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Title: Multi-component frailty assessment tools for older people with psychiatric disorders: A systematic review

Short running title: Frailty assessment and psychiatric disorder

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Word Count: Abstract: 227 words. Main Text: 3800 words. Number of figures in main text: 1. Number of Tables in main text: 0

Funding Source: None.

Impact statement: We certify that this work is novel. To the authors best knowledge this is the first systematic review to consider frailty assessment in the context of psychiatric disorder in older adults. This review highlights that no existing multi-component frailty assessment has been developed for or validated in older adult populations with psychiatric disorders. It also highlights that significant construct overlap and potential confounding exists between the indicators of frailty as conceptualised in existing frailty assessment tools and DSM-5 diagnostic criteria for common psychiatric disorders, including Major Depressive Episode and Generalised Anxiety Disorder. It determines that further research is necessary to establish a reliable and valid tool to assess frailty in this population.

ABSTRACT:

Objective: To review evidence evaluating the use of multi-component frailty assessment tools in assessing frailty in older adults with psychiatric disorders. **Methods:** A systematic literature review was conducted to identify all multi-component frailty assessment tools (i.e. a tool that assesses ≥2 indicators of frailty). The items of each frailty assessment tool were compared to DSM-5 diagnostic criteria for psychiatric disorders to assess construct overlap. Studies conducted in community, inpatient and outpatient clinical settings were considered for inclusion. **Participants:** Adults aged ≥60 years old. **Results:** 5,639 studies in total were identified following the removal of duplicates; 97 of which were included for review. Of the 48 multi-component frailty assessment tools identified, no tool had been developed for, or validated in, older adult populations with psychiatric disorder. 24/48 frailty assessment tools contained a psychological assessment domain, with 18/48 tools using presence of depressed mood and/or anxiety as a frailty indicator. Common areas of construct overlap in frailty assessment tools and DSM-5 diagnostic criteria included weight loss (29/48) and fatigue (21/48). **Conclusions:** Significant construct overlap exists between the indicators of frailty as conceptualised in existing frailty assessment tools and DSM-5 diagnostic criteria for common psychiatric disorders, including Major Depressive Episode and Generalised Anxiety Disorder, which has the potential to confound frailty assessment results. Further research is necessary to establish a reliable and valid tool to assess frailty in this population.

Keywords: frailty assessment, psychiatric disorder.

INTRODUCTION:

Frailty is a prevalent issue in later life, with evidenced links to adverse outcomes including functional decline, falls, institutionalisation and mortality.[1-5] Frailty is a multifactorial clinical state or syndrome; it represents decline in multiple physiological systems resulting in poor maintenance of homeostasis and decreased reserves and resilience to stressors[6,7]. There are number of models to conceptualise frailty, the two most widely accepted being the Canadian Study of Health and Ageing Cumulative Deficit Model[8] and the Cardiovascular Health Study Phenotype Model[9]. The Cumulative Deficit Model assesses frailty through an index of deficits associated with aging including disabilities and diseases; a higher index score indicates a higher level of frailty, with no cut point to distinguish between frail and robust[8]. The Phenotype Model establishes a frailty phenotype consisting of the following frailty indicators; involuntary weight loss, self-reported exhaustion, self-reported sedentary behaviour, slow gait speed and weak grip strength[9]. The presence of zero frailty indicators suggests an individual is robust, 1-2 frailty indicators is suggestive of pre-frail (the intermediate stage between robust and frail) and ≥3 indicators confirms frailty[10].

Frailty and psychiatric disorders, such as Major Depressive Disorder and Generalised Anxiety Disorder, are thought to be distinct but highly related clinical entities.[11,12] Evidence suggests that frailty and psychiatric disorders are highly co-morbid[12,13]. A recent systematic review of evidence exploring comorbidity of frailty and depression found that 4-16% of frail adults aged ≥60 years had major depression, with this rising to 35% in frail older adults aged ≥75 years and in male populations.[13] The rate of co-morbid frailty in depressed older adult populations reached 46-57%.[13]

In addition to comorbidity there is good evidence to support a bidirectional association between depression/anxiety and frailty in later life.[12,14-16] Evidence suggests that older adults with a psychiatric disorder are at an increased risk of becoming frail and often experience the highest levels of frailty.[17,18] For example, a cross sectional observational study by Collard and colleagues[19] found that the overall prevalence of physical frailty in a depressed older adult population was 27.0%, three times higher than the prevalence in the study's non-depressed sample (9.1%). Conversely, evidence suggests that frailty is associated with an increased chance of developing clinically meaningful depression and anxiety symptoms.[12,14-16] Further to this, physical frailty has been shown to adversely affect the course of late-life depression, with increased odds of non-remission associated with increased physical frailty[20]. Brown and colleagues[21] have recently proposed a depressed frail phenotype as a high-risk profile for late life frailty. Given that psychiatric disorders are also pervasive late life issues with increased risks for many of the same adverse outcomes as frailty including dementia and morality,[22,23] frailty in the context of psychiatric disorder warrants specialist clinical detection and intervention.

Frailty is widely considered to be a dynamic process with potential for restorative and preventative clinical interventions.[6,24] The need to develop new treatment modalities to address frailty in the context of psychiatric disorders has been recently highlighted[13,25]. The accurate assessment of frailty is key in the development and provision of such interventions. A recent systematic review of the psychometric properties of existing multi-component frailty assessment tools found the extent and quality of psychometric testing of these tools to be limited[26]. Only two of the thirty-eight tools included for review evidenced reliability and validity data within statistically significant parameters and were of fair-to-excellent quality according to the COnsensus-based Standards for the selection of health

Measurement INstruments (COSMIN) checklist[27]; the Frailty Index-Comprehensive Geriatric Assessment (FI-CGA)[28] and the Tilburg Frailty Indicator (TFI)[29]. To date, there is no frailty assessment tool that is widely accepted as a gold standard.[26]

Given the high co-morbidity of frailty and psychiatric disorders in late life, associations between the two, the increased risk for adverse outcomes and potential for restorative and preventative interventions, the accurate assessment of frailty in older adult psychiatric populations should be a priority. Of the 10 systematic reviews concerning frailty assessment published to date,[7,26,30-37] none have considered frailty assessment in the context of mental illness. Therefore, the aims of this review were to: (1) Establish if any existing multi-component frailty assessment tools have been developed for or validated in older adult populations with a diagnosis of psychiatric disorder, and (2) establish any construct overlap between the assessment domains of existing multicomponent frailty assessment tools and the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) diagnostic criteria for psychiatric disorders in older adults, exploring the potential impact of this on valid and reliable frailty assessment in this population.

