State of the art report on the prevention and management of frailty

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State of the art report on the prevention and management of frailty
ABBREVIATIONS

BMI = Body Mass Index
CD = Chronic diseases
CFS = Clinical Frailty Scale
CHS = Cardiovascular Health Study
CGA = Comprehensive Geriatric Assessment
COPD = Chronic Obstructive Pulmonary Disease
EC = European Commission
eFI = Electronic Frailty Index
EFS = Edmonton Frail Scale
EIPAHA = European Innovation Partnership on Active and Healthy Ageing
EU = European Union
FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight
ICTs = Information and Communication Technologies
JA = Joint Action
MNA = Mini Nutritional Assessment
MS = Member State
SHARE = Survey of Health, Ageing and Retirement in Europe
SOF = Study of Osteoporotic Fractures
SoAR = State of Art report
SPPB = Short Physical Performance Battery
WHO = World Health Organization
WP = Work package
EXECUTIVE SUMMARY

Demographic ageing is one of the most serious challenges that Europe is currently facing. Older people are at greatest risk of becoming frail and developing disability. However, since frailty is not an inevitable consequence of ageing, it can be prevented and treated to foster a longer and healthier life.

There are a number of initiatives taken forward by the European institutions to address these challenges but even so frailty is not yet at the top of the public health agenda. There is an urgent need to develop evidence based support to make frailty a public health priority.

The concern for this situation motivated the European Commission, the Parliament and many of the Member States (MSs) to co-fund, by the Third European Health Programme of the European Union (EU) 2014-2020, the first Joint Action (JA) on the prevention of frailty, ADVANTAGE, which brings together 33 partners from 22 MSs for 3 years.

The first practical step towards this aim has been the preparation of this document: the State of the Art on Frailty Report to support an overview of evidence of what works and what does not work on frailty prevention and management. Evidence on frailty has been researched and discussed by the professionals involved in the ADVANTAGE JA and crystallized here to have a common conceptual framework for further work and to base our recommendations for action for health and social care policies on this area.

ADVANTAGE JA partners summarized and analyzed the evidence obtained from four sources of information: peer-reviewed articles, grey documents, good practices identified at European level and EU funded projects. The main results are presented in this document as answers to key questions that stakeholders might ask when trying to understand how to best address frailty such as: what is frailty?; why is it a public health problem?; what is the relationship with chronic diseases?; how can frailty be prevented?; how should health care and social systems adapt to address frail patients?. For further information on these issues specific reports are available at the JA website www.advantageja.eu

The key messages reflected in this State of the Art document are grounded in scientific knowledge, are assertive and avoid controversial statements whenever further research is needed or results are unclear. Furthermore, they acknowledge the heterogeneity of the MSs health and social care systems and diverse societies in a scenario of demographic change and economic constraints across the EU.

Overall these messages intend to be an instrument of added value to advocate for policy driven decisions on frailty prevention and management in the JA participating MSs and subsequently towards a disability free older population in Europe.
INTRODUCTION

Ageing population in Europe and the importance of frailty

Demographic ageing is one of the most serious challenges that Europe is facing. (European Commission 2012). The percentage of citizens aged over 65 years is predicted to rise from 18% to 28% by 2060; the percentage of over 80s will increase from 5% to 12% during the same time period. Life expectancy at the age of 65 years, and even at 80 years, has increased and is expected to continue increasing beyond 2020 (European Union, 2017).

Older people are at greatest risk of becoming frail and developing disability. These demographic trends suggest that there will be an increase in age-related disability and dependence, which will ultimately impact not only on the wellbeing of the individuals affected but also on the sustainability of healthcare systems (European Commission, 2015).

As a consequence, the models of care should take into account the need to approach older people not just in terms of addressing diseases but also in terms of care and support to prevent functional decline, frailty and disability (Murray et al., 2013).

Despite ongoing controversy over an agreed definition of frailty, it is widely accepted that it is a geriatric syndrome characterized by a diminished physiological reserve of multiple organs, which means increased vulnerability of older people to adverse outcomes such as disability, institutionalization, hospitalization and death (Gill, 2006; Kan et al., 2008; Rodriguez-Mañas et al., 2012; Servicio Madrileño de Salud, 2018).

Frailty is very common with a global weighted prevalence of approximately 11% in people older than 65 years living in the community (Collard et al., 2012).

Frailty has a clear impact on the costs of health services. Recent studies carried out in Germany, France and Spain have determined its costs in older people both in the community and in hospitals. The incremental annual costs ranges from 1,500 to 5,000 €/person depending upon the frailty status (pre-frail or frail) and the setting of care (community or hospital) (Bock et al., 2016; García-Nogueras et al., 2016; Sirven et al., 2016).

However, since frailty is not an inevitable consequence of ageing, it may be prevented and treated to foster a longer and healthier life. Furthermore, the identification of conditions preceding the development of disability is an essential requisite to effectively prevent it. Among them the most important risk factor is frailty (Gill et al., 2011).

An EU approach to address frailty

The above mentioned reasons make frailty an important topic for public health at European level.
In this regard, a number of institutions, such as the European Commission (EC) and the World Health Organization (WHO), are advancing strategies and actions to create awareness about the need to support and care for older people and to build consensus across all sectors of society regarding both the philosophy of care and on how this will be delivered in the most cost-efficient way.

- The European Innovation Partnership on Active and Healthy Ageing (EIPAHA) was launched in 2012 as an EC response to meet Europe’s demographic challenges. Tackling frailty and disability and integrated care are among its priorities and the specific Action Groups on those topics have since contributed significantly to policy debate at the European Union (EU) and to shape new models for screening, treatment and monitoring as well as sharing good practices (European Commission, 2012).

- In the 2014 joint report on adequate social protection for long-term care needs in an ageing society, the Social Protection Committee and the EC agreed that national policy makers should move to an increasingly proactive policy approach, seeking both to prevent the loss of autonomy and thus reduce care demand, and to boost efficient, cost-effective care provision (European Union, 2014).

- The WHO is taking the lead in advocating for a comprehensive public health action on population ageing focusing on supporting action around the new concept of functional ability (WHO, 2015).

In spite of these initiatives, frailty is not yet at the top of the public health agenda. There is an urgent need to develop evidence based support to make frailty a public health priority.

