

## Clinical Nutrition Guidelines

# Diagnostic and application guidelines for malnutrition in adult patients (2025 edition)

Chinese Society for Parenteral and Enteral Nutrition, Clinical Nutrition Branch of Chinese Nutrition Society, Clinical Nutrition and Health Branch of China International Exchange and Promotive Association for Medical and Health Care

Malnutrition is a crucial factor affecting the prognosis of various diseases, especially among elderly, surgical and critically ill patients. With the implementation of Diagnosis Related Groups (DRGs) and Diagnosis-Intervention Packet (DIP) in China, accurate diagnosis and treatment of malnutrition is essential for enhancing clinical decision-making and patient prognosis. These guidelines were developed by multidisciplinary experts through a systematic review of evidence-based medical literature. They adopt the new international standard for malnutrition diagnosis from the Global Leadership Initiative on Malnutrition (GLIM) proposed by the Global Nutrition Organization and categorize evidence levels, providing recommendations tailored to the Chinese population's data and characteristics. The guidelines cover the entire process of malnutrition diagnosis in adult patients, including definition, epidemiology, nutrition risk screening, multi-level nutrition assessment, and diagnostic procedures. They also propose individualized diagnostic strategies for specific patient groups, such as obese or critically ill patients, and establish a standardized process for malnutrition diagnosis. At last, the guidelines form 27 questions, 38 recommendations, in order to improve the practical capacity of malnutrition diagnosis in China.

**Key Words:** malnutrition, nutritional risk screening, nutritional assessment, nutrition diagnosis, clinical guidelines

## INTRODUCTION

Malnutrition refers to the state of energy or nutrient deficiencies or imbalances caused by inadequate intake or utilization disorders, leading to alterations in body composition, declined physiological function, and adverse clinical outcomes.<sup>1</sup> According to the survey on nutritional status of Chinese inpatients, 23.3% of hospitalized patients were at nutritional risk.<sup>2</sup> However, there remains a lack of globally unified diagnostic methods and universally accepted criteria for malnutrition. In 2015, the European Society for Clinical Nutrition and Metabolism (ESPEN) proposed a consensus-based decision tree for malnutrition diagnosis, categorizing nutritional disorders into three types: malnutrition, micronutrient abnormalities, and overnutrition.<sup>3</sup> In 2019, the Global Leadership Initiative on Malnutrition (GLIM) criteria, jointly developed by authoritative global clinical nutrition societies, established a standardized framework for clinical diagnosis of malnutrition.<sup>4</sup> Nevertheless, the clinical application of GLIM requires further validation considering regional variations, economic disparities, age-related factors, and different diseases. Additionally, malnutrition is often accompanied by gastrointestinal dysfunction, decreased immunity, and metabolic disorders, necessitating comprehensive evaluation of these factors during nutritional diagnosis. Over the past three years, Diagnosis Related Groups (DRG) have become a crucial reference for China's basic medical insurance reimbursement system. A holistic diagnostic system for standardized clinical management on malnutrition is urgently needed under these circumstances. To address this imperative, Chinese Society of Parenteral and Enteral Nutrition (CSPEN) together

**Corresponding Author:** Prof. Wei Chen, Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, No.1 Shuai Fu Yuan Wang Fu Jing Dong Cheng District, Beijing, 100730, China

Tel: +86-010-69154095

Email: chenw@pumch.cn

Prof. Hua Jiang, Institute of Emergency Medicine and Disaster Medicine, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, No.32 Yi Huan Lu Xi Er Duan Qing Yang District, Chengdu, 610072, China

Tel: +86-028-87393881

Email: jianghua@uestc.edu.cn

Prof. Hua Yang, Department of General Surgery, Chongqing General Hospital, 118 Xing Guang Avenue Liang Jiang New Area, Chongqing, 401147, China

Tel: +86-023-63390111

Email: hwbyang@126.com

Manuscript received 06 August 2025. Initial review and accepted 08 August 2025.

doi: 10.6133/apjcn.202510\_34(5).0001

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with the Clinical Nutrition Branch of Chinese Nutrition Society and Clinical Nutrition and Health Branch of China International Exchange and Promotive Association for Medical and Health Care jointly convened domestic experts. This multidisciplinary expert panel conducted in-depth discussions on malnutrition diagnostic criteria and ultimately developed this guideline through systematic clinical practice integration

## PART 1: METHODOLOGY FOR GUIDELINE DEVELOPMENT

### I. Literature search strategy

To ensure scientificity, transparency, and applicability, the guideline development group systematically searched for evidence by referencing existing guidelines and expert consensus in related fields.

#### 1. Timeframe

January 1, 2000, to August 30, 2024.

#### 2. Databases

(1) Secondary databases: Guideline Clearing House, Cochrane Library, Sum Search;

(2) Primary databases: Medline, EMBASE, Web of Science, China Biology Medicine (CBM) Database, China National Knowledge Infrastructure (CNKI), Wanfang Database.

#### 3. Publication types

Diagnosis (guidelines, meta-analysis, systematic reviews, controlled diagnostic trials, observational studies, case reports, consensus statements) & Safety (guidelines, meta-analyses, systematic reviews, cohort studies, adverse reaction reports, consensus statements).

(1) Primary search terms: Malnutrition, diagnosis, nutritional risk screening, nutritional assessment, gastroenteric function, immune function, GLIM, etc.

(2) Expanded search terms (including but not limited to): Critical illness, obesity, Wernicke's encephalopathy, sarcopenia, sarcopenic obesity (SO), wasting, sequela, protein-energy malnutrition (PEM), nutrient deficiency, nutritional edema, PEM, cachexia, clinical pathway, management, DRG, etc.

### II. Levels of evidence and grading criteria of recommendations

Based on the Guiding Principles for the Development/Revision of Clinical Diagnosis and Treatment Guidelines in China (2022 Edition),<sup>5</sup> the Grading of Recommendations Assessment, Development and Evaluation

(GRADE) system was adopted to assess quality of evidence and strength of recommendations, thereby formulating recommendations.<sup>6</sup> "GRADE system: classification of quality of evidence" is shown in Table 1. This guideline follows "Question-Recommendation (Quality of Evidence, Strength of Recommendations)-Evidence Summary" framework. Evidence was systematically retrieved and synthesized by clinical questions, followed by evidence evaluation to formulate recommendations. Key clinical evidence was summarized, and final conclusions were made with consideration of health economic impacts. Expert opinions were provided when evidence was insufficient or of low quality, while weighing benefits, risks, and economic burdens.

### III. Target audience

This guideline is intended for use by specialists, nutritionists, dietitians, and other healthcare professionals across disciplines in China. The recommendations in this guideline apply specifically to adult patients in China.

### IV. Identification of clinical question, development process of recommendation, and methodology of consensus development

The guideline development group of this guideline comprised multidisciplinary experts in clinical nutrition, surgery, internal medicine, critical care medicine, epidemiology, and evidence-based medicine. Clinical questions were identified through group discussions addressing urgent challenges in malnutrition diagnosis among Chinese adult patients. Guided by methodology experts, these questions were refined into research topics and clinical questions included in this guideline were finally determined through iterative revisions. Recommendations were formulated after thorough evidence review, balancing benefits, patient preferences, resource utilization, and cost-effectiveness, supplemented by clinical expertise. For contentious recommendations, the Delphi method was employed, involving expert discussions followed by voting to resolve discrepancies and ensure reliability of the guideline. After finalization, 101 domestic experts independently voted on strength of each recommendation via an online platform, selecting "strongly agree", "agree", "disagree", or "strongly disagree". Consensus was achieved if  $\geq 75\%$  of votes reached "agree" or higher.

**Table 1.** GRADE system: classification of quality of evidence

Levels of evidence	Definition
Quality of evidence	
High (A)	Very confident that the true effect lies close to that of the estimate of the effect.
Moderate (B)	Moderate confidence in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low (C)	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low (D)	Very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
Strength of recommendations	
Strong (1)	Strong support for or against an intervention, where benefits outweigh risks.
Weak (2)	Conditional support for or against an intervention, with uncertain benefit-risk balance.

### V. Declaration of interest

All guideline contributors declared no conflicts of interest related to commercial sponsorship and hold no patents associated with the recommendations in this guideline.

### VI. Practice guideline registration

Practice Guideline Registration for Transparency (PRE-PARE-2023CN299).

## PART 2: SCREENING, ASSESSMENT, AND DIAGNOSIS OF MALNUTRITION DEVELOPMENT

Diagnosis of malnutrition is the process of identifying metabolic and nutritional issues in patients to establish a clinical diagnosis, as outlined in Figure 1. Nutritional risk screening, nutritional assessment, and nutritional intervention constitute the three critical steps in nutritional care.<sup>7</sup> Nutritional risk screening is the key method for rapidly identifying nutritional risk.<sup>8</sup> Nutritional assessment further clarifies malnutrition manifestations, etiologies, and severity grading in patients confirmed to have nutritional risk, ultimately leading to a malnutrition diagnosis

### I. Nutritional risk screening

Nutritional risk screening is a simple, widely applicable, and highly reproducible method that serves as the first step in diagnosing malnutrition. Under current healthcare insurance policies in China, conducting nutritional risk screening and identifying nutritional risks are prerequisites for initiating nutritional interventions.<sup>8</sup>

**Question 1:** What is the clinical value of nutritional risk screening in malnutrition diagnosis?

**Recommendation 1:** Nutritional risk screening facilitates rapid identification of patients at nutritional risk or likely to develop malnutrition and predicts clinical out-

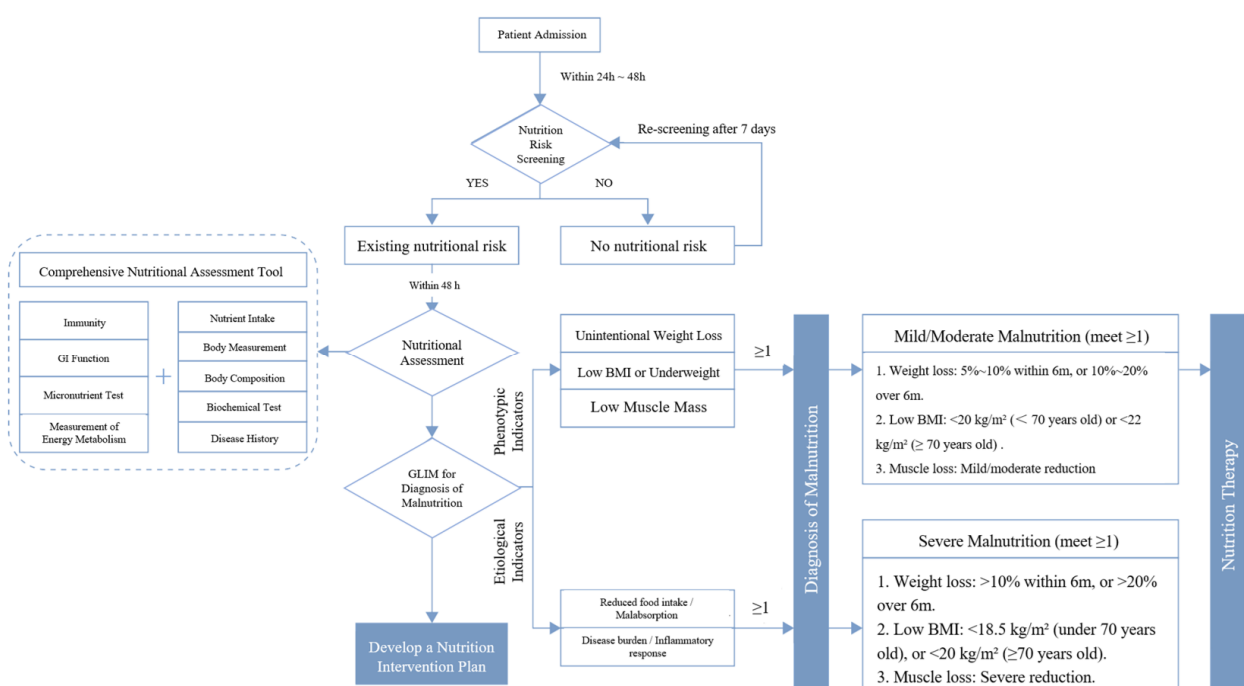
comes. (Grade A, Strong recommendation)

