Malnutrition or frailty? Overlap and evidence gaps in the diagnosis and treatment of frailty and malnutrition.

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Abstract

There is increasing awareness of the detrimental health impact of frailty on older adults and of the high prevalence of malnutrition in this segment of the population. Experts in these two arenas need to be cognizant of the overlap in constructs, diagnosis and treatment of frailty and malnutrition. There is a lack of consensus regarding the definition of malnutrition and how it should be assessed. While there is consensus on the definition of frailty, there is no agreement on how it should be measured. Separate assessment tools exist for both malnutrition and frailty however, there is intersection between concepts and measures. This narrative review highlights some of the intersections within these screening/assessment tools including: weight loss/decreased body mass, functional capacity, and weakness (hand grip strength). The potential for identification of a minimal set of objective measures to identify, or at least, consider risk for both conditions, is proposed. Frailty and malnutrition have also been shown to result in similar negative health outcomes and consequently common treatment strategies have been studied, including oral nutritional supplements (ONS). While many of the outcomes of treatment relate to both concepts of frailty and malnutrition, research questions are typically focused on the frailty concept, leading to possible gaps or missed opportunities in understanding the effect of complementary interventions on malnutrition. A better understanding of how these conditions overlap may improve treatment strategies for frail, malnourished, older adults.

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Introduction

The association between malnutrition and frailty, especially in older adults (over 65 years of age), has been established (Fried 2001; Jeejeebhoy 2012; Vellas et al. 2016), yet consideration of this overlap in research and practice is just beginning. Recent literature has suggested some consistency in constructs, identification tools and treatment methods. For example, in 2012, a review highlighting this overlap concluded that loss of body tissues, resulting in wasting, is a common phenotype for several conditions, including frailty and malnutrition (Jeejeebhoy 2012). Other research suggests that these conditions have the potential to exacerbate each other and further conditions (Vellas et al. 2016), with treatment strategies being generally similar (Vellas et al. 2016; Morley et al. 2013). Research does not typically measure both nutritional status *and* frailty, nor consider both conditions when developing and targeting interventions or in determining the outcomes of interventions. A better understanding of the conceptual overlap of malnutrition and frailty could also help practitioners consider these conditions together with respect to diagnosis and treatment. Légaré et al. (2015) recommend that the oldest old (80+ years), who are typically overlooked, be considered specifically in health policy as they are expected to grow in numbers by 151% between 2005-2030 (National Institute of Aging 2011). As malnutrition and frailty are most common in this segment of the population, a greater understanding of efficient diagnostic methods and effective treatments is needed (Artaza-Artabe et al. 2016; Vellas et al 2016).

In this narrative review, we aim to: 1) describe the constructs of malnutrition and frailty including definitions and health implications, 2) describe the individual and coinciding prevalence of malnutrition and frailty in hospitalized and community living older adults, 3) describe the similarities and differences in assessment tools for malnutrition and frailty, and 4) demonstrate the

potential for improved research on treatment strategies for both malnutrition and frailty, using the example of oral nutritional supplement (ONS) interventions in older adults. Gaps in the literature will be highlighted to provide direction for further work. A literature search was conducted to identify key texts, reports, and journal articles relevant to malnutrition and/or frailty, their associated assessment tools, and ONS interventions. Generic search terms (e.g. malnutrition, frailty, function, ONS, indicators, screening, assessment etc.) in various databases (i.e. MEDLINE, PubMed, Web of Science, the Cochrane Library) were used to identify key literature. Further review of references of identified articles, and indexes of relevant journals were also conducted to help narrow the search and identify any relevant missing documents.

Frailty and Malnutrition

What is frailty?

Frailty is of considerable interest in research and in practice, but agreement on factors necessary for defining frailty is elusive (Conroy 2009; Fried et al. 2004; Fried et al. 2001; Rockwood & Mitnitski 2007). The two main ways to conceptualize frailty are the phenotype model and the cumulative deficit model (Clegg et al. 2013; Fried et al. 2001; Morley et al. 2013; Rockwood & Mitnitski 2007). Despite the conceptual differences between the models, in 2012, experts reached consensus for defining frailty (Figure 1) (Morley et al. 2013). Individuals at risk of developing frailty are typically referred to as “pre-frail,” defined by the presence of one or two of the five Fried criteria (Fried et al. 2001; Fernández-Garridoa 2014). This threshold approach may be problematic as individual criteria may be expressed at varying prevalence. Confirmation of this pre-frail state and its responsiveness to treatment is needed.