The concern for this situation motivated the EC, the Parliament and many of the Member States (MSs) to co-fund, by the Third European Health Programme of the European Union 2014-2020, the first Joint Action (JA) on the prevention of frailty: ADVANTAGE.

The work that ADVANTAGE JA is implementing is particularly relevant in Europe at present as it addresses the demographic change and the associated increasing demands for social and health care from the burden of chronic diseases, frailty, disability and older age, which are a central priority for the EU and its MSs.

Bringing together 33 partners from 22 MSs for 3 years, this JA involves a wide diversity of countries and regions with very different health systems, diverse health and social policies and different cultural, social and economic backgrounds. This scenario represents a formidable challenge but also a great opportunity for concerted action resulting in fostering effective and successful policies in frailty prevention and management in the participating MSs.
ADVANTAGE JA focuses on three lines of action:

1. Building a common understanding on the concept and operative definition of frailty versus chronic diseases (CD) interventions.
2. Developing methodology and tools for assessment of pre-frail and frail people.
3. Preparing common health and social care guidelines or frameworks on frailty prevention and management to promote better health in older people and to reduce the growing burden of health care demands related to frailty, CD and disability.

Why an ADVANTAGE JA State of the Art report on frailty?

The final aim of this State of the Art report (SoAR) is to support an overview of evidence of what works on frailty prevention and management. Subsequently, this will be reflected in the advice that the JA will give to policy makers at national level (this work is to be implemented in 2018-2019).

The purpose of the SoAR is twofold and thus has two different target groups:

1. The Consortium members themselves so as to have a common framework and agreed concepts on which to base the rationale for future actions and deliverables within the ADVANTAGE JA.
2. The stakeholders in general and policy makers in particular from participant MSs who might find it a useful guide so that their own decisions may be informed by the evidence on frailty that has been researched and discussed by the professionals involved in the ADVANTAGE JA and crystallized in this report to base their recommendations for action.

The need for research on known evidence and gaps about frailty was based on the following reasons:

1. The need for concerted action from the ADVANTAGE JA advised to share a common rationale in spite of the different professional backgrounds and country situations of the Consortium.
2. The lack of international consensus on how to define and measure frailty poses challenges for prevention, clinical management and research activities.
3. The need to distinguish between frailty and CDs/ multimorbidity, two syndromes that overlap and are sometimes used interchangeably to describe vulnerable older adults.
4. Due to the lack of a common definition there is wide variation in the results of the studies on the prevalence of frailty, rendering unclear information on how common frailty is in different settings (community, primary care, hospitals,
nursing homes) and whether its frequency varies across countries. Moreover, little is known about how many new cases can be expected in the future, and the proportion of individuals who will become frail or recover from the condition, including the precipitating factors for transitions from robust to pre-frail or frail.

5. The plethora of tools that have been developed and are used to screen and diagnose frailty contributes to further complicate the comparison between prevention and management activities. There is a need to identify and select the most appropriate tools through the application of well-defined criteria.

6. Frailty can potentially be prevented and treated, particularly where appropriate interventions are implemented early. Therefore, it is necessary to update the available evidence and knowledge on four specific areas that have proven so far to be either effective or promising in the prevention and clinical management of frailty: nutrition, physical activity and exercise, drugs, and information and communication technologies (ICTs).

7. Many screening tools for frailty have been recommended at population level, but the feasibility and potential benefits of systematic screening and monitoring programs are yet unclear.

8. Current health and social care models are not attuned to the challenges that an increasing presence of frailty among the individuals they attend bring. Rather than the presence or absence of disease, the most important consideration for older people is usually their level of function. Integrated care has emerged as an effective way to improve outcomes for people with chronic conditions and complex care and support needs; therefore, it could also benefit frail people, although there is currently limited data from cost-effectiveness studies to support this hypothesis.

9. The need for competencies, which are not usually part of the curricula of health and social care professionals during their undergraduate and postgraduate training, to support reshaping of health and social care systems to address frailty.

How this document is organized

The SoAR points out the main facts and draws conclusions from the specific work packages (WPs) state of the art reports. For more detailed information on each of the five knowledge areas they have addressed, the interested reader should consult the specific WP state of the art reports available at the ADVANTAGE JA website: www.advantageja.eu

The SoAR is arranged in five sections: introduction, methodology, results, key messages, and annexes. Results are presented as answers to key questions that stakeholders might ask when trying to understand how to best address frailty, such as: what is frailty?; why is it a public health problem?; what is the relationship with CDs?; how can frailty be prevented?

State of the art report on the prevention and management of frailty
METHODS

Search strategy
The goal of the WP state of the art reports was to summarize and analyze the evidence obtained from four sources of information: Peer-reviewed articles, grey documents, good practices identified at European level and EU funded projects. The process spanned from February to October 2017. Each WP focused on their respective area of knowledge as depicted in Table 1.

Table 1. Area of knowledge evidence researched and analyzed by work packages

<table>
<thead>
<tr>
<th>WP</th>
<th>Area of knowledge covered by each WP</th>
</tr>
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<tbody>
<tr>
<td>WP4</td>
<td>Frailty definition. Relationship of frailty with chronic diseases and multimorbidity. Individual screening and diagnosis.</td>
</tr>
<tr>
<td>WP6</td>
<td>Prevention. Clinical management and treatment (including nutrition, physical activity, drugs and ICTs).</td>
</tr>
<tr>
<td>WP7</td>
<td>Health and social care models for frailty management.</td>
</tr>
<tr>
<td>WP8</td>
<td>Education/training of the workforce. Research.</td>
</tr>
</tbody>
</table>

A homogenous search approach by all WP partners was ensured by agreeing types of articles, period of search, sources of information and inclusion-exclusion criteria.

Only original articles were considered. Letters to the editor, abstract publications, conference proceedings, non-systematic reviews and editorials were excluded. Languages allowed were English and from any of the ADVANTAGE JA MSs.

All WPs reviewed papers published from 2002 to 2017, the period that has witnessed a dramatic increase in publications dealing with the concept of frailty. Exceptions were reviews on the areas of knowledge presented in Table 1 of “education/training of the workforce”, limited to the last 10 years, and “research”, limited to the last 2.5 years. Papers published before 2002 were included on a case-by-case basis if deemed relevant.

