Validated screening tools for the assessment of Cachexia, Sarcopenia and Malnutrition: A systematic review

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Disclaimers: Nil

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Sources of support: No funding was provided for this review. Publishing costs will be provided by the University of Edinburgh and The Yorkshire Cancer Research Endowment Programme.

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Abbreviations: BAPEN (British Association for Parenteral and Enteral Nutrition, BIA (Bioelectrical impedance analysis), BNST (British Nutrition Screening Tool), CASCO (Cachexia Score), CINAHL (Cumulative index to Nursing and Allied Health Literature),CNST (Canadian Nutrition Screening Tool), CONUT (Controlling Nutritional Status), DEXA (dual-energy x-ray absorptiometry), EDC (ESPEN Diagnostic Criteria for Malnutrition), ESPEN (European Society for Clinical Nutrition and Metabolism), GNRI (Geriatric Nutrition Risk Index), INSYST (Imperial Nutritional Screening System), MST (Malnutrition Screening Tool), MSTC (Malnutrition Screening Tool for Cancer), NRI (Nutritional Risk Index), NRS-2002 (Nutritional Risk Screening), NUFFE (Nutritional Form For the Elderly), SGA (Subjective Global Assessment), SNAQ (Short Nutritional Assessment Questionnaire), Spinal NST (Spinal Nutritional Screening Tool), SPSM (Short Portable Sarcopenia Measure), R-NST (Renal Nutritional Screening Tool), 3-MinNS (3 Minute Nutrition Screening), UWL (Unintentional weight loss)

Clinical trial registry number: N/A

Abstract

Background

There is great overlap between the presentation of cachexia, sarcopenia and malnutrition. Distinguishing between these conditions would allow for better targeted treatment for patients.

Objectives

To systematically review validated screening tools for cachexia, sarcopenia and malnutrition in adults and, if a combined tool is absent, make suggestions for the generation of a novel screening tool.

Design

A systematic search was performed in Ovid MEDLINE, EMBASE, CINAHL (Cumulative index to Nursing and Allied Health Literature) and Web of Science. Two reviewers performed data extraction independently. Each tool was judged for validity against a reference method. Psychometric evaluation was performed as was appraisal of the tools ability to assess the patient against consensus definitions.

Results

Thirty-eight studies described 22 validated screening tools.

The Cachexia score (CASCO) was the only validated screening tool for cachexia; performing well against the consensus definition.

Two tools assessed sarcopenia (the Short Portable Sarcopenia Measure [SPSM] and the SARC-F); scoring well against the 1998 Baumgartner definition. The SPSM required large amounts of equipment and the SARC-F had a low sensitivity.

Nineteen tools screened for malnutrition. The 3 minute nutrition score (3 MinNS) scored best meeting consensus definition criteria (ESPEN) and also having sensitivities and specificities >80%.

No tool contained all the currently accepted components to screen for all three conditions. Only three tools were measured against cross-sectional imaging, a clinical tool that is gaining wider interest in body composition analysis.

Conclusion

No one validated screening tool can be implemented for the simultaneous assessment of cachexia, sarcopenia and malnutrition. The development of a tool that encompasses consensus definition criteria and directs clinicians towards the underlying diagnosis would be optimal to target treatment and improve outcomes. We propose that tool should incorporate a stepwise assessment of nutritional status; oral intake; disease status; age; muscle mass/function; and metabolic derangement.

Keywords: Cachexia, Sarcopenia, Malnutrition, Screening, Assessment

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50 **Introduction**

51 Unintentional weight loss (UWL) as a form of nutritional depletion is commonly seen in
52 ageing, cancer and many chronic diseases. The main subtypes can be categorised into three
53 primary syndromes: cachexia, age-related sarcopenia and malnutrition; however, it is not clear
54 whether existing screening tools are able to distinguish between these three conditions. This is
55 due in part to the complex overlap between them. Loss of muscle mass is a key feature in both
56 cachexia and sarcopenia but patients with sarcopenia are not necessarily cachectic. Sarcopenia
57 can occur simply with ageing and leads to functional decline [1,2]. Cachexia involves complex
58 metabolic pathways leading to systemic inflammation, muscle and fat wasting and must be
59 present in association with a chronic disease [3]. Cachexia differs from malnutrition in that it
60 cannot be reversed by simple nutritional support [4]. There are many definitions for each
61 condition, with nutritional depletion playing a part in each, therefore making it difficult to
62 separate them out [1,2,3,4]. These conditions are also often not noticed in their earlier phases
63 but do become apparent following a critical event or development of disability [5].

64

65 More than 70 nutritional screening tools for use in hospitals have been developed to facilitate
66 easy screening or assessment of a patient's nutritional status or to predict poor clinical outcome
67 related to UWL. Despite increasing research, there appears to be a lack of a practical and
68 implementable clinical screening tool to support diagnosis [6]. In the general community, the
69 European Society for Clinical Nutrition and Metabolism (ESPEN) endorses the use of
70 Malnutrition Screening Tool (MUST) [6,7], and Nutritional Risk Screening (NRS-2002) [8]
71 and the Mini Nutritional Assessment – Short Form (MNA-SF) for the elderly [9,10]. Some

This is a pre-copyedited, author-produced version of an article accepted for publication in The American Journal of Clinical Nutrition following peer review. The version of record [Janice Miller, Liz Wells, Ugochinyere Nwulu, David Currow, Miriam J Johnson, Richard J E Skipworth; Validated screening tools for the assessment of cachexia, sarcopenia, and malnutrition: a systematic review, The American Journal of Clinical Nutrition, Volume 108, Issue 6, 1 December 2018, Pages 1196–1208] is available online at: https://doi.org/10.1093/ajcn/nqy244.

tools claim to have been developed to screen in specific target groups however, there are currently no disease specific recommendations. There is no international consensus on a single 'best tool' to identify all three syndromes across populations. The use of different tools in different studies makes drawing any conclusions about their comparison and meta-analyses difficult.

