

Supplement 4. Details of overall recommendation, including the process of deriving individual recommendations

I. Diagnosis and assessment

I-1. Screening of frailty

Key question: Does screening of frailty in community dwelling older adults aged 70 or older help prevent complications (functional decline, fall, hospitalization, death, etc.) and management of frailty?

Recommendations for screening (recommendation 1 and 2):

1. It is recommended to conduct a screening test for frailty among community-dwelling elderly individuals aged 70 years or older. (Strength of recommendation: I, level of evidence A)
2. It is recommended to use validated evaluation tools to conduct screening tests for frailty. (Strength of recommendation: I, level of evidence A)

List of recommendations from existing clinical practice guidelines (CPGs) used to in the adaptation.

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| Frailty in elderly people ³⁵⁾ |
| Subjects over 75 should be always considered potentially frail. The suspect of frailty can be based on observation and/or the patient's narrative, gathering information on health status and in particular on mobility, cognitive function, feeding and life habits, and sensory functions. (Strength of recommendation: A, level of evidence VI) |
| Fit for frailty, part 1 & 2 ³²⁾ |
| Older people should be assessed for the presence of frailty during all encounters with health and social care professionals. Gait speed, the timed-up-and-go test and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) questionnaire are recommended assessments. |
| The Asia-Pacific clinical practice guidelines for the management of frailty ³⁴⁾ |
| We conditionally recommend that older adults with frailty who exhibit unintentional weight loss should be screened for reversible causes and considered for food fortification/protein and caloric supplementation. (Strength of recommendation: conditional) We strongly recommend that frailty be identified using a validated measurement tool. (Strength of recommendation: strong) |
| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| All adults aged 65 years and over should be offered screening for frailty using a validated rapid frailty instrument suitable to the specific setting or context. (Strength of recommendation: strong, level of evidence: low) |

The above two recommendations relating to key question 1 were mentioned in four of the five CPGs used in the adaptation. The four CPGs either provided a low level of evidence for the related recommendations or did not provide a level of evidence. Therefore, additional literature searches were conducted to determine the level of evidence in these recommendations, and two randomized controlled trials (RCTs) confirmed that it would be beneficial to conduct screening tests.^{36,37)} One systematic review (SR) also confirmed the character and usefulness of screening tools.³⁸⁾ Based on these, we determined the level of evidence in both recommendations as A in accordance with the definition of the level of evidence in this CPG. For the strength of recommendation, we determined strength of recommendation: I considering the level of evidences are A, the benefits of implementing the recommendations are expected and utilization at the site of healthcare. The level of evidence and strength of recommendation for two recommendations were confirmed after agreement by the development committee.

I-2. Diagnosis and assessment of frailty

Key question: Is it helpful to conduct diagnostic test and assessment of frailty for prevent complication and manage of frailty in older adults aged 70 or older who are suspected of frailty or pre-frailty in screening test?

Recommendations for diagnosis and assessment (recommendation 3, 4, and 5):

3. Diagnostic tests for patients with frailty or pre-frailty status in the screening test may be considered. (Strength of recommendation: IIb, level of evidence C)
4. It is recommended to conduct a comprehensive geriatric assessment (CGA) in patients diagnosed with frailty. (Strength of recommendation: I, level of evidence A)
5. It is recommended that patients diagnosed with advanced frailty be referred to geriatric medication (Strength of recommendation: I, level of evidence C)

List of recommendations from existing clinical practice guidelines (CPGs) used to in the adaptation

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| Frailty in elderly people ³⁵⁾ |
| The assessment is included within the multi-professional group of primary care, relying on support from other healthcare professionals where necessary. (Strength of recommendation: A, level of evidence I) |
| Frailty in an older adult is confirmed if at least 3 of the following conditions are present: (1) unintended weight loss ($\geq 5\%$ during the last 12 months); (2) rapid onset of fatigue in carrying out daily activities; (3) reduced weekly frequency of physical activity; (4) reduced gait speed (SPPB-gait test ≤ 3); and (5) reduced muscular strength (SPPB-chair test ≤ 2). (Strength of recommendation: A, level of evidence IV) |
| Fit for frailty, part 1 & 2 ³²⁾ |
| Carry out a comprehensive review of medical, functional, psychological and social needs based on the principles of comprehensive geriatric assessment. |
| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| Clinical assessment of frailty should be performed for all older adults screening as positive for frailty or pre-frailty. (Strength of recommendation: strong, level of evidence: low) Where appropriate, persons with advanced (severe) frailty should be referred to a geriatrician. (Strength of recommendation: Consensus Based Recommendations, level of evidence: no data) |