METHODS:

Search strategy

The following databases were searched on 15th February 2017: Medline (1946–present), PsychINFO (1806–present), Embase (1947– present) and the Cochrane Central Register of Controlled Trials. The search strategy used was: frailty AND (older OR elder* OR geriatr*) AND (measure* OR assess*). The reference lists of 10 systematic reviews[7,26,30-37] concerning

frailty assessment identified through the above search strategy were also searched manually.

Selection criteria

Studies were selected for inclusion for review if they met the following criteria:

- All study participants were aged ≥60 years old.
- The study described a multi-component tool, which was defined as a tool that assesses ≥2 indicators of frailty, such as a frailty index.
- The study described a tool that was specifically developed to assess frailty.
- The main purpose of the study was the development and/or evaluation of the reliability and validity of a multi-component tool to assess frailty.
- The study applied the original version of a multi-component tool to assess frailty.
- The full content of the multi-component tool was available (including all indicators of frailty, units of measurement and scoring systems).
- The study reported quantitative data.
- The full peer-reviewed study text was available.
- Studies were available in English or were translated wherever possible.

See supplementary file 1 for an expanded explanation of study selection criteria. The title and abstracts were screened, and potentially eligible studies were selected for inclusion by JLS. Studies were considered for inclusion regardless of their methodological quality.

Data extraction and analysis

Data were extracted regarding: i) study characteristics; ii) the population each tool was developed for and validated in; iii) the content of each frailty assessment tool. Data for items i) and ii) were extracted by two independent raters, while data for items iii) were extracted by JLS.

Following data extraction, the assessment items of each frailty assessment tool were compared to the DSM–5 diagnostic criteria for the seven common psychiatric disorders in older adults; Major Depressive Disorder (MDD), Bipolar Affective Disorder (BAD), Schizophrenia, Generalised Anxiety Disorder (GAD), Social Anxiety Disorder (SAD), Specific phobia (SP) and Panic Disorder (PD).[22,38] An assessment of definite construct overlap between the items of the frailty assessment tools and the DSM-5 diagnostic criteria was then completed. Definite construct overlap was defined as instances where the frailty assessment tool item and DSM-5 diagnostic criteria were conceptually the same (for example, 'troubles with sleeping' and 'Insomnia or hypersomnia'). The exact units and process of measurement did not need to be the same, but they must have assessed the same theoretical construct. The potential for an individual to be assessed as frail or pre-frail based on mental health symptoms alone was also reviewed. Assessment of definite construct overlap was completed by two independent blind raters (JLS, RG, MC, EW, AB, MLS, MS, AR). Any disagreements were resolved through discussion.

Assessment of methodological quality of studies included for review

The COSMIN checklist is a standardized tool for evaluating the methodological quality of studies examining measurement properties of health-related instruments.[27,39,40] It assesses measurement properties across the following domains, awarding ratings of 'excellent',

'good', 'fair', or 'poor' quality; internal consistency, reliability, measurement error, content validity, structural validity, hypotheses testing, cross-cultural validity, criterion validity and responsiveness.[27,39,40] A rating of 'excellent' indicates that the evidence provided for that measurement property is adequate. A rating of 'good' indicates that the evidence provided can be assumed to be adequate. A rating of 'fair' indicates that the evidence is questionable, and 'poor' indicates that the evidence provided is inadequate. The COSMIN checklist was applied to each study and data were extracted by two independent, blind raters (JLS, RLG, MCC, AMB, EVW, MLS, GL). Any disagreements were resolved through discussion.

Reporting

This review followed the PRISMA standards[41] for reporting of systematic reviews.

RESULTS:

Literature search and inclusion for review:

The literature search identified 5,639 records in total following the removal of duplicates; from which 95 studies were included for review following assessment against selection criteria (see Fig. 1).[3,9,28,29,42-132]

Study characteristics

A full outline of study characteristics is provided in supplementary table 1. Forty-eight multi-component frailty assessment tools were examined across 95 studies.[3,9,28,29,42-132] The most frequently observed study design was prospective cohort (32/95 studies).[3,42-46,9,48-51,70-72,74,75,80,82,86,89,91,94,97,99,103,107,109,116,118,131,132] Of the 62 studies with follow-up data available,

follow-up periods ranged from 1 month[53,64,73] to 348 months.[119] The total number of participants per study ranged from 14[121] to 931,541.[67] The overall total percentage of female participants, calculated by pooling the percentage female population from the 84/95 studies with data available, was 65.9%. The overall mean age of participants, calculated by pooling the mean ages from the 73/95 studies with data available, was 74.9 years. Participants were most commonly sampled from The Netherlands (29/95 studies).[29,60-62,68,76,77,84,86-92,95,96,98,101,102,107,111,113-115,125-128] The cohorts were predominantly community based, general older adult populations (51/95).[3,9,29,42,46,48,50,56-58,60-62,67,69,70,74,76,77,79,81,82,84-88,90,95-99,103,105,106,108,109,111,118,119,123-132] Only one of the 95 cohorts consisted of 'psychogeriatric patients' (80.8% diagnosed with dementia, 5% depression, 11% unspecified, 3% no mental disorder).[107] Data regarding participant mental health diagnoses were not available in the remaining 94 studies.

Methodological quality of studies included for review

The COSMIN checklist results are detailed in supplementary table 2. In total, 7/95 studies had one aspect of methodological quality rated as excellent.[48,56,59,84,99,111,132] All ratings of excellent were in relation to content validity. A further 7/95 studies had at least one aspect of methodological quality rated as good; hypothesis testing being the measurement property with the highest number of good ratings (4/7).[67,73,88,101,103,122,123] 70/95 studies had at least one aspect of methodological quality rated as fair.[3,9,28,29,42,44,45,47,48,51-60,62,64,66,69-72,74-77,81-87,89-99,101-103,106,107,109-118,120,124,125,127-129] Hypothesis testing had the greatest number of fair ratings (65/70). 42/95 studies had at least one aspect of methodological quality rated as poor. [43,46,50,52,53,57,58,60,61,63,65,68-70,76,78-80,82,84,86-88,91,98-100,104,105,108,111,112,115,118,119,121,126,129,130]

Criterion validity had the greatest number of poor ratings (30/42). Five studies cited low response rates as a study limitation.[29,76,125,126,128]

Construct overlap between multi-component frailty assessment tool items and psychiatric disorder