Current diagnostic methods for sarcopenia and cachexia include the assessment of body anthropometry using either body mass index (BMI) or estimated weight loss, or by direct assessment of muscle and fat mass using dual-energy X-Ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), CT or MRI scanning. Whilst the latter two radiographic modalities are accurate, they are impractical, expensive and some expose the patient to radiation. This diagnostic approach to detect the presence of sarcopenia is time consuming, expensive and requires highly specialised equipment [11]. Therefore, a screening tool that is implementable in a larger population that allows for early detection is important. This approach would highlight the potential for further assessment with early biomarkers, thus allowing prophylactic intervention in malnutrition and driving further research in sarcopenia and cachexia.

We aimed to systematically review validated screening tools for the general adult population to enable clinicians to distinguish between the three syndromes. The specific strengths and limitations of each tool were assessed, as was the appropriateness of the validation population. Through psychometric evaluation and assessment of the tools against the agreed consensus definitions, we also investigated if any one single tool could be used for the simultaneous assessment of all three.

Methods

Methods for conducting systematic reviews of the effectiveness of interventions have been well described. In accordance with PRISMA guidelines [12] we applied the principles to systematically reviewing validated screening tools used in the assessment of cachexia, sarcopenia and malnutrition.

Literature review

A systematic search was performed on 26th September 2017 in Ovid MEDLINE (1946-2017), EMBASE (1974-2017), CINAHL (Cumulative index to Nursing and Allied Health Literature) and Web of Science. Relevant articles were identified by title and abstract. Reference lists of review articles were also hand searched. Double data extraction was performed by two reviewers independently to ensure consistency. Any disagreements were settled by a third reviewer.

The basic search strategy was "Sarcopenia" OR "Cachexia" OR "Malnutrition" AND "screening" AND "validation study" using MeSH terms and keywords appropriate to each database. No language restriction was imposed. The search was designed to be broad to ensure all validated tools were identified. A full copy of the search used for MEDLINE can be found in the online supplementary material (OSM). There were no disease specific or language limits.

Inclusion and exclusion criteria

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Studies were included if they had developed a screening tool which had been validated for the screening of either cachexia, sarcopenia or malnutrition in adults (**Table 1**). Disease specific tools were included. Papers were excluded if the tools had not been validated or if they assessed malnutrition in children or obesity in adults. Studies which described modified versions of pre-existing tools were also excluded as this was out with the scope of this review. It was intended that studies that included less than 25 patients should be excluded as they were unlikely to yield robust, generalisable psychometric results, however no studies with numbers smaller than this were found.

Assessment of Validity

Studies had to have evaluation of at least two of the following psychometric characteristics:

- Content validity
- Construct validity e.g. including convergent validity, discriminant validity
- Test-retest reliability
- Internal consistency
- Responsiveness
- Factor analysis
- Criterion validity

Primary criteria used to evaluate the tools were construct validity and responsiveness.

Criterion and construct validity, reference method

Studying the validity of a tool usually compares to a gold standard. Although many research groups are now using cross sectional imaging to investigate UWL there is currently the absence of a perfect gold standard. Studies used different reference methods to validate their tools e.g. DXA and assessment by a health professional. The tools SGA and MNA are the tools currently

recognised as the industry standard and were therefore considered valid references. The term criterion validity was used for these comparisons.

Less valid reference methods including the use of other screening tools and blood tests for example albumin which can be influenced by other factors including inflammation and acute disease were included as many research groups vary in their opinion on the optimal reference method. [13] These comparisons were termed construct validity.

Predictive validity

Predictive validity was assessed as the ability of the tool to predict the probability of a better or worse clinical outcome due to nutritional risk.

Diagnostic criteria

Tools were also assessed for their ability to identify the risk of cachexia, sarcopenia or malnutrition by comparison of their components against the components of each set of chosen diagnostic criteria (**Table 2**).

Assessment of bias

Assessment of bias was made using a form of the Newcastle-Ottowa scale adapted for cross-sectional studies [14]. Each study was scored out of 10 and a study with a score of <5 was considered to be at high risk of bias. Full details of the scoring used can be found in **the OSM.**

Secondary criteria

Secondary criteria included face validity, development and content validity, factor analysis, test-retest reliability, internal consistency, respondent and administrative burden (the time and

effort required to complete the tool). These are also summarised in table 1. Data were extracted concerning the study participants, the tool used and psychometric evaluations (Inclusion criteria Table 1). Assessment of sensitivity and specificity was made. A value >80% was considered good, 60-80% fair and <60% poor. Agreement was also assessed as: 0.9-1 = excellent, 0.80-.90 = good, 0.60-0.80 = fair and <0.60 = poor.

Results

Principal findings

Thirty-eight studies were included which described the validation of 22 screening tools. The majority of papers were excluded as they described un-validated tools. This is summarised in **figure 1**.

The Cachexia score (CASCO) was the only screening tool for cachexia that had been validated. It performed well against diagnostic criteria (Fearon 2011) [3], but sensitivities and specificities were not recorded. Only two tools assessed sarcopenia (the Short Portable Sarcopenia Measure [SPSM] and the SARC-F) and scored well against the agreed definition (Baumgartner 1998) [1]. However, the SPSM required a large amount of equipment and the SARC-F had a very low sensitivity. Both were validated for use in the outpatient setting. Nineteen tools screened for malnutrition. The 3 minute nutrition score (3 MinNS) proved to be the best, scoring well against the consensus definition (ESPEN) as well as having sensitivities and specificities >80%. There was no one validated tool which adequately screened for all three conditions. A critical appraisal of all tools can be found in **table 3**.

187 *Tools with evidence of validity, reliability and acceptability*

188 The available validity, reliability and acceptability data are summarised in **tables 4 and 6**.
189 **Table 5** assesses how well each tool encompasses the criteria in the chosen definitions.
190 Assessment of bias is shown in **table 7**.

191

192 *Sarcopenia*

193 In total two tools were found that were validated for the assessment of sarcopenia (SPSM and
194 SARC-F). Three other tools assessed muscle function but no other tools made an assessment
195 of muscle strength, mass or wasting. Both tools which were validated for the assessment of
196 sarcopenia were done so in the community setting. They agreed with the SCWD diagnostic
197 criteria but the SARC-F showed variation in agreement against the three consensus definitions
198 it was validated against (EWGSOP, IWGS criteria and the Asian working group for
199 sarcopenia). The SARC-F had good specificity (94.2-99.1%) but poor sensitivity (3.8-9.9%
200 dependent on sex) and also showed good agreement (0.78-0.90). Values for the SPSM were
201 not assessed.