Sources of information for peer-reviewed articles were databases of references and abstracts on biomedical topics. All WPs searched articles in Medline via PubMed. All but one searched Embase. Other less used databases were CINAHL, Cochrane databases, Up to date, OpenGrey, Scopus and the Web of Science.

Specific search terms for each WP queries can be found in their reports. Overall, the search terms frailty or frail were applied without prejudice as to the specific definition. A
total of 17 areas of knowledge were considered for the search and included key issues related to frailty concept, epidemiology and its management.

In most of the WPs, pairs of reviewers independently assessed each of the studies for inclusion. A third reviewer settled disagreements. A total of 1,291,904 articles were identified by the search and information from 503 was extracted and subsequently analyzed (Annex 1).

The search for grey documents, good practices and initiatives supported by the EC, included searching the websites of the EIPAHA and EU funded projects related to frailty, and reporting by ADVANTAGE JA partners (many of whom are also EIPAHA members) when aware of specific unpublished evidence in their own countries.

Analysis of information

Each WP discussed their main findings within the group and subsequently developed their own topic-specific state of the art report. Each report was critically reviewed by three out of the seven members of an expert panel and later discussed in a two-day session with the expert panel, the coordination team and the WP leaders and co-leaders (Expert Panel meeting, September 2017. Mao Spain). The updated and revised final versions are available at the ADVANTAGE JA website: www.advantageja.eu.

Limitations of the common search strategy

Although the methodology for the review was rigorous, some limitations need to be considered:

• The open definition of the terms frail and frailty makes the comparison between different publications using the same terms for an array of clinical situations difficult.

• The search for grey literature was opportunistic; thus some important documents may not have been identified.
RESULTS

1. What is the definition of frailty adopted by ADVANTAGE JA?

The concept of frailty is a recent one, dating from the last quarter of the 20th century. The definition of frailty is still under debate. ADVANTAGE JA partners have agreed that, irrespective of a given definition, the concept of frailty must refer to a condition with five core attributes:

1. Characteristics (multiple conditions, complexity, relationship to ageing, and a specific trajectory that may be reversible).
2. Pathogenesis (a multicausal process that includes the malfunction of several systems due to intrinsic and extrinsic factors that results in loss of reserve).
3. Triggers (stressors).
4. Vulnerability for adverse outcomes.
5. Phenomenon (characterized by its heterogeneity, fluctuating nature and difficulties in staging the progressive pathway). When describing frailty three different approaches have been raised: the clinical (a clinical state or geriatric syndrome), the functional (losses in human functioning, alterations in several domains of function and reduction of activities) and the multidimensional one (frailty covers different domains including the physical, cognitive and psychosocial domains).

From the many different frailty definitions used in the publications and projects reviewed, only the 2015 WHO definition fully incorporates the first four attributes that are uncontroversial. Thus ADVANTAGE JA has decided to adopt this definition:

“Frailty is a progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes.” (WHO, 2015).

2. What is the relationship between frailty and multi-morbidity?

Multimorbidity, disability and frailty are often used interchangeably to identify vulnerable older adults. However, they are distinct clinical entities that are causally related, often associated and may overlap. Frailty is now considered to be a distinct dimension, aside from comorbidity and functional dependency, and is a pre-disability stage (Kan et al., 2008).

All three occur frequently and have important consequences. There is a need to distinguish between them because frailty is more strongly predictive of adverse outcomes compared to multimorbidity. Compared to disease states, function has a greater impact on quality of life than disease. Furthermore, the best predictor of function is frailty.
Frailty focuses on specific areas for which a general treatment approach can be developed, whereas multi-morbidity moves the focus to the management of each condition separately, although both require multidimensional assessment and management (Morley et al., 2013).

Frailty should be framed as a chronic condition (Harrison et al., 2015). Chronic care strategies to provide accessible information, advice, education and support for self-management to promote participation, independence and wellbeing in later life should be adopted. Support for the caregiver to remain well and continue in their caring role should be also provided.

3. How common is frailty in the ADVANTAGE JA Member States?

The prevalence of frailty reported in multiple studies on community cohort samples ranges from 2% to 60%, contingent on factors such as the age of the population studied and the frailty assessment instrument or classification used. Nine out of every ten studies reviewed, reported prevalence rates below 30% and half reported rates above 11%. This is consistent with the global weighted prevalence of 11% reported in a recent systematic review of community-dwellers over 65 years old (Collard et al., 2012).

There are much fewer studies from other settings. They indicate that frailty is more frequent (≥30%) in primary care and outpatient settings, reaching more than 50% of inpatients in hospital wards and over 60% of residents in long-term care facilities.

Not all ADVANTAGE JA MSs are equally represented in these frailty prevalence studies. Most of the studies reviewed were conducted in just five countries (France, Germany, Italy, the Netherlands and Spain), while another five (Bulgaria, Croatia, Cyprus, Lithuania and Malta), to the best of our knowledge, do not have any published information available.

4. How many new cases should we expect in the future?

As frailty is highly associated with age, we should expect an increase in the number of new cases (incidence) of frailty as the European population gets older. Nevertheless, there is limited information on precisely how many new cases we could expect in the ADVANTAGE JA MSs. Published data ranges from 4% new cases in adults aged over 65 years in Germany to 8% in adults aged over 60 years in Spain after three years of follow-up.

A study in Italy found the following risk factors for frailty: older age; female gender; obesity; cardiovascular disease; osteoarthritis; low vitamin D; smoking; loss of vision; dependence in activities of daily living; cognitive impairment; low monthly income and
poor physical performance (Trevisan et al., 2017). Diabetes was also associated with an increased risk of frailty in a study carried out in Spain (Garcia-Esquinas et al., 2015).

In research conducted outside the EU, acute illness, hospitalisation and polypharmacy were the most common precipitating factors resulting in transitions to more severe frailty states. These associations have not been checked in research conducted in Europe.

5. Can a frail person improve his/her situation (become less frail) spontaneously?

Frailty is a potentially reversible condition that can regress spontaneously to a robust (non-frail) state, especially in its early stages, although little is known about how frequently this can happen without intervention. More advanced frailty states are less likely to be reversible.