Figure 2 summarizes key findings in relation to the review aims. Table 1 provides an overview of construct overlap observed in relation to frailty assessment domains and supplementary table 3 provides an overview of all construct overlap observed. Of the tools reviewed, only 7/48 had no definite construct overlap between frailty assessment tool items and DSM-5 diagnostic criteria for MDD, BAD, Schizophrenia, GAD, SAD, SP or PD; Brief Clinical Instrument to Classify Frailty,[42-44] Clinical Frailty Scale (CFS),[48-51] Frailty predicts death One yeaR after CArdiac Surgery Test (FORECAST),[54,55,73] Frailty Index Based on Common Laboratory Tests (FI-LAB),[75] Korean Longitudinal Study of Health and Aging (KLoSHA) Frailty Index,[99] Palumbo Frailty Index,[102] and the 9-Item Frailty Measure.[132] In 29/48 tools, definite construct overlap was established between the nutritive domains of the frailty assessment tool (weight loss/reduced appetite) and DSM-5 diagnostic criteria for MDD and BAD[38] concerning weight loss and appetite changes.[3,9,28,29,43,44,47,52,59,63-67,70-72,76-79,81,82,84-98,100,101,103-106,108,109,111-131] Definite construct overlap was observed between frailty items concerning fatigue and the DSM-5 diagnostic criteria for MDD, BAD and GAD[38] concerning fatigue in 21/48 tools.[3,9,28,43,47,52-55,68,69,76-79,81,83,85,87,93,97,103-105,108-118,121-131] In 9/48 tools, definite construct overlap was established between cognitive items relating to concentration and processing skills and the DSM-5 diagnostic criteria for MDD, BAD and GAD,[38] concerning diminished ability to think or concentrate.[28,44,45,67,70-72,76,77,80,87,100,107,119-130] Definite construct overlap was observed between the frailty item ‘slowness’ and

psychomotor retardation; a DSM-5 diagnostic criteria for MDD, BAD[38] in 8/48 tools.[3,9,43,53-55,82,103-105,107-109,111-115]Definite construct overlap was observed between frailty indicators concerning reduced activity levels and the DSM-5 diagnostic criteria for schizophrenia,[38] concerning negative symptoms in 8/48 tools.[39,50-52,64,65,77,82,105-108,111,114-118] Definite construct overlap was also identified between sleep disturbance domains and the DSM-5 diagnostic criteria for MDD, BAD and GAD,[38] concerning sleep disturbance in 4/48 tools.[47,67,74,76,77] A detailed summary of all construct overlap between all 48 frailty assessment tool items and DSM-5 diagnostic criteria for MDD, BAD, schizophrenia, GAD, SAD, SP & PD is provided in Supplementary tables 4-10, respectively.

Of the 31 tools for which there is a clear cut-off point to distinguish between individuals who are frail or robust, an individual could be classified as frail solely on the basis of their mental health symptoms in 11/31 tools,[3,9,28,43,44,70-72,78,79,100,103-105,107-109,116-120] and as pre-frail on a further 4/31[45,58,110-115] (15/31total).

21/48 multi-component frailty assessment tools identified in this review contain a psychological assessment domain (domains/items concerning 'psychological indicators of frailty' defined by the author).[28,43-47,52,56,57,59-66,68-72,76-78,81,84-92,94,100,101,109,110]

18/48 tools include the presence of depressed mood and/or anxiety as specific measurement items indicating frailty.[28,43-47,52,56,57,59-66,68-72,76,77,81,84-92,94,100,101] 12/48 tools include items from existing psychiatric assessment tools; five of which use items from the Centre for Epidemiological Studies-Depression Scale (CES-D).[3,9,43,58,68,79,104,105,108] Other tools included the Hospital Anxiety and Depression Scale (HADS)[59] and the Beck Depression Inventory II.[94] However, in the majority of these cases, items included from existing mental

health tools were used to assess fatigue (7/12),[3,9,43,58,68,79,81,93,104,105,108] rather than the presence of mental illness (5/12).[28,44,45,63,70-72,94,100]

DISCUSSION:

To the authors' knowledge, this is the first systematic review that has considered frailty assessment in the context of psychiatric disorder in older people.

In summary, no tool identified in this review has been developed for or validated in older adult populations with psychiatric disorder. One tool that has been tested in a psychogeriatric population; the Prognostic Risk Score,[107]was developed for and validated in a cohort of whom 80.8% had a dementia diagnosis. This identifies a gap in the current research.

Only seven tools were identified as having no definite construct overlap with DSM-5 diagnostic criteria: Brief Clinical Instrument to Classify Frailty[42-44] and CFS,[48-51] which are screening instruments designed for use in general hospitals; FORECAST[54,55,73], which was designed to assess frailty following cardiac surgery; FI-LAB[75], which is based on common laboratory tests for use in long-term residential care facilities; KLoSHA Frailty Index[99], developed for use with community-dwelling elderly Korean population; Palumbo Frailty Index[102], designed to assess frailty in multiple myeloma patients; and 9-Item Frailty Measure[132], designed for use in routine geriatric practice. However, as noted, none of these tools have been developed for use in a mental health setting, or with consideration for the complex interactions between frailty and psychiatric disorder. Significant construct overlap was identified between indicators of frailty as conceptualised in existing frailty assessment tools and DSM-5 diagnostic criteria for seven common psychiatric disorders. The diagnostic criteria for MDD (and thus the depression criteria for BAD) had the highest proportion of

definite construct overlap with frailty assessment items (41/48 tools). The diagnostic criteria for GAD also had a high proportion of definite construct overlap (34/48 tools). The diagnostic criteria for SAD and SP had the lowest proportion of definite construct overlap observed (11/48 tools and 10/48 tools respectively).

21/48 frailty assessment tools contained a psychological assessment domain, with 18/48 tools including the presence of depressed mood and/or anxiety as a frailty indicator. The frailty indicators and DSM-5 diagnostic criteria that had the most construct overlap concerned weight loss (29/48 tools) and fatigue (21/48). This construct overlap was further confounded by the inclusion of questions from existing psychiatric assessment tools to assess fatigue in 7/48 tools. For the tools for which there is a clear cut-off point to distinguish between individuals who are frail or robust; an individual could be classified as frail or pre-frail solely based on their mental health symptoms in half of them (15/31 tools). This thus demonstrates significant potential for inaccurate assessment and recognition of frailty in psychiatric populations.

Specifically, significant construct overlap and confounding was observed for the frailty assessment tools with the most extensive reliability and validity testing;[26] FI-CGA[28] and TFI[29]. FI-CGA[28] items such as 'problems with mood', 'problems with motivation' and 'changes in weight' were observed to have definite construct overlap with DSM-5 diagnostic criteria for MDD. On FI-CGA[28] it is possible to be assessed as frail based on psychiatric symptoms alone; the tool contains a psychological assessment domain and utilises questions from the Geriatric Depression Scale[133] to assess mood, further increasing confounding. TFI[29] items such as 'unexplained weight loss', 'physical tiredness' and 'feeling down' were observed to have definite construct overlap with DSM-5 diagnostic criteria for MDD. The TFI also

includes a psychological assessment domain. Whilst it is not possible to be assessed as frail based purely on the definite construct overlap observed for TFI, the level of overlap is such that it is likely to confound frailty assessment in psychiatric populations. Definite construct overlap was also observed for tools based on the prominent Cumulative Deficit Model[74] and Phenotype Model[9], increasing the risks of confounding when assessing frailty with such tools in psychiatric populations.