202

203 *Cachexia*

204 Only one tool had been validated for the screening of cachexia – the CASCO. Overall six tools
205 quantified weight loss within a specified time frame, with a further three quantifying it within
206 an unspecified time frame. Sixteen tools characterised weight loss as unintentional. Only seven
207 tools asked about the presence of underlying disease and only the CASCO took into account
208 the presence of raised inflammatory markers and quality of life. Sensitivities and specificities
209 were not recorded for the CASCO but it scored well in the assessment of its validity with it
210 being able to quantitatively classify stages of cachexia. Its ability to predict patient's outcome
211 was not assessed.

212

213 *Malnutrition*

214 Nineteen screening tools were found to be validated for the assessment of malnutrition.
215 However, only twelve of these incorporated a question about dietary intake or decline. Six
216 measured percentage weight loss over time and 13 assessed BMI. In particular those tools
217 which had high sensitivities and specificities (MSTC and SNST) did not encompass all parts
218 of the agreed definition: The SNST did not assess BMI and the MSTC made no assessment of
219 quantifying weight loss within a specified time frame. The 3 MinNS was the tool which
220 incorporated the consensus definition criteria and also had high sensitivities and specificities
221 (>80%).

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Discussion

Overview

Whilst recent systematic reviews have described the results of studies examining malnutrition screening tools, to our knowledge this is the first review to examine tools that have been validated against another to assess cachexia, sarcopenia and malnutrition. There has only been one prior review on tools for cachexia, sarcopenia and malnutrition [53]. This review did not include psychometric evaluation, did not comment on the validity of the tools, nor compare them to the agreed consensus definitions. Existing systematic reviews of malnutrition screening tools have been limited to describing tools that are non-disease specific and 'quick and easy' or have been narrative in nature.

Thirty-eight studies describing 22 tools were identified and judged for validity against a reference method. In the absence of a generally recognised gold standard for screening, assessment by a professional, DXA, CT, MRI, anthropometry or the screening tools SGA and MNA were considered 'valid' reference methods by our research group [13,44-46]. Although cross sectional imaging is now used routinely for body composition analysis, only three tools identified were validated against CT. The heterogeneity in populations, age groups, tools and reference methods was large, and therefore pooling of results was impossible. Most tools had only been tested in one population making the drawing of any definitive conclusions difficult. There were too few disease-specific tools to conclude which would be superior for different disease processes.

Problems with current screening tools

For the generalised adult population, all tools showed inconsistent results regarding their validity. The SGA which is often considered to be the industry standard [54] and against which

many tools are validated has not itself been well validated. It performed well against the diagnostic criteria but sensitivities and specificities were either not recorded or poor. Arguably the most well-known tools 'MUST' and 'NRS-2002' showed a variation in results from poor to good [27,29,34-39,42], and consistency between groups in which the tools were studied was poor. The less well-known NUFFE showed good validity, but it has been described in only a small volume of literature and is not implemented widely [43]. The "quick and easy" screening tools, including SNAQ and MST performed reasonably (sensitivities ~80%) in most studies in which they were used [25-30,35,47,48]. Of note because these tools are quick, they require a further detailed assessment by a qualified health professional if screening is positive. They also miss approximately 20% of at risk patients at initial screen and therefore may be more useful in screening high risk patients.

The tool which performed the best for malnutrition was the 3MinNS [52]. It showed high sensitivity and specificity (>80%) and accurately encompassed the correct diagnostic criteria (percentage weight loss over specified time and measurement of BMI) for malnutrition. It was validated in acute medical and surgical patients and proved quick and easy to complete. It has only been validated in one paper and therefore it cannot be assumed that it would perform as well in different patient populations. Both tools which assessed sarcopenia (SPSM, SARC-F) scored well against the agreed definition [15,16]. However, the SPSM required transport of equipment and the SARC-F had a very low sensitivity [13,15]. The CASCO was the only validated screening tool for cachexia [17]. It performed well against diagnostic criteria, but sensitivities and specificities were not recorded. It has also only been validated in the cancer setting; more work would be needed to validate the tool in other cachectic populations or the general adult population.

Most tools were validated in the adult hospital inpatient setting. Tools for sarcopenia have only been validated in the healthy, community dwelling [15,16]. Length of hospital stay is diminishing worldwide and outpatient nutritional screening is advocated to pick up patients at risk. In this review, we identified eight studies in which outpatients were included. More studies focussing on the construct and predictive validity of tools for outpatient screening are warranted, especially since care is shifting to this setting.

The tool which appeared to have the broadest coverage was the CASCO [17]. It is the only tool which screens for cachexia, but also picks up many of the variables required for a diagnosis of malnutrition. However, assessment of muscle mass or function (required for sarcopenia) is not included. One previous review showed that 20 screening tools appeared relevant for starvation, but none contained all the currently accepted components needed to screen for sarcopenia and cachexia risk [53]. Our study supports this.

Outlook and recommendations for future tools

A screening tool needs to be developed that encompasses the criteria to pick up all three possible syndromes. This concept is supported by the notion that, in the human being, there may be no "pure" phenotype of cachexia, as it is usually associated with reduced food intake (potential for malnutrition) and increasing age (increasing sarcopenia) [55]. There is also currently a lack of agreement as to the diagnostic criteria of each syndrome and the relative importance of body composition analysis and the nature of depleted tissue within each definition. We hypothesised that the overlap between syndromes could be illustrated as in **figure 2** along with the identified best performing tools for each aspect.

There are clearly many existing validated screening tools (at least for malnutrition). It is unlikely that any further novel tools will be devised without breakthroughs in biomarker

development. We therefore suggest that the ideal composite tool incorporate a stepwise assessment of nutritional status; oral intake; disease status; patient age; muscle mass/function; and metabolic derangement. The presence of underlying disease is a key question in order to stratify the syndromes. Suggested components for use in creating a new tool are depicted in **table 8**.

By screening for all three syndromes, it will allow for a more targeted intervention. Screening for cachexia, sarcopenia or malnutrition is not warranted unless it is accompanied by an intervening care plan. It would be expected that an adequate intervention would prevent any further decline in health status and therefore lead to a positive effect on disease outcome.