In this CPG, individual recommendations were made for each screening test, diagnostic test, and CGA. CGA is a very important process as a preparation step to implement appropriate interventions in individual frail elderly. However, CAG requires significant time and human resources. Of course, it would be ideal to implement CGAs across patients suspected of frailty or pre-frailty, but considering limited medical resources, it is difficult to implement them. Therefore, it is meaningful in terms of limited medical resources to conduct additional diagnostic test on patients suspected of frailty in screening test. However, the strength of recommendation of recommendation no. 3 was determined IIB considering unclear boundaries with screening test and clinical aspects of the difficulty for conducting tests in primary care settings.³⁹⁻⁴¹⁾ For CGA, the strength of recommendation: I, based on relevant clear evidences, and the clinical significance and benefits.⁴²⁻⁴⁴⁾ In addition, a separate recommendation was made for patients who are judged to be an advanced frail status through the evaluation process, as referral is required to geriatricians. Although the relevant level of evidence is low for the recommendation, the development committee determined the strength of recommendation: I in consideration of its clinical significance.⁴⁵⁾

II. Intervention and monitoring

II-1. Polypharmacy

Key question: Does evaluation and intervention for polypharmacy in older adults aged 70 or older diagnosed with frailty help prevent complications (medication side effects, fall, hospitalization, and admission to nursing home)?

Recommendation for polypharmacy (recommendation 6):

6. It is recommended to assess and review medications being used by elderly patients with frailty and to make adjustment to the drug if necessary. (Strength of recommendation: I, level of evidence A)

List of recommendations from existing CPGs used to in the adaptation

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| Fit for frailty, part 1 & 2 ³²⁾ |
| Conduct evidence-based medication reviews for older people with frailty (e.g., STOPP START criteria). |
| The Asia-Pacific clinical practice guidelines for the management of frailty ³⁴⁾ |
| We strongly recommend that polypharmacy be addressed by reducing or deprescribing any inappropriate/superfluous medications. (Strength of recommendation: strong) |

Polypharmacy was included in two of the five CPGs used in the adaptation, all of which provided no level of evidence for the recommendation. Therefore, additional literature searches were conducted in this CPG to determine the level of evidence for the recommendation, with two SRs and one RCT selected. Selected SRs reported that the number of medications taken was significantly associated with frailty,^{46,47)} and RCT targeting elderly patients showed that intervention of medication was effective in preventing functional decline.⁴⁸⁾ Based on these literature, recommendation for evaluation and intervention of polypharmacy in patient with frailty was determined at the level of evidence: A. The strength of recommendation was given after agreement of the development committee, taking into account the clinical significance, benefit, and harm.

II-2. Physical activities

Key question: Does implementing physical activities in older adults aged 70 or older who are diagnosed with frailty help prevent complications (functional decline due to sarcopenia, fall, and walking disorders)?

Recommendation for physical activity (recommendation 7):

7. It is recommended that physical activities, including resistance, aerobic, and balance exercises, be implemented in frail elderly patients. (Strength of recommendation: I, level of evidence A)

List of recommendations from existing CPGs used to in the adaptation

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| Frailty in elderly people ³⁵⁾ |
| Frailty is caused by several concomitant factors whose main aspect is the progressive reduction of muscular strength and bodyweight. Therefore, the main strategies to stabilize the system and control frailty are promoting physical activity and monitoring diet and bodyweight. (Strength of recommendation: A, level of evidence III) |
| The Asia-Pacific clinical practice guidelines for the management of frailty ³⁴⁾ |
| We strongly recommend that older adults with frailty be referred to a progressive, individualized physical activity program that contains a resistance training component. (Strength of recommendation: strong) |
| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| Older people with frailty should be offered a multi-component physical activity program (or those with pre-frailty as a preventative component). (Strength of recommendation: strong, level of evidence: moderate) Health practitioners are strongly encouraged to refer older people with frailty to physical activity programs with a progressive, resistance-training component. (Strength of recommendation: strong, level of evidence: moderate) |
| Interventions to prevent, delay or reverse frailty in older people ³⁰⁾ |
| We suggest implementing physical interventions, including physical activity/exercise, nutritional interventions, and a combination of exercise and nutritional interventions, to prevent or delay the progression of frailty, or to reverse frailty. (Strength of recommendation: conditional) The recommendation is stronger for group-based supervised exercise programs, either alone or in association with nutritional supplementation. (Strength of recommendation: strong) |