It is of note that there were many frailty assessment items for which a direct plausible association with DSM-5 diagnostic criteria was observed, but which did not meet the criteria for definite construct overlap. For example, tools such as the FI-LAB[75]contain a measure of serum albumin as part of a nutritive domain, with low levels indicating malnutrition. Whilst this cannot be classified as definite construct overlap with the MDD diagnostic criterion 'unintentional weight loss', there is a direct and plausible association. Tools such as the Brief Frailty Index[45] and Prognostic Risk Score[107] included 'low body mass index ' as an indicator of frailty, which again whilst highly associated with 'unintentional weight loss', did not meet the criteria for definite overlap. Another example are tools such as the Palumbo Frailty Index[102] and the KLoSHA Frailty Index[99] which include a functional assessment of instrumental activities of daily living (IADL). Whilst no definite construct overlap was identified, there is a plausible association between IADL assessment performance and the symptoms of fatigue and reduced interest in activities and concentration associated with MDD.

Research and clinical implications

No frailty assessment tool identified in this review has been developed for use with, nor had its reliability or validity tested in older adult psychiatric populations. Consequently, the

evidence-base for each frailty assessment tool lacks interpretability and generalisability in relation to psychiatric populations, significantly increasing the risk of invalid assessment and identification of frailty. Additionally,, the risk of invalid frailty assessment in psychiatric populations is increased with the application of frailty assessment tools: i) for which definite construct overlap was observed between assessment items and DSM-5 diagnostic criteria; ii) that include a psychological assessment domain; and iii) include items derived from psychiatric assessments.

Given the established high level of comorbidity of frailty with psychiatric disorders and evidenced associations between psychiatric disorders and frailty, inaccurate assessment of frailty in psychiatric populations holds substantial clinical risks. If frailty is not recognised and treated within this high-risk population, the potential for adverse outcomes including worsening of psychiatric symptoms and delayed psychiatric remission increases.[13,21,25] Similarly, if an individual is inaccurately assessed as being frail or pre-frail based on psychiatric symptoms alone, then this could inappropriately or unnecessarily inform treatment planning and provisions. At a wider level, the presence of frailty and psychiatric disorders individually represent increased risks of adverse outcomes including functional decline, institutionalisation and mortality.[1-5,22] Accurate assessment and thus treatment of frailty in the context of psychiatric disorder is essential in minimising risks of such adverse outcomes and associated increased healthcare service utilisation.

In research terms, the implications of inaccurately assessing frailty are also substantial, including an increased likelihood of the interpretation and reporting of flawed results. There exists the potential to identify a research population as frail based on their mental health symptoms alone, thus limiting the potential to identify a ‘true’ frail psychiatric population.

Considering the established research priorities specific to this population, including the need to develop specialist treatments and preventative interventions, the impact of this is considerable.

Further research is necessary to establish a reliable and valid tool to accurately assess frailty in older adults with a diagnosis of psychiatric disorder. Some level of construct overlap and confounding between the indicators of frailty and of psychiatric disorder is inevitable. For example, sarcopenia is widely considered to be a fundamental component of the frailty syndrome, and unintentional weight loss is an established symptom of MDD, both of which are highly related concepts. However, it may be possible to minimise this construct overlap by considering the way that indicators are conceptualised and measured, for example, by defining and measuring the frailty indicator 'slowness' in a way that minimises construct overlap with psychomotor retardation. Future research is required to establish this.

Limitations of the review

This review has several limitations. The search strategy was completed in February 2017, therefore any potentially relevant studies published after this date were not considered for review. Studies were assessed against inclusion criteria by the lead author (JLS) only, increasing the risk of selection bias. This was minimised by strict adhesion to the search strategy and following the PRISMA standards for reporting in systematic reviews. Data extraction concerning the content of frailty assessment tools was also completed by JLS only, however all analysis including assessments of construct overlap were completed by two independent raters. Studies concerning tools that were not explicitly developed to assess frailty were excluded, limiting the scope of this review but deemed appropriate given the multifaceted nature of the frailty presentation. The COSMIN checklist applied also has a

number of limitations (see previous review for discussion of these limitations)[16]. However, COSMIN is a standardized tool for evaluating the methodological quality of studies examining measurement properties of health-related instruments, so it was deemed appropriate. In establishing construct overlap between frailty assessment tool items and psychiatric indicators, the use of a different set of diagnostic criteria for mental illnesses such as the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)[134] may have produced variation in the areas of construct overlap identified. Due to the large volume tools reviewed, it was not possible to apply two separate sets of diagnostic criteria. As the DSM-5 provides in-depth descriptions of diagnostic criteria and is widely used, it was considered appropriate. Finally, whilst the majority of construct overlap observed was due to actual construct overlap; a small amount could be attributed to ambiguous wording of the frailty assessment tool items. For example, the term ''problems with'' allows for a large range of symptoms to be scored under one item.

Conclusions

To date, no multi-component frailty assessment tool has been developed for or validated in older adult populations with psychiatric disorders. This review has provided an in-depth analysis of construct overlap and confounding between the indicators of frailty as conceptualised in existing frailty assessment tools and DSM-5 diagnostic criteria for seven common psychiatric disorders. In designing a tool for use with older adults with a diagnosis of psychiatric disorder, special consideration should be given, where possible, to minimising the construct overlap identified in this review. Further research is necessary to establish a reliable and valid tool to accurately assess frailty in this specific population.

ACKNOWLEDGEMENTS

This research was supported by King's College London, NIHR Dementia Biomedical Research Unit, NIHR Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust, University College London and Middlesex University. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The authors would like to express their gratitude and thanks to all those authors who responded to study queries and data requests.

Conflict of Interest: All authors declare that they have no conflicts of interest.

Author Contributions: The research question, concept and design were formulated by Jennifer L. Sutton, Rebecca L. Gould and Robert J. Howard. The trial selection was completed by Jennifer L. Sutton. Data analysis was completed by Jennifer L. Sutton, Rebecca L. Gould, Mark C. Coulson, Emma V. Ward, Aine M. Butler, Megan Smith, Grace Lavelle, Amy Rosa and Margret Langridge. Preparation of manuscript completed by Jennifer L. Sutton. Rebecca L. Gould, Robert J. Howard, Mark C. Coulson, Emma V. Ward, Aine M. Butler, Megan Smith, Grace Lavelle, Amy Rosa and Margret Langridge reviewed and edited the manuscript.

Sponsor's Role: None.

References:

1. Collard RM. Prevalence of frailty in community-dwelling older persons: a systematic review. *Journal of the American Geriatrics Society.* 2012;60.

