# **BMJ Open** Malnutrition assessment methods in adult patients with tuberculosis: a systematic review

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# ABSTRACT

**To cite:** ter Beek L, Bolhuis MS, Jager-Wittenaar H, *et al.* Malnutrition assessment methods in adult patients with tuberculosis: a systematic review. *BMJ Open* 2021;**11**:e049777. doi:10.1136/ bmjopen-2021-049777

Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/ bmjopen-2021-049777).

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Received 04 February 2021 Accepted 19 November 2021

ObjectivesMalnutrition is associated with a twofold<br/>higher risk of dying in patients with tuberculosis (TB) and<br/>considered an important potentially reversible risk factor<br/>for failure of TB treatment. The construct of malnutrition<br/>has three domains: intake or uptake of nutrition; body<br/>composition and physical and cognitive function. The<br/>objectives of this systematic review are to identify<br/>malnutrition assessment methods, and to quantify how<br/>malnutrition assessment methods capture the international<br/>consensus definition for malnutrition, in patients with TB.DesignDifferent assessment methods were identified. We<br/>determined the extent of capturing of the three domains<br/>of malnutrition, that is, intake or uptake of nutrition, body<br/>composition and physical and cognitive function.

**Results** Seventeen malnutrition assessment methods were identified in 69 included studies. In 53/69 (77%) of studies, body mass index was used as the only malnutrition assessment method. Three out of 69 studies (4%) used a method that captured all three domains of malnutrition.

**Conclusions** Our study focused on published articles. Implementation of new criteria takes time, which may take longer than the period covered by this review. Most patients with TB are assessed for only one aspect of the conceptual definition of malnutrition. The use of international consensus criteria is recommended to establish uniform diagnostics and treatment of malnutrition.

PROSPERO registration number CRD42019122832.

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# BACKGROUND

In 2019, tuberculosis (TB) was the worldwide leading cause of death from a single infectious agent, with 10 million new patients, and 1.2 million deaths.<sup>1</sup> TB prevalence is up to 20 times higher among people living in lowincome countries compared with high-income countries.<sup>2</sup> TB, poverty and malnutrition are closely linked. Prevalence of malnutrition in patients with TB is studied to be 50% to 57%, and malnutrition is associated with a twofold risk of dying.<sup>3–9</sup>

# Strengths and limitations of this study

- PubMed, CINAHL and EMBASE were systematically searched for studies in the last decade, to prevent older studies describing outdated supportive care strategies to be eligible for inclusion.
- As there is no instrument for 'risk of bias assessment' of studies on diagnosis (eg, malnutrition assessment), we evaluated risk of bias by scoring the presence of essential components required for adequate assessment and reporting of malnutrition.
- To report on how malnutrition was assessed in studies on tuberculosis (TB), we quantified how malnutrition assessment methods capture the international consensus definition for malnutrition, in patients with TB.
- Implementation of new criteria in study protocols takes time. This implementation might take longer than the time period used in this review.

As hunger-related malnutrition caused by food-insecurity impacts the immune system,<sup>11011</sup> malnutrition is an important risk factor for re-activation of TB, with a reported 27% attributable risk.<sup>112</sup> Malnutrition is considered an important, potentially reversible risk factor for treatment failure.<sup>13</sup> Therefore, a better understanding in assessing malnutrition in patients with TB is urgently needed.<sup>14</sup>

The European Society for Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as 'a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease'.<sup>10</sup> In patients with TB, two types of malnutrition may coexist: malnutrition without disease<sup>10</sup>; and disease-related malnutrition once active disease has developed. The latter is often driven by a combination of loss of appetite, malabsorption and/ or inflammation-driven catabolism.<sup>10 11</sup> A low

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body mass index (BMI) is a characteristic for chronic malnutrition.<sup>15</sup> However, since malnutrition leads to loss of fat-free mass in all individuals, including those who are overweight or obese, patients with either a normal or high BMI may be malnourished as well.<sup>10</sup> In 2015, ESPEN published their first consensus on diagnostic criteria for malnutrition,<sup>15</sup> followed by the Global Leadership Initiative on Malnutrition (GLIM) criteria in 2018, which were established by ESPEN, the American Society for Parenteral and Enteral Nutrition, la Federación Latino Americano de Terapia Nutriconal, Nutricion Clinica y Metabolismo and the Parenteral and Enteral Nutrition Society of Asia.<sup>16</sup>

It was not until 2013 that the WHO presented their first guideline on nutritional care and support for patients with TB. In this guideline, the WHO stressed that all patients with active TB receive individualised nutritional assessment and management, including dietary counselling and nutritional interventions, to improve nutritional status and consequently, prevent TB treatment failure.<sup>17</sup> Nutritional assessment is a necessary step in the 'nutritional care process', enabling the professional to design a treatment plan together with the patient.<sup>18</sup> However, the 2013 WHO guideline only refers to BMI as a method of assessing malnutrition for adults. The important issue of lack of consistency and understanding of how malnutrition can be assessed in patients with TB results from, the complexity of TB being on the one hand strongly associated with malnutrition and on the other by the vertical and siloed nature of TB programmes.

