Assessment and management of frailty in individuals living with dementia: expert recommendations for clinical practice

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Frailty complicates the care of individuals with dementia, increasing their vulnerability to adverse outcomes. This Personal View presents expert recommendations for managing frailty in individuals with dementia, aimed at health-care providers, particularly those in primary care. We conducted a rapid literature review followed by a consensus process involving 18 international experts on dementia and frailty. The experts identified key areas, including diagnosis of frailty, assessment of nutritional status and nutritional management, physical activity, prevention of falls, and polypharmacy management. The recommendations emphasise early identification of frailty and a comprehensive, interdisciplinary approach to care that aims to maintain the individual's daily functioning, quality of life, and independence. The recommendations highlight the importance of tailored interventions, regular monitoring, and the integration of psychosocial support into the therapeutic approach. These recommendations address a crucial gap in existing clinical guidelines, offering practical guidance for clinicians managing frailty in individuals with dementia.

Introduction

Dementia involves cognitive decline, behavioural and physical changes, and progressive functional deterioration. As of 2020, more than 50 million people globally had dementia, a figure projected to rise to 152 million by 2050 owing to population ageing.[1] The estimated economic burden of dementia in 2018 was US$1 trillion, with projections estimating that this figure will double by 2030.[2] Dementia is a leading cause of disability and dependency among older adults worldwide.[3] *The Lancet* Commission on dementia prevention, intervention, and care was updated in 2024.[4]

Frailty, a condition characterised by increased vulnerability and diminished response to stressors, increases the complexity of care for individuals living with dementia.[5] As a condition quite common in ageing, frailty complicates the dementia scenario by introducing additional challenges.[6] People with both dementia and frailty have substantially increased vulnerability compared with those with dementia alone. Although dementia primarily affects cognitive functioning, frailty adds a physical component that weakens resilience and the ability to recover from stressors.[7,8] Furthermore, several studies have shown that older adults with dementia who present a high degree of frailty have worse health trajectories than individuals with lower levels of frailty.[9,10] Frailty can also be diagnosed before the onset of profound cognitive deficits and has been described as a risk factor for the development of dementia.[11] Thus, health-care providers need to adopt early, comprehensive, and effective diagnosis and management strategies for addressing frailty, mainly in the context of dementia.

The expert recommendations presented in this Personal View provide clinicians with tailored advice for managing frailty in individuals with dementia, thereby helping clinicians to address the diverse needs and complex presentations in this population. Given the current scarcity of specific guidelines, raising awareness and enhancing knowledge on frailty in individuals with dementia are essential at all levels of clinical care. This Personal View aims to serve as a valuable resource for clinicians, particularly for primary care doctors but also for neurologists, psychiatrists, physiotherapists, nutrition specialists, and occupational therapists. By summarising current evidence and expert insights, our goal is to slow the rapid functional decline associated with frailty and dementia. Although previous efforts have explored the connection between the two conditions, we bring together multidisciplinary expertise to provide comprehensive, practical recommendations that focus on frailty as a clinical syndrome, in accordance with the geroscience agenda.[12,13]

Methodology

This Personal View is a result of the EU Joint Programme–Neurodegenerative Disease Research-funded consortium "Interdisciplinary perspectives on functional maintenance and frailty in people living with moderate to severe dementia". We developed recommendations with experts in two phases: a literature review and an expert consensus. 18 expert researchers and clinicians from eight different countries were selected on the basis of their expertise in the diagnosis, management, and rehabilitation of dementia; expertise in frailty, sarcopenia, malnutrition, and geriatric syndromes; strong publication record in these areas; and experience in evidence synthesis methodology. A preliminary virtual meeting identified the following key topics: diagnosis of frailty, nutritional management, nutritional supplements, dementia management, physical activity, mood assessment, loneliness, falls, polypharmacy, and sensory loss.