2. Vermeiren S, Vella-Azzopardi R, Beckwée D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *Journal of the American Medical Directors Association.*17(12):1163.e1161-1163.e1117.
3. Ensrud KE, Ewing SK, Taylor BC, et al. Frailty and risk of falls, fracture, and mortality in older women: the study of osteoporotic fractures. *The journals of gerontology Series A, Biological sciences and medical sciences.* 2007;62(7):744-751.
4. Al Snih S, Graham JE, Ray LA, Samper-Ternent R, Markides KS, Ottenbacher KJ. Frailty and incidence of activities of daily living disability among older Mexican Americans. *Journal of rehabilitation medicine.* 2009;41(11):892-897.
5. Boyd CM, Xue QL, Simpson CF, Guralnik JM, Fried LP. Frailty, hospitalization, and progression of disability in a cohort of disabled older women. *The American journal of medicine.* 2005;118(11):1225-1231.
6. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet (London, England).* 2013;381(9868):752-762.
7. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: A review. *European journal of internal medicine.* 2016;31(Supplement C):3-10.
8. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *TheScientificWorldJournal.* 2001;1:323-336.
9. Fried LP. Frailty in older adults: evidence for a phenotype. *The journals of gerontology Series A, Biological sciences and medical sciences.* 2001;56.
10. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *The journals of gerontology Series A, Biological sciences and medical sciences.* 2001;56(3):M146-156.
11. Lohman M, Dumenci L, Mezuk B. Gender Differences in the Construct Overlap of Frailty and Depression: Evidence from the Health and Retirement Study. *Journal of the American Geriatrics Society.* 2014;62(3):500-505.
12. Ni Mhaolain AM, Fan CW, Romero-Ortuno R, et al. Frailty, depression, and anxiety in later life. *International psychogeriatrics.* 2012;24(8):1265-1274.
13. Buigues C, Padilla-Sánchez C, Garrido JF, Navarro-Martínez R, Ruiz-Ros V, Cauli O. The relationship between depression and frailty syndrome: a systematic review. *Aging & Mental Health.* 2015;19(9):762-772.
14. Lohman MC, Mezuk B, Dumenci L. Depression and frailty: concurrent risks for adverse health outcomes. *Aging & Mental Health.* 2017;21(4):399-408.
15. Briana M, Lauren E, Matt L, Moon C, Kate L. Depression and frailty in later life: a synthetic review. *International journal of geriatric psychiatry.* 2012;27(9):879-892.
16. Soysal P, Veronese N, Thompson T, et al. Relationship between depression and frailty in older adults: A systematic review and meta-analysis. *Ageing research reviews.* 2017;36(Supplement C):78-87.
17. Andrew MK, Rockwood K. Psychiatric Illness in Relation to Frailty in Community-Dwelling Elderly People without Dementia: A Report from the Canadian Study of Health and Aging. *Canadian Journal on Aging / La Revue canadienne du vieillissement.* 2010;26(1):33-38.
18. Gale CR, Cooper C, Deary IJ, Aihie Sayer A. Psychological well-being and incident frailty in men and women: the English Longitudinal Study of Ageing. *Psychological medicine.* 2014;44(4):697-706.
19. Collard RM, Comijs HC, Naarding P, Oude Voshaar RC. Physical frailty: vulnerability of patients suffering from late-life depression. *Aging & Mental Health.* 2014;18(5):570-578.
20. Collard RM, Arts MHL, Schene AH, Naarding P, Oude Voshaar RC, Comijs HC. The impact of frailty on depressive disorder in later life: Findings from the Netherlands Study of depression in older persons. *European Psychiatry.* 2017;43:66-72.

21. Brown PJ, Rutherford BR, Yaffe K, et al. The Depressed Frail Phenotype: The Clinical Manifestation of Increased Biological Aging. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry.* 2016;24(11):1084-1094.
22. Skoog I. Psychiatric Disorders in the Elderly. *The Canadian Journal of Psychiatry.* 2011;56(7):387-397.
23. Solfrizzi V, Scafato E, Frisardi V, et al. Frailty syndrome and the risk of vascular dementia: The Italian Longitudinal Study on Aging. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association.* 2013;9(2):113-122.
24. Lang PO, Michel JP, Zekry D. Frailty syndrome: a transitional state in a dynamic process. *Gerontology.* 2009;55(5):539-549.
25. Collard RM, Arts MHL, Schene AH, Naarding P, Oude Voshaar RC, Comijs HC. The impact of frailty on depressive disorder in later life: Findings from the Netherlands Study of depression in older persons. *European Psychiatry.* 2017;43(Supplement C):66-72.
26. Sutton JL, Gould RL, Daley S, et al. Psychometric properties of multicomponent tools designed to assess frailty in older adults: A systematic review. *BMC geriatrics.* 2016;16:55.
27. Terwee CB, Mokkink LB, Knol DL, Ostelo RW, Bouter LM, de Vet HC. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2012;21(4):651-657.
28. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. *Journal of the American Geriatrics Society.* 2004;52(11):1929-1933.
29. Gobbens RJ, van Assen MA, Luijkx KG, Wijnen-Sponselee MT, Schols JM. The Tilburg Frailty Indicator: psychometric properties. *Journal of the American Medical Directors Association.* 2010;11(5):344-355.
30. Sternberg SA, Wershof Schwartz A, Karunananthan S, Bergman H, Mark Clarfield A. The identification of frailty: a systematic literature review. *Journal of the American Geriatrics Society.* 2011;59(11):2129-2138.
31. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age and ageing.* 2015;44(1):148-152.
32. Pijpers E, Ferreira I, Stehouwer CD, Nieuwenhuijzen Kruseman AC. The frailty dilemma. Review of the predictive accuracy of major frailty scores. *European journal of internal medicine.* 2012;23(2):118-123.
33. Drubbel I, Numans ME, Kranenburg G, Bleijenberg N, de Wit NJ, Schuurmans MJ. Screening for frailty in primary care: a systematic review of the psychometric properties of the frailty index in community-dwelling older people. *BMC geriatrics.* 2014;14:27.
34. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Nijhuis-van der Sanden MW. Outcome instruments to measure frailty: a systematic review. *Ageing research reviews.* 2011;10(1):104-114.
35. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC geriatrics.* 2013;13:64.
36. McDonald VSMT, Kimberly A. MD; Lewis, Paul R. DO; Sise, C. Beth MSN; Sise, Michael J. MD; Shackford, Steven R. MD. Frailty in trauma: A systematic review of the surgical literature for clinical assessment tools. *Journal of Trauma and Acute Care Surgery.* 2016;80(5):824–834.
37. Warnier RMJ, van Rossum E, van Velthuijsen E, Mulder WJ, Schols JMGA, Kempen GIJM. Validity, reliability and feasibility of tools to identify frail older patients in inpatient hospital care: A systematic review. *The journal of nutrition, health & aging.* 2016;20(2):218-230.
38. Association AP. *Diagnostic and statistical manual of mental disorders (5th edition).* Washington, DC2013.

39. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2010;19(4):539-549.
40. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *Journal of clinical epidemiology.* 2010;63(7):737-745.
41. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ (Clinical research ed).* 2009;339:b2535.
42. Rockwood K, Stadnyk K, MacKnight C, McDowell I, Hebert R, Hogan DB. A brief clinical instrument to classify frailty in elderly people. *Lancet (London, England).* 1999;353(9148):205-206.
43. Kenig J, Zychiewicz B, Olszewska U, Richter P. Screening for frailty among older patients with cancer that qualify for abdominal surgery. *Journal of geriatric oncology.* 2015;6(1):52-59.
44. Ritt M, Bollheimer LC, Sieber CC, Gaßmann KG. Prediction of one-year mortality by five different frailty instruments: A comparative study in hospitalized geriatric patients. *Archives of gerontology and geriatrics.* 2016;66(Supplement C):66-72.
45. Freiheit EA, Hogan DB, Eliasziw M, et al. Development of a frailty index for patients with coronary artery disease. *Journal of the American Geriatrics Society.* 2010;58(8):1526-1531.
46. Kamaruzzaman S, Ploubidis GB, Fletcher A, Ebrahim S. A reliable measure of frailty for a community dwelling older population. *Health and quality of life outcomes.* 2010;8:123.
47. Goldstein J, Hubbard RE, Moorhouse P, Andrew MK, Mitnitski A, Rockwood K. The validation of a care partner-derived frailty index based upon comprehensive geriatric assessment (CP-FI-CGA) in emergency medical services and geriatric ambulatory care. *Age and ageing.* 2015;44(2):327-330.
48. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne.* 2005;173(5):489-495.
49. Rockwood K, Abeysundera MJ, Mitnitski A. How should we grade frailty in nursing home patients? *Journal of the American Medical Directors Association.* 2007;8(9):595-603.
50. Mitnitski A, Fallah N, Rockwood MR, Rockwood K. Transitions in cognitive status in relation to frailty in older adults: a comparison of three frailty measures. *The journal of nutrition, health & aging.* 2011;15(10):863-867.
51. Kang L, Zhang S-Y, Zhu W-L, et al. Is frailty associated with short-term outcomes for elderly patients with acute coronary syndrome? *Journal of Geriatric Cardiology : JGC.* 2015;12(6):662-667.
52. Studenski S, Hayes RP, Leibowitz RQ, et al. Clinical Global Impression of Change in Physical Frailty: development of a measure based on clinical judgment. *Journal of the American Geriatrics Society.* 2004;52(9):1560-1566.
53. Sundermann S, Dademasch A, Praetorius J, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* 2011;39(1):33-37.
54. Sundermann S, Dademasch A, Rastan A, et al. One-year follow-up of patients undergoing elective cardiac surgery assessed with the Comprehensive Assessment of Frailty test and its simplified form. *Interactive cardiovascular and thoracic surgery.* 2011;13(2):119-123; discussion 123.
55. Sundermann SH, Dademasch A, Seifert B, et al. Frailty is a predictor of short- and mid-term mortality after elective cardiac surgery independently of age. *Interactive cardiovascular and thoracic surgery.* 2014;18(5):580-585.

56. De Witte N, Gobbens R, De Donder L, et al. The comprehensive frailty assessment instrument: development, validity and reliability. *Geriatric nursing (New York, NY).* 2013;34(4):274-281.
57. De Witte N, Gobbens R, De Donder L, et al. Validation of the Comprehensive Frailty Assessment Instrument against the Tilburg Frailty Indicator. *European geriatric medicine.* 2013;4(4):248-254.
58. Buchman AS, Wilson RS, Bienias JL, Bennett DA. Change in frailty and risk of death in older persons. *Experimental aging research.* 2009;35(1):61-82.
59. Cohen HJ, Smith D, Sun C-L, et al. Frailty as determined by a comprehensive geriatric assessment-derived deficit-accumulation index in older patients with cancer who receive chemotherapy. *Cancer.* 2016;122(24):3865-3872.
60. van Kempen JA, Schers HJ, Jacobs A, et al. Development of an instrument for the identification of frail older people as a target population for integrated care. *The British journal of general practice : the journal of the Royal College of General Practitioners.* 2013;63(608):e225-231.
61. van Kempen JA, Schers HJ, Melis RJ, Olde Rikkert MG. Construct validity and reliability of a two-step tool for the identification of frail older people in primary care. *Journal of clinical epidemiology.* 2014;67(2):176-183.
62. van Kempen JAL, Schers HJ, Philp I, Olde Rikkert MGM, Melis RJF. Predictive validity of a two-step tool to map frailty in primary care. *BMC Medicine.* 2015;13:287.
63. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age and ageing.* 2006;35(5):526-529.
64. Haley MN, Wells YD, Holland AE. Relationship between frailty and discharge outcomes in subacute care. *Australian health review : a publication of the Australian Hospital Association.* 2014;38(1):25-29.
65. Graham MM, Galbraith PD, O'Neill D, Rolfson DB, Dando C, Norris CM. Frailty and outcome in elderly patients with acute coronary syndrome. *The Canadian journal of cardiology.* 2013;29(12):1610-1615.
66. Perna S, Francis MDA, Bologna C, et al. Performance of Edmonton Frail Scale on frailty assessment: its association with multi-dimensional geriatric conditions assessed with specific screening tools. *BMC geriatrics.* 2017;17:2.
67. Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age and ageing.* 2016;45(3):353-360.
68. de Vries NM, Staal JB, Olde Rikkert MG, Nijhuis-van der Sanden MW. Evaluative frailty index for physical activity (EFIP): a reliable and valid instrument to measure changes in level of frailty. *Physical therapy.* 2013;93(4):551-561.
69. Vernerey D, Anota A, Vandel P, et al. Development and validation of the FRAGIRE tool for assessment an older person's risk for frailty. *BMC geriatrics.* 2016;16:187.
70. Jones D, Song X, Mitnitski A, Rockwood K. Evaluation of a frailty index based on a comprehensive geriatric assessment in a population based study of elderly Canadians. *Aging clinical and experimental research.* 2005;17(6):465-471.
71. Pilotto A, Rengo F, Marchionni N, et al. Comparing the prognostic accuracy for all-cause mortality of frailty instruments: a multicentre 1-year follow-up in hospitalized older patients. *PloS one.* 2012;7(1):e29090.
72. Ritt M, Rádi KH, Schwarz C, Bollheimer LC, Sieber CC, Gassmann KG. A comparison of frailty indexes based on a comprehensive geriatric assessment for the prediction of adverse outcomes. *The journal of nutrition, health & aging.* 2016;20(7):760-767.
73. Kobe AR, Meyer A, Elmubarak H, et al. Frailty Assessed by the FORECAST Is a Valid Tool to Predict Short-Term Outcome After Transcatheter Aortic Valve Replacement. *Innovations (Philadelphia, Pa).* 2016;11(6):407-413.

74. Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K. Frailty, fitness and late-life mortality in relation to chronological and biological age. *BMC geriatrics.* 2002;2:1.
75. Rockwood K, McMillan M, Mitnitski A, Howlett SE. A Frailty Index Based on Common Laboratory Tests in Comparison With a Clinical Frailty Index for Older Adults in Long-Term Care Facilities. *Journal of the American Medical Directors Association.* 2015;16(10):842-847.
76. Drubbel I, Bleijenberg N, Kranenburg G, et al. Identifying frailty: do the Frailty Index and Groningen Frailty Indicator cover different clinical perspectives? a cross-sectional study. *BMC family practice.* 2013;14:64.
77. Drubbel I, de Wit NJ, Bleijenberg N, Eijkemans RJ, Schuurmans MJ, Numans ME. Prediction of adverse health outcomes in older people using a frailty index based on routine primary care data. *The journals of gerontology Series A, Biological sciences and medical sciences.* 2013;68(3):301-308.
78. Tocchi C, Dixon J, Naylor M, Jeon S, McCorkle R. Development of a frailty measure for older adults: the frailty index for elders. *Journal of nursing measurement.* 2014;22(2):223-240.
79. Cesari M, Demougeot L, Boccalon H, et al. A self-reported screening tool for detecting community-dwelling older persons with frailty syndrome in the absence of mobility disability: the FiND questionnaire. *PloS one.* 2014;9(7):e101745.
80. Doba N, Tokuda Y, Goldstein NE, Kushiro T, Hinohara S. A pilot trial to predict frailty syndrome: the Japanese Health Research Volunteer Study. *Experimental gerontology.* 2012;47(8):638-643.
81. Woo J, Yu R, Wong M, Yeung F, Wong M, Lum C. Frailty Screening in the Community Using the FRAIL Scale. *Journal of the American Medical Directors Association.* 2015;16(5):412-419.
82. Garcia-Garcia FJ, Carcaillon L, Fernandez-Tresguerres J, et al. A new operational definition of frailty: the Frailty Trait Scale. *Journal of the American Medical Directors Association.* 2014;15(5):371.e377-371.e313.
83. Kajsa E, Katarina W, Sten L, Synneve I-D. Screening for frailty among older emergency department visitors: Validation of the new FRESH-screening instrument. *BMC Emergency Medicine.* 2016;16(1):27.
84. Bielderman A, van der Schans CP, van Lieshout MR, et al. Multidimensional structure of the Groningen Frailty Indicator in community-dwelling older people. *BMC geriatrics.* 2013;13:86.
85. Coelho T, Paúl C, Gobbens RJJ, Fernandes L. Frailty as a predictor of short-term adverse outcomes. *PeerJ.* 2015;3:e1121.
86. Daniels R, van Rossum E, Beurskens A, van den Heuvel W, de Witte L. The predictive validity of three self-report screening instruments for identifying frail older people in the community. *BMC public health.* 2012;12:69.
87. Hoogendijk EO, van der Horst HE, Deeg DJ, et al. The identification of frail older adults in primary care: comparing the accuracy of five simple instruments. *Age and ageing.* 2013;42(2):262-265.
88. Metzelthin SF, Daniels R, van Rossum E, de Witte L, van den Heuvel WJ, Kempen GI. The psychometric properties of three self-report screening instruments for identifying frail older people in the community. *BMC public health.* 2010;10:176.
89. Meulendijks FG, Hamaker ME, Boereboom FTJ, Kalf A, Vögtlander NPJ, van Munster BC. Groningen frailty indicator in older patients with end-stage renal disease. *Renal Failure.* 2015;37(9):1419-1424.
90. Schuurmans H, Steverink N, Lindenberg S, Frieswijk N, Slaets JP. Old or frail: what tells us more? *The journals of gerontology Series A, Biological sciences and medical sciences.* 2004;59(9):M962-965.
91. Smets IH. Four screening instruments for frailty in older patients with and without cancer: a diagnostic study. *BMC geriatrics.* 2014;14.
92. Tegels JJ, de Maat MF, Hulsewe KW, Hoofwijk AG, Stoot JH. Value of geriatric frailty and nutritional status assessment in predicting postoperative mortality in gastric cancer surgery.

Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2014;18(3):439-445; discussion 445-436.
93. Guilley E, Ghisletta P, Armi F, et al. Dynamics of Frailty and ADL Dependence in a Five-Year Longitudinal Study of Octogenarians. *Research on Aging.* 2008;30(3):299-317.
94. Kwon M, Kim S-A, Roh J-L, et al. An Introduction to a Head and Neck Cancer-Specific Frailty Index and Its Clinical Implications in Elderly Patients: A Prospective Observational Study Focusing on Respiratory and Swallowing Functions. *The Oncologist.* 2016;21(9):1091-1098.
95. Chin APMJ, Dekker JM, Feskens EJ, Schouten EG, Kromhout D. How to select a frail elderly population? A comparison of three working definitions. *Journal of clinical epidemiology.* 1999;52(11):1015-1021.
96. Chin APMJ, de Groot LC, van Gend SV, et al. Inactivity and weight loss: effective criteria to identify frailty. *The journal of nutrition, health & aging.* 2003;7(1):55-60.
97. Di Bari M, Profili F, Bandinelli S, et al. Screening for frailty in older adults using a postal questionnaire: rationale, methods, and instruments validation of the INTER-FRAIL study. *Journal of the American Geriatrics Society.* 2014;62(10):1933-1937.
98. Morris JN, Howard EP, Steel KR. Development of the interRAI home care frailty scale. *BMC geriatrics.* 2016;16(1):188.
99. Jung HW, Kim SW, Ahn S, et al. Prevalence and outcomes of frailty in Korean elderly population: comparisons of a multidimensional frailty index with two phenotype models. *PloS one.* 2014;9(2):e87958.
100. Amici A, Baratta A, Linguanti A, et al. The Marigliano-Cacciafesta polypathological scale: a tool for assessing fragility. *Archives of gerontology and geriatrics.* 2008;46(3):327-334.
101. Warnier RM, van Rossum E, van Leendert JA, et al. Screening for Frailty in Hospitalized Older Adults: Reliability and Feasibility of the Maastricht Frailty Screening Tool for Hospitalized Patients (MFST-HP). *Research in gerontological nursing.* 2016;9(5):243-251.
102. Palumbo A, Bringhen S, Mateos M-V, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. *Blood.* 2015;125(13):2068-2074.
103. Paulson D, Lichtenberg PA. The Paulson-Lichtenberg Frailty Index: Evidence for a Self-Report Measure of Frailty. *Aging & mental health.* 2015;19(10):892-901.
104. Kim H, Higgins PA, Canaday DH, Burant CJ, Hornick TR. Frailty assessment in the geriatric outpatient clinic. *Geriatrics & gerontology international.* 2014;14(1):78-83.
105. Kulminski AM, Ukraintseva SV, Kulminskaya IV, Arbeev KG, Land K, Yashin AI. Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: lessons from the Cardiovascular Health Study. *Journal of the American Geriatrics Society.* 2008;56(5):898-903.
106. Carriere I, Colvez A, Favier F, Jeandel C, Blain H. Hierarchical components of physical frailty predicted incidence of dependency in a cohort of elderly women. *Journal of clinical epidemiology.* 2005;58(11):1180-1187.
107. Pijpers E, Ferreira I, van de Laar RJ, Stehouwer CD, Nieuwenhuijzen Kruseman AC. Predicting mortality of psychogeriatric patients: a simple prognostic frailty risk score. *Postgraduate medical journal.* 2009;85(1007):464-469.
108. Nunes DP, Duarte YAdO, Santos JLF, Lebrão ML. Screening for frailty in older adults using a self-reported instrument. *Revista de Saúde Pública.* 2015;49:2.
109. Yamada M, Arai H. Predictive Value of Frailty Scores for Healthy Life Expectancy in Community-Dwelling Older Japanese Adults. *Journal of the American Medical Directors Association.* 2015;16(11):1002.e1007-1002.e1011.
110. Barreto Pde S, Greig C, Ferrandez AM. Detecting and categorizing frailty status in older adults using a self-report screening instrument. *Archives of gerontology and geriatrics.* 2012;54(3):e249-254.

111. Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC geriatrics.* 2010;10:57.
112. Romero Ortuno R. [The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe (SHARE-FI): results of the Spanish sample]. *Revista espanola de geriatria y gerontologia.* 2011;46(5):243-249.
113. Romero-Ortuno R, O'Shea D, Kenny RA. The SHARE frailty instrument for primary care predicts incident disability in a European population-based sample. *Quality in primary care.* 2011;19(5):301-309.
114. Romero-Ortuno R. The SHARE operationalized frailty phenotype: a comparison of two approaches. *European geriatric medicine.* 2013;4(4).
115. Romero-Ortuno R. The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe predicts mortality similarly to a frailty index based on comprehensive geriatric assessment. *Geriatrics & gerontology international.* 2013;13(2):497-504.
116. Bilotta C, Nicolini P, Case A, Pina G, Rossi S, Vergani C. Frailty syndrome diagnosed according to the Study of Osteoporotic Fractures (SOF) criteria and adverse health outcomes among community-dwelling older outpatients in Italy. A one-year prospective cohort study. *Archives of gerontology and geriatrics.* 2012;54(2):e23-28.
117. De Buyser SL, Petrovic M, Taes YE, et al. Validation of the FNIH sarcopenia criteria and SOF frailty index as predictors of long-term mortality in ambulatory older men. *Age and ageing.* 2016;45(5):602-608.
118. Ensrud KE, Ewing SK, Taylor BC, et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. *Archives of internal medicine.* 2008;168(4):382-389.
119. Strawbridge WJ, Shema SJ, Balfour JL, Higby HR, Kaplan GA. Antecedents of frailty over three decades in an older cohort. *The journals of gerontology Series B, Psychological sciences and social sciences.* 1998;53(1):S9-16.
120. Matthews M, Lucas A, Boland R, et al. Use of a questionnaire to screen for frailty in the elderly: an exploratory study. *Aging clinical and experimental research.* 2004;16(1):34-40.
121. Andreasen J, Lund H, Aadahl M, Gobbens RJJ, Sorensen EE. Content validation of the Tilburg Frailty Indicator from the perspective of frail elderly. A qualitative explorative study. *Archives of gerontology and geriatrics.* 2015;61(3):392-399.
122. Andreasen J, Sorensen EE, Gobbens RJ, Lund H, Aadahl M. Danish version of the Tilburg Frailty Indicator--translation, cross-cultural adaption and validity pretest by cognitive interviewing. *Archives of gerontology and geriatrics.* 2014;59(1):32-38.
123. Coelho T, Santos R, Paúl C, Gobbens RJJ, Fernandes L. Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation. *Geriatrics & gerontology international.* 2015;15(8):951-960.
124. Freitag S, Schmidt S, Gobbens RJJ. Tilburg frailty indicator. *Zeitschrift für Gerontologie und Geriatrie.* 2016;49(2):86-93.
125. Gobbens RJ, van Assen MA. The prediction of quality of life by physical, psychological and social components of frailty in community-dwelling older people. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2014;23(8):2289-2300.
126. Gobbens RJ, van Assen MA, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Determinants of frailty. *Journal of the American Medical Directors Association.* 2010;11(5):356-364.
127. Gobbens RJ, van Assen MA, Luijkx KG, Schols JM. The predictive validity of the Tilburg Frailty Indicator: disability, health care utilization, and quality of life in a population at risk. *The Gerontologist.* 2012;52(5):619-631.

128. Gobbens RJ, van Assen MA. Frailty and its prediction of disability and health care utilization: the added value of interviews and physical measures following a self-report questionnaire. *Archives of gerontology and geriatrics.* 2012;55(2):369-379.
129. Roppolo M, Mulasso A, Gobbens RJ, Mosso CO, Rabaglietti E. A comparison between uni- and multidimensional frailty measures: prevalence, functional status, and relationships with disability. *Clinical interventions in aging.* 2015;10:1669-1678.
130. Uchmanowicz I, Jankowska-Polanska B, Loboz-Rudnicka M, Manulik S, Loboz-Grudzien K, Gobbens RJ. Cross-cultural adaptation and reliability testing of the Tilburg Frailty Indicator for optimizing care of Polish patients with frailty syndrome. *Clinical interventions in aging.* 2014;9:997-1001.
131. Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. *Journal of the American Geriatrics Society.* 2005;53(8):1321-1330.
132. Ravaglia G, Forti P, Lucicesare A, Pisacane N, Rietti E, Patterson C. Development of an easy prognostic score for frailty outcomes in the aged. *Age and ageing.* 2008;37(2):161-166.
133. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research.* 1982;17(1):37-49.
134. Organization WH. International statistical classification of diseases and related health problems. In. Vol 10th revision: WHO Library Cataloguing-in-Publication Data; 2016.