steps to Avoid Falls in the Elderly Study. *Arch Phys Med Rehabil* 2017;98:1086e1096.
132. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: A systematic review. *J Aging Res* 2011;2011:569194.
133. Chou CH, Hwang CL, Wu YT. Effect of exercise on physical function, daily living activities, and quality of life in the frail older adults: A meta-analysis. *Arch Phys Med Rehabil* 2012;93:237e244.
134. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older adults: A systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154.
135. Raymond MJ, Bramley-Tzerefos RE, Jeffs KJ, et al. Systematic review of highintensity progressive resistance strength training of the lower limb compared with other intensities of strength training in older adults. *Arch Phy Med Rehabil* 2013;94:1458e1472.
136. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exer* 2009;41:1510e1530.
137. Schreier MM, Bauer U, Osterbrink J, et al. Fitness training for the old and frail. Effectiveness and impact on daily life coping and self-care abilities. *Zeitschrift fur Gerontologie und Geriatrie* 2016;49:107e114.
138. Oh SL, Kim HJ, Woo S, et al. Effects of an integrated health education and elastic band resistance training program on physical function and muscle strength in community-dwelling elderly womenHealthy Aging and Happy Aging II. study. *Geriatr Gerontol Int* 2017;17:825e833.

139. Forti LN, Van Roie E, Njemini R, et al. Load-specific inflammation mediating effects of resistance training in older persons. *J Am Med Dir Assoc* 2016;17:547e552.
140. Chung CL, Thilarajah S, Tan D. Effectiveness of resistance training on muscle strength and physical function in people with Parkinson's disease: A systematic review and meta-analysis. *Clin Rehabil* 2016;30:11e23.
141. Fiatarone Singh MA, Gates N, Saigal N, et al. The Study of Mental and Resistance Training (SMART) study-resistance training and/or cognitive training in mild cognitive impairment: A randomized, double-blind, double-sham controlled trial. *J Am Med Dir Assoc* 2014;15:873e880.
142. Liu CJ, Latham N. Can progressive resistance strength training reduce physical disability in older adults? A meta-analysis study. *Disabil Rehabil* 2011;33:87e97.
143. Cadore EL, Moneo AB, Mensat MM, et al. Positive effects of resistance training in frail elderly patients with dementia after long-term physical restraint. *Age*(Dordrecht, Netherlands) 2014;36:801e811.
144. Singh NA, Quine S, Clemson LM, et al. Effects of high-intensity progressive resistance training and targeted multidisciplinary treatment of frailty on mortality and nursing home admissions after hip fracture: A randomized controlled trial. *J Am Med Dir Assoc* 2012;13:24e30.
145. Steib S, Schoene D, Pfeifer K. Dose-response relationship of resistance training in older adults: A meta-analysis. *Med Sci Sports Exer* 2010;42:902e914.
146. Landi F, Marzetti E, Martone AM, et al. Exercise as a remedy for sarcopenia. *Curr Opin Clin Nutri Metab Care* 2014;17:25e31.
147. Hagstrom AD, Marshall PW, Lonsdale C, et al. Resistance training improves fatigue and quality of life in previously sedentary breast cancer survivors: A randomised controlled trial. *Eur J Cancer Care* 2016;25:784e794.
148. Liu JY, Lai CK, Siu PM, et al. An individualized exercise programme with and without behavioural change enhancement strategies for managing fatigue among frail older people: A quasi-experimental pilot study. *Clin Rehabil* 2016;31:521e531.
149. Franklin BA, Whaley MH, Howley ET, Balady GJ. ACSM's Guidelines for Exercise Testing