In phase one, four experts (MGB, LCV-S, IR-S, and MS-C), who were selected based on their qualifications and expertise in conducting the information search, performed rapid literature reviews for each topic, focusing on dementia and frailty.[14] The literature search was conducted

Lancet Healthy Longev 2024

Published Online
https://doi.org/10.1016/j.lanhl.2024.100666

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See online for appendix

in PubMed, Scopus, and Cochrane Library, from the date of inception of the databases to May, 2024, without restrictions on study type or language. The core search terms included "frailty" or "prefrailty" and "dementia", with additional terms for specific topics (nutrition, treatment, physical exercise, depression, social isolation, falls, polypharmacy, hearing loss, and vision loss). The inclusion criteria focused on studies that explored interventions and health assessments for individuals with all types and stages of dementia and frailty, covering a range of study types (excluding narrative reviews and letters to the editor). Considering that the available evidence about management of dementia and frailty might be insufficient, the search was not restricted by study design. Given that the proposed methodology was a rapid review, some components typical of a standard systematic review were not included.[14] The full details of the terms and filters used in this search are available in the appendix (p 1).

Phase two involved in-person meetings at the International Congress on Dementia, Frailty, and Sarcopenia: Advancing Research, Enhancing Care, and Promoting Healthy Aging, held in May, 2024 in Stavanger, Norway, where the four experts who conducted the literature review presented review findings in subgroups, formulated recommendations, and held discussions to reach consensus. The final recommendations incorporated new insights from the whole expert group, resulting in a comprehensive consensus document.

Recommendations

Recommendation 1: identifying frailty

Early identification and grading of the degree of frailty in individuals with dementia are essential for effective management of the condition.[15,16] The diagnostic tool should be brief and straightforward, and should be accessible to a wide range of clinicians, including family medicine practitioners, psychiatrists, and other practitioners such as medical doctors belonging to other specialties, nutritionists, and therapists. One example is the FRAIL scale,[17,18] a tool that quickly assesses frailty through the following five components: fatigue, resistance, ambulation, illnesses, and weight loss. Similarly, the Clinical Frailty Scale is a practical tool for frailty detection and severity grading to guide decision making, with a scale from 1 (very fit) to 9 (terminally ill).[19] Additionally, tools such as the Fried frailty phenotype and the frailty index are valuable in detecting frailty in individuals with cognitive impairments.[20]

Identifying cognitive impairment in older adults with frailty is as essential as identifying frailty itself, given the bidirectional relationship between the two conditions. Regular evaluation of both conditions, either through comprehensive geriatric assessment (CGA) or standalone screenings, is crucial in the care of older adults. CGA allows for the early detection of treatable issues, thereby mitigating the effects of frailty and dementia on the affected individuals and their caregivers. The positive effects of CGA on the health of older adults highlight its potential as a high-yield tool that is particularly beneficial for long-term care in individuals with dementia.[21]

Recommendation 2: establishment of early interventions

Early management actions after frailty identification are essential to minimise the adverse effects of frailty. Early diagnosis is crucial for counteracting the negative progression of both dementia and frailty. Identifying frailty at an early stage enables clinicians to implement timely interventions that could slow the progression of dementia, preserve functional abilities, and enhance quality of life.[15]

Recommendation 3: assessment and diagnosis of nutritional status

Continuous assessment and diagnosis of nutritional status is a fundamental step in managing frailty in individuals with dementia, as malnutrition is a frequent issue that affects the prognosis of both conditions.[22,23] A quick and simple tool, such as the Mini Nutritional Assessment - Short Form, is recommended for initial nutritional screening.[24] If the screening results are positive for malnutrition, then further evaluation should follow the criteria outlined by the Global Leadership Initiative on Malnutrition, requiring at least one phenotypic criterion (eg, weight loss or low BMI) and one aetiological criterion (eg, reduced intake or inflammation) to confirm the diagnosis of malnutrition.[25] Regular monitoring of nutritional status (ideally every 3 months) is also essential, focusing on weight tracking to address emerging issues and to monitor treatment goals.

Recommendation 4: management of nutrition

Nutritional management should be done on the basis of nutritional assessment and the level of risk.

Individuals with dementia tend to eat less owing to forgetfulness about eating, challenges in preparing food, issues related to depression, swallowing difficulties, or physical weakness. Being frail further increases the risk of malnutrition in people with dementia and restricts their ability to obtain and consume food independently. Therefore, nutritional education is recommended in this population, involving educating the affected people and caregivers about the importance of nutrition and practical ways to improve dietary habits.[26,27] Given the challenges with respect to diet adherence among individuals with dementia, the mode of instruction should be simple and engaging, possibly involving visual aids or reminders.