**Recommendation 2:** Developing nutritional intervention plans based on screening results improves clinical outcomes and demonstrates favorable health economic benefits. (Grade B, Strong recommendation)

Nutritional risk screening tools are evidence-based scales composed of composite indicators and questionnaires, including Nutrition Risk Screening 2002 (NRS-2002), Mini-Nutritional Assessment Short Form (MNA-SF), Malnutrition Universal Screening Tool (MUST), Simplified Nutrition Appetite Questionnaire (SNAQ), Malnutrition Screening Tool (MST), Nutrition Risk in the Critically Ill (NUTRIC), Nutritional Risk Index (NRI), Prognostic Nutritional Index (PNI), Prognostic Inflammatory and Nutritional Index (PINI), Controlling Nutritional Status (CONUT), Malnutrition Screening Tool for Cancer Patients (MSTC), Control of Food Intake, Protein, and Anthropometry (CIPA) and so on.<sup>9-11</sup>

Multiple studies demonstrated that nutritional risk screening effectively predicted clinical outcomes. Hersberger et al.<sup>12</sup> found that NRS-2002 identified nutritional risk as a significant predictor of short-term (30-day) and long-term (180-day) outcomes in medical inpatients. Williams et al.<sup>13</sup> found perioperative nutritional screening predicted the risk of postoperative adverse outcomes. A systematic review by Hu et al.<sup>14</sup> of 36 studies involving 25,141 heart failure patients showed nutritional risk screening predicted all-cause mortality of heart failure. Additionally, two cohort studies validated its predictive value for mortality risk in corona virus disease 2019 (COVID-19) and critically-ill hematologic malignancy patients.<sup>15-16</sup> A systematic review of 128 randomized controlled trials (RCT) highlighted that patients with nutritional risk identified by NRS-2002 were more likely to benefit from nutritional support.<sup>17</sup>

Timely nutritional interventions for inpatients with



**Figure 1.** Diagnostic flowchart for malnutrition in adults. GI: Gastrointestinal; GLIM: Global Leadership Initiative on Malnutrition; BMI: Body Mass Index

nutritional risk accelerate recovery, reduce hospital stays, and improve outcomes. A study on general surgical inpatients revealed that CIPA-guided nutritional decisions shortened hospitalization and lowered intensive care unit (ICU) admission rates.<sup>18</sup> For gastric cancer patients, post-screening nutritional support improved treatment efficacy and accelerated postoperative recovery.<sup>19</sup> Another RCT trial demonstrated preoperative nutritional support in colorectal cancer patients with nutritional risk improved postoperative nutritional status, reduced surgical stress and promoted recovery.<sup>20</sup> The prospective cohort study of Zhang et al.<sup>21</sup> found nutritional support shortened hospitalization and reduced infectious complications of patients with nutritional risk, with a cost of \$392 per prevented case. Another RCT showed NRS-2002-guided preoperative nutritional support in colorectal cancer patients decreased complications, shortened stays, and lowered costs.<sup>22</sup> Nutritional therapy based on screening also demonstrated cost-effectiveness in total knee arthroplasty patients.<sup>23</sup>

**Question 2:** What role does nutritional risk screening play in diagnosing malnutrition across different clinical settings?

**Recommendation 3:** Nutritional risk screening enables early and rapid identification of individuals at nutritional risk in diverse clinical scenarios, typically demonstrating high sensitivity but low specificity. Therefore, subsequent nutritional assessment is necessary to confirm malnutrition diagnosis and severity. (Grade C, Weak recommendation)

Nutritional risk screening tools such as MUST, NRS-2002, and MNA-SF are widely used across clinical settings. A systematic review of 105 studies evaluating the reliability, validity, and consistency of screening tools found that MST and NRS-2002 exhibited moderate validity in adult populations, while MNA-SF demonstrated moderate validity in elderly patients.<sup>24</sup>

For patients with cirrhosis, specialized screening tools improve diagnostic accuracy for malnutrition.<sup>25</sup> In patients with cancer, heterogeneity exists in the utility of nutritional risk screening. A systematic review comparing various tools with the Patient-Generated Subjective Global Assessment (PG-SGA) in adult patients with gastrointestinal cancer revealed variability in screening outcomes based on treatment modality, phase, and patient characteristics.<sup>26</sup> An observational study of 165 patients with upper gastrointestinal, colorectal, or head & neck cancers compared five screening tools: MNA-SF showed the highest sensitivity (0.99) but low specificity (0.45), whereas CONUT exhibited low sensitivity (0.21) but high specificity (0.89). NUTRISCORE also demonstrated significant heterogeneity in diagnostic performance across tumor types by sites.<sup>27</sup> Sobrini et al.<sup>28</sup> evaluated the effectiveness of MNA-SF in elderly cancer patients, reporting perfect sensitivity (1.00) but poor specificity (0.50).

## II. Nutritional assessment

Nutritional assessment follows risk screening to determine etiology, type, and severity of malnutrition. It encompasses multidimensional metrics, including clinical history, dietary evaluation, anthropometry, body composition analysis, and laboratory tests.

**Question 3:** What is the role of clinical history in nutritional assessment?

**Recommendation 4:** Clinical history is integral to nutritional assessment, encompassing nutrition-related manifestations, disease history, dietary intake, food & drug allergies, appetite, and digestive function. It provides multidimensional insights to guide assessment, intervention, and monitoring. (Grade D, Weak recommendation)

Clinical history provides subjective and retrospective data on factors influencing nutrient intake, gastrointestinal motility, and digestive function, including chronic or acute illnesses, psychiatric disorders, infections, and metabolic stressors. This information aids in evaluating energy expenditure, protein catabolism, and muscle loss. Additional factors include family history, food/drug allergies, lifestyle, dietary intake, physical activity, socioeconomic status, and psychological state.<sup>10, 29-30</sup> Additionally, clinical history should document routine medication use, particularly vitamins, minerals, and nutritional supplements, to evaluate potential drug-nutrient interactions and associated adverse effects.

In assessing dietary and nutritional intake, factors such as dietary patterns, dietary habits, and contributors to specific nutrient deficiencies, including cultural practices, specialized diets, and food allergies, must be evaluated, along with fluid and alcohol intake. Cong Minghua et al. developed a simple diet self-assessment tool to quantify dietary intake in cancer patients, aiding in the determination of food intake.<sup>31</sup> Furthermore, changes in appetite significantly impact nutritional intake; appetite scales can objectively measure subjective appetite, enabling timely dietary adjustments.

**Question 4:** What is the role of anthropometry and body composition analysis in nutritional assessment?

**Recommendation 5:** Body weight and Body Mass Index (BMI) reflect overall nutritional status, while body composition analysis evaluates muscle, fat, and water content. Low BMI,  $\geq 5\%$  weight loss within 6 months, and reduced muscle mass correlate with malnutrition prognosis across diseases. (Grade B, Strong recommendation)

**Recommendation 6:** Calf circumference (CC) and mid-arm muscle circumference (MAMC) reflect muscle reserves and correlate with sarcopenia and malnutrition prognosis. (Grade C, Weak recommendation)

**Recommendation 7:** Handgrip strength (HGS) reflects muscle function and predicts sarcopenia, malnutrition-related quality of life, and prognosis. (Grade B, Strong recommendation)

**Recommendation 8:** The Five-Times-Sit-to-Stand Test (FTSST) serves as a practical alternative for assessing lower limb muscle strength. (Grade B, Weak recommendation)

Anthropometry and body composition analysis are critical for nutritional evaluation. Weight and unintentional weight loss in short term is strongly associated with mortality.<sup>32</sup> Gaddey et al. linked  $\geq 5\%$  unintentional weight loss within 6–12 months to increased morbidity and mortality in older adults across diseases.<sup>33</sup> A 14-year follow-up study of 2,935 community-dwelling elderly patients showed that  $\geq 5\%$  weight loss elevated mortality risk, while weight gain did not.<sup>34</sup> BMI is widely used to diagnose malnutrition and obesity, and low BMI correlates

with mortality and complications.<sup>35</sup> A 5-year cross-sectional study of 10,298 nursing home residents across 13 countries demonstrated that weight loss and low BMI were associated with mortality in the elderly.<sup>36</sup>

Patients with sarcopenia exhibit reduced predicted value of forced expiratory volume in one second (FEV1), diminished exercise tolerance, and poorer quality of life.<sup>37</sup> A systematic review investigating the association between sarcopenia and health-related quality of life (HRQoL) confirmed that sarcopenia correlated with decreased HRQoL.<sup>38</sup> In chronic kidney disease and dialysis patients, low muscle strength, low muscle mass, and reduced physical performance are associated with higher mortality.<sup>39</sup>

CC, MAMC, and HGS serve as prognostic indicators in nutritional assessment. Studies demonstrated that CC predicted nutritional risk.<sup>40-41</sup> Tarnowski et al.<sup>42</sup> reported that reduced CC correlated with prolonged hospitalization. Maeda et al.<sup>43</sup> found that low CC as a marker for early sarcopenia and malnutrition, was linked to in-hospital mortality. Kim et al.<sup>44</sup> found MAMC and inflammatory markers were equally predictive of prognosis in advanced cancer patients.

HGS serves as an efficient indicator for nutritional assessment as well. Based on UK Biobank data, Petermann-Rocha et al.<sup>45</sup> found that lower muscle mass and strength were associated with increased risk of severe non-alcoholic fatty liver disease. Bobos et al.<sup>46</sup> systematically validated the reliability and efficacy of HGS assessment across diverse populations. McNicholl et al.<sup>47</sup> demonstrated the superior practicality of HGS over gait speed in a multicenter study. In patients with cirrhosis, HGS assessment outperformed subjective global assessment (SGA) and PNI in predicting major complications within one year.<sup>48</sup>

While handgrip strength currently remains the most accessible measure of muscle strength, strength of knee flexion and extension, though more precise, is less feasible to obtain. FTSST provides a practical alternative for estimating strength of quadriceps, balance control, and fall risk.<sup>49</sup> Multiple studies confirmed its reliability in assessing lower limb muscle strength in healthy individuals and patients with stroke, chronic obstructive pulmonary disease (COPD), Parkinson's disease, spinal cord injury, and hip osteoarthritis.<sup>50-51</sup>

**Question 5:** What is the role of laboratory indicators in nutritional assessment?

**Recommendation 9:** Visceral proteins such as serum albumin, prealbumin, transferrin, and retinol-binding protein reflect nutritional status but should not be used in isolation to diagnose malnutrition. (Grade B, Weak recommendation)

**Recommendation 10:** Hypoalbuminemia is a risk factor for mortality or poor prognosis in multiple diseases. (Grade B, Strong recommendation)

**Recommendation 11:** Lymphocyte count and neutrophil-to-lymphocyte ratio (NLR) hold potential value in assessing nutritional status and predicting clinical outcomes. (Grade C, Weak recommendation)