Most studies did not comment on intervention, which depending on the balance of the three syndromes may need to include varying attention to nutrition, exercise and measures to combat inflammation.

Strengths, limitations and assessment of bias

One of the strengths of this review is that it provides a complete overview of tools that have been validated for cachexia, sarcopenia and malnutrition. We did not describe reliability, repeatability or other clinical outcome measures in any great detail. The review used the consensus definitions of each syndrome, we are aware however that many other definitions exist. However, there were a number of study limitations. There was a risk of bias when assessing each tool for their predictive validity. Studies may have been biased if they did not adjust for factors such as cancer stage or disease severity. As clinical outcome is affected by more than just nutritional status alone adjusting for these variables is important. Nutritional intervention is likely to improve outcomes for malnutrition but potentially not for age-related sarcopenia or established cachexia. Only one study discussed whether they did this. There is no agreed ‘gold standard’ tool and therefore we chose cross sectional imaging and the SGA

and MNA based on the results of previous studies [13]. Tools that were compared to potentially less valid standards were also included to allow a wider analysis. Full nutrition assessments were different in each study ranging from anthropometric to biochemical measures and full assessment by a medical professional. Conclusions from this study were based upon the original papers in which there may have been varying definitions with regards to the subject group, syndrome or assessment undertaken. Another potential limitation is that we excluded modified versions of pre-existing tools. They were excluded as reliability and validity data would only relate to the modified tool and it was therefore difficult to assess improvements from the original. It is possible that these tools were being improved or evaluated more thoroughly.

Conclusion

We have highlighted that many practitioners who regularly come into contact with patients suffering from weight loss are not able to easily screen between the conditions of cachexia, sarcopenia and malnutrition as there is no one validated tool which can be implemented for the assessment of all three conditions. The adaptation of existing screening tools incorporating all relevant criteria described in this review would be optimal for diagnosis and to direct the content of complex interventions.

Acknowledgements

Conflict of interest

The authors declare no conflicts of interest.

Authors contributions

347 MJ and LW designed the project. JM and UN conducted the review. JM and LW wrote the
348 manuscript. RJES, DC and MJ critically appraised the manuscript. MJ and RJES had overall
349 responsibility for the final content.
350

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Tables

Table 1 Inclusion criteria

Types of participants Adults (>18 years) undergoing routine screening for cachexia, sarcopenia, or malnutrition	Includes patients with advanced cancer, end stage cardiac, renal and liver disease
Types of tools Validated, quantitative measurements of cachexia, sarcopenia or malnutrition	Tools developed for clinical or research purposes. Completed by health care professionals
Psychometric evaluation	**Demonstration of at least 2 criteria:**
Content Validity	Breadth of scope of tool; to what extent does it appear to capture the relevant aspects of unintentional weight loss; are there gaps?
Construct validity, including convergent validity, discriminant validity	How well the tool relates to other measures of the same construct; lack of correlation with dissimilar or unrelated constructs or variables
Test-retest reliability	How consistent an individual's scores are over a defined time-period presuming weight stays constant
Internal consistency	How closely related are the different items in the tool?
Responsiveness	Ability to detect clinically meaningful change for individuals
Factor analysis	For a tool comprising several items, a way of grouping them into factors which may tap into a particular construct

Criterion validity	A shortened version of a scale, concurrent validity with the longer version which has been validated

Table 2 Summary of proposed diagnostic criteria for identification of cachexia, sarcopenia and malnutrition

Syndrome	**Diagnostic criteria**
Cachexia	Weight loss greater than 5%, or weight loss greater than 2% in individuals already showing depletion according to current bodyweight and height (body-mass index [BMI] <20 kg/m^2) or skeletal muscle mass (sarcopenia) [3]
Sarcopenia	Loss of function – 6-minute walk < 400m OR gait speed <1.0m/s Muscle mass – low appendicular lean mass/height [2] (2 standard deviations below the mean diagnostic on DXA) [1,2]
Malnutrition	Protein/energy deficiency - risk indicated by low BMI <18.5 kg/m^2 OR weight loss >10% (indefinite time)/5% over last 3 months AND BMI <20 (if <70 years)/ <22 (if>70 years) or FFMI < 15 and 17 kg/m^2 in men and women respectively [4]

BMI (Body Mass Index) DXA (Dual-energy –ray absorptiometry) FFMI (Fat-free mass index)

Table 3 Critical appraisal of tools to measure unintentional weight loss

	Author	Tool	Description	Validation population	Validation reference	Strengths	Limitations
Sarcopenia	Woo et al, 2014 (15)	SARC-F	A questionnaire regarding ability to carry a heavy load, walking, rising from a chair, climbing stairs and falls frequency	Community dwelling Chinese (n=4000)	3 consensus definitions of sarcopenia	Not dependent on cut off values	No assessment of muscle mass, not validated in hospital populations
	Miller et al, 2009 (16)	SPSM	Portable measure that combines estimates of muscle quantity and function into a single scale	Community dwelling African Americans (n=998)	DXA	Portable	Time consuming, equipment dependent, muscle mass not measured
Cachexia	Argiles et al, 2017 (17)	CASCO	Score to classify cachectic patients into three different groups. Includes five components: body weight loss & composition, inflammation/metabolic disturbances/immunosuppression, physical performance, anorexia and quality of life	Cancer patients (n=186)	Assessment by oncologist	Encompasses all diagnostic criteria	Involves many questions and measurements, does not include questions on disease state
Malnutrition	Weekes et al, 2004 (18)	BAPEN	Tool based on four nutritional parameters (weight, height, recent unintentional weight loss and appetite)	Acute medical and elderly care wards (n=100)	Dietician	Quick and easy	Percentage weight loss not quantified
	Mimiram et al, 2011 (19)	BNST	Score based on UWL, unintentional eating loss and being unable to eat for >5 days	Medical and surgical (n=446)	Dietician	Easily completed by nursing staff	Low importance given to amount of weight loss
	Laporte et al, 2015 (20)	CNST	Tool containing two items: Weight loss and decreased food intake	Medical and surgical (n=150)	SGA	Very brief, can be completed by non-trained rater	Assessed on admission only. Validity of re-screening unknown
	Ignacio et al, 2005 (21)	CONUT	Evaluates nutrition using albumin, cholesterol and lymphocyte count. Automated system	Medical and surgical inpatients (n=53)	SGA	Simple, automated	Markers vary depending on disease state, only done on patients who have bloods taken
	Guerra et al, 2017 (22)	EDC	Screening tool based on ESPEN criteria for diagnosis malnutrition	Medical and surgical inpatients (n=632)	PG-SGA	Includes FFM assessment	Very low sensitivity
	Abd-El-Gawad et al, 2014 (23)	GNRI	Modified nutritional risk index for geriatric patients (based on albumin, current and previous weight)	Acute geriatrics ward (n=131)	MNA	Good prognosticator, does not require capacity	Diseases associated with high mortality or hypoalbuminaemia excluded