Meeting the recommended protein intake of 1·2–1·8 mg/kg per day should be encouraged in all older adults, especially those with dementia, frailty, or with a risk of frailty.[28] For individuals with kidney disease, the European Society for Clinical Nutrition and Metabolism advises a personalised approach to protein intake. When the estimated glomerular filtration rate is greater than 30 mL/min/1·73 m^2 and is stable, a daily protein intake of at least 1 g/kg per day is recommended under close monitoring of kidney function. If the estimated glomerular filtration rate is less than

30 mL/min/1·73 m^2 or is declining, then protein intake should be reduced to 0·6–0·8 g/kg per day.[29,30]

Tools such as the Mini Nutritional Assessment - Short Form should be used to track changes in nutritional status regularly, ensuring timely interventions, with involvement of the caregiver for consistency. Nutritional supplements should be considered to address deficiencies or enhance overall nutrient intake.[31,32]

People with dementia and frailty and their caregivers need to be educated about the importance of maintaining a balanced diet, including adequate protein intake.[31] A comprehensive nutritional assessment should be carried out, which involves assessing the individual's nutritional status and daily diet, including typical food intake. This assessment would help to identify gaps and areas for improvement.[33] The use of simple questions, such as "What do you eat on a normal day?", is important.

Furthermore, physical examinations should be conducted, comprising an oral cavity assessment to check for abnormalities in the teeth, gums, tongue, and oral mucosa, along with questions about issues with dentures, pain, or chewing. If any problems are identified, referral to a dentist is recommended. Enquiring about swallowing difficulties to detect potential deglutition issues is also important. If such issues are suspected, then the Eating Assessment Tool-10 scale (a 10-item questionnaire positive for swalloing difficulties at a score of 3 or higher) should be administered; a referral to a specialist is recommended upon a positive result.[34]

Assessment for sarcopenia is recommended in older adults, especially those with dementia and frailty, following the guidelines established by the European Working Group on Sarcopenia in Older People 2.[35] Sarcopenia is a crucial component of frailty, and the brain–muscle axis highlights the bidirectional relationship between muscle health and cognitive decline.[36,37]

The individual's dietary habits should be discussed and specific supplements should be recommended to meet the protein and calorie requirements. Input from a dietitian, wherever available, will ensure that the recommendations are tailored to the individual's needs.

Recommendation 5: hydration

As individuals with dementia often forget to intake fluids, individuals with dementia and frailty and their caregivers should be advised to ensure adherence to hydration recommendations. A daily fluid intake of 1·6 L for women and 2·0 L for men is recommended.[30] Consistent monitoring helps to identify issues with fluid consumption, allowing timely interventions to prevent dehydration, which can worsen frailty and cognitive decline. An example question would be, "How many glasses of water, coffee, juice, or other liquids do you consume in a normal day?"

Regarding the above recommendations on nutrition management and hydration, a multidisciplinary team approach can enhance care by monitoring diet, recommending supplements, and educating people with dementia and frailty and their caregivers. Management of these conditions should be tailored to the specific care setting. In community settings, care plans should focus on education, nutritional support, and regular monitoring for those with mild to moderate dementia. In long-term care, care plans should be adapted to meet the complex needs of residents, especially those with advanced dementia, by providing additional support for daily activities. In acute care settings, nutritional management should be prioritised during care transitions, and continuity should be ensured to address both immediate and ongoing needs, particularly in emergencies and during hospital stays.

Recommendation 6: micronutrients, trace elements, and vitamins

A personalised assessment needs to be conducted to identify vitamin and nutrient deficiencies on the basis of the individual's requirements and risks. Although strong recommendations are not possible on account of insufficient evidence and varying individual needs and circumstances, some supplements, such as vitamin D, B12, and folate, warrant consideration, particularly for individuals with deficiencies. Individuals who consume less than 1500 kcal per day need to be recommended a daily multivitamin supplementation since these individuals often have difficulty meeting their micronutrient needs through regular food intake alone.[38]

Recommendation 7: dementia-focused pharmacological interventions

Pharmacological treatment for dementia should be initiated or continued regardless of the individual's frailty status. No particular recommendation was made here since no evidence exists to suggest that specific dementia medications improve frailty status or physical performance.