Prevalence of frailty

Many recognize frailty, yet it is difficult to quantify and diagnose, contributing to variable prevalence rates; the estimated range in community dwelling older adults (>65 years) is from 4-59% (Clegg et al. 2013). Other research suggests that prevalence may be higher among women than men (Collard et al. 2012; Song et al. 2010). Estimates also suggest that at least one million (Hoover et al. 2013) and up to one quarter of Canadians over 65 are frail (Muscedere et al. 2016). Pre-frailty is anticipated to be higher at 35-50% in those over age 60, and especially women, with weakness being the most common criteria reported (Fernández-Garridoa 2014).

The variation in prevalence may be due to inconsistencies in measuring frailty and the population being measured. Using the cumulative deficit model, Song et al. (2010) found that 22.7% of a sample of community dwelling older adults (age 65-102) were frail with higher rates among women (25.3%). Using the phenotype model, a similar prevalence of 24% was only found in an extreme old age group of 90-94 year olds; those over 95 years had a prevalence of 39.5% (Lee et al. 2016). Based on this comparison, it is worth contrasting the two methods of diagnosis in generalizable samples to determine the potential for over-estimation with different criteria.

Differences in prevalence are also noted by medical condition and location within the healthcare sector where diagnosis is made. In hospital patients >75 years of age on geriatric wards, almost all patients were considered frail, while on all other wards (e.g. medicine, surgery) prevalence was lower (50-85%) for the same age category (Andela et al. 2010). With the presence of a chronic disease, rates of frailty also increase significantly. For example, over 50% of older cancer patients are considered pre-frail or frail (Handforth et al. 2015). Although frailty is not unique to older adults, frailty rates increase with age (Fried et al. 2001; Song et al. 2010; Collard et al. 2012). Statistics Canada predicts that by 2036, nearly 1 in 4 Canadians will be over age 65,

thus leading to increases in frailty prevalence (StatsCan 2015). With a large proportion of the population at risk, screening and assessing frailty in a reliable manner is important (Muscedere et al. 2016) to ensure that effective treatments are targeted.

Health implications of frailty

Frailty is associated with risk of functional decline, loss of independence, deterioration in health status, increased risk of hospitalization, and ultimately increases an individual's risk of death (Bollwein et al. 2013; Boyd et al. 2005; Muscedere et al. 2016; Song et al. 2010). For example, when adjusted for age and sex, the presence of frailty increased the risk of death in those aged 65-102 years by 57% (Song et al. 2010).

Prevention of frailty is of particular importance among the pre-frail population, as reversing frailty itself may be more challenging than returning a pre-frail individual to a “fit” state (Cederholm et al. 2016). Early identification and treatment of frailty and pre-frailty is important for attenuating the progression of complications or preventing the exacerbation of conditions (Fried et al. 2004; Walston et al. 2002). Interventions for preventing or minimizing the effects of frailty in older adults include physical activity, nutrition, and lifestyle changes (Chou et al. 2012; Daniels et al. 2008; Cadore et al. 2013; de Vries et al. 2012; Artaza-Artabe et al. 2016). The pre-frail population may benefit from treatment, yet are often excluded from interventions comparing frail to non-frail participants (Fernández-Garridoa 2014).

What is malnutrition?

There is no universally accepted definition or method/criteria to diagnose malnutrition. In attempts to standardize terminology, consensus statements were released jointly by the Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) (White et al. 2012) as well as a recent statement by the European Society of

Clinical Nutrition and Metabolism (ESPEN) (Cederholm et al. 2016). Several definitions of malnutrition and their common concepts are outlined in Figure 2.