- and Prescription. 9th ed. 2013. Philadelphia, Pa: Lippincott Williams & Wilkins.
150. Bray NW, Smart RR, Jakobi JM, Jones GR. Exercise prescription to reverse frailty. *Appl Physiol Nutri Metab* 2016;41:1112e1116.
151. Thiebaud RS, Funk MD, Abe T. Home-based resistance training for older adults: A systematic review. *Geriatr Gerontol Int* 2014;14:750e757.
152. Thomas S, Mackintosh S, Halbert J. Does the 'Otago exercise programme' reduce mortality and falls in older adults?: A systematic review and metaanalysis. *Age Ageing* 2010;39:681e687.
153. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: The LIFE study randomized clinical trial. *JAMA* 2014;311:2387e2396.
154. Jefferis BJ, Merom D, Sartini C, et al. Physical activity and falls in older men: The critical role of mobility limitations. *Med Sci Sports Exercise* 2015;47:2119e2128.
155. Izquierdo M, Rodriguez-Manas L, Casas-Herrero A, et al. Is it ethical not to prescribe physical activity for the elderly frail? *J Am Med Dir Assoc* 2016;17:779e781.
156. Santanasto AJ, Glynn NW, Lovato LC, et al; LIFE Study Group. Effect of physical activity versus health education on physical function, grip strength and mobility. *J Am Geriatr Soc* 2017 Feb 21 [Epub ahead of print].
157. Manini TM, Beavers DP, Pahor M, et al; LIFE study investigators. Effect of physical activity on self-reported disability in older adults: Results from the LIFE Study. *J Am Geriatr Soc* 2017;65:980e988.
158. Freiberger E, Blank WA, Salb J, et al. Effects of a complex intervention on fall risk in the general practitioner setting: A cluster randomized controlled trial. *Clin Intervent Aging* 2013;8:1079e1088.
159. Freiberger E, Kemmler W, Siegrist M, Sieber C. Frailty and exercise interventions: Evidence and barriers for exercise programs. *Zeitschrift fur Gerontologie und Geriatrie* 2016;49:606e611.
160. de Souto Barreto P, Morley JE, Chodzko-Zajko W, et al. Recommendations on physical activity and exercise for older adults living in long-term care facilities:A taskforce report.

J Am Med Dir Assoc 2016;17:381e392.

161. Hawley-Hague H, Horne M, Campbell M, et al. Multiple levels of influence on older adults' attendance and adherence to community exercise classes. Gerontologist 2014;54:599e610.
162. Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: Five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol 2012;65:989e995.
163. Rolland Y, Morley JE. Editorial: Frailty and polypharmacy. J Nutr Health Aging 2016;20:645e646.
164. Flaherty JH, Perry HM III, Lynchard GS, Morley JE. Polypharmacy and hospitalization among older home care patients. J Gerontol A Biol Sci Med Sci 2000;55:M554eM559.
165. Bronskill SE, Gill SS, Paterson JM, et al. Exploring variation in rates of polypharmacy across long term care homes. J Am Med Dir Assoc 2012;13:309.e15e309.e21.
166. Moulis F, Moulis G, Balardy L, et al. Searching for a polypharmacy threshold associated with frailty. J Am Med Dir Assoc 2015;16:259e261.
167. Resnick B, Pacala JT. 2012 Beers Criteria. J Am Geriatr Soc 2012;60:612e613.
168. Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging definition of 'deprescribing' with network analysis: Implications for future research and clinical practice. Br J Clin Pharmacol 2015;80:1254e1268.
169. Frank C, Weir E. Deprescribing for older patients. CMAJ 2014;186:1369e1376.
170. Potter K, Flicker L, Page A, Etherton-Bee C. Deprescribing in frail older people: A randomised controlled trial. PLoS One 2016;11:e0149984.
171. Tjia J, Velten SJ, Parsons C, et al. Studies to reduce unnecessary medication use in frail older adults: A systematic review. Drugs Aging 2013;30:285e307.
172. Hamilton H, Gallagher P, Ryan C, et al. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Arch Intern Med 2011;171:1013e1019.
173. O'Mahony D, O'Sullivan D, Byrne S, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. Age Ageing 2015;44:213e218.
174. Gallagher P, Ryan C, Byrne S, et al. STOPP (Screening Tool of Older Person's Prescriptions)

