# Call to Improve Coding of Cancer-Associated Cachexia

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## ABSTRACT

Cachexia is a systemic wasting syndrome prevalent in patients with cancer that significantly affects quality of life, health care costs, and therapeutic outcomes. Despite its clinical importance, cachexia is rarely formally diagnosed. This deficiency presents a challenge for effective patient management and care, health care resource allocation, and the advancement of therapeutic approaches. Here, we highlight impedances to the diagnosis and coding of cachexia, including the absence of standardized therapy, a lack of incentives for accurate coding, and overlapping clinical features with other conditions. We differentiate cachexia from related conditions like unintentional weight loss, sarcopenia, frailty, and protein-calorie malnutrition, outlining their distinct clinical features and inter-relations. We propose an approach to enhance diagnostic accuracy and coding for cachexia. This effort will enable better prevalence data, translation of mechanism-based therapy development, patient identification and stratification, and ultimately advanced diagnostics and US Food and Drug Administration–approved treatments for cachexia.

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Correct patient management requires correct diagnoses. Diagnostic uncertainty can be the consequence of incomplete understanding of a syndrome or disease, unclear or nonvalidated diagnostic criteria, incomplete evaluation of patients, and/or administrative uncertainty around documentation and coding. Here, we explore the challenges and potential solutions around the diagnosis and miscoding of patients with cancer-associated cachexia, a common and deadly condition. We focus on evaluation and code assignment and propose immediately actionable steps to improve clarity in the diagnosis and management of patients with cachexia.

## CANCER CACHEXIA

Cachexia is a systemic wasting condition that occurs frequently in the setting of chronic diseases, especially in patients with progressive cancer.[1] Weight loss is diagnostic of cachexia when it exceeds 5% or more in a 6-month period on the basis of the latest consensus definition.[2] This degree of weight loss is highly prevalent, occurring in about one third of patients with early-stage disease and nearly three quarters of patients with advanced cancer.[3-5] The prevalence varies on the basis of the primary site of cancer. For example, the Eastern Cooperative Oncology Group found that the frequency of weight loss ranged from 31% for favorable non-Hodgkin's lymphoma to 87% in gastric cancer.[3] Unlike the generalized tissue wasting observed with starvation, the lost weight during cachexia is primarily from atrophy of skeletal muscle and adipose tissue with large amounts of heterogeneity among patients.[6,7]

Cancer cachexia is not only common but also highly relevant to patient management. The presence of cachexia is associated with worse quality of life, more treatment-related complications, worse treatment responses, and poor overall survival in patients with cancer.[8-11] Cachexia can also strain the supporting network of friends and family of patients, leading to well-intended, but potentially distressing repeated conversations and conflict around body weight, mealtimes and food intake, and assistance for activities of daily living.[12,13] Furthermore, cachexia contributes to overall health care costs by increasing the number of hospitalizations and prolonging the length of inpatient stays, thereby raising the total cost of admissions.[14,15]

## BARRIERS TO CACHEXIA DIAGNOSIS

Despite the simple diagnostic criteria of body weight change, there are several barriers that limit the diagnosis of cachexia. First and foremost, obtaining accurate historical body weight data can be a significant challenge. Patients and their family members often do not recall their usual body weight or how their weight has changed over time. Some families and cultures do not discuss the subject of weight as a sign of respect or privacy, making discussions of weight changes related to cancer treatment more complicated. Measuring height and weight is not performed consistently or accurately in different care settings such as a doctor's office, treatment facility, or hospital. Furthermore, hydration status, fluid balance from intravenous fluid administration, and/or medication effects can influence weight measurements and mask changes in body composition. These factors

are operational hurdles to precise determinations of 5% weight loss over the past 6 months.

In addition to the operational limitations, several other factors may contribute to the under-reporting of cachexia. First, cachexia has no standard approved therapy or validated treatment algorithm in the United States, resulting in clinicians seeing no benefit in formally diagnosing or billing for the condition.[16] Second, oncology providers are tasked with the management of many complex medical conditions and complications. Cachexia may not reach a sufficient priority until patients appear overtly wasted on physical examination and the cancer treatment plan is compromised. Third, the physician or the health care facility may not receive any additional reimbursement for managing patients with cachexia, so they are not incentivized to provide correct diagnostic coding. In other words, the correct or incorrect coding of cachexia seemingly has no consequence on care provision or delivery.