In 2016, ESPEN published a consensus statement regarding definitions and terminology, which subdivides malnutrition (undernutrition) into disease-related malnutrition with/without inflammation, and malnutrition/undernutrition without disease (Cederholm et al. 2016). Sarcopenia and frailty were also considered in this terminology (Cederholm et al. 2016). Sarcopenia is the gradual and general loss of skeletal muscle mass and performance, accompanied by risk of adverse outcomes (Cruz-Jentoft et al. 2010; Fielding et al. 2011; Morley et al. 2010), which can lead to frailty (Cederholm et al. 2016). An additional concern is with older adults who are obese, but also meet criteria for sarcopenia, a condition defined as sarcopenic obesity (Baumgartner 2000). In the ESPEN statement, frailty is discussed as a state of susceptibility with limited physiological reserve capacity (Cederholm et al. 2016). Although frailty is distinguished from malnutrition and sarcopenia, the overlap in these conditions is apparent as they present with similar phenotypes of weight loss/shrinking/loss of muscle mass, however may respond differently to treatment, due to their different etiology (Jeejeebhoy, 2012).

As with pre-frailty, (mal)nutrition risk, which is rarely defined, is a commonly used term (Bales, 2001). Nutrition risk is listed as a step in the nutrition care process, followed by diagnosis (ESPEN terminology), which suggests that the malnourished are a subset of those nutritionally at risk. Others have suggested it is the presence of risk factors known to lead to impaired nutritional status if left unchecked (Council on Practice, 1994; Keller 2007; Rijk et al, 2016). Similar to frailty and pre-frailty, is the view that nutrition risk is not as detrimental as malnutrition and earlier identification results in easier or more successful treatment (Brotherton et al. 2011). A variety of valid and reliable screening tools are available, often specific to a healthcare setting or population.

Overall, this lack of agreement regarding the definitions of malnutrition and nutrition risk leads to challenges with developing and using screening/assessment tools and the identification of when treatment should be instituted, as discussed in subsequent sections. It is important to note that decreased body size (or wasting) and/or impaired function are consistent with the phenotype definition of frailty (Fried 2001), emphasizing the significance of considering the intersection in the concepts of malnutrition and frailty.

Prevalence of malnutrition and nutrition risk

As nutrition risk is conceptualized to precede malnutrition (Keller 2007) it should be more common. However, prevalence of risk is elusive not only due to the different tools and populations assessed, but also as tools designed for screening are sometimes referred to as assessment tools (Bales, 2001). In a large Canadian population survey from 2008/2009, more than 4 million (~34%) older adults (over 65) living in the community were at risk of malnutrition (Ramage-Morin and Garriguet 2013). However, a systematic review of nutrition screening in community dwelling older adults found the prevalence of risk ranged from 0%-83% (Hamirudin et al. 2016), while in long-term care, about half of residents were at risk of malnutrition (Bell et al. 2013).

Malnutrition diagnosis in the community is believed to be relatively uncommon, although focus has been placed predominately on the older adult population or specific disease states (e.g. cancer). A recent review based on a single diagnostic measure, the Mini Nutritional Assessment (MNA®), for older adults suggests that prevalence in the community is less than 5%, while hospital, rehabilitation and long term care prevalence ranges between 20-30% (Cereda 2016). Malnutrition has been more commonly researched at admission to hospital with prevalence

ranging from 20-50% (Allard et al. 2016a; Agarwal et al. 2013; Barker et al. 2011; Russell et al. 2014).

Health implications of malnutrition

Being malnourished while in hospital has been shown to independently increase mortality, length of hospital stay (LOS), rates of infection, impair wound healing and increase risk of readmission, all of which affect patient flow and ultimately, healthcare costs (Allard et al. 2016a; Agarwal et al. 2013; Barker et al. 2011; Charlton 2010; Jeejeebhoy et al. 2015; Lim et al. 2012; Russell et al. 2014; Zisberg et al. 2015). The cost for treating a malnourished patient in hospital is approximately \$2,000 (CAD) more per patient than the cost to treat a well-nourished patient (Curtis et al. 2016; Norman et al. 2011; Barker et al. 2011; Correia et al. 2003). Canadian research also demonstrates that most patients remain in the nutritional state in which they were admitted or decline further while in hospital; a similar pattern is observed 30-days after discharge, leading to readmission (Allard et al., 2016a,b). In the community, nutrition risk may lead to increased number of visits to the General Practitioner (BAPEN 2003), more hospital visits, and increased risk of falling, among other complications (Visvanathan et al. 2003).