Recent studies suggest that inflammatory cytokines may suppress visceral protein synthesis, casting doubt on the reliability of albumin, prealbumin, transferrin, and

retinol-binding protein as standalone biomarkers.<sup>52</sup> Despite the correlation between inflammation and malnutrition, these proteins should be interpreted alongside inflammatory markers for comprehensive assessment.<sup>53</sup>

Serum albumin, the most extensively studied visceral protein, reflects disease severity. In emergency patients, hypoalbuminemia predicts 30-day mortality.<sup>54</sup> Burn patients exhibit albumin levels linked to injury severity.<sup>55</sup> Low albumin also associates with increased mortality or poor prognosis in conditions like end stage renal failure, cancer, and major surgery.<sup>56-61</sup> Prealbumin and other visceral proteins, with the shorter half-life period, more sensitively reflect nutritional changes and prognosis.<sup>62</sup> A study of ICU patients found that prealbumin fluctuations correlated with in-hospital mortality.<sup>63</sup> A study of elderly COVID-19 inpatients found a linear relationship between low prealbumin and increased risk of adverse outcomes.<sup>64</sup>

Lymphocyte count holds potential value in the assessment of nutritional status and prediction of clinical outcomes. Patients with malnutrition showed reduced lymphocyte ratios that were associated with malnutrition.<sup>65</sup> Total lymphocyte count (TLC) identified mortality risk in myelofibrosis patients.<sup>66</sup> Eminovic et al. found that elderly inpatients undergoing total hip replacement surgery with preoperative hypoalbuminemia and low TLC had increased rates of postoperative complications.<sup>67</sup>

Furthermore, NLR holds significant value in assessing nutritional status and predicting patient outcomes. Kang et al.<sup>68</sup> found NLR predictive of functional status, nutritional risk, and indicators of nutritional status in 21,457 cancer patients. Males with hypertension or coronary heart disease (CHD) were more prone to systemic inflammation, which further impaired physical function, worsened nutritional status, and increased malnutrition risk and affected fat and muscle metabolism. Another cohort study that enrolled 1,207 heart failure patients demonstrated that NLR correlated with all-cause mortality in community-dwelling heart failure patients and exhibited predictive value.<sup>69</sup> Wang et al.<sup>70</sup> demonstrated that NLR aided in evaluating and managing nutritional status in cirrhotic patients. Furthermore, a prospective cohort study revealed that NLR in hemodialysis patients correlated with nutritional indicators and predicted hospitalization risk.<sup>71</sup>

**Question 6:** How to diagnose micronutrient deficiency?

**Recommendation 12:** Diagnosis of micronutrient deficiency relies on clinical history, symptoms, signs, and standardized laboratory tests. (Grade C, Strong recommendation)

Under various disease conditions, malnutrition patients are prone to micronutrient deficiencies of varying severity due to factors such as inadequate intake, malabsorption, and traumatic stress, which may exacerbate disease progression and compromise clinical outcomes. Therefore, adequate micronutrient supplementation should be initiated at the outset of nutritional therapy. For patients with malnutrition, micronutrient deficiencies, disease-related metabolic abnormalities, or increased postoperative drainage, routine micronutrient monitoring is essential.

Micronutrient deficiencies typically present with distinct clinical history, symptoms, and signs. Diagnosis

involves laboratory testing of circulating micronutrient levels combined with disease context to determine deficiency type and severity. Although standardized assays exist for nearly all vitamins and trace elements, routine micronutrient testing remains uncommon in most Chinese healthcare facilities, particularly primary care settings, due to low demand, technical complexity, and high costs, thereby hindering timely diagnosis. For detailed protocols, refer to Guidelines for Clinical Application of Micronutrients in Chinese Adult Patients (2024 Edition),<sup>72</sup> specifically its section on clinical micronutrient testing (Clinical manifestations and reference diagnostic criteria for biochemical markers of common micronutrient deficiencies are described in Supplementary Table 1).

**Question 7:** Which micronutrients require prioritized monitoring in specific diseases?

**Recommendation 13:** Severe burn patients often exhibit deficiencies in vitamin D and other micronutrients. Patients with inflammatory bowel disease (IBD) are prone to iron and multiple vitamin deficiencies. Those with short bowel syndrome (SBS) frequently experience impaired absorption of iron and fat-soluble vitamins. Patients undergoing distal ileum resection are at higher risk for vitamin B12 deficiency, necessitating regular micronutrient monitoring. (Grade B, Strong recommendation)

Burn patients frequently experience significant micronutrient losses due to wound exudation and impaired cutaneous vitamin D biosynthesis, making vitamin D deficiency particularly prevalent.<sup>73</sup> A multicenter retrospective study by Garner et al.<sup>74</sup> revealed that 56.8% of burn patients exhibited vitamin D deficiency, with a 2.4-fold higher infection risk compared to non-deficient patients.

Anemia, the most common extraintestinal manifestation of IBD, complicates disease progression.<sup>75</sup> The primary anemia types in IBD patients include iron deficiency anemia, anemia of chronic disease, and mixed anemia, which are diagnosed through complete blood count, serum ferritin, and C-reactive protein (CRP) testing.<sup>76</sup> IBD patients in remission or with mild disease activity should undergo testing every 6 to 12 months, while those with active disease require monitoring at least every 3 months. Iron supplementation is recommended for all patients with iron deficiency anemia, regardless of age, to improve quality of life.<sup>77</sup>

Disrupted enterohepatic circulation in SBS patients commonly leads to deficiencies in iron, fat-soluble vitamins, and essential fatty acids.<sup>78</sup> Studies indicate that even with intermittent parenteral nutrition support and oral vitamin supplementation, patients may still develop vitamin D and E deficiencies.<sup>79</sup>

Vitamin B12 is primarily absorbed in the distal ileum, and thus patients with short bowel syndrome following distal ileum resection are at high risk for vitamin B12 deficiency.<sup>80</sup>

**Question 8:** Which populations require gastrointestinal (GI) function assessment to prevent malnutrition?

**Recommendation 14:** Patients with severe stress, acute organs injury, or those using non-steroidal anti-inflammatory drugs (NSAIDs) that increased the risk of upper gastrointestinal bleeding (UGIB) should routinely evaluate GI function to prevent malnutrition. (Grade B, Strong recommendation)

GI dysfunction refers to structural or functional impairment of GI tract, leading to digestive/absorptive failure and intestinal barrier dysfunction, which predisposes to malnutrition. Clinical manifestations include dysmotility, feeding intolerance, intestinal barrier dysfunction, constipation, and diarrhea.<sup>81</sup>

Under severe stress, factors such as ischemia, hypoxia, and metabolic disturbances trigger GI dysfunction, leading to reduced intestinal blood flow and digestive secretions, impaired chemical/mucosal barriers, ultimately creating a vicious cycle.<sup>82-85</sup> Traumatic brain injury (TBI) frequently causes acute GI injury, potentially due to impaired gastric motility and emptying, neurogenic damage, or medication effects.<sup>86</sup> Reduced gastric mucosal blood flow in TBI patients may also precipitate gastrointestinal bleeding.<sup>87-90</sup> A prospective cohort study in 2019 reported a 34.4% incidence of UGIB in cirrhotic patients with acute decompensation.<sup>91</sup> Other high-risk conditions include acute stroke,<sup>92</sup> acute respiratory failure,<sup>93</sup> acute coronary syndromes,<sup>94-95</sup> acute kidney injury,<sup>96</sup> polytrauma,<sup>97</sup> postpartum hemorrhage,<sup>98-99</sup> and septic shock.<sup>100</sup>

**Question 9:** Which GI assessment methods can be used to predict clinical outcomes?

**Recommendation 15:** Acute Gastrointestinal Injury (AGI) grading and Intake, Feeling nauseated, Emesis, Exam, and Duration of symptoms scoring system (I-FEED) are applicable for postoperative GI evaluation. (Grade C, Weak recommendation)

**Recommendation 16:** AGI grading predicts mortality and prognosis in critically ill patients. (Grade B, Weak recommendation)

**Recommendation 17:** Chronic intestinal failure (CIF) severity can be classified by type and volume of parenteral nutrition, which correlates with clinical outcomes. (Grade B, Weak recommendation)

Over a dozen GI function assessment tools exist, but few studies have investigated their prognostic relevance.<sup>101</sup> Reintam et al.<sup>102</sup> demonstrated that the Gastrointestinal Failure Score (GIF score) is a predictive factor for ICU mortality. Patients with Gastrointestinal Dysfunction Score (GIDS score) 2–4 exhibit higher 28-day mortality and longer ICU stays compared to those with GIDS 0–1. When combined with the SOFA score, GIDS also serves as the risk factor for 28- and 90-day mortality.<sup>103-104</sup>

Postoperative GI assessment primarily relies on the AGI grading and I-FEED scoring systems. In 2020, the observational study by Hou Jingyue et al.<sup>105</sup> revealed that AGI-guided nutritional interventions after liver cancer resection promoted wound healing, reduced diarrhea incidence, and improved nutritional status. Seilitz et al.<sup>106</sup> prospectively observed 501 cardiac surgery patients and found that elevated AGI within the first three postoperative days correlated with increased 30-day gastrointestinal complications and mortality.

In 2012, the European Society of Intensive Care Medicine (ESICM) proposed the AGI grading system, categorizing GI function into four grades in critically ill patients.<sup>107</sup> Multiple studies confirm that AGI severity positively correlates with ICU mortality, multiorgan failure, and prolonged mechanical ventilation. A 2016 multicenter prospective study and a 2022 retrospective study demonstrated that patients with AGI grades III/IV had

higher 28-day mortality, overall mortality, and extended mechanical ventilation durations.<sup>108-109</sup> Additionally, higher AGI grades inversely correlate with enteral nutrition (EN) feeding rates and 7-day energy intake adequacy.<sup>86, 108-114</sup>

CIF is characterized by progressive and persistent metabolic disturbances. The ESPEN classifies CIF severity based on parenteral nutrition (PN) requirements: patients requiring only intravenous fluids/electrolytes have milder disease than those needing PN with macronutrients. A 1-year prospective study linked PN type/volume to outcomes including total PN (TPN) weaning rates, intestinal failure-associated liver disease (IFALD), cholestasis, hepatic failure, and catheter-related bloodstream infections.<sup>115</sup>

**Question 10:** Which biomarkers can be used for diagnosing GI dysfunction?

**Recommendation 18:** Combined detection of biomarkers such as serum intestinal fatty acid-binding protein (I-FABP), citrulline, D-lactate (D-LAC), and diamine oxidase (DAO) improves the predictive efficacy for GI dysfunction and guides the implementation of early EN. (Grade C, Weak recommendation)

An ideal biomarker should directly correlate with GI dysfunction, reflect the severity of dysfunction through quantitative changes in concentration, and allow real-time dynamic monitoring. However, no currently available biomarker fully meets these criteria. Studies indicate that a combination of multiple biomarkers such as I-FABP, citrulline, D-LAC and DAO can predict GI dysfunction. Elevated serum I-FABP levels are a risk factor for GI dysfunction,<sup>116</sup> positively correlating with GI function scores, duration of mechanical ventilation, and inflammatory markers. Its concentration increases with higher AGI grades.<sup>117-126</sup>

Patients with GI dysfunction exhibit lower serum citrulline levels,<sup>127-129</sup> which further decline with AGI progression.<sup>125, 130-131</sup> Controversy persists regarding optimal diagnostic cut-off value of GI dysfunction. Noordally et al.<sup>130</sup> proposed that citrulline concentration <15 µmol/L suggested small intestinal dysfunction in critically ill patients. Wang et al.<sup>118</sup> proposed that <9.7 µmol/L was the optimal cut-off value. Additionally, a prospective study in 2017 showed that plasma citrulline level ≤19.07 µmol/L predicted post-traumatic AGI with 89.13% sensitivity and 80.77% specificity in critically ill patients with GI dysfunction.<sup>132</sup>

Concentrations of D-LAC and DAO correlate with GI injury severity, SOFA scores, and acute physiology and chronic health evaluation II (APACHE II) score, increasing alongside AGI grades.<sup>125, 127,129, 133, 134</sup> A study by Du Gongliang et al.<sup>122</sup> involving 156 polytrauma patients demonstrated that combining citrulline, I-FABP, and D-LAC achieved an area under the curve (AUC) of 0.960 for predicting AGI, with 87.23% sensitivity and 93.26% specificity. Therefore, while the combined detection of multiple biomarkers may improve predictive efficacy, optimal integration strategies need further investigation. Additional studies indicated that intestinal trefoil factor,<sup>116</sup> intestinal alkaline phosphatase (IAP),<sup>135</sup> vasoactive intestinal peptide (VIP),<sup>136</sup> heparin-binding pro-

tein<sup>134</sup> and other biomarkers exhibited potential value in predicting GI dysfunction.