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	Tammam et al, 2009 (24)	INSYST	Two-tiered tool – first is a simple pre-screen aiming to establish if malnourished, second provides a more detailed evaluation	Medical, surgical and oncological inpatients (n=61)	MUST and MNA	Doesn't require height and BMI, quick and easy	Ease of completing dependent on patient's cognitive state
	Ferguson et al, 1999 (25) Isenring et al, 2006 (26) Neelemaat et al, 2011 (27) Nursal et al, 2005 (28) Young et al, 2013 (29) Wu et al, 2012 (30) Bhuachalla et al, 2018 (31) Leipold et al, 2018 (32)	MST	Two questions regarding appetite and unintentional weight loss	Medical and surgical inpatients (n=408) Oncology outpatients (n=51) Acute hospitalised (n=193) Medical and surgical inpatients (n=2211) Elderly medical inpatients (n=134) Elderly inpatients (n=157) Oncology patients (n=725) Rehabilitation patients (n=160)	SGA PG-SGA Malnutrition definition CT	Very quick, does not require calculations	Non-specific
	Kim et al, 2011 (33)	MSTC	Tool based on intake change, weight loss, ECOG performance status and BMI	Oncology inpatients (n=1057)	PG-SGA	Cancer specific	Designed to be performed by dieticians, not nurses
	Boleo-Tome et al, 2012 (34) Leistra et al, 2013 (35) Sharma et al, 2017 (36) Neelemaat et al, 2011 (27) Kyle et al, 2006 (37) Young et al, 2013 (29) Almedia et al, 2012 (38) Velasco et al, 2011 (39) Bhuachalla et al, 2018 (31)	MUST	Five step tool including BMI, unplanned weight loss and presence of acute disease	Oncology inpatients (n=450) Medical and surgical outpatients (n=2236) Acute medical inpatients (n=132) Elderly inpatients (n=198) Medical and surgical (n=995) Medical inpatients (n=134) Surgical inpatients (n=300) Medical and surgical (n=400) Oncology patients (n=725)	PG-SGA Malnutrition definition CT	Quick, easy	Does not pick up patients with normal BMI who are malnourished, UWL reported by patients is subjective
	Prasad et al, 2012 (40) Faramarzi et al, 2013 (401) Bhuachalla et al, 2018 (31)	NRI	Derived from serum albumin concentration and ratio of usual to present weight	Peritoneal dialysis patients (n=283) Colorectal cancer (n=52) Oncology patients (n=725)	SGA CT	Assesses dialysis patients at risk	Relies on previous weight – limited use with changes in fluid status
	Neelemaat et al, 2011 (27) Kyle et al, 2006 (37) Young et al, 2013 (29) Almedia et al, 2012 (38) Bauer et al, 2005 (42) Velasco et al, 2011 (39)	NRS-2002	Tool containing nutritional components of the MUST along with disease severity	Elderly inpatients (n=198) Medical and surgical (n=995) Elderly medical patients (n=134) Surgical inpatients (n=300) Acute geriatrics ward (n=121) Medical and surgical (n=400)	Definition of malnutrition SGA	Includes disease severity therefore applicable in ITU	Ease of completing dependent on patient's cognitive state
	Soederhamn et al, 2002 (43)	NUFFE	Three-point ordinal scale with 15 items assessing weight loss, dietary history, appetite and general activity	Elderly care rehab ward (n=114)	MNA	Simple as lacks anthropometric measurements	Many confounding factors in questionnaire

	Duerksen et al, 2000 (44) Cooper et al, 2002(45) Moriana et al, 2014 (46)	SGA	Assessment of nutritional status based on history and examination	Acute elderly care and elderly rehab (n=95) End stage renal disease (n=76) Medical and surgical inpatients (n=197)	Geriatric and internal medicine resident, Total body Nitrogen, Anthropometric and biochemical data	Current gold standard	Reproducibility less than in non-elderly, unable to predict severe malnutrition in ESRD, requires experienced operator to carry out
	Kruizenga et al, 2005(47) Leistra et al, 2013 (35) Harada et al, 2017 (48) Neelemaat et al, 2011 (27) Young et al, 2013 (29)	SNAQ	26 questions related to eating and drinking difficulties, defecation, condition and pain	Medical, surgical and oncological inpatients (n=291) Medical and surgical outpatients (n=2236) Oncology outpatients undergoing chemotherapy (n=300) Medical and surgical inpatients (n=2211) Elderly medical inpatients (n=134)	Malnutrition criteria, CONUT	Corresponds to ESPEN criteria	High NPV, no outcome data
	Susetyowati et al, 2014 (49)	SNST	Six questions including weight loss, appetite and health status	Medical and surgical inpatients (n=495)	SGA	Can be done by non-trained staff	No anthropometric assessment, all subjective
	Wong et al, 2011(50)	Spinal NST	Tool which assesses eight criteria including appetite, weight loss and level of spinal cord injury	Spinal cord injury patients (n=150)	Dietetic assessment	Disease specific	Requires specialised scales to measure paralysed patients
	Xia et al, 2016 (51)	R-NST	Nine questions assessing malnutrition risk/symptoms combined with albumin, CRP and urea	Renal inpatients (n=122)	SGA	Renal specific	Patients picked up for conditions other than malnutrition e.g. hyperkalaemia
	Lim et al, 2009 (52)	3-MinNS	Questionnaire based on diagnostic criteria for malnutrition and muscle wastage	Medical and surgical inpatients (n=818)	SGA	Quick and easy	Dependent on cognitive state