The practitioner should evaluate the potential risks and benefits of each medication in relation to the individual's overall health and treatment goals.[39] For example, in the case of rivastigmine, which can produce side-effects such as dizziness and weight loss, the practitioner should identify whether the potential benefits of rivastigmine in improving cognition outweigh the risks and side-effects for the individual.[40] If the medication is ineffective or causing substantial adverse effects, it should be withdrawn or alternative options should be explored. In individuals with high levels of frailty, close monitoring of the safety, tolerability, and effectiveness of the treatment for dementia is recommended.

Recommendation 8: exercise prescription for older adults with dementia and frailty

Practitioners should prescribe an individualised multicomponent physical exercise programme, given its benefits for both frailty and dementia.[41] Ideally, the multidisciplinary team should include a physical activity expert or physical therapist.[42,43] The exercise programme should be tailored to the individual's physical and cognitive functioning and

their level of social support[44] and should incorporate a combination of aerobic, resistance, balance, and gait exercises to target different aspects of physical fitness and functionality.

The aerobic exercise should consist of sessions of 10–20 min each, 3–7 days per week, at an intensity of 12–14 on the Borg scale (equivalent to 55–70% of the heart rate reserve).[45] For the resistance exercise, 1–3 sets of 8–12 repetitions are recommended, 2–3 days per week, starting at 20–30% of one-repetition maximum and progressing to 60–80% of one-repetition maximum, incorporating daily activities.[46] 1–2 sets of 4–10 different balance exercises, targeting both static and dynamic postures, are recommended to be done 2–7 days per week. Sessions as brief as 5–10 min to as long as 15–30 min of daily gait training should be incorporated, focusing on improving walking ability and endurance.

A total duration of 50–60 min of exercise per day should be encouraged, but the exercise does not need to be completed in a single session. Since mental and physical fatigue can occur, especially in individuals with dementia and frailty, distributing the exercise sessions throughout the day to accommodate individual preferences and capabilities is recommended.

The practitioner should emphasise the importance of maintaining the exercise programme over time for sustained benefits and prevention of physical and cognitive decline. Regular participation and adherence to the exercise regimen should be encouraged to optimise outcomes. Since individuals with dementia can face unique challenges in adhering to exercise regimens, additional support such as reminders or greater involvement of caregivers might be necessary to improve adherence and effectiveness.

Recommendation 9: individualised multidomain exercise programme

An individualised multidomain exercise programme combining physical activity (20–30 min per day) with cognitive training, tailored to the person's abilities, enhances physical and cognitive health.[47,48] Mind–body exercises, such as yoga or tai chi, can support relaxation and wellbeing; however, evidence of the effectiveness of these exercises in individuals with both dementia and frailty is scarce.[49,50] Regular monitoring of adherence to exercise and the response to the intervention is essential to manage potential adverse events such as joint pain or falls in frail individuals.[51] Exercise and protein supplementation together improve muscle mass and strength, thereby aiding in the management of sarcopenia and frailty.[52]

Recommendation 10: assessment of depression

Depression and mood disorders in individuals with dementia and frailty should be assessed using a short and simple tool. As depression can substantially affect the overall wellbeing and functional status of these individuals, it is important that clinicians recognise the importance of considering depression in the diagnostic process.[53] Although various screening tools for depression are available, clinicians should consider using a short tool that is widely used and validated in this population, such as the Patient Health Questionnaire-2.[54]

Recommendation 11: management of depression

Practitioners should provide individualised and appropriate treatments for depression or other mood disorders, considering the risk of adverse effects, comorbidities, and the presence of behavioural and psychological symptoms associated with these mental health disorders.