- and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *Int J Clin Pharmacol Therapeut* 2008;46:72e83.
175. McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: A national consensus panel. *CMAJ* 1997;156:385e391.
176. Lund BC, Carnahan RM, Egge JA, et al. Inappropriate prescribing predicts adverse drug events in older adults. *Ann Pharmacother* 2010;44:957e963.
177. Basger BJ, Chen TF, Moles RJ. Inappropriate medication use and prescribing indicators in elderly Australians: Development of a prescribing indicators tool. *Drugs Aging* 2008;25:777e793.
178. Scott IA, Anderson K, Freeman CR, Stowasser DA. First do no harm: A real need to deprescribe in older patients. *Med J Australia* 2014;201:390e392.
179. Page AT, Etherton-Bee CD, Clifford RM, et al. Deprescribing in frail older peopleDo doctors and pharmacists agree? *RSAP* 2016;12:438e449.
180. Tang NKY, Lereya ST, Boulton H, et al. Nonpharmacological treatments of insomnia for long-term painful conditions: A systematic review and metaanalysis of patient-reported outcomes in randomized controlled trials. *Sleep* 2015;38:1751e1764.
181. Basunia M, Fahmy SA, Schmidt F, et al. Relationship of symptoms with sleepstage abnormalities in obstructive sleep apnea-hypopnea syndrome. *J Commun Hosp Intern Med Perspect* 2016;6:32170.
182. Stadje R, Dornieden K, Baum E, et al. The differential diagnosis of tiredness: A systematic review. *BMC Fam Pract* 2016;17:147.
183. Taylor WD. Clinical practice. Depression in the elderly. *N Engl J Med* 2014;371:1228e1236.
184. Dominguez LJ, Bevilacqua M, Dibella G, Barbagallo M. Diagnosing and managing thyroid disease in the nursing home. *J Am Med Dir Assoc* 2008;9:9e17.
185. Briani C, Dalla Torre C, Citton V, et al. Cobalamin deficiency: Clinical picture and radiological findings. *Nutrients* 2013;5:4521e4539.
186. Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: Clinical, research, and policy implications of a core geriatric concept. *J Am Geriatr Soc* 2007;55:780e791.

187. Vitiello MV, McCurry SM, Shortreed SM, et al. Short-term improvement in insomnia symptoms predicts long-term improvements in sleep, pain, and fatigue in older adults with comorbid osteoarthritis and insomnia. *Pain* 2014;155:1547e1554.
188. Lakey SL, LaCroix AZ, Gray SL, et al. Antidepressant use, depressive symptoms, and incident frailty in women aged 65 and older from the Women's Health Initiative Observational Study. *J Am Geriatr Soc* 2012;60:854e861.
189. Morley JE, Malmstrom TK, Rodriguez-Manas L, Sinclair AJ. Frailty, sarcopenia and diabetes. *J Am Med Dir Assoc* 2014;15:853e859.
190. Morley JE. Anorexia, weight loss, and frailty. *J Am Med Dir Assoc* 2010;11:225e228.
191. Morley JE. Undernutrition in older adults. *Fam Pract* 2012;29:i89ei93.
192. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. *Cochrane Database Syst Rev* 2009;Cd003288.
193. Milne AC, Avenell A, Potter J. Meta-analysis: Protein and energy supplementation in older people. *Ann Intern Med* 2006;144:37e48.
194. Wright OR, Connelly LB, Capra S, Hendrikz J. Determinants of foodservice satisfaction for patients in geriatrics/rehabilitation and residents in residential aged care. *Health Expectations* 2013;16:251e265.
195. Collins J, Porter J. The effect of interventions to prevent and treat malnutrition in patients admitted for rehabilitation: A systematic review with metaanalysis. *J Human Nutri Dietetics* 2015;28:1e15.
196. Bounoure L, Gomes F, Stanga Z, et al. Detection and treatment of medical inpatients with or at-risk of malnutrition: Suggested procedures based on validated guidelines. *Nutrition* 2016;32:790e798.
197. Beck AM, Dent E, Baldwin C. Nutritional intervention as part of functional rehabilitation in older people with reduced functional ability: A systematic review and meta-analysis of randomised controlled studies. *J Hum Nutr Diet* 2016;29:733e745.
198. Beck AM, Holst M, Rasmussen HH. Oral nutritional support of older (65years+) medical and surgical patients after discharge from hospital: Systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil* 2013;27:19e27.