Frailty and Malnutrition Concept and Prevalence Overlap

Correspondence in the constructs of frailty and malnutrition, particularly the phenotype concept of frailty, is evident. Shrinkage or weight loss, exhaustion, weakness and slowness are all symptoms consistent with malnutrition and also represent four of the five Fried criteria (Fried 2001). Jeejeebhoy (2012) highlighted this overlap in his review of the consistencies and differences among malnutrition, sarcopenia, cachexia, and frailty. This review highlighted that the loss of body tissues contribute to a phenotype common to each of these syndromes, although etiology of this loss of tissue varies with the condition (Jeejeebhoy 2012). Jeejeebhoy noted the

differences between malnutrition (specifically protein/energy deficit and not micronutrient deficiency) and frailty. Those who have loss of body tissue due to inadequate food intake or increased requirement are malnourished and thus, tissue accretion will result with refeeding. Loss of body tissue due to other root causes such as inactivity, a myriad of hormonal, cytokine, metabolic or medical challenges could result in sarcopenia and/or frailty, both of which may not respond to improvements in protein and energy intake (Jeejeebhoy 2012). In clinical practice the reality is that for many older adults these conditions overlap in their occurrence and causes, and treatment should be multifactorial.

Boulos et al. (2016) also recognized the significant association between malnutrition and frailty, indicating that these constructs share common socio-demographic, physical and cognitive risk factors (Boulos et al. 2016). As malnutrition and frailty share risk factors, it is anticipated that many individuals will present with both frailty and malnutrition. It has been reported that malnutrition/risk of malnutrition is related to an almost four-fold increase in risk of frailty (Boulos et al. 2016) and these conditions are often concordant in those over the age of 65 years. In the community, nutritional risk in older adults increases the risk of frailty and associated consequences, including risk of hospitalization and loss of independence (Bollwein et al. 2013; Boyd et al. 2005). Bollwein et al. (2013), found that among non-frail community dwelling individuals in Germany, roughly 98% were considered well-nourished, and among the frail individuals, only around 50% had normal nutritional status. In a group of rural elderly Lebanese patients, of those identified to be frail, nearly 64% also had poor nutritional status, while 36% were well nourished. In contrast, for those identified as non-frail, roughly 90% were considered well nourished, with only 1.8% malnourished (Boulos et al. 2016).

Most studies have focused on community dwelling older adults, and there is a need to understand the overlapping prevalence within populations such as hospitalized patients, younger adults

vulnerable to frailty, and those with high risk of chronic disease. More focus should be placed on understanding and reversing the effects of pre-frailty, as this is the population that may receive the most benefit from intervention. Nutritional treatment is one avenue, and can be combined with other interventions including exercise and/or rehabilitation given the emphasis on muscle mass and strength highlighted in the frailty definition. Frailty and pre-frailty should also be examined across all populations and healthcare settings. Consistent terminology and assessment tools are required to gain a clear picture of the overlap in prevalence of malnutrition and frailty with direction for potential interventions.

Overlap in Screening/Assessment Tools

Several screening and/or assessment tools exist to identify frailty or malnutrition, but no tool currently considers both conditions.

Frailty screening/assessment tools

Although there is agreement regarding the importance of identifying and treating frailty, there is currently no consensus on what elements are necessary for its diagnosis (Conroy 2009; Fried et al. 2004; Fried et al. 2001; Rockwood and Mitnitski 2007). The two main models for conceptualizing frailty (phenotype and cumulative deficit) form the basis for many screening and assessment tools created to date (Clegg et al. 2013; Fried et al. 2001; Morley et al. 2013; Rockwood and Mitnitski 2007). Examples of tools include: FRAIL (Abellan van Kan et al. 2008), the Cardiovascular Health Study Frailty Screening Measure (Fried et al. 2001), the Clinical Frailty Scale (Rockwood et al. 2005), the Grontople Frailty Screening Tool (Subra et al. 2012), the interRAI Assessment Urgency Algorithm (Elliott 2016), or simply, walking speed (Mathias et al. 1986; Muscedere et al. 2016). Many of these tools use inconsistent terminology, yet there is overlap in characteristics such as weight loss, weakness etc. as shown in Table 1. For

the cumulative deficit model, primary and ambulatory care can use existing electronic medical record data to identify key risk factors while long term care can use the interRAI Minimum Data Set (MDS) (Muscedere et al. 2016).