In a study conducted in the Netherlands within the FP7-funded PERSSILAA project, in a sample of 169 participants 25% of frail participants transitioned back to pre-frail, while 25% of pre-frail participants transitioned to robust after two years follow-up. Studies in the USA have reported much smaller favourable transitions, with less than 1% reversing spontaneously after four and a half years follow-up (Gill, 2006).

Being overweight, having a low-moderate alcohol consumption, a higher educational level and living alone appear to be associated with improvements in frailty status, while some chronic conditions like diabetes or chronic obstructive pulmonary disease (COPD) are associated to a poor evolution (Trevisan et al., 2017; Pollack et al., 2017), although this has to be confirmed with other studies.

Physical activity and physical exercise has a role in reversing frailty status: Moderate physical activity reduced frailty progression in some age groups (particularly those aged over 65 years) and vigorous activity significantly reduced the trajectory towards frailty. However, mild physical activity was insufficient to slow progression (Rogers et al., 2017).

6. How can frailty be screened in clinical practice?

An international consensus group stated there is sufficient evidence to recommend that all persons older than 70 years should be screened for frailty by health care providers (Morley et al., 2013). The Ministry of Health of Spain (2014) also recommends as a national strategy the opportunistic screening for frailty in patients aged over 70 years attending primary health care centers and active search for frailty in patients with CD.

ADVANTAGE JA supports the recommendation of opportunistic screening of individuals aged over 70 years receiving health care at any level of the system.
In order to screen for frailty, many instruments have been proposed and are used to identify frail individuals in clinical practice and public health level frailty detection programs.

Frailty screening instruments used in clinical practice must be sensitive, so as to detect most patients needing special attention, and specific, so as to avoid providing unneeded interventions to robust patients falsely classified as pre-frail or frail. Available instruments tend to have high sensitivity but limited specificity. Frailty screening instruments must also have good positive and negative predictive values, which are influenced by the prevalence of frailty. These will be the instruments most useful at population level.

ADVANTAGE JA proposes the use of screening tools that fulfill four characteristics:

- Quick to administer (taking no more than 10 minutes to complete).
- Do not require special equipment.
- Have been validated.
- Are meant for screening (see Annex 2).

These four characteristics are met by the following instruments: Clinical Frailty Scale (CFS); Edmonton Frail Scale (EFS); Fatigue, Resistance, Ambulation Illness, Loss of Weight Index (FRAIL Index); Inter-Frail; Prisma-7; Sherbrooke Postal Questionnaire; Short Physical Performance Battery (SPPB) or Study of Osteoporotic Fractures Index (SOF). All of these instruments appear in a recent review of tools for frailty assessment (Dent et al., 2016).

Although gait speed is not a scale, it has been shown to be a good predictor of frailty and other significant adverse events. It is also one of the screening tools recommended in the Frailty Strategy of the Ministry of Health of Spain (2014). For these reasons, ADVANTAGE JA adds it to the list of recommended tools.

In the absence of a “gold standard”, the instrument to screen and diagnose frailty should be chosen according to the characteristics of the population being studied, the aims of the assessment and the clinical context (Cesari et al., 2016).

7. How can frailty be diagnosed?

Frailty status in older adults without disability should be determined using a validated scale (Annex 3). ADVANTAGE JA proposes as frailty diagnostic instruments the Frailty Index of accumulative deficits, the Frailty Phenotype of the Cardiovascular Health Study (CHS), or the Frailty Trait Scale as frailty diagnostic instruments. The first and the last one allow tracking of the evolution of the frailty status. These scales appear in a recent review of tools for the assessment of frailty (Dent et al., 2016).

These three diagnostic tools do not assess all the dimensions of comprehensive individual needs that must be considered. These dimensions are best assessed through the process...
of Comprehensive Geriatric Assessment (CGA), which has become the internationally established method to assess and manage older people in clinical practice.

As the aim of diagnosing frailty is to prevent functional decline and disability, assessing frailty status is a controversial issue in patients with established disability and a low Barthel Index.

Frailty is viewed as continuum of changes in intrinsic capacity, preceded by a pre-frail state, where early intervention is more likely to reverse frailty or delay progression to frailty (Rodríguez-Mañas & Walston, 2017). Although the therapeutic approach to pre-frail and frail patients is quite similar, it is important to differentiate between these two clinical situations as it also determines the treatment of other pathologies that may be present, for example diabetes (Sinclair et al., 2015).

8. How can frailty be managed?

It is important to encourage a healthy life-style from midlife, which will include interventions such as stopping smoking and reducing alcohol consumption, increasing physical activity, and improving the diet to achieve and maintain a healthy weight, to improve health status in general and to reduce the risk of becoming frail in later life (National Institute for Health and Care Excellence, 2015; Graciani et al., 2016).

There is sufficient evidence supporting that the Mediterranean diet is useful to prevent frailty (Goisser et al., 2016; León-Muñoz et al., 2014).

A recent meta-analysis has confirmed that exercise and nutrition are effective interventions to reduce frailty (Puts et al., 2017). Although some drugs have shown some potential benefits, up to now no drug treatment has been approved for frailty.

Today, the gold standard for management of frailty is the CGA and its associated interventions (Morley et al., 2013). CGA is a multidimensional, interdisciplinary assessment process to determine the medical, psychological, social and functional capabilities of a frail older person and to develop a co-ordinated and integrated plan for treatment and long-term follow up (Rubenstein et al., 1991). CGA allows structuring of the specific actions needed to be adopted by different professionals according to the range of problems identified with the frail individual and his/her caregiver.

Figure 1 presents an algorithm for the prevention and management of frailty.
Figure 1. Algorithm for the management of frailty at individual level

All persons 70 years or older attending health care services

SCREENING with any of the following scales
Clinical Frailty Scale; Edmonton Frailty Scale; Fatigue, Resistance, Illness, Loss of Weight Index (FRAIL Index); Gait Speed; Inter-Frail; Prisma-7; Sherbrooke Postal Questionaire; Short Physical Performance Battery (SPPB) or Study of Osteoporotic Fractures Index (SOF).