SPSM (Short Portable Sarcopenia Measure), CASCO (Cachexia Score), BAPEN (British Association for Parenteral and Enteral Nutrition, BNST (British Nutrition Screening Tool), CNST (Canadian Nutrition Screening Tool), CONUT (Controlling Nutritional Status), EDC (ESPEN Diagnostic Criteria for Malnutrition), GNRI (Geriatric Nutrition Risk Index), INSYST (Imperial Nutritional Screening System), MST (Malnutrition Screening Tool), MSTC (Malnutrition Screening Tool for Cancer), NRI (Nutritional Risk Index), NRS-2002 (Nutritional Risk Screening), NUFFE (Nutritional Form For the Elderly), SGA (Subjective Global Assessment), SNAQ (Short Nutritional Assessment Questionnaire), Spinal NST (Spinal Nutritional Screening Tool) R-NST (Renal Nutritional Screening Tool), 3-MinNS (3 Minute Nutrition Screening)

Table 4 Psychometric evaluation of tools to measure unintentional weight loss

	Scale	Environment	Context (OP/IP)	Face validity	Content validity	Factor analysis	Construct validity	Discriminant validity	Predictive validity	Test-retest	Internal consistency	Responsiveness	Acceptability	Time to complete
Sarcopenia	SARC-F	Community dwelling	Outpatients	◆	-	-	◆	-	◆	-	◆	-	◆	-
	SPSM	Community dwelling	Outpatients	-	-	◆	X	◆	◆	◆	◆	◆	-	◆
Cachexia	CASCO	Oncology	Outpatients	◆	◆	◆	◆	◆	-	-	◆	◆	-	-
Malnutrition	BAPEN	Acute medical and elderly care	Inpatients	◆	-	-	◆	-	-	◆	-	◆	◆	◆
	BNST	Spinal cord injuries	Inpatients	◆	-	◆	-	-	-	◆	-	-	-	-
	CNST	Medical and surgical	Inpatients	◆	-	-	◆	-	◆	◆	-	-	-	-
	CONUT	Medical and surgical	Inpatients	◆	-	X	◆	-	-	-	-	◆	◆	-
	EDC	Medical and surgical	Inpatients	◆	-	-	-	-	◆	-	◆	-	-	-
	GNRI	Acute geriatrics	Outpatients	◆	-	◆	-	-	◆	-	-	-	◆	-
	INSYST	Medical, surgical and oncology	Inpatients	◆	◆	-	◆	-	-	◆	-	◆	◆	◆
	MST	Medical, surgical and oncology	Inpatients Outpatients	◆	◆	◆	◆	-	◆	◆	◆	-	◆	-
	MSTC	Oncology	Inpatients	◆	X	◆	◆		-	-	-	-	X	◆
	MUST	Medical, surgical and oncology	Inpatients Outpatients	◆	◆	X	◆	- -	◆	-	-	◆	◆	◆
	NRI	Peritoneal dialysis and	Inpatients	-	-	◆	-	-	◆	-	-	-	◆	-

		colorectal cancer												
	NRS-2002	Elderly, medical and surgical	Inpatients	◆	◆	-	◆	-	◆	◆	-	◆	◆	◆
	NUFFE	Elderly care rehab	Inpatients Outpatients	◆	◆	◆	◆	-	◆	◆	◆	-	-	-
	R-NST	Renal	Inpatients	◆	◆	◆	◆	-	-	-	-	-	X	◆
	SGA	Elderly, renal, medical and surgical	Inpatients	◆	◆	◆	◆	-	◆	◆	◆	-	-	-
	SNAQ	Medical, surgical and oncology	Inpatients Outpatients	◆	◆	-	◆	◆	◆	◆	-	◆	◆	◆
	SNST	Medical and surgical	Inpatients	◆	-	◆	-	◆	◆	◆	◆	◆	◆	◆
	Spinal NST	Spinal cord injuries	Inpatients	◆	-	◆	-	-	-	◆	-	-	◆	◆
	3-MinNS	Medical and surgical	Inpatients	◆	◆	-	◆	◆	◆	◆	-	◆	◆	◆

◆ = tool assessed for and found to be valid X = tool assessed for and found not to be valid - = tool not assessed for/not enough information provided

SPSM (Short Portable Sarcopenia Measure), CASCO (Cachexia Score), BAPEN (British Association for Parenteral and Enteral Nutrition, BNST (British Nutrition Screening Tool), CNST (Canadian Nutrition Screening Tool), CONUT (Controlling Nutritional Status), EDC (ESPEN Diagnostic Criteria for Malnutrition), GNRI (Geriatric Nutrition Risk Index), INSYST (Imperial Nutritional Screening System), MST (Malnutrition Screening Tool), MSTC (Malnutrition

Screening Tool for Cancer), NRI (Nutritional Risk Index), NRS-2002 (Nutritional Risk Screening), NUFFE (Nutritional Form For the Elderly), SGA (Subjective Global Assessment), SNAQ (Short Nutritional Assessment Questionnaire), Spinal NST (Spinal Nutritional Screening Tool) R-NST (Renal Nutritional Screening Tool), 3-MinNS (3 Minute Nutrition Screening)

Table 5 Domains assessed by tools to measure relevant parameters required to identify risks of malnutrition, sarcopenia and cachexia [adapted from 51]