Several studies have explored the predictive value of citrulline for early EN failure in patients with severe gastrointestinal injury. Multivariate logistic regression analysis identified age, 24-h citrulline change (ΔCit), and 48-hour feeding volume escalation as independent risk factors for early EN failure. A ΔCit <0.74 µmol/L or rapid feeding increases within 48 h may elevate the risk of EN intolerance. Dynamic monitoring of citrulline levels could provide guidance for successful feeding strategies in these patients.<sup>137</sup>

### III. Comprehensive nutritional assessment

Comprehensive nutritional assessment is a diagnostic process integrating nutrition-related medical history, physical examination, and malnutrition-associated manifestations. SGA in the 1980s emerged as a pioneering method for comprehensive nutritional assessment and has since gained widespread clinical acceptance. In 2019, the GLIM became a globally recognized framework for nutritional assessment. Importantly, malnutrition diagnosis should not only assess patients' current nutritional phenotype but also elucidate underlying pathophysiological mechanisms and etiologies to guide targeted nutritional interventions.

**Question 11:** Which comprehensive nutritional assessment tools can diagnose malnutrition?

**Recommendation 19:** Tools such as SGA, PG-SGA, MNA, and GLIM enable integrated evaluation of nutritional status and malnutrition diagnosis. GLIM is increasingly recognized as a global standard. (Grade A, Strong recommendation)

SGA is applicable to general inpatients with validated reliability and validity across clinical settings, including chronic kidney failure, cancer, critical illness, and geriatric populations.<sup>138-139</sup> PG-SGA, a questionnaire adapted from SGA specifically for cancer patients, demonstrates high sensitivity (0.95) and specificity (0.85) for diagnosing malnutrition in this population, as shown in a systematic review.<sup>140</sup> Another systematic review linked PG-SGA-assessed malnutrition to poorer survival and increased postoperative complication risks in cancer patients.<sup>141</sup> MNA not only assesses malnutrition in older adults but also serves as a metric for evaluating the efficacy of nutritional interventions.<sup>142</sup>

Since 2019, GLIM has emerged as a globally recognized universal diagnostic tool for malnutrition in adult patients. Prospective studies demonstrated that GLIM-diagnosed malnutrition predicted impaired functional status, cancer-related symptoms, and reduced quality of life.<sup>143</sup> Furthermore, GLIM-diagnosed malnutrition is a predictor of 90-day mortality and postoperative complications in patients undergoing major abdominal surgery.<sup>144-145</sup> Studies also indicated elevated long-term mortality risk in critically ill patients diagnosed with malnutrition by GLIM.<sup>146</sup> Validity of GLIM has been confirmed in Chinese populations, establishing GLIM as a key method for diagnosing and stratifying severe malnutrition.<sup>147-148</sup>

#### IV. GLIM-based diagnosis of malnutrition

**Question 12:** What workflow should be followed for GLIM-based diagnosis of malnutrition?

**Recommendation 20:** The GLIM malnutrition diagnostic process adopts a two-step approach. The first step involves nutritional risk screening to determine whether a patient is at nutritional risk. For those identified as at risk, the second step entails malnutrition diagnosis. The diagnosis requires meeting at least 1 phenotypic criterion (3 in total) and 1 etiologic criterion (2 in total) to confirm malnutrition. (Grade A, Strong recommendation)

**Question 13:** How to select appropriate nutritional risk screening tools for the first step of the GLIM diagnostic process?

**Recommendation 21:** Adopt validated nutritional risk screening tools compatible with GLIM, including MUST, MNA-SF, NRS-2002, SNAQ, and others. (Grade B, Strong recommendation)

Lima et al.<sup>149</sup> applied five screening tools, including MST, MUST, Nutritional Risk in Emergency-2017 (NRE-2017), NRS-2002, and SNAQ, to 601 hospitalized patients for GLIM diagnosis. Results showed that patients screened via NRE-2017, MST, or MUST had increased risks of in-hospital mortality, prolonged hospitalization, and readmission rates. Among these, MUST demonstrated the highest sensitivity (73.6%) and accuracy, with a negative predictive value (NPV) of 83.6% and positive predictive value (PPV) of 93.4%.<sup>149</sup>

Xu et al.<sup>150</sup> studied 7,311 elderly hospitalized patients and found that MNA-SF-based GLIM diagnosis predicted mortality in those aged over 70 years. Aloy et al.<sup>151</sup> retrospectively analyzed 5,270 hospitalized patients in Brazil, revealing that MUST and MST-positive status correlated with longer hospital stays and increased mortality risk. Lian Yuying et al.<sup>152</sup> compared one-step (direct GLIM diagnosis) and two-step (screening followed by diagnosis) approaches in 385 cancer patients, noting discrepancies in malnutrition diagnosis rates, though clinical outcome impacts were not validated.

**Question 14:** What are the phenotypic criteria in GLIM diagnosis?

**Recommendation 22:** The GLIM phenotypic criteria include low BMI, weight loss, and reduced muscle mass: (1) Low BMI: BMI <18.5 kg/m<sup>2</sup> for patients aged <70 years; BMI <20 kg/m<sup>2</sup> for patients aged ≥70 years. (2) Weight loss: Moderate malnutrition: 5%–10% weight loss within 6 months or 10%–20% weight loss over >6 months. Severe malnutrition: ≥10% weight loss within 6 months or ≥20% weight loss over >6 months. (3) Incorporate relative muscle mass (RMM) assessment into GLIM diagnosis. Meeting at least one phenotypic criterion fulfills the GLIM diagnostic criteria. (Grade A, Strong recommendation)

Domestic researchers have conducted multiple observational validation studies of GLIM across diverse diseases and populations. For the weight loss criterion, most studies define >5% weight loss within 6 months or >10% weight loss over >6 months as meeting the phenotypic standard. Yin et al.<sup>153</sup> analyzed 1,219 lung cancer patients from the China Nutritional Oncology Database (Investigation on Nutrition Status and its Clinical Outcome of Common Cancers (INSCOC) study), revealing median

survival times of 1,896 days (no malnutrition), 1,248 days (mild-to-moderate malnutrition), and 1,049 days (severe malnutrition).

Most studies employ BMI criteria for Asian populations to define low BMI: BMI <18.5 kg/m<sup>2</sup> for individuals aged <70 years or BMI <20 kg/m<sup>2</sup> for those aged ≥70 years. Wang et al.,<sup>154</sup> based on the observation that the average BMI of Chinese adults increased by 1.49 kg/m<sup>2</sup> over the past two decades, used BMI <20 kg/m<sup>2</sup> as the cut-off value for moderate malnutrition in 8,725 patients. However, this study did not analyze the association between malnutrition defined by this BMI threshold and clinical outcomes.

In Japan, Maeda et al.<sup>155</sup> enrolled 6,783 hospitalized patients aged >40 years and established optimal BMI cut-off values for severe malnutrition: <17.8 kg/m<sup>2</sup> for patients ≥70 years and <17.0 kg/m<sup>2</sup> for those <70 years (derived from 1,987 patients). These cut-off values were validated in 4,796 patients, showing higher mortality in GLIM-diagnosed malnourished patients versus non-malnourished individuals. Shimizu et al.<sup>156</sup> further validated these cut-off values in 26,098 Asian elderly patients with pneumonia. For patients ≥70 years, BMI <17.8 kg/m<sup>2</sup> predicted increased 30-day mortality, prolonged hospitalization, and 30-day readmission rates.

Zhuang et al.<sup>157</sup> applied GLIM criteria to 16,104 cancer patients (mean age 58 years; 52.5% male). Using the optimal stratification method, BMI cut-off values <16.7 kg/m<sup>2</sup> for both sexes demonstrated superior predictive value for mortality risk. However, due to the lack of large-scale, multi-disease studies in China defining BMI cutoffs for severe malnutrition, this guideline does not currently recommend specific BMI cut-off values for severe malnutrition in Chinese populations.

GLIM diagnosis builds upon the ESPEN 2015 malnutrition diagnostic criteria,<sup>3</sup> further emphasizing the critical role of RMM in malnutrition diagnosis.<sup>158</sup> Chinese studies incorporating RMM criteria showed that malnutrition significantly predicts adverse clinical outcomes.<sup>159–162</sup>

**Question 15:** How to assess muscle mass reduction indicators and cut-off values in GLIM?

**Recommendation 23:** Use skeletal muscle index (SMI), appendicular skeletal muscle mass index (ASMI), or fat-free mass index (FFMI) as criteria for muscle mass reduction. When these metrics are unavailable, calf circumference may serve as a surrogate indicator. (Grade C, Weak recommendation)

To determine skeletal muscle mass, Zhuang et al.<sup>163</sup> evaluated the third lumbar skeletal muscle index (L3 SMI) via computed tomography (CT) in 937 gastric cancer patients undergoing radical surgery. Low SMI (cut-off values ≤40.8 cm<sup>2</sup>/m<sup>2</sup> for males, ≤34.9 cm<sup>2</sup>/m<sup>2</sup> for females) predicted postoperative severe complications and poorer 5-year overall survival (OS) and disease-free survival (DFS). Xu et al.<sup>159</sup> analyzed the third lumbar total psoas muscle mass index (TPMI) via CT in 152 duodenectomy patients. Optimal cut-off values were 4.78 cm<sup>2</sup>/m<sup>2</sup> for males and 3.46 cm<sup>2</sup>/m<sup>2</sup> for females. Based on data from acute pancreatitis patients, Fu et al.<sup>160</sup> found that the cut-off values of psoas muscle area (PMA) were <11.50 cm<sup>2</sup> for males and <8.22 cm<sup>2</sup> for females. Patients with PMA below these cut-off values exhibited increased complica-



tion risks and could predict the severity of acute pancreatitis.

ASMI measured by bioelectrical impedance analysis (BIA) can also serve as an indicator of muscle mass reduction. Currently, RMM criteria from the Asian Myopathy Working Group (AWGS) are widely adopted for GLIM-based malnutrition diagnosis.<sup>164</sup> Ji et al.<sup>161</sup> analyzed BIA data from 2,477 cancer patients in the Chinese INSCOC database, revealing that 22.0% had muscle mass reduction confirmed by ASMI, while 26.6% were identified by FFMI, with overlapping cases. Low FFMI was associated with severe malnutrition, whereas low ASMI predicted overall survival.