POSSIBLY FRAIL

DIAGNOSIS
Apply Frailty Index of accumulative deficits, Frailty Phenotype, or Frailty Trait Scale in the context of the CGA.

FRAILTY OR PREFRAILTY

INTERVENTION
Advice to stop smoking, reduce alcohol consumption, increase physical activity, and improve diet

ROBUST

MANAGEMENT CONSISTING OF:
- Comprehensive Geriatric Assessment to develop a personalised care plan and carry out a personalized multi-dimensional interventions
- Take into account the frailty or pre-frailty stage to tailor the correct treatment of concomitant diseases.
- Provide structured multicomponent exercise programs (consisting of endurance, flexibility, balance, and resistance training) performed with low to moderate intensity, in 30 to 45 minutes sessions, three times a week. Followed or substituted by exercise programs of strength training: minimum of 8 weeks and medium to high exercise load (from 8 to 12 repetitions, from 30% - 60-70% of maximum intensity).
- Assess and optimise nutrition (Mini Nutritional Assessment).
- Apply tools to minimise risk from inappropriate drugs and polypharmacy (Beers criteria, STOPP-START or Laroche criteria).
- Advise patients with a body mass index greater than 35 kg/m2 to achieve a moderate weight loss of 0.5-1 kg per week or 8-10% of initial body weight after 6 months, with a final target of a body mass index between 30-35; always combined with physical activity and/or physical exercise.
- Consider Vitamin D supplementation in frail patients who are at high risk for falls and fracture level and with a 25-OH vitamin D level < 30 ng/ml, with doses of 20 to 25 µg/day (800 a 1000 IU/day) of vitamin.
- ICT solutions should also be considered and advised to enable self-management and promote independence.
8.1 How useful is physical activity and exercise for the management of frailty?

In order to reduce frailty it is necessary to act on one of its main risk factors: inactivity. Interventions that have focused on physical activity have demonstrated its effectiveness in delaying and even reversing symptoms of both frailty and disability.

A systematic review provides evidence on the positive effects of multicomponent exercise programs on the functional ability and the overall health of frail people. The most frequently used program consists of endurance, flexibility, balance, and resistance training performed with low to moderate intensity, in 30 to 45 minutes sessions, three times a week. Exercise seems to be more effective in earlier stages of frailty than on its later stages.

Several clinical trials (Cadore et al., 2013; Pahor et al., 2014), show that frailty and frailty related syndromes (falls, sarcopenia) respond positively to structured exercise programs of strength training, consisting on low to medium exercise load (from 30% -low- to 60-70% -medium- of maximum intensity). The duration of the trials was extremely variable, from eight weeks minimum to a year and a half maximum, but even the shortest trial duration produced an increase in strength.

There is also evidence that physical exercise is more useful if combined with a nutritional programme (Theou et al., 2011).

8.2 What should be done about nutrition for the treatment of frailty?

There is sufficient evidence that nutrition and frailty status are related; thus nutritional status should be assessed in frail and pre-frail patients using a validated tool such as the Mini Nutritional Assessment (MNA) (Guigoz, 2006).

One recent revision analyzed the relationship between nutrition and frailty. It suggested to try in those who are obese a “moderate weight loss of 0.5-1 kg per week (or 8-10% of initial body weight after six months) in order to reach a body mass index (BMI) of 30-35 kg/m² maximum, while assuring a protein intake of at least 1 g per kilogram of body weight per day and an appropriate intake of micronutrients” (Goiser et al. 2016). Moreover, the implementation of a simultaneous physical exercise program (combined aerobic and resistance exercise) to the diet is the best strategy for improving function in obese frail patients (Villarreal et al., 2017)

Frail older patients who are at high risk of falls or fracture and with a 25-OH vitamin D level < 30 ng/ml should receive doses of 20 to 25 µg/day (800 a 1000 IU/day) of vitamin D (Bruyère et al., 2017).
8.3 What is the relationship between polypharmacy and frailty?

Frailty increases the risk of side effects from drug treatments.

Polypharmacy does not cause frailty but is associated with increased rates of mortality, disability, hospitalization, and emergency department visits in frail and pre-frail older adults. Polypharmacy (especially when more than 10 drugs are taken) should be monitored in these patient subgroups to optimize health outcomes (Bonaga et al., 2017).

Besides the number of drugs, prescribing medicines which are either inappropriate or no longer indicated increases adverse drug reactions, drug interactions, hospitalisations and costs of care, and may exacerbate frailty (Gnjidic et al., 2012). Hence, reduction in inappropriate medicines can clearly decrease costs and medication side effects in frail populations (Morley et al., 2013).

There are useful tools to manage inappropriate prescribing and reduce polypharmacy in frail patients. The most widely used include the Beers, STOPP-START and Laroche criteria (Kaufmann et al., 2014).

8.4 Are ICTs useful in the management of frailty?

A wide range of technological solutions have been developed to enable older people to remain independent at home, support caregivers, facilitate remote monitoring and self-management, provide decision support, and improve information sharing and coordination of services. Examples include the CareWell, SmartCare and FACET European projects.

There is evidence that show there are substantial potential benefits from the use of ICTs in older people especially for aspects of smart home technologies and monitoring of chronic conditions. In addition, Scotland has developed a strategy in this setting, and telecare has been shown to delay entry to long term care (The Deloitte Centre for Health Solutions, 2015). Although ICTs have been shown to be beneficial in the provision of care for older people with disabilities, up to now it is not quite clear if these benefits expand to frail individuals.

The most effective Telehealth intervention is automated vital signs monitoring in order to reduce health service use, according to a systematic review of home Telehealth and telecare for frail older people and patients with chronic conditions (Barlow et al., 2007). However, there is still limited evidence on the cost-effectiveness of these interventions and on the effects of home safety and security alert systems at scale.

Furthermore, results of this review suggest that the acceptance and deployment of these new technologies remains problematic, especially for frail older people. Some reasons for the latter are that clinicians and patients are lost in the variety of services that apparently exist, that they doubt about the clinical effectiveness and acceptance of the services, and
that they have no idea on how to start the implementation in clinical practice (Niehaves et al., 2013).

9. Do we need programs to screen for frailty at population level?

Screening for frailty in older populations would provide the opportunity to intervene at earlier stages when treatments are more likely to reverse or at least delay the progression of the condition. Nevertheless, to date there is little empirical evidence on the acceptability and effectiveness of population screening programmes.