199. Fukagawa NK. Protein and amino acid supplementation in older humans. *Amino Acids* 2013;44:1493e1509.
200. Bauer JM, Verlaan S, Bautmans I, et al. Effects of a vitamin D and leucineenriched whey protein nutritional supplement on measures of sarcopenia in older adults, the PROVIDE study: A randomized, double-blind, placebocontrolled trial. *J Am Med Dir Assoc* 2015;16:740e747.
201. Cramer JT, Cruz-Jentoft AJ, Landi F, et al. Impacts of high-protein oral nutritional supplements among malnourished men and women with sarcopenia: A multicenter, Randomized, Double-Blinded, Controlled Trial. *J Am Med Dir Assoc* 2016;17:1044e1055.
202. Morley JE, Argiles JM, Evans WJ, et al. Nutritional recommendations for the management of sarcopenia. *J Am Med Dir Assoc* 2010;11:391e396.
203. Paddon-Jones D, Short KR, Campbell WW, et al. Role of dietary protein in the sarcopenia of aging. *Am J Clin Nutr* 2008;87:1562se1566s.
204. Bauer J, Biolo G, Cederholm T, et al. Evidence-based recommendations for optimal dietary protein intake in older people: A position paper from the PROT-AGE Study Group. *J Am Med Dir Assoc* 2013;14:542e559.
205. Ng TP, Feng L, Nyunt MS, et al. Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal Among Older Adults: A Randomized Controlled Trial. *The American journal of medicine* 2015;128:1225e1236.e1.
206. Tieland M, van de Rest O, Dirks ML, et al. Protein supplementation improves physical performance in frail elderly people: A randomized, double-blind,placebo-controlled trial. *J Am Med Dir Assoc* 2012;13:720e726.
207. Kim HK, Suzuki T, Saito K, et al. Effects of exercise and amino acid supplementation on body composition and physical function in communitydwelling elderly Japanese sarcopenic women: A randomized controlled trial. *J Am Geriatr Soc* 2012;60:16e23.
208. Cesari M, Landi F, Calvani R, et al. Rationale for a preliminary operational definition of physical frailty and sarcopenia in the SPRINTT trial. *Aging Clin Exp Res* 2017;29:81e88.
209. Landi F, Cesari M, Calvani R, et al. The “Sarcopenia and Physical fRality IN older people: Multicomponent Treatment strategies” (SPRINTT) randomized controlled trial: Design