Recommendations related to physical activities were included in the four CPGs, with an average levels of evidence being moderate, while the strengths of recommendation were relatively strong. In this CPG, further literature searches on frailty and physical activities have identified several research findings to support the strength of recommendation of existing guidelines. Two SRs and meta-analyses showed that physical activities reduced the risk of frailty.^{49,50)} Several RCTs also confirmed that physical activities has beneficial effects on frailty scores, physical function, and mental health.^{15,16)} Physical activity is a very important part of intervention for frailty, as has been found in several literature, but due to different individual ability of physical activity in older adults, this may result in an accidents such as damage or fall. A study of physical activity in patients with osteoporosis which is relatively high-risk group, reported more damage, such as minor muscle and joint pain. However, even in such patients, serious side effects from physical activity are rare, and these have rarely affected physical activity. Based on these results, the strength of recommendation was determined by considering the relatively clear level of evidence supporting the recommendation and the clinical significance, benefit, and harm of implementing the recommendation.

II-3. Nutrition and oral health

Key question: Does nutritional assessment and intervention help prevent complications (infection, functional decline due sarcopenia, and hospitalization) in older adults aged 70 or older who are diagnosed with frailty?

Recommendations for nutrition and oral health (recommendation 8 and 9):

8. It is recommended to evaluate body weight loss and nutritional status in frail elderly patients and perform interventions. (Strength of recommendation: I, level of evidence A)

9. Evaluation and training of oral health in frail elderly patients should be considered. (Strength of recommendation: IIa, level of evidence A)

List of recommendations from existing CPGs used to in the adaptation

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| The Asia-Pacific clinical practice guidelines for the management of frailty ³⁴⁾ |
| We conditionally recommend that older adults with frailty who exhibit unintentional weight loss should be screened for reversible causes and considered for food fortification/protein and caloric supplementation. (Strength of recommendations: conditional) |
| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| Protein/caloric supplementation can be considered for persons with frailty when weight loss or undernutrition has been diagnosed. (Strength of recommendation: conditional, level of evidence: very low) Health practitioners may offer nutritional/protein supplementation paired with physical activity prescription. (Strength of recommendation: conditional, level of evidence: low) Advise older adults with frailty about the importance of oral health. (Strength of recommendation: Consensus Based Recommendations, level of evidence: no data) |
| Interventions to prevent, delay or reverse frailty in older people ³⁰⁾ |
| We suggest implementing physical interventions, including physical activity/exercise, nutritional interventions, and a combination of exercise and nutritional interventions, to prevent or delay the progression of frailty, or to reverse frailty. (Strength of recommendation: conditional) |

The recommendations for assessment and intervention of nutritional status of frailty patients were included in three of CPGs used in the adaptation, in which the levels of evidence for the recommendations were not undervalued or presented. Further literature searches were conducted to find evidence related to nutritional problems in patients with frailty. Several SRs have confirmed that poor nutritional conditions are associated with the occurrence of frailty.^{24,25)} Further research is needed, of course, as to whether nutritional conditions can affect the prevention and improvement of frailty. Nevertheless, considering the need for rapid evaluation and intervention of nutritional conditions, ease of evaluation tool, and related evidence, the recommendation (recommendation no. 9) was given a higher strength of recommendation.

Oral health has been addressed in one of CPGs used in the adaptation. No data on the level of evidence were presented in the CPG, and the strength of the recommendation was determined by the relevant expert agreement. In this CPG, further literature searches confirm that oral health is significant as predictors of frailty.²⁶⁾ Based on this, the recommendation was assessed to have a high level of evidence: A. Despite the importance of oral health in frailty and relevant evidence, the strength of recommendation was determined IIa, taking into account the practical difficulties of assessment and education of oral health in primary care settings.

II-4. Vitamin and hormones

Key question: Does vitamin or hormone supplementation help prevent complications caused by frailty (fall, fracture, functional decline, hospitalization, and admission to nursing home)?