General practitioners have been identified as the preferred healthcare professional to identify physical health problems and risks (Lette et al., 2015) and therefore seem very appropriate to screen and monitor for frailty at population level.

There are both ongoing and completed EU funded projects and initiatives showing the feasibility and acceptance of screening approaches for frailty in primary care or the community in ADVANTAGE JA MSs. They are based on a two-step approach, consisting of the use of a short screening instrument to identify possible frail individuals followed by a more comprehensive evaluation to confirm the diagnosis. Different approaches to the first step have been tried, including the use of questionnaires, an Electronic Frailty Index (eFI) to be used with patient’s primary care records, or scales administered by healthcare professionals or even the individual him/herself. The second step is always a more structured assessment using validated diagnostic tools.

In Spain, the Ministry of Health, in agreement with all regional ministries and professional associations, developed in 2014 a common protocol to screen for frailty in primary care. Furthermore, the region of Andalusia has implemented a programme to screen and manage/monitor frailty at population-level, on-going since 2008. In the United Kingdom, the routine use of an eFI in primary care has been promoted since 2017. None of these strategies have been evaluated yet.

Challenges in the uptake of screening programs remain, with concerns raised about inconsistencies in the definition of frailty; difficulty in eliciting psychosocial issues through questionnaires compared to home visits; overlapping of preventive initiatives between services; the weak evidence-base of many initiatives; ill-defined target groups and limited consideration of how to follow-up the detected problems.

There is a need to pilot throughout Europe regional screening programmes in primary care using a two-step strategy and to evaluate the existing programmes in countries like Spain and the United Kingdom, to build the evidence base for future routine screening programs.
10. Is there a need to monitor frailty in Europe?

As frailty is highly prevalent in Europe and is very much associated with disability, monitoring its evolution seems a reasonable way to proceed.

Longitudinal studies across Europe (Survey of Health, Ageing and Retirement in Europe-SHARE) and in specific countries (Germany, Italy, Spain) and the recent inclusion of an assessment of frailty into English National Health Service primary care contracts show that identifying and monitoring frailty is feasible and useful to provide information on its prevalence, incidence and outcomes. This may help healthcare providers calibrate the extent to which appropriate interventions are provided and to assess their impact over time.

Despite this, no country in Europe has adopted a systematic process for the surveillance or monitoring of this condition. Cross-national experiences like the SHARE project (http://www.share-project.org/) can serve as basis to establish these programmes. Furthermore, monitoring would be much easier if the next review of the International Classification of Diseases includes a specific code for frailty.

11. What components should health and care systems adopt to manage frailty?

Most of the key components of an effective model of integrated care for frailty have been signalled by Béland et al. (2011) and reflected in the Multimorbidity Care Model developed by the JA on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (CHRODIS) (Navickas et al., 2016) and the Integrated Care for Older People (ICOPE) Guidelines on community-level interventions to manage declines in intrinsic capacity (WHO, 2017). They include:

- The establishment of a single entry point for the system and individualised assessment and care plans (for both older people and their caregivers).
- Focusing on case management.
- The coordination of home and community services across the continuum of care, by a continuous partnership between the case manager and the family physician.
- Tailoring multiple physical, cognitive, social and functional interventions by an interdisciplinary team (both in hospitals and community) with a prioritisation of the interventions that should avoid the risk of overtreatment and adverse events.
- The effective management of care transitions.
- Using electronic information tools and technology enabled care solutions.
- The adoption of clear policies and procedures for eligibility and care processes.

Other additional elements that care systems need to consider are: targeting interventions towards high risk frail community dwelling older adults, detected through the two-step procedure mentioned above; enabling individuals to achieve their personal goals and to...
regain functional abilities; supporting self-management, both for the patient and the caregivers, as is done with chronic conditions (Harrison et al., 2015); supporting the adoption of changes in the way of delivering care and assuring their implementation; and giving more importance to outcomes relevant to patients, clients and service users such as their care experience, quality of life and participation.

12. Is the health and social care workforce ready to meet the challenges of frailty?

In its “World report on ageing and health”, the WHO (2015) concluded that health professionals are often unprepared to deliver the holistic, anticipative and based-on-function type of care that old people require. They usually lack the skills and knowledge on gerontology and geriatrics and on topics not directly related to these disciplines like shared decision-making, team-based care implementation, use of ICTs and continual quality improvement, needed to achieve that objective. They are then especially ill-equipped to deal with the clinical and organizational challenges posed by frailty and therefore require specific training both at the undergraduate and postgraduate level.

However, the search of the literature has not retrieved any evidence on the efficacy, effectiveness or sustainability of frailty specific training programs for any profession involved in the care of frail patients. The evaluation of the on-going EU-funded projects FACET and SUNFRAIL, and finished PERSILAA, which include educational components targeting professionals, patients and caregivers, will provide evidence to fill this gap. PERSILAA, for example, has proved the feasibility of a train-the-trainers intervention to increase the literacy on frailty of two older populations, adapting the information provided to their sociocultural contexts.

There are also current initiatives on continuous health professional education at national level. One example is Spain, where the Ministry of Health put in place in 2015 a 30 hours online programme on the detection and management of frailty and falls in older people, which has trained so far 2,698 health care professionals. Another example is Ireland, where the Health Service Executive and the Royal College of Physicians have launched in 2017 a National Frailty Education Programme based on the training the trainers of health professionals with the support of e-learning materials. France includes several in-person training initiatives on this topic under the umbrella of a national education strategy. All these experiences are promising and, after their evaluation, may be seen as a hallmark for future recommendations within participants MSs.
13. What are the future areas of research on frailty?