The AWGS-recommended calf circumference cut-off values are  $\leq 34.0$  cm for males and  $\leq 33.0$  cm for females.<sup>164</sup> Yin et al.<sup>162</sup> studied 3,998 Chinese cancer patients and demonstrated that GLIM-defined malnutrition using calf circumference (cut-off values cited in the ESPEN consensus:  $<30.0$  cm for males,  $<29.5$  cm for females) predicted mortality risk.<sup>165</sup>

**Question 16:** How to define inflammatory criteria for etiology positivity in GLIM diagnosis?

**Recommendation 24:** Inflammatory response is one of the etiologic criteria in GLIM. Elevated CRP / hypersensitive CRP (hs-CRP) combined with NLR, hypoalbuminemia, or neutrophilia may serve as inflammatory markers for GLIM-defined malnutrition. It is proposed to define mild-to-moderate inflammation as CRP levels of 3.0–50 mg/L and severe inflammation as  $>50$  mg/L. (Grade B, Weak recommendation)

Inflammation is a critical etiologic criterion in GLIM. Studies show that the choice of inflammatory biomarkers impacts the clinical relevance of malnutrition diagnoses. Xie et al.<sup>166</sup> compared GLIM diagnoses using tumor status (all cancer patients as etiology-positive) versus specific inflammatory markers-inflammatory burden index (IBI), CRP, NLR, and albumin in 1,683 cancer patients from the INSCOC study. GLIM criteria incorporating hypoalbuminemia ( $<37.6$  g/L) demonstrated optimal performance in predicting long-term adverse outcomes. Inflammatory states increase capillary permeability and reprioritize hepatic protein synthesis, leading to reduced albumin levels. Combining hypoalbuminemia with elevated CRP may better identify inflammatory status. The ESPEN guidelines (2024) recommend defining mild-to-moderate inflammation as CRP 3–50 mg/L and severe inflammation as  $>50$  mg/L to identify inflammatory states.<sup>167</sup>

Zhang L et al.<sup>168</sup> studied 502 patients with head and neck cancer, all classified as inflammation-positive under GLIM criteria, showing a Kappa agreement index of 0.681 with ESPEN 2015 diagnoses. Wu Y et al. analyzed 113 cirrhotic patients, revealing that malnourished patients had longer hospital stays, higher 3-month mortality, and elevated readmission rates.<sup>169</sup>

**Question 17:** What role does artificial intelligence (AI) play in assisting GLIM-based malnutrition diagnosis?

**Recommendation 25:** AI technology aids GLIM diagnosis by improving accuracy and efficiency. (Grade B, Weak recommendation)

In 2020, Yin et al.<sup>170</sup> developed a binary machine learning model using GLIM results in 1,219 lung cancer

patients to predict malnutrition. Logistic regression analysis and decision algorithm in this model achieved an accuracy of 0.980 and AUC of 0.987. In another study, Yin et al.<sup>171</sup> constructed a three-class decision tree model for GLIM-based nutritional status prediction in 3,998 multi-cancer patients, achieving an accuracy of 0.955 and multiclass AUC of 0.964. Wang et al.<sup>172</sup> built a malnutrition diagnostic model using random forest algorithms in 2,660 elderly patients, with an accuracy of 0.743 and AUC of 0.923. Furthermore, Yin et al.<sup>173</sup> developed an AI system for malnutrition identification and grading in 14,134 multi-cancer patients from the China Nutritional Oncology Database. Sun et al.<sup>174</sup> evaluated an AI rapid malnutrition diagnostic system in 5,763 multicenter inpatients, demonstrating that AI implementation enhanced diagnostic efficiency, improved patient prognosis, and offered health economic benefits. AI technology is poised to revolutionize clinical nutrition by optimizing healthcare decisions and enabling personalized nutritional therapies.<sup>175</sup>

## PART 3: DIAGNOSIS OF MALNUTRITION IN SPECIAL POPULATIONS

### I. Malnutrition diagnosis in obese patients

**Question 18:** How should nutritional screening and assessment be conducted for obese patients?

**Recommendation 26:** Nutritional screening and assessment in obesity should prioritize body composition changes and emphasize functional status evaluation to identify SO. (Grade C, Weak recommendation)

Obesity is defined as excessive fat accumulation that impairs health.<sup>176</sup> High BMI often masks underlying malnutrition, while overnutrition cannot counteract disease-induced negative nitrogen balance and hypercatabolism. Studies indicate that 25%–30% of ICU patients are obese,<sup>177</sup> and many developing countries face coexisting obesity and malnutrition.<sup>178</sup>

Obesity may coexist with cardiopulmonary dysfunction, endocrine disorders, and proinflammatory states, increasing the risk of adverse outcomes.<sup>177,179</sup> Stress-induced enhanced gluconeogenesis, insulin resistance, and impaired substrate utilization exacerbate fat-free mass loss, leading to SO and elevating risks of functional decline and poor outcomes.<sup>180–181</sup> Cross-sectional studies suggest that functional status assessment is more sensitive than weight- or BMI-based screening alone.<sup>182–183</sup>

Assessment of body fat and fat-free mass is critical for identifying malnutrition risk in obese patients and guiding nutritional interventions. Studies indicate that relying solely on body weight or BMI inadequately reflects nutritional status; assessments in obesity should prioritize body composition changes and functional decline.<sup>183–184</sup> ESPEN guidelines<sup>181</sup> recommend screening and evaluating SO by integrating BMI, waist circumference, age, chronic diseases, hospitalization or surgical needs, and mobility. The Simple Five item Scoring Scale for Sarcopenia (SARC-F) can identify sarcopenia risk, followed by handgrip strength, knee extension strength, or chair stand tests for skeletal muscle function and physical performance. Dual-energy X-ray absorptiometry (DXA) or BIA is recommended for body composition assessment.<sup>176</sup> Large prospective cohort studies reveal that reduced FFMI and increased fat mass index (FMI) correlate with

prolonged hospitalization in obese inpatients, though diagnostic cutoffs for FFMI/FMI remain undefined. In 2009, Canadian researchers Sharma et al.<sup>185</sup> developed the Edmonton Obesity Staging System (EOSS), which stratifies obese individuals based on functional status, metabolic comorbidities, and overall health to guide prognosis management. Multicenter studies indicate that higher EOSS stages in COVID-19 patients with obesity predict greater risks of adverse outcomes.<sup>186</sup>

**Question 19:** How to perform nutritional diagnosis of SO?

**Recommendation 27:** Diagnose SO through a screening-diagnosis-staging workflow, involving separate assessments of excess adiposity, muscle insufficiency, and muscle dysfunction, followed by staging based on comorbidity severity. (Grade B, Strong recommendation)

SO is characterized by the coexistence of sarcopenia and obesity, marked by increased fat mass, reduced skeletal muscle mass, and impaired muscle function.<sup>187</sup> Obesity and sarcopenia mutually exacerbate each other, forming the core of malnutrition in obese populations.<sup>188</sup> Patients with SO face higher risks of frailty, disability, decreased quality of life, systemic diseases, chronic inflammation, reduced muscle mass and function, further increasing mortality. Studies show that obese individuals with low muscle mass/function have greater frailty and disability risks than non-obese counterparts.<sup>189</sup> ESPEN recommends a three-step SO diagnostic approach: screening, diagnosis, and staging.<sup>181</sup>

Screening for SO can be conducted through BMI and waist circumference measurements to preliminarily identify excessive adiposity. Risk factors such as age, chronic diseases, history of hospitalization, surgical needs, and reduced mobility are then assessed. Validated questionnaire tools (e.g., SARC-F) are used to screen for sarcopenia risk.

Diagnosis of SO typically involves two steps. First, assess skeletal muscle function: Measure muscle strength and physical performance via handgrip strength, knee extension strength tests (BMI-adjusted), or chair stand tests. According to sarcopenia criteria for Asian populations, the thresholds are as follows:

Handgrip strength: <28.0 kg for males and <18.0 kg for females; Gait speed: <1.0 m/s; Short Physical Performance Battery (SPPB) score: ≤9, or 5-time chair stand test >12 seconds.

Second, perform body composition measurement: Use DXA or BIA to evaluate skeletal muscle mass and fat distribution.<sup>176</sup>

Stage based on complications associated with high adiposity and low muscle mass:

Stage I: No complications.

Stage II: Presence of one or more secondary complications (e.g., metabolic disorders, functional impairment, cardiovascular diseases, respiratory diseases).

## II. Diagnosis of malnutrition in critically ill patients

**Question 20:** Which method should be used for nutritional screening in critically ill patients?

**Recommendation 28:** Critically ill patients should undergo nutritional risk screening within 24 hours of admis-

sion using the NRS-2002 or NUTRIC score. (Grade A, Strong recommendation)

**Recommendation 29:** For patients with an NRS-2002 score <5, continue to monitor body weight, energy and protein intake, and re-evaluate nutritional status after 3 days. (Grade A, Strong recommendation)

Due to the severe inflammatory response and the hypercatabolic state, accompanied by inadequate nutritional supplementation and impaired intestinal absorption, the prevalence of malnutrition in critically ill patients reaches 37.8%–78.1%.<sup>190-191</sup> Studies indicate that malnutrition is associated with increased rates of complications, mortality, infection risks, and prolonged hospitalization.<sup>192-193</sup> Therefore, timely, comprehensive, and accurate nutritional screening and assessment are crucial for critically ill patients.

Currently, there is no consensus on the optimal tool for nutritional risk screening in critically ill patients. Commonly used tools include the NRS-2002, MNA-SF, and NUTRIC score. One study demonstrated that the NRS-2002 exhibited high sensitivity, while the MNA-SF demonstrated high specificity.<sup>194</sup> The joint guidelines from American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society for Critical Care Medicine (SCCM) recommend using the NRS-2002 or NUTRIC score for nutritional screening in critically ill patients.<sup>195</sup> The NUTRIC score is incorporated as a key indicator influencing nutritional status and prognosis, and the modified NUTRIC (m-NUTRIC) score can effectively identify ICU patients likely to benefit from early nutritional support.<sup>196</sup> Research shows that both the NRS-2002 and NUTRIC scores demonstrate robust nutritional screening capabilities.<sup>197</sup> Higher NRS-2002 scores are typically associated with prolonged mechanical ventilation duration, extended length of hospital stay, and increased 28-day mortality.<sup>198-199</sup> The NUTRIC score reliably predicts in-hospital mortality risk in critically ill patients.

**Question 21:** How to accurately assess muscle mass in critically ill patients?

**Recommendation 30:** Muscle mass is a critical indicator of nutritional status in critically ill patients. CT and magnetic resonance imaging (MRI) can be used to assess muscle mass, while bedside ultrasound is simple and feasible, which is recommended for evaluating muscle mass and quality in critically ill patients. (Grade C, Weak recommendation)

**Recommendation 31:** BIA can be used to assess and monitor body composition changes in critically ill patients, particularly muscle mass, phase angle, and fluid balance. Regular monitoring facilitates timely adjustment of treatment plans. (Grade C, Weak recommendation)

Studies show that the prevalence of sarcopenia in ICU patients is as high as 41%, with even higher rates among mechanically ventilated patients, and it is associated with one-year mortality.<sup>200-201</sup> CT and MRI can serve as reference standard methods for assessing muscle mass,<sup>202</sup> measuring skeletal muscle index to predict mortality risk.<sup>203-204</sup> However, due to radiation exposure and operational constraints, they are rarely used routinely in the ICU. In recent years, bedside ultrasound, as a visualizable technique, has gained widespread use for assessing muscle mass and trends due to its convenience, repeatability,

and dynamic monitoring capabilities. It can measure structural parameters such as muscle thickness, cross-sectional area, and fiber length, and evaluate muscle fat infiltration via grayscale values, demonstrating good accuracy and reliability.<sup>205-206</sup> Additionally, ultrasound can assess diaphragm function through thickening fraction and excursion, identifying diaphragm dysfunction in respiratory critically ill patients.<sup>207</sup> A prospective study of 70 sepsis patients revealed that early reductions in muscle thickness were good predictors of in-hospital mortality.<sup>208</sup>

In the ICU, BIA provides rapid information on nutritional status and fluid balance, assisting in timely adjustment of treatment plans and allowing repeated monitoring without additional radiation exposure.<sup>209</sup> The phase angle measured by BIA reflects cellular membrane integrity and functional status, with higher phase angles indicating better cellular health and nutritional status.<sup>210</sup> Studies suggest that low phase angle scores correlate with increased mortality and prolonged ICU stays.<sup>211-216</sup> Assessing phase angle at ICU admission may serve as a prognostic marker, and dynamic monitoring of its changes can guide nutritional interventions to improve outcomes.