- and methods. *Aging Clin Exp Res* 2017;29:89e100.
210. Bauer JM, Kaiser MJ, Anthony P, et al. The Mini Nutritional Assessment: Its history, today's practice, and future perspectives. *Nutr Clin Pract* 2008;23:388e396.
211. Kaiser MJ, Bauer JM, Ramsch C, et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): A practical tool for identification of nutritional status. *J Nutr Health Aging* 2009;13:782e788.
212. Stratton RJ, Hackston A, Longmore D, et al. Malnutrition in hospital outpatients and inpatients: Prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' ('MUST') for adults. *Br J Nutr* 2004;92:799e808.
213. Chang HH, Tsai SL, Chen CY, Liu WJ. Outcomes of hospitalized elderly patients with geriatric syndrome: Report of a community hospital reform plan in Taiwan. *Arch Gerontol Geriatr* 2010;50:S30eS33.
214. Chan M, Lim YP, Ernest A, Tan TL. Nutritional assessment in an Asian nursing home and its association with mortality. *J Nutr Health Aging* 2010;14:23e28.
215. Tsai AC, Yang SF, Wang JY. Validation of population-specific Mini-Nutritional Assessment with its long-term mortality-predicting ability: Results of a population-based longitudinal 4-year study in Taiwan. *Br J Nutr* 2010;104:93e99.
216. Tsai AC, Chang TL, Wang JY. Short-form Mini-Nutritional Assessment with either BMI or calf circumference is effective in rating the nutritional status of elderly TaiwaneseResults of a national cohort study. *Br J Nutr* 2013;110:1126e1132.
217. Chao PC, Chuang HJ, Tsao LY, et al. The Malnutrition Universal Screening Tool (MUST) and a nutrition education program for high risk cancer patients: Strategies to improve dietary intake in cancer patients. *BioMedicine* 2015;5:17.
218. Wilson MM, Thomas DR, Rubenstein LZ, et al. Appetite assessment: Simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. *Am J Clin Nutr* 2005;82:1074e1081.
219. Leung RY, Cheung BM, Nguyen US, et al. Optimal vitamin D status and its relationship with bone and mineral metabolism in Hong Kong Chinese. *Bone* 2017;97:293e298.
220. Bolland MJ, Grey A, Cundy T. Vitamin D and health in adults in Australia and New Zealand:

A position statement. Med J Australia 2012;197:553. Author reply-4.

221. Wahlqvist ML. Vitamin D in North-East Asian clinical nutrition practice. Asia Pac J Clin Nutr 2013;22:166e169.
222. Nowson CA, McGrath JJ, Ebeling PR, et al. Vitamin D and health in adults in Australia and New Zealand: A position statement. Med J Australia 2012;196:686e687.
223. Jayaratne N, Hughes MC, Ibiebele TI, et al. Vitamin D intake in Australian adults and the modeled effects of milk and breakfast cereal fortification. Nutrition 2013;29:1048e1053.
224. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): The Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab 2003;88:5766e5772.
225. Tieland M, Brouwer-Brolsma EM, Nienaber-Rousseau C, et al. Low vitamin D status is associated with reduced muscle mass and impaired physical performance in frail elderly people. Eur J Clin Nutr 2013;67:1050e1055.
226. Wong YY, McCaul KA, Yeap BB, et al. Low vitamin D status is an independent predictor of increased frailty and all-cause mortality in older men: The Health in Men Study. J Clin Endocrinol Metab 2013;98:3821e3828.
227. Flicker L, Mead K, MacInnis RJ, et al. Serum vitamin D and falls in older women in residential care in Australia. J Am Geriatr Soc 2003;51:1533e1538.
228. Shimizu Y, Kim H, Yoshida H, et al. Serum 25-hydroxyvitamin D level and risk of falls in Japanese community-dwelling elderly women: A 1-year follow-up study. Osteoporosis Int 2015;26:2185e2192.
229. Zhou J, Huang P, Liu P, et al. Association of vitamin D deficiency and frailty: A systematic review and meta-analysis. Maturitas 2016;94:70e76.
230. Artaza-Artabe I, Saez-Lopez P, Sanchez-Hernandez N, et al. The relationship between nutrition and frailty: Effects of protein intake, nutritional supplementation, vitamin D and exercise on muscle metabolism in the elderly. A systematic review. Maturitas 2016;93:89e99.
231. Halfon M, Phan O, Teta D. Vitamin D. A review on its effects on muscle strength, the risk of fall, and frailty. BioMed Res Int 2015;2015:953241.