Contrary to nutrition tools, there is a minimal distinction between frailty screening (identification of potential risk) and assessment (diagnosis of condition) tools. Another challenge is that many tools recommended for fast-paced clinical environments are long and/or solely subjective, making them difficult to administer in clinical settings. The feasibility of the tool within the target setting should always be considered. A recent review offers a broad understanding of frailty tools in various healthcare settings and highlights that the setting often determines the tool that is utilized (Muscedere et al. 2016). Screening for pre-frailty should be incorporated into various clinical environments.

Nutrition assessment and screening tools

Different definitions of malnutrition have led to various diagnostic frameworks. AND/A.S.P.E.N. recommend that diagnosis is made when at least two of the following six criteria are present: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation, and diminished functional status (White et al. 2012). ESPEN has also released very minimal malnutrition diagnostic criteria out of the desire to have simple, objective measures that can be used in a variety of contexts and clinical populations (Cederholm et al. 2015). ESPEN suggests that body mass index (BMI) $<18.5 \text{ kg/m}^2$, or the combination of unintentional weight loss along with a reduced BMI or a low fat free mass index can be used to diagnose malnutrition (Cederholm et al. 2015). Since this set of diagnostic criteria was released, there has been criticism (Soeters et al. 2016; Bahat 2016; Mokaddem 2016), especially with using BMI as the basis for diagnosis. This index does not

account for fat distribution; cannot distinguish between muscle, fat or other tissues that may be dynamically changing during the aging and/or disease process; cut-points vary with ethnicity; and this index lacks predictive ability at the individual level (Bray 1979; Heymsfield et al. 2016; Paris and Mourtzakis, 2016; Soeters et al. 2016). Further, these diagnostic criteria are focused on the phenotype and do not include inadequate food intake, which is the root cause of malnutrition. A recent validation study also demonstrated poor sensitivity of the ESPEN diagnostic framework (17.1%) when compared to Patient Generated-Subjective Global Assessment (PG-SGA) (Guerra et al. 2016). In the more recent ESPEN definitions and terminology consensus statement, PG-SGA, subjective global assessment (SGA) and MNA® are singled out as assessment tools that can be used to standardize the diagnosis of malnutrition. These tools provide a more comprehensive view of malnutrition including food intake, risk factors for food intake, function and body mass or composition. Short versions intended for screening for nutrition risk are available for both the PG-SGA (Abbott et al. 2016) and the MNA® (Vellas et al, 1999). Experts in Canada, Australia and Brazil recommend SGA to assess malnutrition (Keller et al. 2015; DAA 2009; Raslan et al. 2011).

In addition to these diagnostic methods, a variety of nutrition screening tools exist. These tools are designed so non-nutrition professionals, such as admission nurses, can quickly and sufficiently identify if a patient is at (mal)nutrition risk. All screening tools result in false positives and negatives, and diagnostic methods are required to confirm malnutrition. A recent review suggests that no single tool is best (van Bokhost-de van der Schueren et al. 2014). Screening tools commonly include patient recall of weight change, food intake and if there are objective measures, height and weight to determine BMI (Elia 2003; Ferguson et al. 1999; Laporte et al. 2015; Stratton et al. 2004). Height and weight can be difficult to obtain in a busy clinical environment (Laporte et al. 2015). In Canada, the Canadian Nutrition Screening Tool

(CNST) is recommended for use in hospital. CNST contains only two questions, and has been demonstrated as valid and reliable for this setting, when compared to the SGA (Laporte et al. 2015). Other screening tools specific to older adults that provide a more up-stream view of nutrition risk are available; these are designed for and potentially more appropriate for a community-based or primary care population (Keller 2007; Keller et al. 2001; Akhtar et al. 2015).