		Patient reported weight loss						BMI & FFM measurements		Nutritional intake				Assessment of muscle mass and function		Disease state		Measures of metabolic derangement				Quality of life
Disease	Screening tool	Weight loss quantified within specified time frame	Weight loss quantified without timeframe	Weight loss unquantified with time frame	Weight loss unquantified, without time frame	UWL specified	Muscle mass	BMI	FFMI	Loss of appetite	Poor dietary intake/ intake decline	Supplemental feeding in use?	Symptoms that would prevent eating e.g. vomiting, ulcers	Physical performance	Muscle strength	Presence of illness	Fatigue	Increased inflammatory markers	Anaemia	Low serum albumin	Other blood Tests e.g. glucose/urea	QOL
Sarcopenia	SARC-F	X	X	X	X	X	X	X	X	X	X	X	X	✓	✓	X	X	X	X	X	X	X
	SPSM	X	X	X	X	X	X	✓	✓	X	X	X	X	✓	✓	X	X	X	X	X	X	X
Cachexia	CASCO	X	✓	X	X	✓	X	X	✓	✓	✓	X	X	✓	X	X	✓	✓	✓	✓	✓	✓
Malnutrition	BAPEN	X	X	X	✓	✓	X	✓	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	BNST	X	X	X	✓	✓	X	✓	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	CNST	X	X	✓	X	✓	X	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	CONUT	X	X	X	X	X	X	✓	X	X	X	X	X	X	X	X	✓	X	X	✓	✓	X
	EDC	X	X	✓	✓	X	X	✓	✓	X	✓	X	X	X	X	X	X	X	X	X	X	X
	GNRI	X	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	✓	X	X	✓	X	X
	INSYST	✓	X	✓	X	✓	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X	X
	MST	X	X	X	X	✓	X	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	MSTC	X	X	X	✓	✓	X	✓	X	X	✓	X	X	X	✓	X	✓	X	X	X	X	X
	MUST	✓	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	NRI	X	X	✓	✓	x	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	NRS-2002	X	X	X	X	✓	X	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	NUFFE	X	X	X	✓	X	X	X	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	R-NST	✓	X	X	X	✓	X	X	X	✓	✓	X	X	X	✓	X	X	X	X	X	X	X
	SGA	✓	X	X	X	✓	X	✓	X	✓	✓	✓	✓	X	X	X	X	X	X	X	X	X
	SNAQ	X	X	X	✓	✓	X	X	X	X	✓	X	X	X	X	X	✓	X	X	X	X	X
	SNST	X	X	✓	X	✓	X	✓	X	✓	✓	X	X	X	X	X	✓	X	X	X	X	X
	SpinalNST	✓	X	X	X	✓	X	✓	X	X	✓	X	X	X	X	X	X	X	X	X	X	X
	3-MinNS		X	X	X		X		X													

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Table 6 Sensitivity, specificity, predictive values, and reproducibility of the studies included

Author	Screening tool	Sensitivity	Specificity	PPV	NPV	Agreement
Woo et al, 2014 (15)	SARC-F	3.8-9.9	94.2-99.1	8.4-54.8	78.4-94.9	0.78-0.90
Miller et al, 2009 (16)	SPSM	-	-	-	-	-
Argiles et al, 2017 (17)	CASCO	-	-	-	-	-
Weekes et al, 2004 (18)	BAPEN	-	-	-	-	0.77
Mirmiram et al, 2011 (19)	BNST	86.7	61.7	79.1	73.1	0.74
Laporte et al, 2015 (20)	CNST	72.6	85.1	81.2	77.0	0.88
Ignacio et al, 2005 (21)	CONUT	92.3	85	-	-	0.488
Guerra et al, 2017 (22)	EDC	17.1	98.3	89.1	58.9	0.803
Abd-El-Gawad et al, 2014 (23)	GNRI	83.1	51.2	78.95	58.33	0.713
Tammam et al, 2009 (24)	NSYST	95-100	65-83	-	-	0.73
Kim et al, 2011 (31)	MST	93	93	98.4	72.7	0.7
Ferguson et al, 1999 (25)		100	92	80	100	0.83
Isenring et al, 2006 (26)		67	86	-	-	0.53
Neelemaat et al, 2011 (27)		49	86	-	-	0.33
Nursal et al, 2005 (28)		73	55	-	-	0.28
Young et al, 2013 (29)		73	70	-	-	-
Wu et al, 2012 (30)		39	93	-	-	0.21
Bhuachalla et al, 2018 (31)		39.4-100	47-74.6	-	-	0.71
Leipold et al, 2018 (32)		72.2	83.8	69.6	85.4	-
Kim et al, 2011 (33)	MSTC	94	84.2	67.8	97.6	0.70
Boleotome et al, 2012 (34)	MUST	80	89	100	100	-
Leistra et al, 2013 (35)		75	94	43	98	-
Sharma et al, 2017 (36)		69.7	75.8	75.4	70.1	0.49
Neelemaat et al, 2011 (27)		96	80	-	-	-
Kyle et al, 2006 (37)		61	79	-	-	-
Young et al, 2013 (29)		87	86	-	-	-
Almedia et al, 2012 (38)		85	93	-	-	-
Velasco et al, 2011 (39)		72	90	-	-	-

Bhuachalla et al, 2018 (31)		20.8-72.8	48-98.3	-	-	0.816
Prasad et al, 2012 (40)	NRI	92.9	32.39	80.41	60.53	0.63
Faramarzi et al, 2013 (41)		66	60	64	62	0.267
Bhuachalla et al, 2018 (31)		21.2-95	21.2-92.1	-	-	-
Neelemaat et al, 2011 (27)	NRS-2002	92	85	-	-	-
Kyle et al, 2006 (37)		62	93	-	-	-
Young et al, 2013 (29)		90	83	-	-	-
Almeida et al, 2012 (38)		80	89	-	-	-
Bauer et al, 2005 (42)		70	85	-	-	-
Velasco et al, 2011 (39)		74	87	-	-	-
Soederhamn et al, 2002 (43)	NUFFE	71	86	-	-	-
Xia et al, 2016 (51)	R-NST	97.3	74.4	88.0	93.6	0.95
Duerksen et al, 2000 (44)	SGA	-	-	-	-	-
Cooper et al, 2002 (45)		59-68	61-65	41-42	70-83	0.6
Moriana et al, 2014 (46)		-	-	-	-	-
Kruizenga et al, 2005 (47)	SNAQ	79	83	70	89	-
Leistra et al, 2013 (35)		43	99	78	96	-
Harada et al, 2017 (48)		43	99	-	-	-
Neelemaat et al, 2011 (27)		75	84	-	-	-
Young et al, 2013 (29)		79	90	-	-	-
Susetyowati et al, 2014 (49)	SNST	97	80	78	92	-
Wong et al, 2011 (50)	Spinal NST	85.7	76.1	62	92	0.57
Lim et al, 2009 (52)	3-MinNS	86	83	67	94	-