232. Wong YY, Flicker L. Hypovitaminosis D and frailty: Epiphenomenon or causal? *Maturitas* 2015;82:328e335.
233. Bruyere O, Cavalier E, Buckinx F, Reginster JY. Relevance of vitamin D in the pathogenesis and therapy of frailty. *Curr Opin Clin Nutr Metab Care* 2017;20:26e29.
234. Song HR, Kweon SS, Choi JS, et al. High prevalence of vitamin D deficiency in adults aged 50 years and older in Gwangju, Korea: The Dong-gu Study. *J Korean Med Sci* 2014;29:149e152.
235. Zhen D, Liu L, Guan C, et al. High prevalence of vitamin D deficiency among middle-aged and elderly individuals in northwestern China: Its relationship to osteoporosis and lifestyle factors. *Bone* 2015;71:1e6.
236. van Schoor NM, Lips P. Worldwide vitamin D status. *Best practice and research Clin Endocrinol Metab* 2011;25:671e680.
237. Bacon CJ, Kerse N, Hayman KJ, et al. Vitamin D status of Maori and non-Maori octogenarians in New Zealand: A Cohort Study (LiLACS NZ). *Asia Pac J Clin Nutr* 2016;25:885e897.
238. G R, Gupta A. Vitamin D deficiency in India: Prevalence, causalities and interventions. *Nutrients* 2014;6:729e775.
239. Chan R, Chan CC, Woo J, et al. Serum 25-hydroxyvitamin D, bone mineral density, and non-vertebral fracture risk in community-dwelling older men: Results from Mr. Os, Hong Kong. *Arch Osteoporosis* 2011;6:21e30.
240. Chin KY, Ima-Nirwana S, Ibrahim S, et al. Vitamin D status in Malaysian men and its associated factors. *Nutrients* 2014;6:5419e5433.
241. Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. *Am J Clin Nutr* 2008;87:1080se1086s.
242. Cancer Council of Australia. Position statement on sun exposure and vitamin D risks and benefits. Available at: http://wiki.cancer.org.au/policy/Position_statement_-_Risks_and_benefits_of_sun_exposure; 2017. Accessed January 16, 2017.
243. Nowson CA, McGrath JJ, Ebeling PR, Haikerwal A, Daly RM, Sanders KM, Seibel MJ, Mason RS. Working Group of the Australian and New Zealand Bone and Mineral Society,

- Endocrine Society of Australia and Osteoporosis Australia. Vitamin D and health in adults in Australia and New Zealand: a position statement. *Med J Australia* 2012;196:686e687.
244. Powe CE, Evans MK, Wenger J, et al. Vitamin D-binding protein and vitamin D status of black Americans and white Americans. *N Engl J Med* 2013;369:1991e2000.
245. Nair R, Maseeh A. Vitamin D. The “sunshine” vitamin. *J Pharmacol Pharmacotherapeut* 2012;3:118e126.
246. Annweiler C, Schott AM, Berrut G, et al. Vitamin D-related changes in physical performance: A systematic review. *J Nutr Health Aging* 2009;13:893e898.
247. Dix CF, Robinson A, Bauer JD, Wright ORL. Vitamin D: Australian dietitian’s knowledge and practices. *Nutr Diet* 16 Jun 2016 [Epub ahead of print].
248. Muir SW, Montero-Odasso M. Effect of vitamin D supplementation on muscle strength, gait and balance in older adults: A systematic review and metaanalysis. *J Am Geriatr Soc* 2011;59:2291e2300.
249. Sanders KM, Seibel MJ. Therapy: New findings on vitamin D₃ supplementation and fallsWhen more is perhaps not better. *Nat Rev Endocrinol* 2016;12:190e191.
250. Sanders KM, Stuart AL, Williamson EJ, et al. Annual high-dose oral vitamin D and falls and fractures in older women: A randomized controlled trial. *JAMA* 2010;303:1815e1822.
251. Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, et al. Monthly high-dose vitamin D treatment for the prevention of functional decline: A randomized clinical trial. *JAMA Intern Med* 2016;176:175e183.
252. Rosendahl-Riise H, Spielau U, Ranhoff AH, et al. Vitamin D supplementation and its influence on muscle strength and mobility in community-dwelling older persons: A systematic review and meta-analysis. *J Hum Nutri Diet* 2016;30:3e15.
253. Rejnmark L, Avenell A, Masud T, et al. Vitamin D with calcium reduces mortality: Patient level pooled analysis of 70,528 patients from eight major vitamin D trials. *J Clin Endocrinol Metab* 2012;97:2670e2681.
254. Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: A systematic review. *J Am Geriatr Soc* 2003;51:1219e1226.