Taken together, these considerations may explain why cachexia is rarely diagnosed formally despite the high prevalence and clinical impact. Only 2% of patients with cancer experiencing the cachexia weight loss criteria (≥5% weight loss) receive the correct diagnosis using International Classification of Disease, 10th edition (ICD-10) codes.[17] Even by expanding the coding to include other cachexia-related ICD-10 codes (ie, anorexia, abnormal weight loss, and feeding difficulties), only 5% of those meeting the cachexia weight loss criteria are captured.[17] Similarly, a broader analysis of patients with and without cancer found that only 14% of patients with text descriptors of cachexia in their electronic medical record notes receive an ICD-10 code for cachexia.[18] These results imply that physicians observe the features of cachexia, but coders do not specifically code for it, which likely leads to an under-reporting of cachexia in large-scale data collection and analysis efforts.

There is also evidence of undercoding cachexia during hospital admissions. On the basis of data from community hospital admissions in the United States, only 3% of patients with cancer receive a diagnosis of cachexia.[14] This finding contrasts with studies that report that 20%-30% of hospitalized patients with cancer experience significant weight loss. These data are striking given that coding tends to be more systematic in the hospital with standardized protocols, compliance requirements, and closer monitoring by coders and billing teams, as opposed to the outpatient setting.

It is important to accurately diagnose and code for all patient conditions, procedures, and diseases using ICD-10 codes. Large-scale data analyses that inform health care payment policies and resource allocation and track health care delivery and patient outcomes over time, such as those conducted through the US. Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project, are reliant on coded diagnoses added to claims forms. The undercoding of cachexia results in less visibility for the diagnosis and under-recognition of the health care resources required to treat this disease, thereby leading to inadequate therapy and poor patient outcomes.

## OVERLAPPING CONDITIONS

From the oncologist's perspective, cachexia may be difficult to identify because the signs and symptoms overlap with other conditions. For example, cachexia shares features and may occur concomitantly with other conditions associated with loss of body weight and muscle mass, including unintentional weight loss (ICD-10 R63.4), sarcopenia (ICD-10 M62.84), frailty (ICD-10 R54), and protein-calorie malnutrition (ICD-10 E43 for severe, E44 for moderate, and E44.1 for mild). The significant overlap between these conditions was exemplified by a study of older medical patients where 31% had more than one of these conditions (11% two, 12% three, and 8% all four).[19] Since oncologists may not be familiar with the subtleties underlying the diagnosis of wasting conditions, we next review their major clinical features.

Unintentional weight loss is an umbrella term used in the early phases of clinical diagnoses when the etiology of weight loss is not apparent. The most common causes of unintentional weight loss are malignancy, nonmalignant GI disorders, and psychiatric conditions such as depression and dementia.[20] Similar to cachexia, weight loss is considered clinically significant when it reaches between 5% and 10% compared with usual body weight within the preceding 3-12 months.[21] The prevalence of unintentional weight loss in US adults varies between 7% and 13%, with differences attributable to both demographics and duration of follow-up.[22] A rational, stepwise approach to the patient presenting with unintentional weight loss has been previously described.[23] When someone with unintentional weight loss is found to have cancer as a cause, then the most appropriate diagnosis is cachexia.

Sarcopenia is a general term referring to a state of muscle loss and reduced strength that can be physiologic because of aging (primary) or secondary to diseases like cancer.[24,25] Secondary sarcopenia should be diagnosed as cachexia, and therefore, we reserve the term sarcopenia for muscle loss related to aging. It typically begins in the third decade of life, and by age 80 years, there is approximately a 30% reduction in muscle mass.[26] Sarcopenia is a highly prevalent condition occurring in about 10% of adults older than 60 years and nearly 30% of persons older than 80 years.[24] It is thought to result from age-related neurodegeneration, endocrine dysfunction (insulin resistance, low testosterone, and growth hormone), and chronic reductions in food and protein intake, a contributor that overlaps with the negative energy balance that results in cachexia. Sarcopenia can precede the onset of cancer, and its effects may compound resultant effects of cancer-associated cachexia.[27] Both conditions cause muscle loss and functional deficits; however, cachexia is a consequence of an underlying, unresolved

pathology that promotes the wasting process. Although there is overlap, the treatment responses are different. For example, sarcopenia typically responds well to diet and exercise interventions, whereas no such evidence exists for cachexia.[28-30]

The loss of muscle in sarcopenia and cachexia causes a physiologic decline that places people at risk of adverse health outcomes, a state generally referred to as frailty.[31] The prevalence of frailty in the United States ranges from 4% to 16% in community-dwelling men and women 65 years and older and was up to 43% in older patients with cancer.[32] Frail adults have weakness and fatigue, more medical comorbidities, and reduced tolerance to medical and surgical interventions as compared with nonfrail adults. As a general rule of thumb, frail adults have sarcopenia and/or cachexia, but not all those with sarcopenia and cachexia have frailty.