Continuing research is needed not only to better understand the nature of frailty but also to improve screening and diagnostic tools and test the effectiveness of interventions. Main areas identified are:

- In basic research, the most relevant issues are the identification of subtle systemic dysfunctions prone to develop frailty and the definition of patterns of risk combining different –omics.
- In the field of epidemiology, European studies on frailty prevalence, incidence and trajectories (including their precipitating factors) should be developed with a sound common methodological approach.
- Concerning assessment and treatment, knowing which screening and diagnosing scales suit best different settings is warranted. More clinical trials should be conducted to determine if the Mediterranean diet, loss of weight, vitamin D and proteins supplementation, withdrawal of psychoactive drugs, control of polypharmacy and use of scales such as MNA, STOPP-START, BEERS and Laroche, are effective for the prevention or treatment of frailty.
- Acceptance and use by older people of ICTs to manage frailty should be further investigated.
- More research is needed on the impact on frailty of the quality of outdoor and indoor air, especially the one produced by climate-control equipment for nursing homes.
- In relation to frailty management by care systems, further research is required to identify the most effective combinations of community health and social care interventions for frailty and to understand the stages in which people benefit most from these approaches. There is a requirement for well-designed trials of CGA for frail older people within more general intermediate care services that operate at the interface between hospital and community.
- More local, national and European projects for education/training of the workforce need to be funded.

KEY MESSAGES

ADVANTAGE JA key messages, reflected in this SoAR, are grounded in scientific knowledge, are assertive and avoid controversial statements whenever further research is needed or results are unclear. This is because overall they are intended to be an instrument of added value to support policy driven decisions on frailty prevention and management in the JA participating MSs.
1. Frailty is not an inevitable consequence of ageing, it may be prevented and treated to foster a longer and healthier life. In addition, it has a clear negative impact on the costs of health services. In spite of that, frailty is not yet at the top of the public health agenda.

2. Despite ongoing controversy over an agreed definition of frailty, it is widely accepted that it is a geriatric syndrome characterized by a progressive age-related decline in physiological systems that results in decreased functional reserves and a low intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes (WHO definition which ADVANTAGE JA supports).

3. Frailty is very common, although the prevalence reported varies considerably contingent on factors such as the definition used, the age of the population studied and the frailty assessment instrument/classification used. A prevalence of more than 11% in community-dwellers over 65 years old seems a reasonable estimate of the current situation in the EU.

4. Frailty is a potentially reversible condition that may revert spontaneously to a robust (non-frail) state, especially in its early stages, although little is known about how frequently this can happen without intervention.

5. Multi-morbidity, disability and frailty are distinct clinical entities that are causally related, often associated and may overlap. All three occur frequently and have important clinical consequences. What really affects quality of life is function and not disease, and the best predictor of function is frailty.

6. To prevent disability in older age and support healthy ageing in the JA participating MSs, the first step is to identify the population group at the highest risk and could benefit most from an intervention aimed at delaying or reversing disability and dependence. These are the frail individuals.

7. Many instruments have been proposed and are used to identify (screen and diagnose) frail individuals in clinical practice and for public health level frailty detection programs. From all tools available, ADVANTAGE JA proposes those that fulfill certain characteristics. For screening: Clinical Frailty Scale; Edmonton Frailty Scale; Fatigue, Resistance, Illness, Loss of Weight Index (FRAIL Index); Gait Speed; Inter-Frail; Prisma-7; Sherbrooke Postal Questionaire; Short Physical Performance Battery (SPPB) and Study of Osteoporotic Fractures Index (SOF). For diagnosis: Frailty Index of accumulative deficits, Frailty Phenotype and Frailty Trait Scale.
8. It is recommended to screen opportunistically for frailty in populations aged over 70 years, giving the possibility of designing and implementing preventive, population-based interventions targeting identified risk factors.

9. Individual interventions, either in the community or in every setting of care, often share a three-step structure: 1) frailty screening to identify pre-frail or frail older persons, 2) use of diagnostic tools to diagnose frailty, and 3) a CGA to assess individual needs and develop multidimensional interventions to match these needs in the frame of individual care plans.

10. Early stages of frailty are the most appropriate target for intervention because they are more likely to be reversible.

11. The specific components of frailty interventions (both for prevention and treatment) include adequate physical activity and exercise, adequate nutrition, healthy lifestyles and drugs revision.

12. General practitioners have been identified as the preferred healthcare professional to identify physical health problems and risks and as such to potentially screen and monitor for frailty at population level.

13. Models of care should take into account the need to approach older people not just in terms of their diseases but also in terms of physical, cognitive and psychosocial care and support to prevent functional decline, frailty and disability. Key components to address frailty are those that define also integrated care, with the addition of targeting high risk frail individuals, an enablement attitude and a focus on outcomes most relevant to frail individuals and their caregivers. For these purposes, a coordinated system able to provide the most effective care in the different settings (community, primary care, hospitals and institutions) needs to be provided.

14. Health and social care professionals across settings and countries need to be trained to address future needs related to ageing, frailty and disability.

15. Further research is needed not only to better understand the nature of frailty but also to improve screening and diagnostic tools and test the effectiveness of interventions. In this regard, ADVANTAGE JA has identified a number of areas that will benefit from EU funding.
REFERENCES


Ministry of Health of Spain (2014). Consensus document on frailty and falls prevention among the elderly. The prevention and health promotion strategy of the Spanish NHS. Available at: https://www.msssi.gob.es/profesionales/saludPublica/prevPromocion/Estrategia/docs/Frailtyandfalls_Elderly.pdf [Last access: 13/12/2017]


National Institute for Health and Care Excellence (NICE) (2015). Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset. NICE Guideline [NG16]. Available at: https://www.nice.org.uk/guidance/ng16 [Last access: 14/12/2017]


Annex 1. Papers in the areas reviewed for the ADVANTAGE State of the Art report

<table>
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<tr>
<th>Areas of knowledge reviewed</th>
<th>Papers identified</th>
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<tr>
<td>Definition</td>
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<td>Relation with chronic diseases</td>
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<td>Prevalence and incidence</td>
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<td>Individual screening and diagnosis</td>
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<td>Nutrition</td>
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<td>Physical activity</td>
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<td>Drugs</td>
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<td>ICTs</td>
<td>124,634</td>
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<td>Population screening</td>
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<td>Trajectories and transitions</td>
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<td>Health care models</td>
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<td>Research</td>
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<td><strong>Total</strong></td>
<td><strong>1.291.904</strong></td>
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ICTs: Information and communication technologies.
Annex 2. Tools for the screening of frailty recommended by ADVANTAGE JA