Recommendations for vitamin and hormones (recommendation 10 and 11):

10. Vitamin D supplementation is recommended only for frail patients with vitamin D deficiency. (Strength of recommendation: I, level of evidence A)
11. Hormone supplementation therapy aimed at treating frailty is not recommended. (Strength of recommendation: III, level of evidence A)

List of recommendations from existing CPGs used in the adaptation

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| The Asia-Pacific clinical practice guidelines for the management of frailty ²⁴⁾ |
| We conditionally recommend that vitamin D be prescribed for persons found to be deficient in Vitamin D. (Strength of recommendation: conditional) |
| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| Vitamin D supplementation is not recommended for the treatment of frailty unless vitamin D deficiency is present. (Strength of recommendation: Consensus Based Recommendations, level of evidence: very low) |
| Hormone therapy is not recommended for the treatment of frailty. (Strength of recommendation: Consensus Based Recommendations, level of evidence: very low) |

Recommendations for vitamin and hormones in frail patients were included in two of the CPGs referenced. Supplementation for treatment of frailty was not recommended in the mentioned recommendations, unless insufficient. It is reported that low vitamin D concentrations increase the risk of frailty or associated with degree of frailty.^{27,51)} In RCT for vitamin D and function, it has been presented that the deficiency of vitamin D is significantly more likely to cause physical and cognitive problem.⁵²⁾ Regarding vitamin D supplementation, studies have shown that supplementing vitamin D in older adults aged 65 or older with vitamin D deficiency is positive for improvement of muscle strength.^{53,54)} Based on these results, we recommend that vitamin D supplementation be implemented only for frailty patients with vitamin D deficiency. The level of evidence: A and strength of recommendation: I were determined considering the positive effects of vitamin D supplementation in patients with vitamin D deficiency.

Several SR and meta-analysis have shown that there is a lack of evidence for hormone supplementation to prevent the development and progression of frailty.^{55,56)} There have been some studies on testosterone, dehydroepiandrosterone and growth hormone, assuming that hormone administration in frail patients will improve their frailty status, but neither has shown positive results such as hypothesis. Overall, it was decided that the implementation of hormone supplementation therapy was not recommended (strength of recommendation: III), and the relevant evidences for this were clear (level of evidence: A).

II-5. Cognitive function

Key question: Dose evaluation and intervention of cognitive functions in older adults aged 70 or older diagnosed with frailty help prevent and manage complications (functional decline, delirium, admission to nursing home due to abnormal behavior) of frailty?

Recommendations for cognitive function (recommendation 12 and 13):

12. Evaluation of cognitive function in patients diagnosed with frailty should be considered. (Strength of recommendation: IIa, level of evidence B)
13. Interventions to prevent cognitive impairment should be considered selectively in patients diagnosed with frailty. (Strength of recommenda-

tion: IIa, level of evidence A)

List of recommendations from existing CPGs used to in the adaptation

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| Physical frailty: ICFSR international clinical practice ²¹⁾ |
| Cognitive or problem-solving therapy is not systematically recommended for the treatment of frailty. (Strength of recommendation: Consensus Based Recommendations, level of evidence: very low) |
| Interventions to prevent, delay or reverse frailty in older people ³⁰⁾ |
| We suggest considering interventions to prevent or delay the progression of frailty, or to revert frailty, based on cognitive training, alone or in combination with exercise and nutritional supplementation, and on exercise combined with diet consultation, at least in pre-frail populations. (Strength of recommendation: conditional) |

The CPGs used in the adaptation did not provide clear recommendations for evaluation and intervention of cognitive function in patient with frailty. Further literature reviews related to cognitive functions were conducted under the agreement that cognitive functions need to be addressed in frailty interventions, considering the impact of cognitive dysfunction on later life. Literature reviews have reported that frailty acts as a predictive factor or is associated with cognitive dysfunction in several SRs.^{28,29,57)} However, there was limited evidence to support the assessment and intervention of cognitive dysfunction in frail patient.

Although there are observational study that suggested that evaluation of cognitive function is required along with evaluation of physical frailty in frail elderly, there is lack of evidence for the need for individual evaluation of cognitive impairment in patients with frailty.⁵⁸⁾ Based on these results, the development committee granted level of evidence: B to the recommendation for evaluation of cognitive function. In addition, the strength of recommendation was determined IIa, considering the need and clinical significance at the field of health care , as evaluation of cognitive function is an item included in the CGA.

Research results, including physical activity and nutritional intervention, have been reported by several RCTs as cognitive intervention for patients with frailty.^{31,59)} Such studies have reported that multi-dimensional interventions, including cognitive function, have a positive effect on the improvement of cognitive function or frailty itself. Based on these results, it was determined that the level of evidence for intervention related to cognitive function in patients with frailty was relatively clear. However, since most of these evidences address the preventive dimension of cognitive function, and patients with severe cognitive impairment are difficult to manage in primary care settings, so this CPG recommends selective implementation of interventions to prevent cognitive impairment. In addition, the strength of recommendation was determined IIa, considering the clinical conditions associated with the implementation of recommendation.