**Question 22:** What inflammatory markers can assist in assessing malnutrition in critically ill patients?

**Recommendation 32:** CRP/hs-CRP is the primary marker for evaluating the severity of inflammatory responses in critically ill patients. Comprehensive assessment combined with interleukin-6 (IL-6) and serum amyloid A (SAA) improves diagnostic accuracy. (Grade C, Weak recommendation)

In critically ill patients, injury-induced inflammatory responses are regulated by cytokines and hormones, leading to increased insulin resistance, reduced appetite, and impaired nutritional metabolism.<sup>217-218</sup> Inflammation is a key driver of muscle catabolism.<sup>219</sup> A multicenter RCT in 2020 by Merker et al.<sup>219</sup> demonstrated that patients with lower CRP levels after 30 days of nutritional support exhibited reduced mortality, while those with extremely high CRP levels (>100 mg/L) showed no significant improvement in mortality post-intervention, which may be related to more severe underlying conditions.

A study by As'habi et al.<sup>220</sup> on cardiovascular disease patients undergoing dialysis revealed a positive correlation between CRP and malnutrition scores, but a negative correlation with albumin levels. Research by Gui Zhihong et al.<sup>221</sup> on maintenance peritoneal dialysis patients found that the malnutrition-inflammation score (MIS) negatively correlated with prealbumin, while positively correlating with hs-CRP and IL-6 ( $p < 0.05$ ).

Other inflammatory markers, such as IL-6, play critical roles in acute inflammatory diseases and are included as a key parameter in the NUTRIC score.<sup>167,222</sup> SAA, an acute-phase protein, elevates during acute infections or persistent inflammation.<sup>223-224</sup> Studies suggest that combining multiple inflammatory markers improves diagnostic accuracy for identifying inflammatory states compared to single-marker assessments.<sup>225-226</sup>

**Question 23:** How to diagnose energy requirements in critically ill patients?

**Recommendation 33:** Indirect calorimetry (IC) is recommended for diagnosing energy requirements in critically ill patients. If IC is unavailable, energy expenditure

may be calculated using carbon dioxide discharge ( $VCO_2$ ) measured by ventilators or oxygen consumption ( $VO_2$ ) obtained via pulmonary artery catheters. If neither method is feasible, predictive equations may be used for estimation. (Grade B, Weak recommendation)

Energy requirements in critically ill patients vary depending on individual differences, disease phase, and functional status. Multiple ICU guidelines internationally recommend IC as the standard for energy assessment, particularly in mechanically ventilated patients,<sup>227-229</sup> except those on extracorporeal membrane oxygenation (ECMO). IC can accurately reflect energy metabolism, guide nutritional therapy, reduce risks of underfeeding or overfeeding, and promote recovery.<sup>230</sup> The ESPEN ICU guidelines indicate that IC-guided energy delivery improves short-term mortality in critically ill patients.<sup>231</sup> The tight calorie control study (TICACOS) study also found that IC-based nutritional protocols reduced in-hospital mortality compared to predictive equations.<sup>232</sup> If IC is unavailable,  $VCO_2$  measured by ventilators or  $VO_2$  from pulmonary artery catheters may be used, offering higher accuracy than predictive equations.<sup>233-234</sup> Predictive equations should only be employed as a last resort.

**Question 24:** How to monitor gastric residual volume (GRV) in critically ill patients?

**Recommendation 34:** GRV can assess gastric retention in critically ill patients. Routine GRV monitoring is unnecessary for low-risk patients with EN tolerance. For high-risk patients, bedside ultrasound or gastric tube aspiration may be used to measure GRV. (Grade C, Weak recommendation)

GRV monitoring aims to evaluate gastric retention and emptying capacity, enabling early detection of feeding intolerance and reducing complication risks. A prospective cohort study by Lindner et al.<sup>235</sup> found that 34% of critically ill patients exhibited high GRV, which correlated with gastrointestinal symptoms and disease severity but not with ventilator weaning time or mortality. High GRV may serve as a marker of gastrointestinal dysfunction and clinical severity. Faramarzi et al.<sup>236</sup> similarly linked high GRV to disease severity. Guidelines from ASPEN and ESPEN recommend using high GRV to identify early feeding intolerance during EN.<sup>227-228, 237</sup> For patients with high GRV, strategies such as post-pyloric feeding, pharmacologic interventions, and positional adjustments may maintain EN delivery.

Common GRV monitoring methods include gastric tube aspiration and ultrasound. While aspiration is convenient, it risks nutrient/fluid loss, tube occlusion, and infection. Bedside ultrasound provides more accurate assessment of GRV and gastrointestinal function, validated by multiple studies.<sup>238-240</sup>

For critically ill patients on EN with low intolerance risk, routine GRV measurement is unnecessary.<sup>241-242</sup> Instead, gastrointestinal symptoms, intra-abdominal pressure monitoring, and gastrointestinal scoring systems should guide comprehensive evaluation of high-risk GRV patients.

#### PART 4: IMPLEMENTATION AND MANAGEMNT OF MALNUTRITION DIAGNOSIS

**Question 25:** How to train personnel responsible for diagnosing and managing malnutrition?

**Recommendation 35:** Healthcare professionals involved in nutritional care should receive standardized education and training. (Grade D, Weak recommendation)

Studies reveal that nearly half of hospitalized patients with malnutrition are not diagnosed promptly or are misclassified. Despite high prevalence rates, only 5% of patients are diagnosed with malnutrition during hospitalization, underscoring the critical role of clinical dietitians and healthcare professionals in accurate assessment and diagnosis. Current literature consistently highlights insufficient nutrition training among healthcare professionals, particularly in malnutrition evaluation and diagnosis.<sup>243</sup>

In clinical practice, the shortage of nutrition specialists and limited training time hinder personalized and comprehensive nutritional interventions for malnourished patients.<sup>244</sup> Some hospitals integrate malnutrition into quality indicators and improvement programs. Research demonstrates that the Malnutrition Quality Improvement Initiative (MQii) enhances healthcare professionals' awareness of malnutrition and improves the timeliness of screening, diagnosis, and intervention.<sup>245</sup> Another study based on ASPEN's 2015 criteria for adult malnutrition showed that educational videos improved healthcare professionals' understanding of cancer-related malnutrition assessment and diagnosis.<sup>243</sup>

**Recommendation 36:** Training should align the consensus between clinical dietitians and physicians on malnutrition diagnostic criteria. (Grade C, Weak recommendation)

A study found that among 1,391 patients diagnosed with malnutrition, only 768 (55.6%) received concurrent diagnoses from both physicians and dietitians, indicating low diagnostic consistency for at-risk patients. Discrepancies in malnutrition assessment may hinder effective nutritional interventions, stemming from differences in documentation practices, disease severity, and insufficient physician training.<sup>246</sup> Thus, unifying diagnostic criteria between clinicians and dietitians is essential.

**Question 26:** What are the timing and frequency for diagnosing malnutrition?

**Recommendation 37:** Nutritional assessment and diagnosis should occur within 48 h of identifying nutritional risk. Weekly nutritional risk screening is recommended during hospitalization. (Grade B, Strong recommendation)

Within 24 h of admission, validated nutritional risk screening tools should be applied to identify patients at risk. If nutritional risk is identified, clinical dietitians or physicians must conduct a comprehensive nutritional assessment within 48 h to diagnose malnutrition, evaluate its severity, and develop a care plan.<sup>247-248</sup> Weekly screening during hospitalization is advised.

Studies indicate that 20–50% of patients remain malnourished at discharge.<sup>249-250</sup> Therefore, nutrition assessment at discharge is also advisable to adjust post-discharge nutrition interventions and optimize follow-up services to prevent and improve clinical outcomes.<sup>251-252</sup>

**Question 27:** How to optimize malnutrition diagnosis management and application?

**Recommendation 38:** Malnutrition diagnoses, coding, and care plans should be fully documented in medical records. Multidisciplinary nutrition support teams should manage patients with complex nutritional needs. (Grade D, Weak recommendation)

Malnutrition diagnoses and management plans must be recorded in medical records, with diagnostic codes included in discharge summaries and other clinical records. A multicenter RCT demonstrated that multidisciplinary nutrition support teams improve nutritional status and reduce the risk of adverse outcomes in elderly patients.<sup>253</sup> Thus, such teams are critical for managing complex cases.

#### PART 5: TERMS AND DEFINITIONS RELATED TO MALNUTRITION DIAGNOSIS

To align with the World Health Organization's diagnostic standards, the writing committee referenced the International Classification of Diseases 11th Revision (ICD-11) and China Healthcare Security Diagnosis-Related Groups (CHS-DRG). Nutritional disorders are categorized under 05 Endocrine, Nutritional, or Metabolic Diseases.

1. **Nutritional Risk:** An existing or potential risk related to nutritional factors that may lead to adverse clinical outcomes. Nutritional risk is screened using evidence-based tools such as NRS-2002, with a score  $\geq 3$  indicating risk.

2. **Kwashiorkor (Malignant Malnutrition):** A disease caused by severe dietary protein deficiency. Clinical manifestations include widespread edema of the limbs, extreme irritability, anorexia, desquamating rash, abnormal hair pigmentation, and fatty liver. Diagnostic requires an edema index [extracellular water (ECW)/total body water (TBW) (ECW/TBW) ratio]  $\geq 0.4$  with  $\geq 1$  clinical manifestation.

3. **Nutritional Marasmus:** A condition resulting from inadequate energy intake, leading to body weight significantly below normal, accompanied by significant fat and muscle wasting. Diagnosis can be made if either of the following criteria is met:

(1) Involuntary weight loss ( $>5\%$  within 6 months or  $>10\%$  beyond 6 months);

(2) BMI  $<18.5 \text{ kg/m}^2$  with poor general condition.

4. **Severe Malnutrition with Marasmus:** A condition of marked deficiency of energy, protein, and other nutrients, leading to significant loss of fat and muscle mass and adversely affecting physiological function and clinical outcomes. Diagnostic criteria: weight loss ( $>10\%$  within 6 months or  $>20\%$  beyond 6 months) or low BMI ( $<18.5 \text{ kg/m}^2$  for age  $<70$ ;  $<20 \text{ kg/m}^2$  for age  $\geq 70$ ).

5. **Marasmic Kwashiorkor:** A state of severe protein-energy malnutrition combining features of kwashiorkor and marasmus. Diagnosis requires involuntary weight loss ( $>5\%$  within 6 months or  $>10\%$  beyond 6 months) or BMI  $<18.5 \text{ kg/m}^2$  with poor general condition, plus clinical manifestations of kwashiorkor.