One of the most difficult distinctions to make in clinical practice is the differentiation between cachexia and protein-calorie malnutrition. Malnutrition, a state of inadequate intake of food resulting in depletion of the body's nutrient reservoirs, is one of the most prevalent problems in patients with cancer and has been shown to negatively affect cancer treatment, quality of life, and mortality.[33] Differentiating malnutrition from cachexia can be hard because many of the same physiologic features used to identify malnutrition, such as poor food intake, weight loss, and nutritional deficiencies,[34-36] are also present in those with cachexia. However, some differences have been described. For example, the low food intake that drives malnutrition activates a systemic starvation response that depletes all organs of their mass, which differs from cachexia where the atrophy is specific to fat and muscle.[37] This starvation state is responsive to medical nutrition therapy,[38] which is not the case for cachexia. Cachexia, by definition, excludes individuals where weight loss can be fully reversed by conventional nutritional support.[2] Therefore, if someone with cancer responds positively to a nutritional intervention, then the best diagnosis is malnutrition. However, clinical studies and those in clinical practice rarely assess the response to nutritional therapy, and, therefore, weight loss alone is commonly used as the primary diagnostic criteria for both diagnoses. This approach cannot distinguish cachexia and malnutrition.

## CACHEXIA IDENTIFICATION AND DIAGNOSIS

To improve the identification and care of patients with cancer cachexia, we propose the following approach (Fig 1). Patients should be weighed and queried about subjective weight loss at each visit. Questions surrounding loose fitting clothing, appetite, early satiety, or number of meals may be helpful when weight is not being monitored by the patient and family directly. If the data are available, the current body weight should be compared with that in previous months to determine the trajectory of weight loss. When long-term data are not available, other indicators may reveal a cachexia diagnosis. For example, a low BMI (<20 kg/m$^2$), a negative weight loss trajectory (>1 kg/month loss), obvious physical wasting, or a positive malnutrition screening test should prompt a focused evaluation for cachexia. For example, the Global Leadership Initiative on Malnutrition (GLIM) criteria identify patients who simultaneously have a combination of at least one phenotypic criterion (weight loss and/or low BMI for age and/or low fat free mass for age) and one etiologic criterion (decreased intake, chronic GI condition, disease burden, and inflammatory condition of cancer).[39] GLIM has a positive likelihood ratio of 3.9 and a negative likelihood ratio of 0.35 for diagnosing malnutrition.[40] Regular screening should be integrated into routine clinical visits to address any emerging nutritional deficiencies or signs of cachexia promptly. These screening sessions can be performed by any member of the medical team and at opportunistic moments, such as during treatment infusions or while patients are waiting for interval imaging studies. A concern for cachexia note can be placed in the medical chart for subsequent evaluation.

The full cachexia evaluation should occur at diagnosis and subsequent therapeutic response intervals. A defined member of the medical team should confirm and document the weight trajectory using the electronic medical records and subjective recall of the patient's stable young adult weight or usual weight. More information should be gathered on the patient's eating habits and nutrition impact symptoms (anorexia, pain, nausea, dysgeusia, etc). Of note, the Functional Assessment of Anorexia/Cachexia Therapy Anorexia Cachexia Scale is a validated instrument designed to assess symptoms and concerns related to anorexia and cachexia in patients with cancer.[41] A GI review of systems should be performed, and a history of functional deficits should be documented. Findings of fat and muscle wasting on physical examination are important to note as well as objective measures of physical function, including the 30-second chair stand or hand grip strength, which have good test characteristics and can be quickly performed in the office[42-45] (normative values can be found in the references and CDC STEADI).[46] Finally, as part of the diagnostic workup, other differential diagnoses should be considered and, if appropriate, further investigated.[47] In particular, physicians should consider and evaluate reversible or at least treatable causes of weight loss, including hyperthyroidism, hypogonadism, malabsorption, and depression. On the basis of this approach, a proper diagnosis of cachexia can usually be reached.