Interventions addressing depression can positively affect frailty outcomes. Non-pharmacological treatments such as exercise, psychotherapy, and behavioural interventions can help to alleviate depressive symptoms and improve mental health.[55,56] Pharmacotherapy, particularly selective serotonin reuptake inhibitors, is effective and well tolerated in older adults with dementia; however, antidepressants with an anticholinergic burden, such as tricyclics, should be avoided for older adults in general and especially for those with frailty and dementia. Among selective serotonin reuptake inhibitors, fluoxetine is generally not recommended for older adults owing to its long half-life and side-effects, whereas venlafaxine, vortioxetine, and mirtazapine are safer options in terms of drug interactions.[57]

Interventions targeting frailty can also positively affect depression. Programmes focused on physical activity, nutrition optimisation, social engagement, and cognitive stimulation improve physical function and quality of life, helping to reduce depressive symptoms.[58]

Recommendation 12: loneliness and social isolation

Practitioners should assess an individual's perceived loneliness and social isolation and should refer individuals to local social assistance programmes, when necessary.[59] In particular, practitioners should routinely screen for loneliness.[60,61] Although various detection scales and indices are available, assessment tools should be chosen on the basis of individual circumstances and preferences. While the 3-item UCLA Loneliness Scale is commonly used,[62] practitioners should also include open-ended questions that allow individuals to express their feelings of loneliness freely.

Following the assessment of loneliness, practitioners should familiarise themselves with the social interventions and support services available within their region or community.[59] They need to be aware of the local social assistance programmes, support groups, and community centres[63] to be able to inform individuals with dementia and frailty and their families about these options, thereby empowering them to make informed choices for social engagement and support.

Recommendation 13: assessment of the risk of falls

A thorough assessment of the risk of falls should be conducted, including evaluating any history of falls and the

presence of adverse outcomes related to falls (ie, fractures, lesions, dependence, and fear of falling).

Assessment of the risk of falls in individuals with dementia and frailty enables the implementation of targeted interventions. Both dementia and frailty are associated with falls, as previous studies have shown that individuals with both cognitive impairment and frailty have a higher risk of falling than those with cognitive decline or frailty alone.[39,64] For this reason, it is important to assess the history of falls and other risk factors, such as the use of concomitant drugs, muscle weakness, sensory deficits, environmental conditions, use of walking aids, nutritional deficits, and mood disorders, among other factors.

Currently, no evidence exists regarding a specific tool for evaluating the risk of falls in individuals with dementia and frailty. Therefore, the recommendation is to use any validated assessment tool to identify the risk of falls. Additionally, conducting osteoporosis and fracture risk assessments for all individuals with dementia and frailty is important. The affected individuals should also undergo a comprehensive gait assessment using computerised methods in settings where such resources are available.

Recommendation 14: management of the risk of falls

Individuals with dementia, frailty, and a high risk of falls should receive a personalised, multimodal intervention based on their specific risk factors.[65,66] Key intervention strategies include physical exercise (aerobic, strength, balance, and stability training), management of comorbidities, review of medication(s), environmental modifications, use of mobility assistance devices, and cognitive interventions, which can further enhance safety.[67,68]

Collaboration of an interdisciplinary team, including physiotherapists, occupational therapists, pharmacists, and social workers, should be encouraged to implement comprehensive strategies for prevention of falls.[69]

Recommendation 15: polypharmacy and deprescribing

Both frailty and dementia are associated with a high burden of polypharmacy and inappropriate prescriptions, which are risk factors for decline in both cognition and functional state.[70–72] Therefore, a systematic, comprehensive review of medications is encouraged for all individuals with dementia and frailty, and deprescribing unnecessary or inappropriate medication as per published criteria is recommended. Additionally, it is essential to assess any potential drug—drug or drug—disease interactions.

General practitioners and non-geriatric medical specialists should consider using established criteria such as the STOPP/START or Beers criteria to assess potentially inappropriate medications.[73] If possible, medications such as anticholinergics, benzodiazepines, antipsychotics, and opioids should be discontinued owing to their potential adverse effects.[74] Furthermore, health-care providers should evaluate potential interactions between medications and medical conditions. Educating individuals with dementia and frailty and their caregivers about proper medication management is important.