II-6. Fall

Key question: Does the implementation of fall risk assessment and intervention in older adults aged 70 or older who are diagnosed with frailty help prevent and manage complications (walking and mobility disorders, hospitalization, and admission to nursing home) of frailty?

Recommendation for fall (recommendation 14):

14. Fall screening test (history taking for fall, assessment of gait and balance) should be conducted in frail elderly, and interventions should be considered for multi-dimensional fall risk assessment and fall prevention in high-risk groups. (Strength of recommendation: IIa, level of evidence B)

List of recommendations from existing CPGs used to in the adaptation

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| Fit for frailty, part 1 & 2 ³²⁾ |
| Develop local protocols and pathways of care for older people with frailty, taking into account the common acute presentations of falls, delirium and sudden immobility. Wherever the patient is managed, there must be adequate diagnostic facilities to determine the cause of the change in function. Ensure that the pathways build in a timely response to urgent need. |

Fall-related recommendation were included in one CPG, and no level of evidence and strength of recommendation were given. Additional literature reviews were conducted in consideration of the clinical significance of falls, and limited evidence was identified for evaluation and intervention of falls in frail elderly. Some SRs have reported benefits in implementing multifactorial intervention related to falls, and RCTs have shown that fall-related interventions have improved quality of life and risk factors associated with falls, but do not actually reduce fracture or fall incidences. In consider the limited benefits of fall intervention identified in the findings mentioned, and the lack of high level of evidence literature reporting gains on fall screening, the level of evidence in this recommendation was evaluated as B. In addition, although mixed results related to intervention exist, the recommended strength was agreed to be IIa, considering clinical significance of falls in patients with frailty.

II-7. Social frailty

Key question: Dose the assessment and intervention of social frailty in older adults aged 70 or older who are diagnosed with frailty help prevent and manage complications (depression, sleep disorders, and functional decline) of frailty?

Recommendation for social frailty (recommendation 15):

15. Evaluation and intervention for social frailty in patients diagnosed with frailty are recommended. (Strength of recommendation: IIa, level of evidence B)

List of recommendations from existing CPGs used to in the adaptation

| Physical frailty: ICFSR international clinical practice ²¹⁾ |
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| All persons with frailty may be offered social support as needed to address unmet needs and encourage adherence to the Comprehensive Management Plan. (Strength of recommendation: strong, level of evidence: very low) |

Recommendation regarding social frailty was included in one of the CPGs used in the adaptation. The CPG gave a strong recommendation strength considering the clinical importance although the level of evidence associated with social frailty is low. Several observational studies have presented that social frailty is independently associated with negative health outcomes,^{33,60)} and preventive intervention of physical frailty is also important for prevention of social frailty.⁶¹⁾ These results cannot be a direct evidences for the assessment and intervention of social frailty, so this recommendation corresponds to the level of evidence: C, but maintains the strong strength of recommendation, such as referenced CPG, considering the clinical importance of social frailty.

II-8. Monitoring

Key question: Does periodic evaluation and monitoring of older adults aged 70 or older who are diagnosed with frailty help prevent and manage complications (hospitalization, admission to nursing home) of frailty?

Recommendation for monitoring (recommendation 16):

16. Periodic evaluation and monitoring may be considered in patients diagnosed with frailty. (Strength of recommendation: IIb, level of evidence D)

List of recommendations from existing CPGs used to in the adaptation

| Frailty in elderly people ³⁵⁾ |
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| A subject defined frail should be regularly monitored and assessed within a primary care setting using specific tools for data collection. (Strength of recommendation: A, level of evidence: I) |
| Information on subjects' frailty should be updated and available, if possible, through a computer system covering each step of the healthcare network. (Strength of recommendation: A, level of evidence: I) |

One of the five CPGs used in the adaptation included recommendations related to monitoring of frail elderly, with relatively high level of evidence and strength of recommendation. However, in additional relevant literature reviews, we were unable to find literature that would serve as evidences for periodic evaluation and monitoring of frail patients. Therefore, the level of evidence for this recommendation was evaluated as D. Nevertheless, the strength of recommendation was IIb, considering the recent positive studies on monitoring of intervention in frail patients using internet of thing (IoT) technology, wearable devices and the importance of continuous evaluation as on ongoing condition of frailty.