Overlap in malnutrition and frailty tools

There are many areas of overlap between malnutrition and frailty screening/assessment tools. An example of this correspondence was demonstrated by Bollwein et al. (2013), which highlights the close relationship between the MNA® and frailty using Fried's (2001) criteria. A significant association between 12 of the 18 MNA® items and frailty status appeared to exist, some of which included: anorexia, weight loss, impaired mobility, and psychological problems (Bollwein et al. 2013). As shown in Table 1, there is considerable overlap in frailty and malnutrition criteria within commonly used screening/assessment tools. However, a recent article suggests that there are important differences between frailty and malnutrition tools. Jeejeebhoy et al. (2015) found that HGS added additional predictive value to a diagnosis of malnutrition using SGA in acute care to predict LOS and mortality, suggesting that HGS is potentially measuring something in addition to malnutrition as assessed by SGA (Jeejeebhoy et al. 2015). These results suggest that use of malnutrition and frailty tools in combination may be valuable in a hospital setting, and the apparent overlap further suggests that a minimum set of indicators should be further defined and researched to determine their utility. This minimum set of measures would need to be: a) responsive to change with intervention, b) predict adverse outcomes in the medical setting, c) and be feasible in the fast-paced clinical environment.

Which objective indicator of frailty could be added to nutrition tools?

Long, subjective frailty measures are challenging to complete in a clinical setting (Cesari et al. 2016). Two objective frailty measures are worthy of consideration in a minimum set of indicators that could be added to current nutrition screening tools to identify malnutrition and frailty in the clinical setting. Decreased gait speed or 'slowness' is one of the components of the phenotype concept of frailty, as defined by Fried (2001), making it a potentially useful single indicator of frailty. Slow gait speed has been reported to successfully characterize older adults who have experienced adverse outcomes (Clegg et al. 2013; Jeejeebhoy 2012; Morley et al. 2013). Specifically, recent literature has provided a cut-point of >6 seconds as an indicator of frailty during the timed 5-metre walk test (The Society of Thoracic Surgeons 2016; Wilson et al. 2013). However, the feasibility of conducting this assessment may be of concern for particular settings and patient populations with mobility issues, and needs to be explored further.

Recent studies have also suggested that decreased muscle strength (specifically HGS) is an appropriate indicator of frailty (Bohannon 2008; Jeejeebhoy 2012; Morley et al. 2013; Roberts et al. 2011). An important component of Fried's phenotype model of frailty is weakness, or decreased strength, highlighting the importance of considering HGS as a useful indicator of frailty (Fried, 2001). Sydal et al. (2003) went as far as suggesting that HGS could be a single indicator of frailty.

One of the challenges with HGS is that it is not specific to frailty. A systematic review highlighting decreased muscle function in relation to nutritional deprivation, found that HGS is often being used as a proxy for nutritional status (Norman et al. 2011). Flood et al. (2014) investigated whether or not HGS could be used as a single marker of nutritional status among hospital patients. This study noted that PG-SGA scores and categories were significantly

correlated with HGS scores. However, as discussed previously, other studies suggest that HGS measures more than nutrition (Jeejeebhoy et al. 2015). HGS reference values for healthy Canadians were published in 2016 (Wong 2016), although a variety of cut-points have been used to predict various outcomes such as mortality (Rijk et al. 2016). Despite the evidence for using HGS as a clinical measure, it is important to consider some of its limitations. HGS is not strictly objective, as it is heavily dependent on mood, motivation and encouragement from the clinician administering the test (White et al. 2013). As with gait speed, some patients will not be able to complete HGS (e.g. musculoskeletal diseases, neurological disorders, stroke).

Improving Research on Treatment by Considering Both Malnutrition and Frailty

It is not surprising that after discussing the overlap in definitions and ways of assessing frailty and malnutrition, there would also be an overlap in research on treatment efforts for these often comorbid conditions. Yet, confusion surrounding definitions and assessment methods has led to challenges in researching appropriate treatments. In intervention studies focused on malnutrition and/or frailty there is little consistency in the way that these conditions were determined or outcome measures used. Studies using ONS as a treatment strategy have been selected to highlight these gaps in the literature because of the sizable body of research conducted using these products in a variety of contexts. Three reviews have been published on ONS and nutrition and/or frailty, which highlight its potential benefits on weight status and mortality (Milne et al., 2009), frailty indicators (Manal et al., 2016, Artaza-Artabe et al., 2016) and nutritional status (Manal et al., 2016). While there are some consistencies identified in these reviews, mixed findings are still common regarding many outcomes relating to frailty and malnutrition (Milne et al., 2009; Manal et al. 2016). For this review, two issues will be specifically highlighted: differences in participant inclusion and choice of outcome measures.