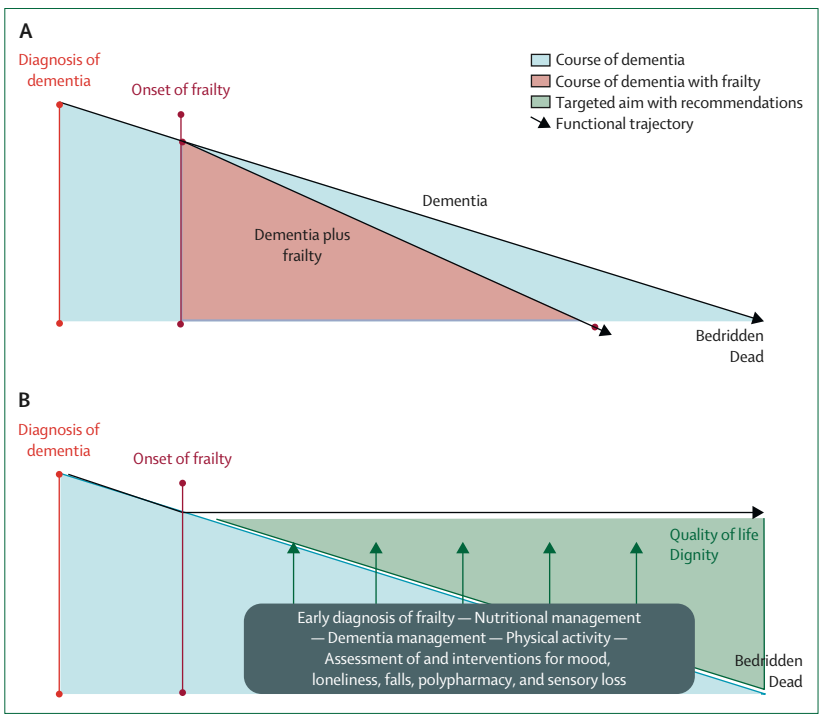


Figure: **(A) Functional prognosis of a person with dementia alone or with dementia and frailty. (B) The aim of the comprehensive interventions referred to in the recommendations. Another common scenario exists in which frailty precedes the onset of dementia but exhibits the same synergistic negative effect. Figure created with BioRender.com. To access the original source of this presentation, visit: https://app.biorender.com/illustrations/6683f81f55d8c74c562a6617**

Recommendation 16: hearing and vision loss

Hearing and visual impairments are common in older adults and are linked to cognitive decline, social isolation, functional impairment, mood disorders, and poor rehabilitation outcomes.[75] These impairments exacerbate the existing challenges of people with dementia and frailty. Thus, assessing these functions as part of evaluations in older adults is essential. Prompt referral for management of sensory impairments could help to prevent further cognitive and functional decline.

Discussion

In these recommendations, we provide health-care practitioners (especially those without a specialised geriatric medicine training) with advice on how to manage frailty in individuals living with dementia. Maintaining daily functioning, quality of life, dignity, and independence in older adults living with these conditions should be the main goals. These recommendations target the individual as a whole, aiming to improve his or her overall health rather than just one specific organ or bodily system. These recommendations are focused on several current challenges: diagnosis of frailty, nutrition, dementia management, physical activity and exercise, mood and behaviour, loneliness, falls, polypharmacy, and sensory impairments.

One of the main reasons for providing these guidelines is to highlight the need to offer geriatric care to all older adults who require it. However, the field of geriatrics faces unique challenges owing to a global shortage of qualified personnel and the rapidly growing ageing population.[76] Addressing important geriatric issues affecting millions of people is a pressing priority.[77] The recommendations presented in this Personal View aim to educate other specialties to address these needs effectively. Moreover, most people living with dementia are cared for by primary care physicians, and thus, making this knowledge available to these physicians in a practical, accessible, and time-efficient way is a priority.

Geriatric syndromes are frequently overlooked owing to the absence of a systematic approach, the normalisation of various age-related pathologies, and the persistent belief that health issues relevant to middle-aged adults (typically defined as those aged 40–65 years) can be directly applied to older populations.[78] Evidence on frequent health issues often fails to account for the unique complexities of ageing. Additionally, individuals with common geriatric conditions are often excluded from prevention trials due to frailty.[79] For example, excluding individuals with delirium from dementia studies can result in missed opportunities to prevent the progression or onset of the disease.