<table>
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<tr>
<th>Tool name</th>
<th>Original reference</th>
<th>Tool description</th>
<th>Time needed to perform</th>
<th>Number of items</th>
<th>Special equipment needed</th>
</tr>
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<tbody>
<tr>
<td>Clinical Frailty Scale</td>
<td>Roockwood et al. Can Med Assoc J 2005</td>
<td>Single descriptor of a person’s state of frailty (fitness)</td>
<td>5 min</td>
<td>NA</td>
<td>No</td>
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<td>Edmonton Frail Scale</td>
<td>Rolfson et al, Age Ageing. 2006</td>
<td>Timed up and Go Test, Clock draw test, 7 Questions exploring frailty domains</td>
<td>&lt;5 min</td>
<td>9</td>
<td>No</td>
</tr>
<tr>
<td>Inter-Frail</td>
<td>Bari et al. J Am Geriatr Soc 2014</td>
<td>1 disability and 10 frailty items (yes-or-no questions)</td>
<td>10 min</td>
<td>11</td>
<td>No</td>
</tr>
<tr>
<td>Prisma-7</td>
<td>Raiche et al. Arch Gerontol Geriatr 2007</td>
<td>Self-reported. 7 questions on demographics and performance</td>
<td>5 min</td>
<td>7</td>
<td>No</td>
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<tr>
<td>Sherbrooke Postal Questionnaire</td>
<td>Hebert et al. Age Ageing 1996</td>
<td>Self-reported questionnaire. 6 items: living alone, polypharmacy, mobility, eyesight, hearing, memory.</td>
<td>&lt; 5 min</td>
<td>6</td>
<td>No</td>
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<tr>
<td>Short Physical Performance Battery (SPPB)</td>
<td>Guralnik et al. J Gerontol 1994</td>
<td>3 dimensions: balance, gait and weakness.</td>
<td>&lt;10 min</td>
<td>12</td>
<td>No</td>
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<tr>
<td>Study of Osteoporotic Fractures Index (SOF)</td>
<td>Ensrud et al. Arch Intern Med. 2008</td>
<td>3 items: weight loss, reduced energy level and inability to rise from a chair.</td>
<td>&lt; 5 min</td>
<td>3</td>
<td>No</td>
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</table>
## Annex 3. Tools for the diagnosis of frailty recommended by ADVANTAGE JA

<table>
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<tr>
<th>Tool</th>
<th>Original reference</th>
<th>Tool description</th>
<th>Time</th>
<th>Number of items</th>
<th>Special equipment needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frailty Index of accumulative deficits</td>
<td>Mitnitsky et al. Sci World J. 2001</td>
<td>Number of health deficits present / Number of health deficits measured</td>
<td>20-30 min</td>
<td>&gt;30</td>
<td>No</td>
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<tr>
<td>Frailty Trait Scale (FTS)</td>
<td>García-Garcia et al. J Am Med Dir Assoc. 2014</td>
<td>Seven dimensions: energy balance and nutrition, activity, nervous system, vascular system, weakness, endurance, slowness</td>
<td>20 min</td>
<td>12</td>
<td>Yes (albumin, dynamometer)</td>
</tr>
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</table>
Annex 4: Glossary

**Active ageing**: the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age.

**Assessment**: the action of making judgement about something. It refers in this context to screening and diagnosis of frailty.

**Comprehensive geriatric assessment**: a multidimensional assessment of an older person that includes medical, physical, cognitive, social and spiritual components; may also include the use of standardized assessment instruments and an interdisciplinary team to support the process.

**Chronic condition**: a disease, disorder, injury or trauma that is persistent or has long-lasting effects.

**Disability**: any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner, or within the range, considered to be normal for a human being. The term disability reflects the consequences of impairment in terms of functional performance and activity by the individual.

**Drug**: a chemical substance used as a medicine.

**Functional ability**: the ability to perform activities of daily living, including bathing, dressing, and other independent living skills, such as shopping and housework. Many functional assessment tools are available to quantify functional ability.

**Frailty**: is a geriatric syndrome which can be regarded as a progressive age-related deterioration in physiological systems that results in extreme vulnerability to stressors and increases the risk of a range of adverse outcomes including care dependence and death.

**Geriatric syndrome**: the multifaceted dynamics between underlying physiological change, chronic disease, and multi morbidity can also result in health states in older age that are not captured at all by traditional disease classifications and that are therefore often missing in disease-based assessments of health. These are commonly known as geriatric syndromes, although there is still some debate as to what disorders these include.

**Good practice**: is a practice that has been proven to work well and produce good results, and is therefore recommended as a model. It is a successful experience, which has been tested and validated, in the broad sense, which has been repeated and deserves to be shared so that a greater number of people can adopt it.

**Intrinsic capacity**: the composite of all the physical and mental (including psychosocial) capacities that an individual can draw on at any point in time.
**Long term care:** the activities undertaken by others to ensure that people with a significant ongoing loss of intrinsic capacity can maintain a level of functional ability consistent with their basic rights, fundamental freedoms and human dignity.

**Management:** to bring about or succeed in accomplishing, sometimes despite difficulty or hardship. In this context it refers to treatment and prevention of frailty.

**Multi-morbidity:** the co-occurrence of two or more chronic medical disorders in one person at the same time. It can lead to interactions between disorders; between one disorder and treatment recommendations for another; and between drugs prescribed for different disorders. As a result, the effect of multi-morbidity on functioning, quality of life, and mortality risk might be much greater than the individual effects that might be expected from these disorders.

**Older person:** a person whose age has passed the median life expectancy at birth.

**Prevalence:** it is an epidemiological measure of the proportion of cases of a disease that are present in a particular population at a given time, whereas incidence refers to the number of new cases that develop in a given period of time in a defined population. Incidence can also be expressed as the proportion of a population that develops the disease in a given period of time.

**Polypharmacy:** the simultaneous administration of multiple drugs (medication) to the same patient.

**Work package:** is a building block of the work breakdown structure that allows the JA management to define the steps necessary for completion of the work. Breaking it down into WP allows multiple teams to work simultaneously or sequentially on different components of the JA.
### Annex 5: Contributors to this report

<table>
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<tr>
<th>National Flag</th>
<th>Name and Affiliation</th>
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<td>Lucia Galluzzo</td>
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