Participants included in efficacy studies

Many ONS interventions target either ‘malnourished’ and/or ‘frail’ participants but do not explicitly select patients who have both conditions for inclusion. The way subjects are defined as malnourished or frail differs greatly among studies. Some studies use the phenotype model of frailty (Abizanda, et al. 2015; Tieland et al. 2012), nutritional assessment or screening tools (Abizanda, et al. 2015; Kim and Lee, 2013; Smoliner et al. 2008; Stange et al. 2013), or specific characteristics (e.g. BMI, reported weight loss) (Neelemaat et al. 2010; Edington et al. 2004; Wouters-Wesseling et al. 2003; Payette et al. 2002) for patient recruitment. Other studies simply report using frail populations without clearly defining the criteria for classification (Bonney et al. 2003; Gray-Donald et al. 1995; Paw et al. 2002; Payette et al. 2002). Efficacy research on ONS and other treatments is likely impacted by not targeting treatment to persons who could benefit most. Due to the inconsistencies in diagnosis of malnutrition and frailty, it is anticipated that many studies to date included patients who did not have malnutrition or frailty, thus potentially diluting the benefit of treatment. Exclusion of those with cachexia, and potentially sarcopenia, is also needed as these individuals may respond differentially to refeeding (Jeejeebhoy 2012). Consistent diagnostic criteria, or at least a minimum data set of key indicators is needed to target patients who can benefit from ONS treatment and measure outcome with respect to these conditions. Intervention studies targeting pre-frail and nutrition risk could also demonstrate the success of targeting interventions earlier in the trajectory of these conditions.

Choice of outcome measures

In ONS intervention research, a variety of frailty and malnutrition indicators are included as outcome measures. Although standardized assessment or screening tools may be used for eligibility criteria, they are rarely used as outcome measures (Kim & Lee, 2013; Tieland et al., 2012). Further, researchers rarely explicitly state ‘malnutrition’ or ‘frailty’ as an outcome, but

rather use a combination of measures relating to both concepts (e.g. function, falls) without connecting them to the specific condition (Neelemaat et al., 2010; Edington et al., 2004). One exception was a study on ONS and physical exercise as the intervention (Abizanda et al. 2015). Outcomes covered both malnutrition and frailty concepts with standardized diagnostic tools (e.g. MNA-SF, Short Physical Performance Battery, Short-Form-Late-Life Function & Disability Instrument, and HGS). Lack of use of frailty or malnutrition assessment tools as outcomes may be due to concern about responsiveness to treatment of these measures. Improvements are not only needed in the conceptualization of frailty and malnutrition but also in measurement that is sensitive to intervention.

Complementary interventions

Considering the overlap in prevalence in malnutrition and frailty, it has been recommended that combining ONS and physical activity as interventions may be the way forward for treating both conditions (Goisser et al. 2016; Morley et al. 2010; Volkert et al. 2011). A range of outcome measures relating to physical function in these complementary intervention studies include performance battery tests (Abizanda et al. 2015; Kim and Lee 2013), HGS or gait velocity tests (Abizanda et al. 2015; Bonnefoy et al. 2003; Edington et al. 2004; Fiatarone et al. 1994; Kim and Lee, 2013; Payette et al. 2002; Stange et al. 2013), and muscle mass and strength (Bonnefoy et al. 2003; Fiatarone et al. 1994; Neelemaat et al. 2010; Tieland et al. 2012; Wouters-Wesseling et al. 2003). While many of these outcomes relate to both concepts of frailty and malnutrition, research questions seem to focus on only the frailty concept, leading to possible gaps or missed opportunities in their understanding of the effect of these complementary interventions on malnutrition.