The primary aim of this review is to identify malnutrition assessment methods that are used in adult patients with TB. The secondary aim is to quantify how malnutrition assessment methods capture the international consensus definition for malnutrition in this population.

#### **METHODS**

The protocol for this review was registered at PROSPERO with number CRD42019122832. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used.<sup>19</sup>

#### Search strategy

In September 2020, PubMed, CINAHL and EMBASE were systematically searched for studies in any language. The search term consisted of a domain describing 'malnutrition' and a domain describing 'tuberculosis', while excluding in vitro, animal and paediatric studies. Details of the search strategy can be found in online supplemental material 1.

# Inclusion and exclusion criteria

Studies in the English language that aimed to assess malnutrition and described a method for assessment of malnutrition in patients with microbiologically confirmed or clinically diagnosed TB, published between 1 January 2009 and 18 September 2020 were considered eligible for inclusion. Since the aim of the review is to identify how malnutrition is assessed in current research, 2009 was chosen as a starting point. Restricting the search to the last decade will prevent older studies describing outdated supportive care strategies to be eligible for inclusion.

Only studies that focused on adult patients with TB were included, because the assessment of malnutrition in children requires different methods than in adults as children are growing, and the criteria for measuring their nutritional status differ per by age.<sup>20</sup>

Reviews and study protocols were excluded since they do not present original data. Case reports and abstracts/ posters were also excluded since the information provided on methods used in this type of publication is considered too limited.

#### **Study selection**

Screening of title and abstract was done independently by two authors using the Rayyan web application.<sup>21</sup> Evaluation of the screening of the first 10 articles was used to define the criteria that determine which studies were eligible for final inclusion. Final inclusion was based on an independent judgement of the full text of both authors. Disagreements about inclusion were resolved through discussion and if consensus was not reached, a third author was consulted, which resulted in consensus in all cases.

#### Patient and public involvement

No patient involved

# **Data collection**

Data collection was performed by two authors independently. The following characteristics were extracted from each study: citation, first author, country, years of publication and data collection, aim of the malnutrition assessment, number of included patients, number of HIV coinfected patients, disease location, drug susceptibility of the *Mycobacterium tuberculosis* isolate.

### **Data analysis**

To report on how malnutrition was assessed in studies on TB, we determined the extent of capturing of the three domains of malnutrition, malnutrition included in the ESPEN conceptual definition of malnutrition, that is, intake or uptake of nutrition (Domain A), body composition (Domain B), and physical and cognitive function (Domain C).<sup>10 22 23</sup>

Domain A was considered to be covered to some extent (+) if the method addressed nutritional intake or uptake at all. It was considered to be covered extensively (++) if the method addressed nutritional intake or uptake in depth. For domain B, weight change, BMI and anthropometric measurements, such as skinfold measurements were considered covering domain B to some extent (+). It was considered extensively addressed (++) if the method

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included identification of muscle mass, lean mass or fatfree mass. Domain C was considered to be covered to some extent (+) if functionality was addressed. Domain C was considered extensively covered (++) if physical (eg, handgrip strength), mental and cognitive function tests were performed, or questions about activities of daily living were addressed.

As micronutrient or trace elements in serum are not representative for intake or uptake of protein or energy,<sup>10</sup> laboratory tests were not considered to attribute to any of the malnutrition domains. Serum albumin and C reactive protein are parameters for inflammation but are not related to parameters of protein/energy intake or functionality, nor do they represent body composition and were therefore not taken into consideration. In addition, while prealbumin (ie, transthyretin) is sensitive for changes in protein and energy intake, this marker is influenced by inflammation activity.<sup>10</sup>

As there is no instrument for 'risk of bias assessment' of studies on diagnosis (eg, malnutrition assessment), we evaluated risk of bias by scoring the presence of essential components required for adequate assessment and reporting of malnutrition. The risk of bias in included studies was assessed by rating the following four characteristics:

- Rationale for the assessment of malnutrition.
- ► Malnutrition was assessed and clear cut-off points were described in the method section. For example: 'malnutrition was assessed as BMI <18.5 kg/m<sup>2</sup>.
- ► Malnutrition was reported in the results section.
- ► The results with regard to malnutrition were reflected on in the discussion section.

The characteristics were graded for quality of the study. Risk of bias was rated by - (meaning high risk of bias), + (medium risk of bias), or ++ (low risk of bias). The scores were added and the total was translated into very low ( $\geq$ 7 plusses), low (5–6 plusses), medium (3–4 plusses) or high risk of bias ( $\leq$ 2 plusses).