255. Cameron ID, Gillespie LD, Robertson MC, et al. Interventions for preventing falls in older people in care facilities and hospitals. *Cochrane Database Syst Rev* 2012;Cd005465.
256. Chan R, Chan D, Woo J, et al. Not all elderly people benefit from vitamin D supplementation with respect to physical function: Results from the Osteoporotic Fractures in Men Study, Hong Kong. *J Am Geriatr Soc* 2012;60:290e295.
257. Beard JR, Officer A, de Carvalho IA, et al. The World report on ageing and health: A policy framework for healthy ageing. *Lancet* 2016;21:2145e2154.
258. Holroyd-Leduc J, Resin J, Ashley L, et al. Giving voice to older adults living with frailty and their family caregivers: Engagement of older adults living with frailty in research, healthcare decision making, and in health policy. *Res Involvement Engagement* 2016;2:23.
259. Baillie L, Gallini A, Corser R, et al. Care transitions for frail, older people from acute hospital wards within an integrated healthcare system in England: A qualitative case study. *Int J Integrated Care* 2014;14:e009.
260. Parsons JG, Sheridan N, Rouse P, et al. A randomized controlled trial to determine the effect of a model of restorative home care on physical function and social support among older people. *Arch Phys Med Rehabil* 2013;94: 1015e1022.
261. Senior HE, Parsons M, Kerse N, et al. Promoting independence in frail older people: A randomised controlled trial of a restorative care service in New Zealand. *Age Ageing* 2014;43:418e424.
262. Manderson B, McMurray J, Piraino E, Stolee P. Navigation roles support chronically ill older adults through healthcare transitions: A systematic review of the literature. *Health Soc Care Commun* 2012;20:113e127.
263. Cameron ID, Fairhall N, Langron C, et al. A multifactorial interdisciplinary intervention reduces frailty in older people: Randomized trial. *BMC Med* 2013;11:65.
264. Fairhall N, Sherrington C, Cameron ID, et al. A multifactorial intervention for frail older people is more than twice as effective among those who are compliant: Complier average causal effect analysis of a randomised trial. *J Physiother* 2017;63:40e44.
265. Metzelthin SF, van Rossum E, de Witte LP, et al. The reduction of disability in community-dwelling frail older people: Design of a two-arm cluster randomized controlled trial. *BMC*

Public Health 2010;10:511.

266. Muntinga ME, Hoogendijk EO, van Leeuwen KM, et al. Implementing the chronic care model for frail older adults in The Netherlands: Study protocol of ACT (frail older adults: Care in transition). BMC Geriatr 2012;12:19.
267. Bleijenberg N, Drubbel I, Ten Dam VH, et al. Proactive and integrated primary care for frail older people: Design and methodological challenges of the Utrecht primary care PROactive frailty intervention trial (U-PROFIT). BMC Geriatr 2012;12:16.
268. Hoogendijk EO. How effective is integrated care for community-dwelling frail older people? The case of The Netherlands. Age Ageing 2016;45:585e588.
269. Gagliardi AR, Alhabib S. Trends in guideline implementation: A scoping systematic review. Implement Sci 2015;10:54.
270. Cesari M, Prince M, Thiagarajan JA, et al. Frailty: An emerging public health priority. J Am Med Dir Assoc 2016;17:188e192.