Conclusion

Prevalence of malnutrition and frailty across the continuum of care warrants further research understanding their potential overlap in prevalence, diagnosis and treatment. Focus on building consensus for definitions and diagnosis, and improving screening and assessment methods, potentially by identifying a minimum set of indicators or tools that capture both conditions is required. Increased attention should also be placed on intervention studies that look at the impact on the nutrition and frailty status of the participants. Complex interventions that address mechanisms for frailty and malnutrition are needed. It is believed that considering the intersection between malnutrition and frailty may lead to improved and complementary interventions, such as the use of physical activity training and ONS. A summary of key literature gaps and future directions is presented in Figure 3. Progress is being made in the field, and considering frailty and malnutrition together may be the way forward to provide appropriate care to at risk older adults. Future research needs to further demonstrate the overlap between malnutrition and frailty (and pre-frailty) in diverse populations and carefully plan and target interventions, while measuring frailty and malnutrition with valid, comprehensive tools.

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Table 1: Key frailty and malnutrition assessment tools and their overlapping characteristics.

Identifying Frailty	Identifying Malnutrition	Overlapping Characteristics
<i>FRAIL</i> : Fatigue, Resistance, Aerobic, Illness, Loss of body weight (Abellan et al. 2008).	<i>ESPEN</i> : BMI, weight loss , Fat free mass index (FFMI)) (Cederholm et al. 2015).	<ul style="list-style-type: none"> • Weight loss/ decreased body mass • Functional capacity • Weakness (grip strength) • Cognitive status
<i>Cardiovascular Health Study Frailty Screening Measure</i> : Weight loss , exhaustion, low activity, gait speed, grip strength (Fried et al. 2001).	<i>AND/A.S.P.E.N</i> : Insufficient energy intake, weight loss , loss of muscle mass, loss of subcutaneous fat/fluid accumulation, diminished functional status (need 2 of 6) (White et al. 2012).	
<i>Clinical Frailty Scale</i> : Activity, fatigue, illness, functional status , cognitive status (Rockwood et al. 2005).	<i>CMTF</i> : Subjective Global Assessment (SGA): dietary intake, weight , symptoms, functional capacity and metabolic requirements; physical exam for fat, muscle, edema (Detsky et al. 1987).	
<i>Gérontopôle Frailty Screening Tool</i> : Functional status , living situation, gait speed, fatigue, cognitive status (Subra et al. 2012).	<i>Mini Nutritional Assessment (MNA®)</i> : anorexia, weight loss , impaired mobility, disease, cognitive status , BMI , living status, drug intake, meal intake, protein intake, fluid intake, fruit intake, eating dependency, perceived nutritional health status, perceived health status, arm circumference (Vellas et al. 1999).	

AND: Academy of Nutrition and Dietetics; A.S.P.E.N: American Society of Parenteral and Enteral Nutrition; CMTF: Canadian Malnutrition Task Force; ESPEN: European Society of Parenteral and Enteral Nutrition; BMI: Body Mass Index; Similar characteristics are bolded.

Figure 1: Definitions of frailty and a recent consensus statement. (1) Fried et al. 2001 p.148; (2) Rockwood and Mitnitski 2007; (3) Morley et al. 2013 p.393

Figure 2: A sample of definitions of malnutrition and their overlapping characteristics. (1) Meier and Stratton 2008; (2) Soeters et al. 2008 p708; (3) Sobotka, 2012, p21.

Figure 3: Summary of gaps and future directions for addressing frailty and malnutrition.

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Gaps in the Literature

- Work contrasting diagnosis methods is rare
- Screening tools and interventions specific to the pre-frail are needed
- Lack of understanding of overlapping prevalence in certain populations
- Frail/malnourished samples are common in ONS research, but interventions do not aim to address both issues explicitly
- Validated nutrition and frailty screening tools are often used to identify patients, but are less commonly used as outcome measures.

Future Directions

- Compare diagnostic methods of frailty and malnutrition; associations between current frailty and nutrition indicators
- Develop and test screening tools specific to pre-frailty and nutrition risk
- Identify a minimum set of indicators for nutrition risk/malnutrition and pre/frailty
- Research on the overlapping prevalence rates in younger adults, hospitalized patients, and those with chronic diseases
- Consistently use screening or assessment tools to target treatment to the right patient populations
- Develop interventions that address both malnutrition and frailty for hospital and community sectors, for example ONS and physical activity.

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