Metabolic syndrome, which predominantly affects middle-aged adults, differs significantly from geriatric syndromes seen in older adults. A key distinction lies in the nature of these conditions; metabolic syndrome primarily involves vascular issues, such as hyperglycaemia and hypertension, whereas geriatric syndromes are characterised by functional decline and its interaction with chronic diseases. In the case of geriatric syndromes, maintaining strict glycaemic control or achieving strict blood pressure targets might not be the primary objective. The overlap between these syndromes in frail older adults highlights the need for targeted interventions that consider both vascular and functional challenges, prioritising quality of life and overall health.

Managing frailty in individuals with dementia requires a multidimensional approach that involves moving away from the traditional medical model based on specific diseases to a more person-centred approach focused on individual objectives.[12,80] The proposed recommendations go beyond treating dementia or frailty as isolated. Therefore, the recommendations are designed to address the underlying factors that affect ageing as a whole. This comprehensive care model is essential for improving patient outcomes, enhancing quality of life and independence, and reducing the care burden on caregivers and society (figure).

The expert recommendations are intended to guide clinical practice, influence policy, and shape resource allocation, emphasising specialised training for health-care providers and advocating for resources to implement effective care strategies. By shaping policy, these expert recommendations aim to prepare health-care systems to meet the increasing demand for dementia and old age care.[81] The recommendations also promote consistency and standardisation of care, ensuring that individuals with dementia and frailty receive high-quality care across settings. Standardised practices enable better monitoring and evaluation, fostering continuous improvement in clinical outcomes.

This Personal View outlines the key challenges in managing frailty and dementia together. Since most recommendations are drawn from evidence on each condition in isolation, more specific research focusing on the combination of dementia and frailty is urgently needed. Implementing these guidelines consistently can be difficult, especially in cases of patients with advanced dementia and insufficient health, social, or financial support. Regional differences in the availability of resources and trained professionals further affect the quality and uniformity of care. Additionally, although these recommendations aim for a personalised approach, standardised protocols can sometimes overlook individual preferences and cultural nuances, making interventions less acceptable or effective. Therefore, adapting these guidelines to various cultural and regional contexts is essential.

In conclusion, this expert consensus offers guidance and advice on managing frailty in individuals with dementia, emphasising the maintenance of daily functioning, dignity, and independence. Our recommendations are based on existing evidence and expert input, despite the scarcity of research on the co-occurrence of dementia and frailty. These recommendations aim to support medical specialties, particularly primary care doctors, in meeting the needs of an ageing population. The presented approach represents a shift from a traditional disease-based model to a person-centred model, integrating physical and psychosocial care. Although these recommendations could improve clinical practice and influence policy, challenges such as insufficient evidence on the co-occurrence of and interventions for dementia and frailty, non-adherence to guidelines, regional variability, and cultural adaptations require further research and tailored approaches to improve effectiveness.

Contributors

MGB conceptualised the study. MGB and DA were responsible for the acquisition of funding and project administration. MGB, GEB, IR-S, MC, MUP-Z, MS-C, and LCV-S investigated the study. MGB, FL, TC, LCV-S, GD, HW, IR-S, MC, MUP-Z, CC-G, and MS were responsible for the methodology. FL, TC, GD, GEB, CC-G, MUP-Z, KR, IT, CB, and DA supervised the study. FL, TC, GD, and GEB validated the data. MGB, HW, CC-G, and DA wrote the original draft. All authors revised and edited the manuscript. All authors meet the authorship criteria as defined by the International Committee of Medical Journal Editors.

Declaration of interests

We declare no competing interests.

Acknowledgments

This work is supported by the EU Joint Programme–Neurodegenerative Disease Research under the project "Interdisciplinary perspectives on functional maintenance and frailty in people living with moderate to severe dementia" (number 354885). In addition, this work represents independent research supported by the Norwegian Government, through Helse Vest (Western Norway Regional Health Authority) and the Norwegian Health Association. This work is also funded by the National Institute for Health Research Biomedical Research Centre at South

London and Maudsley National Health Service Foundation Trust and Kings College London. The views expressed are those of the author(s) and not necessarily of the funding organisations. The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

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