At present, there are no advanced diagnostics nor US Food and Drug Administration–approved treatments for the workup or management of cachexia, which creates a barrier to proper coding. Several promising pharmacologic agents targeting poor oral intake and tissue wasting are in late stages of development and may soon be approved for use. Accurate understanding of the prevalence of cachexia and identifying patients who will benefit from therapies are

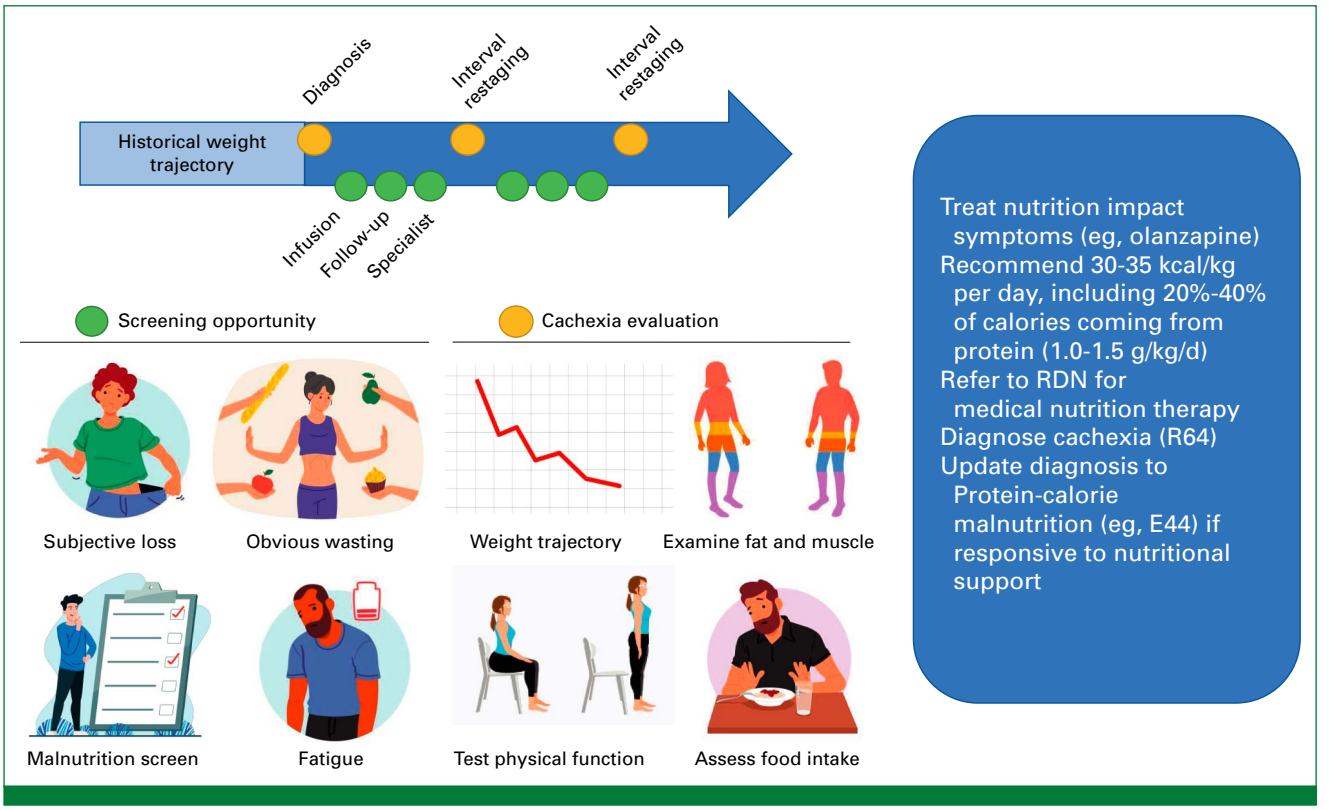


**FIG 1.** Cachexia screening and evaluation opportunities. To improve the identification and care of patients with cancer cachexia, we propose screening and evaluation at multiple time points over the course of diagnosis and treatment. Obtaining historical weight information is useful at diagnosis to understand the extent of weight loss, which commonly occurs before patients present with cancer. If no previous objective body weight measures are available in the medical record, then patients can be queried on their recall of body weight 6 and 12 months ago. When previous body weights are not available, other indicators may reveal a cachexia diagnosis. For example, a low BMI (<20 kg/m$^2$), a negative weight loss trajectory (>1 kg/month loss), obvious physical wasting, or a positive malnutrition screening test should prompt a focused evaluation for cachexia. The GLIM criteria can effectively identify patients with malnutrition.[40] Baseline assessments of body composition (fat and muscle mass), physical function, and food intake can be efficiently performed by office staff at diagnosis and then interval restaging appointments (yellow dots). We recommend direct observation of subcutaneous fat amount and muscle bulk for assessment of body composition, a 30-second sit-to-stand test for physical function (normative values found in references and CDC[42,45,46]), and the FAACT Anorexia Cachexia Scale to assess symptoms of low food intake.[41] If cachexia is not identified, then every subsequent touch point (green dots) is an opportunity to screen for cachexia. Patients should be weighed and queried about subjective weight loss and weakness at each visit. These screening sessions can be performed by any member of the medical team and at opportunistic moments, such as during treatment infusions or while patients are waiting for interval imaging studies. A concern for cachexia note can be placed in the medical chart for subsequent evaluation. If cachexia is confirmed, it should be diagnosed and coded (eg, R64). Key interventions involve treating nutrition-impact symptoms (may offer olanzapine), recommending a daily caloric intake of 30-35 kcal/kg with 20%-40% of calories from protein (1.0-1.5 g/kg/day), and referring patients to a RDN for personalized medical nutrition therapy. If the patient responds positively to nutritional support, the diagnosis can be updated to protein-calorie malnutrition (eg, E44 series). FAACT, Functional Assessment of Anorexia/Cachexia Therapy; GLIM, Global Leadership Initiative on Malnutrition; RDN, registered dietitian nutritionist.



needed so that efforts to reduce their suffering can be streamlined. Furthermore, proper coding can benefit patients with cancer now. One study found that 93% of patients with an ICD-based diagnosis of cachexia were offered an intervention to address the diagnosis.[17] Although evidence does not support the recommendation of any pharmacologic therapy as of yet, ASCO recommends referral to a dietician with the goals of providing patients practical and safe advice for feeding, with particular emphasis on education regarding high-protein, high-calorie, nutrient-dense food.