# RESULTS

The search resulted in 2175 studies after removal of duplicates. After screening by title and abstract, 272 studies were selected for a full text eligibility check. Review of the full text resulted in inclusion of 69 studies.<sup>3 24–91</sup> A flow diagram of the selection process is visualised in figure 1.



Figure 1 Flow diagram of the selection process of studies describing assessment in the context of malnutrition.

# **Open access**

Table 1 Cut-off values	BMI exclusively used
Cut-off value	Studies using only BMI for assessment of malnutrition n=53
$\leq 20.0 \text{ kg/m}^2$	1
<20.0 kg/m <sup>2</sup>	2
<18.5 kg/m <sup>2</sup>	34
$\leq$ 18.5 kg/m <sup>2</sup>	3
<18.49 kg/m <sup>2</sup>	1
<18.4 kg/m <sup>2</sup>	1
<17.0 kg/m <sup>2</sup>	2
<16.0 kg/m <sup>2</sup>	2
No clear cut-off value described in study	7
BMI, body mass index.	

In total, among 69 studies, 17 different methods were used to assess malnutrition. Four studies used multiple (ie, two to four) methods to assess malnutrition. Four studies used multiple criteria but integrated these together into one method to perform an assessment. In 53/69 (77%) of the studies, BMI was used as single assessment method. Among these studies eight different cut-off points were used, 34/53 studies (64%) used BMI < $18.5 \text{ kg/m}^2$ . In seven studies, no cut-off values for BMI were described. Table 1 shows all the cut-off values of BMI used as single method.

# Capturing of the domains of malnutrition

Table 2 presents the capturing of the domains of malnutrition per assessment method.<sup>324-91</sup> Uptake or intake of nutrition (A) was addressed to some extent by four methods that were used in five of the 69 studies. Body composition (B) was addressed to some extent by all but two studies, 67/69 (97%). Two methods did not address domain B, as these were methods that used self-reporting of diet quality and a food frequency questionnaire as assessment methods. Physical and/or cognitive functionality (C) was addressed to some extent by only 3/69 studies (4%).

Only 2 of the 17 different assessment methods that were used in the 69 studies captured all three domains of the definition, that is, the Subjective Global Assessment was used in two studies and the Mini Nutritional Assessment was used in one study. Forty-one studies (59%) assessed malnutrition for the purpose of their primary aim. The three studies that used a method that captured all three domains of the definition, had a primary aim related to malnutrition.

Table 2      Comparison of 17 different assessment methods by malnutrition domain capturing						
Domains	Α	В	С			
Description of domain	Intake or uptake of nutrition	Body composition	Physical and cognitive function	Total		
PIBW, BMI, albumin, TLC, cholesterol, Hb	-	+	-	+		
Weight change	-	+	-	+		
BMI & MUAC	-	+	-	+		
Self-report of diet quality	+	-	-	+		
MNA	++	+	++	+++++		
MUST	+	+	-	++		
AMA	-	++	-	++		
BMI/albumin	-	+	-	+		
BMI, MUAC, TSF, MAMC, Hb, Ht, albumin, total protein, globulin, iron fixation capacity, retinol, tocopherol Zn, SE, Fe	-	+	-	+		
MAMC	-	++	-	++		
Underweight	-	+	-	+		
TSF/TST	-	+	-	+		
SGA	++	++	++	+++++		
BMI	-	+	-	+		
BIA: (body fat%)	-	+	-	+		
MUAC	-	+	-	+		
FFQ	++	-	-	++		

AMA, arm muscle area; BIA, bio-electrical impedance analysis; BMI, body mass index; Fe, iron; FFQ, Food Frequency Questionnaire; Hb, haemoglobin; Ht, haematocrit; MAMC, mid arm muscle circumference; MNA, mini nutritional assessment; MUAC, mid upper arm circumference; PIBW, percent ideal body weight; SE, selenium; SGA, subjective global assessment; TLC, total lymphocyte count; TSF, triceps skin fold ; TST, triceps skinfold thickness; Zn, zinc.

Table 3	Subanal	ysis of	malnutrition	assessment	methods
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Year of start data collection	No of studies (n=69)	BMI as the only assessment method N %	Use of an assessment method that attributes to three domains %
2000–2004	9	9 89	-
2005–2009	12	7 58	-
2010–2014	14	13 93	-
2015–2019	19	15 79	-
No available data on year of data collection	15	10 67	3 20
Total	69	53 77	3 4

A descriptive subanalysis, as shown in table 3, was performed to compare studies regarding their use of assessment tools, by their period of data collection.<sup>3</sup>  $^{24-91}$  No differences were found between 5-year periods regarding the use of BMI as the only assessment method. The studies that used methods that capture all three domains of the ESPEN definition of malnutrition did not describe when their data was collected Of the 69 included studies, 18 studies (26%) were on inpatients, 26 studies (38%) on outpatients, 7 (10%) on both type of patients and in 18 studies (26%) the type of patients was not described.