6. **Protein-Energy Malnutrition (PEM):** A form of nutritional deficiency caused by inadequate protein or energy intake. Clinically, it's classified into skinny type, edematous type, and mixed type.

(1) **Skinny Type:** Predominantly energy deficiency, characterized by severe fat and muscle wasting, and growth retardation in infants and young children.

(2) **Edematous Type:** Predominantly protein deficiency over time, presenting with visceral protein depletion, hair loss, edema, delayed wound healing, hypoalbuminemia, and lymphocytopenia.

(3) **Mixed Type:** The most severe form, resulting from combined protein and energy deficiencies.

**7. Severe Protein-Energy Malnutrition:** A state of extreme deficiency of energy, protein, and other nutrients, leading to significant weight loss or failure to thrive. A body weight  $\geq 3$  standard deviations below the reference population mean strongly indicates this condition.

**8. Severe Malnutrition:** A state of extreme deficiency of energy, protein, and other nutrients, with deleterious effects on body function and clinical outcomes. The GLIM criteria may be used for diagnosis, requiring at least two of the following:

(1) Weight loss:  $>10\%$  within 6 months or  $>20\%$  beyond 6 months;

(2) Low BMI:  $<18.5 \text{ kg/m}^2$  for age  $<70$ ;  $<20 \text{ kg/m}^2$  for age  $\geq 70$ .

**9. Nutritional Edema:** A severe complication or comorbidity of malnutrition, often caused by reduced plasma osmotic pressure due to protein deficiency. Diagnosis requires an edema index (ECW/TBW ratio)  $\geq 0.4$ .

**10. Moderate Protein-Energy Malnutrition:** A state of deficiency of energy, protein, and other nutrients resulting in weight loss or inadequate weight gain in adults or children. A body weight 2–3 standard deviations below the reference population mean increases diagnostic likelihood.

**11. Moderate Malnutrition:** A state of moderate deficiency of energy, protein, and other nutrients adversely affecting physiological function and clinical outcomes. The GLIM criteria are recommended, requiring at least one of each:

(1) Weight loss ( $5\%–10\%$  within 6 months or  $>10\%–20\%$  beyond 6 months);

(2) Low BMI ( $<20 \text{ kg/m}^2$  for age  $<70$ ;  $<22 \text{ kg/m}^2$  for age  $\geq 70$ ).

**12. Mild Protein-Energy Malnutrition:** A state of mild deficiency of energy, protein, and nutrients causing mild weight loss or impaired weight gain in children. This condition is more likely when body weight falls 1–2 standard deviations below the reference population mean.

**13. Mild Malnutrition:** A state of mild deficiency of energy, protein, and nutrients with adverse effects on function and outcomes.

**14. Malnutrition:** A state of deficiency of energy, protein, and/or other nutrients that impairs body function and clinical outcomes. According to DRG guidelines, diagnosis is based on the two-step GLIM approach: first perform nutrition risk screening; if positive, apply GLIM diagnostic criteria-requiring at least one phenotypic criterion and one etiologic criterion-and then grade as moderate or severe malnutrition.

**15. Vitamin A Deficiency:** A disease caused by insufficient intake or absorption of vitamin A and carotenoids, manifesting primarily with ocular symptoms (e.g., night blindness, xerophthalmia) and skin/mucosal changes

(e.g., dry skin, follicular hyperkeratinization). Diagnosis is based on dietary history, clinical manifestations, and laboratory measurements; serum retinol is the recommended biomarker. According to World Health Organization (WHO), serum retinol  $<0.35 \text{ } \mu\text{mol/L}$  ( $100 \text{ } \mu\text{g/L}$ ) indicates deficiency;  $0.35–0.70 \text{ } \mu\text{mol/L}$  ( $100–200 \text{ } \mu\text{g/L}$ ) indicates marginal deficiency. Chinese experts recommend a serum retinol cut-off of  $<0.70 \text{ } \mu\text{mol/L}$  ( $200 \text{ } \mu\text{g/L}$ ) in adults to define deficiency.

**16. Wernicke Encephalopathy:** A classic syndrome of vitamin B1 deficiency characterized by psychosis, disorientation, ocular motor dysfunction (ophthalmoplegia, nystagmus, diplopia), ataxia, memory impairment, and confabulation. Diagnosis requires at least two of the following: (1) malnutrition; (2) ocular motor abnormalities; (3) cerebellar dysfunction; (4) altered mental state or memory loss.

**17. Vitamin B1 Deficiency (Thiamine Deficiency):** Also known as beriberi, a condition resulting from inadequate dietary intake of vitamin B1 (thiamine), affecting the gastrointestinal, nervous, and cardiovascular systems. Diagnosis is typically by biochemical testing: a thiamine tolerance test with urinary excretion  $<100 \text{ } \mu\text{g}$ , or 24h urinary thiamine  $<40 \text{ } \mu\text{g}$ , indicates deficiency. The 2023 Chinese Dietary Reference Intakes (DRIs) recommend a thiamine (Vitamin B1) Recommended Nutrient Intake (RNI) of 1.4 mg per day for adult males and 1.2 mg per day for adult females.

**18. Vitamin B2 Deficiency (riboflavin deficiency):** A nutritional disorder due to insufficient intake or excessive loss of riboflavin, leading to metabolic disorder and inflammatory lesions of the eyes, mouth, and skin. Diagnosis is based on dietary history, clinical manifestations, and laboratory tests: an erythrocyte glutathione reductase activation coefficient  $>1.4$  indicates deficiency; urinary riboflavin excretion  $<400 \text{ } \mu\text{g}$  in a load test or a urine riboflavin/creatinine ratio  $<27$  also suggests deficiency. The 2023 Chinese DRIs recommend daily intakes of 1.4 mg for adult males and 1.2 mg for adult females.

**19. Vitamin B6 Deficiency:** A condition caused by inadequate intake of vitamin B6 or altered metabolism due to disease or medications, presenting with skin lesions, stomatitis, glossitis, and neuropsychiatric symptoms. Diagnosis relies on dietary and medication history, clinical manifestations, and laboratory tests: plasma pyridoxal-5'-phosphate  $<14.6 \text{ nmol/L}$  ( $3.6 \text{ } \mu\text{g/L}$ ) indicates deficiency; in a tryptophan load test, a ratio of 24 h urinary xanthurenic acid excretion to tryptophan  $>12$  also suggests deficiency. The recommended nutrient intake (RNI) by the 2023 Chinese DRIs is 1.4 mg/d for adults.

**20. Vitamin B12 Deficiency:** Characterized by megaloblastic anemia and neurological demyelination. Diagnosis is based on serum vitamin B12  $<148 \text{ pmol/L}$ ; elevated methylmalonic acid and homocysteine levels can provide supportive evidence. The 2023 Chinese DRIs recommend a daily vitamin B12 intake of 2.4  $\mu\text{g}$  for adults.

**21. Folic Acid Deficiency:** Caused by insufficient dietary intake or malabsorption of folate, leading to hematologic, neurologic, psychiatric, and gastrointestinal manifestations, primarily megaloblastic anemia and neural tube defects in the fetus. Diagnosis is based on serum folate  $<3 \text{ } \mu\text{g/L}$  indicating deficiency, and red blood cell

folate <140 µg/L suggesting long-term deficiency. The 2023 Chinese DRIs recommend an RNI of 400 µg/day for adults.

22. Biotin Deficiency: Due to inadequate intake, restrictive diets, or certain medications, manifesting with dermatologic, mucosal, and neurologic signs such as periorificial dermatitis, alopecia, and atrophic tongue papillae. Diagnosis incorporates history, clinical manifestations, and laboratory tests: 24-hour urinary biotin excretion <1 µg or whole-blood biotin <100 ng/L. The 2023 Chinese DRIs set the appropriate intake (AI) for adults at 40 µg/day.

23. Pantothenic Acid Deficiency: A rare condition of nutritional disorder due to low pantothenic acid levels, characterized by nausea, vomiting, abdominal cramps, irritability, headache, depression, paralysis, muscle spasms, and limb paresthesia. It often coexists with deficiencies of other macronutrients and vitamins. Diagnosis should be based on medical history, clinical manifestations, and laboratory tests: urinary pantothenic acid excretion <1 mg/day or blood pantothenic acid <1 mg/L. The 2023 Chinese DRIs recommend an AI of 5.0 mg/day for adults, 6.0 mg/day in pregnancy, and 7.0 mg/day during lactation.

24. Vitamin B-Complex Deficiency: A state of malnutrition due to insufficient levels of one or more B vitamins, commonly presenting with oral mucositis, skin lesions, and neuropsychiatric symptoms. Diagnosis requires dietary history, clinical manifestations, and measurement of specific B vitamins in blood/urine.

25. Scurvy: Caused by vitamin C deficiency, clinically characterized by petechiae, gingival swelling, stomatitis, and osteoporosis. Diagnosis is based on history, clinical manifestations, and laboratory tests, with differential diagnosis excluding arthritis and hemorrhagic disorders.

26. Vitamin C Deficiency (Ascorbic Acid Deficiency): Caused by inadequate vitamin C intake or increased requirements, presenting with scurvy. Diagnosis integrates history, clinical manifestations, and laboratory tests (e.g., urinary vitamin C load test, plasma ascorbate measurement); urinary vitamin C <5 mg/day or plasma vitamin C <2 mg/L indicates deficiency. The 2023 Chinese DRIs recommend an RNI of 100 mg/day for adults and pregnant women, and 150 mg/day during lactation.

27. Vitamin D Deficiency: A disorder resulting from insufficient intake, synthesis, or metabolism of vitamin D, presenting as rickets in children or osteomalacia in adults. Diagnosis is based on clinical manifestation and serum 25-hydroxyvitamin D measurement. International criteria classify 25-hydroxyvitamin D levels of 50–75 nmol/L as insufficient, 25–50 nmol/L as mild deficiency, 12.5–25 nmol/L as moderate deficiency, and <12.5 nmol/L as severe deficiency. Chinese experts recommend ≥50 nmol/L as normal, 30–50 nmol/L as insufficient, and <30 nmol/L as deficient. The 2023 Chinese DRIs set the RNI at 10 µg/day for adults 18–64 years (including pregnant/lactating women) and 15 µg/day for those ≥65 years.

28. Dietary Calcium Deficiency: A state of inadequate calcium intake. In infants and children, it may cause growth retardation, osteomalacia, skeletal deformities, and rickets; in older adults, osteomalacia and osteoporosis are common. The 2023 Chinese DRIs recommend: AI of

200 mg/day for infants 0–6 months, 350 mg/day for 7–12 months; RNI of 500 mg/day for children 1–3 years, 600 mg/day for 4–6 years, 800 mg/day for 7–8 years and adults (including pregnant/lactating women), and 1 000 mg/day for adolescents 9–17 years.

29. Keshan Disease: A regional cardiomyopathy first identified in the Keshan region of Heilongjiang Province, China, characterized by multifocal myocardial necrosis in children aged 2–6 years and women of childbearing age. Clinical features include myocardial necrosis, cardiomegaly, cardiac insufficiency, and arrhythmias; severe cases may progress to cardiogenic shock or heart failure. Selenium deficiency is the primary cause. Radiography shows globular cardiomegaly; laboratory tests reveal plasma selenium <0.4 µmol/L (<32 µg/L) and reduced erythrocyte glutathione peroxidase activity. Widespread use of selenium-fortified salt has rendered Keshan disease exceedingly rare in China.