SPSM (Short Portable Sarcopenia Measure), CASCO (Cachexia Score), BAPEN (British Association for Parenteral and Enteral Nutrition, BNST (British Nutrition Screening Tool), CNST (Canadian Nutrition Screening Tool), CONUT (Controlling Nutritional Status), EDC (ESPEN Diagnostic Criteria for Malnutrition), GNRI (Geriatric Nutrition Risk Index), INSYST (Imperial Nutritional Screening System), MST (Malnutrition Screening Tool), MSTC (Malnutrition Screening Tool for Cancer), NRI (Nutritional Risk Index), NNP (Negative predictive value) NRS-2002 (Nutritional Risk Screening), NUFFE (Nutritional Form For the Elderly), PPV (Positive predictive value) SGA (Subjective Global Assessment), SNAQ (Short Nutritional Assessment Questionnaire), Spinal NST (Spinal Nutritional Screening Tool) R-NST (Renal Nutritional Screening Tool), 3-MinNS (3 Minute Nutrition Screening)

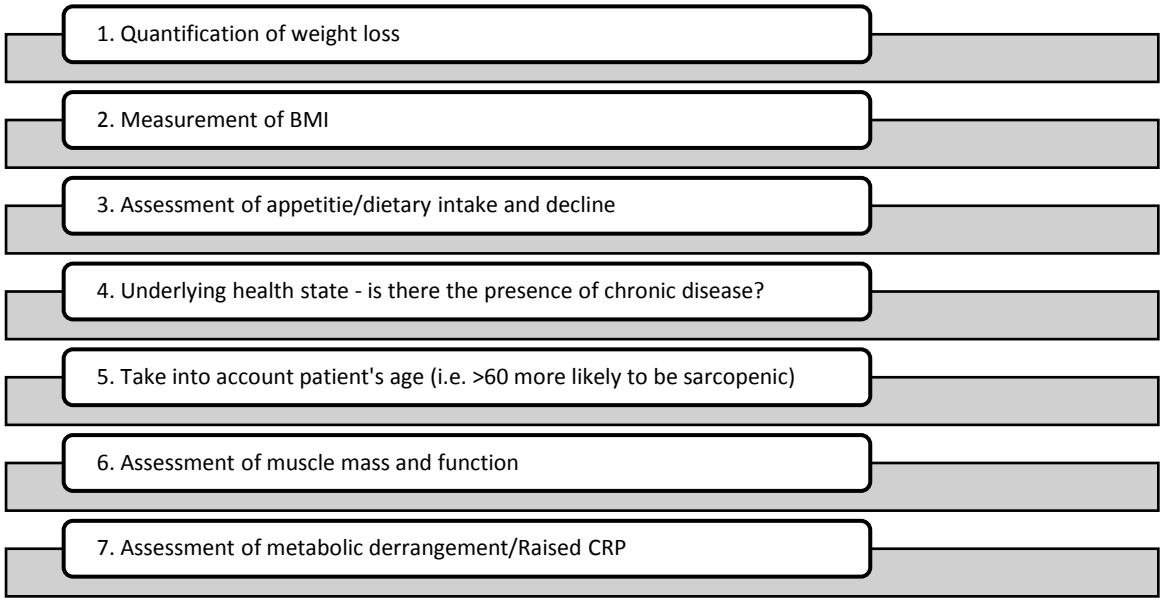
Table 7 Newcastle-Ottawa scale adapted for cross-sectional studies

	Woo et al, 2014	Miller et al, 2009	Argiles et al, 2017	Weekes et al, 2004	Mirmiram et al, 2011	Laporte et al, 2015	Ignacio et al, 2005	Guerra et al, 2017	Abd-El-Gawad et al, 2014	Tammam et al, 2009	Ferguson et al, 1999	Isenring et al, 2006	Neelemaat etal, 2011	Nursal et al, 2005	Young et al, 2013	Bhuachalla et al, 2018	Leiopold et al, 2018	Wu et al, 2012	Kim et al, 2011	Boleo-Tome et al, 2012	Leistra et al, 2013	Sharma et al, 2017	Kyle et al, 2006	Almedia et al, 2012	Velasco et al, 2011	Prasad et al, 2012	Faramarzi et al, 2013	Bauer et al, 2005	Soederhamn et al, 2002	Duerksen et al, 2000	Cooper et al, 2002	Moriana et al, 2014	Kruizenga et al, 2005	Harada et al, 2017	Susetyowati et al, 2014	Wong et al, 2011	Xia et al, 2016	Lim et al, 2009
Selection (max 5 stars)																																					
1.Representativeness of the sample 2. Sample size justified 3. Response rate satisfactory 4. Ascertainment of exposure (validated measurement tool used)	* * * *	* * * *	* * * *	* * * *	* * * *	* * * *	* * * * *	* * * * *	* * * *	* * * * *	* * * * *	* * * * *	* * * *	* * * * * *	* * * * *	* * * * *	* * * * * *	* * * * *	* * * * *	* * * * *	* * * *	* * * * *	* * * * * *	* * * * * *	* * * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * *	* * * * * *	* * * * * *	* * * * *	* * * * *	* * * *	* * * *	* * * * *	* * * * *
Comparability (max 2 stars)																																					
1.The study controls for disease severity 2. Study controls for other confounding factors	* * *	* * *	*					*	* * *										*				*							*								
Outcome (max 3 stars)																																					
1. Assessment of outcome 2. Appropriate statistical test described	* * *	*	*	*	* * * *	* * * *	* * * *	*	*	* * * *	* * * *	* * * *	*	*	*	** * *	*	* * * *	*	*	*	* * * *	*	*	*	*	*	*	*	* * * *	* * * *	*	*	*	*	*	*

Total (Out of 10)	7	6	5	5	6	6	6	5	6	6	6	6	4	5	4	7	4	7	5	4	4	6	6	5	6	5	4	5	5	7	7	6	4	6	6	4	5	5

*= Assessed in study and found to be present
Score <5 = high risk of bias

Table 8 **Suggested components for use in creating a new screening tool**



Figures

Figure 1 PRISMA flow diagram [12]

Figure 2 Diagram to show overlap between cachexia, sarcopenia and malnutrition

Legend figure 2: The sizes of the circles represent the perceived sizes of each clinical problem