# **Risk of bias assessment**

Online supplemental material 2 shows the risk of bias assessment and details of the 69 included studies.<sup>3 24-91</sup> Twenty-one of the 69 studies (30%) did not describe the rationale for the assessment of malnutrition. Fifteen of the 69 studies (22%) described their assessment method without clear cut-off values. Risk of bias was very low in 24 studies (35%), low in 20 studies (29%), medium in 20 studies (29%) and high in five studies (7%).

#### DISCUSSION

This review showed that most patients with TB are assessed for only one aspects of the construct of malnutrition. BMI is often used assessment method for malnutrition in studies with patients with TB, even though it only partly covers just one malnutrition domain (domain B). In addition, while some studies did not report a cut-off value for BMI, in other studies different cut-off values for BMI were used, therefore making it difficult to compare these studies. The use of BMI could be justified from a public health perspective, since a low BMI is a characteristic of chronic malnutrition that involves loss of both fat and muscle tissue.<sup>15</sup> However, the use of BMI alone for assessing malnutrition in this population is debatable. In clinical settings, disease-related malnutrition is

the predominant type of malnutrition. Disease-related malnutrition is a (sub)acute condition, in which loss of weight and muscle/fat-free mass does not automatically result in a low BMI, while loss of weight and fat-free mass are related to poor clinical outcomes including increased morbidity and mortality.<sup>15 92</sup> With the current global overweight and obesity epidemic, patients with catabolic diseases such as TB may lose more than 20% of their weight and muscle mass within 3–6 months, and still show BMI values at or above normal range.<sup>93</sup> When assessing malnutrition in patients with TB solely based on BMI, these patients will not be identified when they are malnourished, despite the therapeutic and prognostic implications of malnutrition.<sup>94</sup>

This review indicates that the international criteria for the assessment of malnutrition have not yet found their way into studies with patients with TB. The 2013 WHO guideline on nutritional care only refers to BMI as a method of assessing malnutrition for adults, which may contribute to the status quo. BMI is by far the most frequently used assessment method for malnutrition (77%) in studies with patients with TB. Only a few (4%)of the studies that reported on the assessment methods addressed all domains of the conceptual definition of malnutrition. For the studies performed after the ESPEN criteria of 2015<sup>95</sup> and the GLIM criteria of 2018,<sup>16</sup> this may be explained by the fact that the WHO does not yet refer to these criteria in their communications. The GLIM criteria have been developed for global use and is therefore recommended to be used in any setting for all patients with TB. The GLIM framework does not include the domain of functionality as criterion.

There are some limitations in our study. First, our study focused on published articles and not on the underlying study protocol. In some cases, detailed information on the assessment and operationalisation of malnutrition might be available in the study protocol, however, it was not addressed in the article making it unavailable to the public domain. Second, implementation of new criteria in study protocols takes time. This implementation might take longer than the time period used in this review. Third: research and clinical practice are different settings and the results from our review are not a reflection of clinical practice. Nevertheless, we postulate that BMI is used the most commonly used method in clinical practice since the WHO recommends that BMI is the method to assess undernutrition/malnutrition.

Awareness of the presence of malnutrition and concept of malnutrition assessment in healthcare professionals working with patients with TB needs improvement. Future studies regarding malnutrition assessment in patients with TB should aim at implementation of international consensus criteria regarding malnutrition assessment. Using the same terminology for malnutrition may make a difference to our patients, improve outcomes as well as reduce chronic sequelae and help to end TB.

It should be stressed that we need to agree on using standardised methods for malnutrition assessment and interventions. However, malnutrition assessment should always be preceded by malnutrition screening with a validated tool (online supplemental material 3).<sup>16</sup>

In conclusion, most studies in adult patients with TB did not describe their assessment method for malnutrition. Most patients with TB are assessed for only one or two aspects of the conceptual definition of malnutrition. Various methods for assessing of malnutrition have been used, and only a very small proportion of the published studies on TB used an assessment method that fully reflects the definition of malnutrition. The use of international consensus criteria is recommended to establish systematic and uniform diagnostics and treatment of malnutrition.

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Acknowledgements We thank Martine Sealy for her contribution to the conceptualisation and visualisation of this review.We thank Giovanni Sotgiu for his feedback on the manuscript. We thank the Central Medical Library of the University of Groningen for their help with designing our search strategy.

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**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** HJ-W was codeveloper of the Patient-Generated Subjective Global Assessment©-based Pt-Global© app/web tool.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. No additional data available.

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