30. Dietary Selenium Deficiency: Caused by inadequate selenium intake, leading to Keshan disease, Kashin-Beck disease, immune dysfunction, reduced antioxidant capacity, and thyroid dysfunction. The 2023 Chinese DRIs recommend selenium intakes of 60 µg/day for adolescents and adults, 65 µg/day for pregnant women, and 78 µg/day during lactation.

31. Zinc Deficiency: A state of insufficient body zinc stores. Mild zinc deficiency is often overlooked due to lack of obvious clinical symptoms; severe deficiency may cause growth retardation, impaired wound healing, taste disturbances, increased incidence of gastrointestinal disorders, and immunodeficiency. Zinc nutritional status is evaluated primarily by biochemical and functional markers in conjunction with dietary assessment. Plasma zinc is diagnostically useful only in severe deficiency; it is not recommended for individual diagnosis of mild to moderate deficiency. The early symptom of zinc deficiency is reduced taste sensitivity. Salivary zinc correlates well with taste sensitivity and may serve as a reference indicator of individual zinc status. Functional assessment may include zinc-dependent enzyme activity, taste tests, and dark-adaptation measures. Monocyte metallothionein mRNA has emerged as a reliable indicator of mild zinc deficiency and is considered a relative gold standard for zinc nutritional assessment.

32. Dietary Zinc Deficiency: A state of inadequate zinc intake leading to suboptimal body zinc status, which may result in immunodeficiency or impaired growth and development in children. According to the 2023 Chinese DRIs, the recommended intakes are:

- Infants 0–6 months: 1.5 mg/day
- Infants 7–12 months: 3.2 mg/day
- Children 1–3 years: 4.0 mg/day
- Children 4–6 years: 5.5 mg/day
- Children 7–11 years: 7.0 mg/day
- Adolescents 12–14 years: boys 8.5 mg/day, girls 7.5 mg/day
- Adolescents 15–17 years: boys 11.5 mg/day, girls 8.0 mg/day
- Adults 18–29 years: men 12.5 mg/day, women 8.5 mg/day
- Adults ≥30 years: men 12.0 mg/day, women 8.5 mg/day

- Pregnant women: 10.5 mg/day
- Lactating women: 13.0 mg/day

33. **Copper Deficiency:** Insufficient body copper stores that may cause anemia, leukopenia, hypercholesterolemia, arrhythmias, osteoporosis, anorexia, and hepatosplenomegaly. Common in patients after bariatric or other non-duodenal abdominal surgery, those with unexplained neuropathies, severe burns, long-term renal replacement therapy, jejunal feeding, or prolonged PN. Serum copper and ceruloplasmin levels should be measured every 6–12 months in at-risk patients. The 2023 Chinese DRIs recommend an RNI of 0.80 mg/day for adults, 0.91 mg/day in early pregnancy, 0.90 mg/day in mid- and late pregnancy, and 1.50 mg/day during lactation. Normal serum copper is ~10–24.6  $\mu\text{mol/L}$  (640–1 560  $\mu\text{g/L}$ ); ceruloplasmin <150 mg/L suggests deficiency, though it may rise and cannot be as an indicator of copper nutritional status in cases of liver disease, malignancy, or inflammation.

34. **Iron Deficiency:** A deficit of body iron stores leading to iron-deficiency anemia, characterized by pallor of skin and mucous membranes (notably lips, buccal mucosa, and nail beds), often with anorexia or pica. The 2023 Chinese DRIs recommend daily iron intakes of 12 mg for adult men; 18 mg for adult women; 18 mg in early pregnancy; 25 mg in mid-pregnancy; 29 mg in late pregnancy; and 24 mg during lactation. Serum ferritin, reflecting iron stores, is the most reliable method for diagnosing iron-deficiency anemia. Serum ferritin <15  $\mu\text{g/L}$  indicates iron-store depletion; serum transferrin receptor rises 3–4 times in iron-deficiency anemia; free erythrocyte protoporphyrin (FEP) >0.9  $\mu\text{mol/L}$  (whole blood) or FEP/hemoglobin >4.5  $\mu\text{g/g}$  diagnoses anemia and is recommended by WHO for population prevalence. Hemoglobin normal ranges: men 120–160 g/L, women 110–150 g/L; mean corpuscular volume (MCV) <80 fL and red cell volume distribution width (RDW) >15% also suggest iron deficiency.

35. **Magnesium deficiency:** A state of low serum magnesium causing neuromuscular hyperexcitability (muscle tremor, carpopedal spasm, hyperreflexia, ataxia) and delirium, psychosis, seizures, or coma in severe cases. Serum magnesium <0.7 mmol/L defines hypomagnesemia. The 2023 Chinese DRIs recommend daily magnesium intakes of 330 mg for adults 18–29 years, 320 mg for adults 30–64 years, 310 mg for adults 65–74 years, 300 mg for adults  $\geq 75$  years, 370 mg for pregnant women, and 330 mg for lactating women.

36. **Manganese Deficiency:** Insufficient manganese intake potentially resulting in growth retardation, skeletal deformities, reproductive dysfunction, seizures, movement disorders, dermatologic problems, severe hypocholesterolemia, weight loss, and slowed hair and nail growth. No reliable biomarkers exist; diagnosis is based on intake assessment, history, and clinical manifestations. The 2023 Chinese DRIs set adequate intakes of 4.5 mg/day for adult men, 4.0 mg/day for adult women (including pregnancy), and 4.2 mg/day during lactation.

37. **Chromium Deficiency:** A condition of low body chromium causing growth arrest, hyperlipidemia, impaired glucose tolerance, hyperglycemia, and glycosuria. Diagnosis is challenging due to undetectably low blood

chromium; urinary chromium measurements apply only to supplemented individuals for nutrition assessment. The 2023 Chinese DRIs recommend adequate intakes of 35  $\mu\text{g/day}$  for adult men, 30  $\mu\text{g/day}$  for adult women, 30  $\mu\text{g/day}$  in early pregnancy, 33  $\mu\text{g/day}$  in mid-pregnancy, and 35  $\mu\text{g/day}$  in late pregnancy and lactation.

38. **Multiple Nutrient Deficiencies:** A condition of severe deficiency in one or more nutrients, impairing physical functions and increasing disease risk. This condition encompasses deficiencies in both macronutrients and micronutrients. Diagnosis requires integration of clinical manifestations, biochemical markers, and dietary intake. The presence of deficiencies in  $\geq 2$  nutrients confirms the diagnosis.

39. **Overnutrition:** Excessive nutrient intake beyond physiological needs, typically from surplus energy or specific macronutrients (e.g., fats, sugars, refined carbohydrates). Clinically, overnutrition may manifest as obesity, fatty liver, dyslipidemia, and hyperuricemia. Diagnosis is based on dietary history, clinical manifestations, anthropometry (weight, BMI, waist circumference), and laboratory tests.

40. **Protein-Energy Malnutrition Sequelae:** Long-term or severe protein and energy deficiency leading to stunted growth, organ dysfunction, and long-term health issues. Common in children and occasionally in adults under extreme conditions including diseases and poverty. Manifestations include growth retardation, weight loss, dehydration, anemia, muscle wasting, and osteoporosis. ICD-10 defines sequelae as residual signs and symptoms after the acute disease has resolved. Diagnosis combines dietary history, clinical manifestations, laboratory tests, and imaging.

41. **Overnutrition Sequelae:** Long-term excess intake of energy and/or specific nutrients resulting in health issues and complications, often linked to obesity, metabolic syndrome, and elevated cardiovascular risk. Manifestations include obesity, hyperuricemia, fatty liver, and dyslipidemia. Diagnosis integrates dietary history, clinical manifestations, anthropometry, laboratory tests, and imaging.

42. **Sarcopenia:** A syndrome characterized by progressive loss of skeletal muscle mass, strength, and function, prevalent in bedridden, sedentary, malnourished, alcohol- or tobacco-using individuals, cancer patients, and frail older adults. According to the AWGS criteria, diagnosis requires appendicular skeletal muscle mass plus muscle strength and/or physical performance:

(1) **Skeletal muscle mass** (appendicular lean mass/height<sup>2</sup>): measured by DXA (men <7.0 kg/m<sup>2</sup>; women <5.4 kg/m<sup>2</sup>) or BIA (men <7.0 kg/m<sup>2</sup>; women <5.7 kg/m<sup>2</sup>).

(2) **Muscle strength:** grip strength <28.0 kg in men and <18.0 kg in women.

(3) **Physical performance:** gait speed <1.0 m/s (4 m walk test), Timed Up and Go  $\geq 12$  s, or Short Physical Performance Battery (SPPB)  $\leq 9$  points.

Diagnosis is confirmed by low skeletal muscle mass plus low strength and/or poor physical performance.

## SUPPLEMENTARY MATERIALS

All supplementary materials are available upon request to the editorial office.

## ACKNOWLEDGEMENTS

List of Expert Committee Members for Guideline Development.

### *Authors (listed in alphabetical order by surname)*

Wei Chen (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Ting Han (Department of Clinical Nutrition, Shanghai Tenth People's Hospital, Tenth People's Hospital of Tongji University, Shanghai); Hua Jiang (Institute of Emergency Medicine and Disaster Medicine, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu); Zhenyi Jia (Department of General Surgery, Shanghai Sixth People's Hospital, Shanghai); Hailong Li (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Rongrong Li (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Zengning Li (Hebei Key Laboratory of Nutrition and Health, The First Hospital of Hebei Medical University, Shijiazhuang); Yumei Qi (Department of Nutrition, Tianjin Third Central Hospital, Tianjin); Huanlong Qin (Department of General Surgery, Suzhou Municipal Hospital, Suzhou); Chunhai Shao (Department of Clinical Nutrition, Huashan Hospital, Fudan University, Shanghai); Xinying Wang (Department of General Surgery, Central Hospital of Eastern Theater Command, Nanjing); Yi Wang (Department of Medical Records, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Hongxia Xu (Department of Clinical Nutrition, Daping Hospital, Army Medical University, Chongqing); Hua Yang (Department of General Surgery, Chongqing General Hospital, Chongqing); Picong You (Department of Internal Medicine Intensive Care Unit, Tianjin Hospital, Tianjin); Li Zhang (Department of General Surgery, Central Hospital of Eastern Theater Command, Nanjing); Mingwei Zhu (Department of General Surgery, Beijing Hospital, Beijing).

### *Methodology experts*

Hua Jiang (Institute of Emergency and Disaster Medicine, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Affiliated Hospital of University of Electronic Science and Technology of China, Chengdu); Wei Chen (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing).

### *Secretariat of the writing group (listed in alphabetical order by surname)*

Liru Chen (Department of Clinical Nutrition, Beijing Hospital, Beijing); Hongzhen Du (Hebei Key Laboratory of Nutrition and Health, The First Hospital of Hebei Medical University, Shijiazhuang); Yan Liu (Clinical and Epidemiological Research Center, Beijing Anzhen Hospital, Capital Medical University, Beijing); Xiaodong Shi (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Mingyao Sun (Department of Clinical Nutrition, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou); Yu Wang (Department of Clinical Nutrition, Chinese Academy of Medical Sciences & Peking Union Medical College, Peking Union Medical College Hospital, Beijing); Huijuan

Xiao (Department of Nutrition, Tianjin Third Central Hospital, Tianjin); Jing Yang (Department of Clinical Nutrition, The First Affiliated Hospital of Soochow University, Suzhou); Liangyu Yin (Department of Nephrology, Xinqiao Hospital, Army Medical University, Chongqing).

## CONFLICT OF INTEREST AND FUNDING DISCLOSURES

All authors have declared no conflicts of interest.

This research was funded by the National Natural Science Foundation of China (72074222); National High Level Hospital Clinical Research Funding (2022-PUMCH-B-054).

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