[16] Specifically, a daily consumption of 30-35 kcal/kg including 20%-40% of calories coming from protein (1.0-1.5 g/kg/d) is recommended.[16,33] The lack of reimbursement for nutrition assessment and counselling is a known barrier to timely recognition of cancer cachexia.[48] In addition, contemporary management of cachexia includes proper supportive care by addressing associated symptoms, including anorexia, nausea, fatigue, pancreatic exocrine insufficiency, and diarrhea through a multidisciplinary approach.[49] In a rapid recommendation update, ASCO recommended that clinicians may offer low-dose olanzapine once daily to improve weight gain and appetite in patients experiencing cancer cachexia.[50] Physicians should clearly document cachexia treatments and their effectiveness in medical files, with proper coding,

to facilitate academic analysis and aid future research efforts.

Future improvements in the diagnosis and management of cachexia could be realized by integrating systematic monitoring practices within the clinical workflow. For example, implementing a program in the electronic medical record that tracks body weight for all patients with cancer and alerts the care team when levels are dropping would facilitate early identification of those at risk of cachexia and allow for timely intervention. This approach would also allow researchers to combine body weight changes with other clinical measures to identify factors that correlate with the presence of cachexia, such as tumor genetic variants, which has been done for obesity.[51] Furthermore, computed tomography imaging for body composition assessments offers a viable method for evaluating both fat and muscle mass in patients with cancer.[6,52] We and others are actively working to develop artificial intelligence–based tools to track and report body composition changes in all patients with cancer across the health care system.[53] This approach would provide clinicians with actionable data to detect and monitor cachexia. As this area evolves, distinguishing cachexia from other overlapping metabolic conditions will be critical. Large, prospective, observational studies are ongoing to search for novel phenotypes and biomarkers of cachexia that may aid in this effort (eg, ClinicalTrials.gov identifier: NCT06073431).[6] The establishment of automated pipelines to track body weight and body composition, in addition to the identification of novel clinical features and blood based biomarkers, could support earlier and more accurate identification of cachexia, positioning oncology teams to deliver tailored supportive care and improve patient outcomes.

In addition to benefiting patients, correct workup and coding of patients with cancer cachexia could help clinical research in multiple ways. It would aid correct documentation and will provide a quantifiable count of cachexia frequency. Most importantly, it will facilitate therapy of patients with cachexia, accurately identify resources required to treat this disease in different care settings, promote appropriate communication of the diagnosis for all health care team members and active management of the condition by caregivers, and aid enrollment of patients into clinical trials that may help refine the care, the increasingly mechanistic understanding of the syndrome, and ultimately treatment of this challenging condition.



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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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