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# Unintentional Weight Loss

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## Abstract

Unintentional weight loss (UWL) is a common symptom, particularly among older patients. In one site, patients with UWL have increased morbidity and mortality; in the other site, the prognosis of the patients is related to primary cause of the UWL. The differential diagnosis of the underlying diseases leading to UWL is broad and includes both malignant and nonmalignant gastrointestinal (GI) diseases, as well as endocrine, infectious, cardiopulmonary, and psychiatric disorders and side effects of medications. Patients with UWL should be investigated. The diagnostic approach to patients with UWL includes comprehensive medical history, physical examination, laboratory testing, imaging, and endoscopy. The imaging and endoscopy should be targeted according to the symptom, physical examination findings, and laboratory results. The treatment of UWL should be targeted to the primary disease causing weight loss. Non-pharmacologic nutrition intervention is the important treatment, and some pharmacologic treatment could be helpful in part of the patients.

**Keywords:** unintentional, unexplained, weight loss, diagnosis, gastrointestinal disorders, gastrointestinal malignancy, endoscopic investigation, morbidity

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## 1. Introduction

The most accepted and most frequently used definition of significant unintentional weight loss (UWL) is the loss of at least 5% of usual body weight over 6–12 months [1, 2]. The weight loss is unintentional and unexplained and should be further investigated.

UWL is a common phenomenon among older adults, with an annual incidence of approximately 13% [3]. Other epidemiologic studies have shown that about 15–20% of elderly patients experience weight loss and this prevalence increases in high-risk patients [4–6].

The body weight changes during the life cycle include increasing of the body weight during early adulthood until the fifth to sixth decade of life, the reason for this increase is the increasing of the body [7]. But regarding the lean body mass, there is a decline at a rate of 0.3 kg/year, beginning in the third decade. Total body mass remains stable from the fifth decade until about age 70; it then slowly decreases at a rate of only 0.1–0.2 kg/year [7].

Different Inflammatory cytokines and interleukins are involved in the pathogenesis of UWL. Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 $\beta$ , and interleukin-6 have been implicated in cachexia and weight loss [3].

One of these important mediators is the TNF- $\alpha$ , which considered to be a primary mediator of the muscle wasting of cachexia [3]. Cytokines may act both centrally and peripherally; the most important effects include inhibiting feeding behavior, by decreasing gastric motility, gastric emptying, and intestinal motility and by modifying gastric secretion [3].

## 2. Risk factors of UWL

On the basis of several studies, different risk factors were found for UWL among adults older than 65 years, subgrouped as:

1. Physiologic factors: acute illness, hospitalization, exacerbation of chronic diseases, dementia, constipation, pressure ulcers, daily pain, medications, compromised motility, recurrent falls, eating and swallowing problems, reduced appetite, low food intake, thirst, serum albumin <35 g/l, and total cholesterol <4.2 mmol/l were found to be factors for UWL [8–13].
2. Psychological factors: depression and bereavement [11, 13].
3. Social factors: reduced social activity and low income [9, 10].

## 3. Unintentional weight loss morbidity, mortality, and prognosis

Increased fracture risk has been associated with weight loss in postmenopausal women; significant association was found between unintentional weight loss and fracture of the hip, spine, and clavicle within 1 year of weight loss; and these associations were still present at 5 years [14]. Another study showed that unexplained weight loss may be important predictors of suicide [15].

Functional decline, infections, decubitus ulcers, exacerbation of cognitive and mood disorders, and increased use of acute and long-term care facilities are important clinical consequences of the UWL [16].

In general, the result of different studies has shown that UWL is associated with mortality rates ranging between 9 and 38% in elderly adults [17–20].

UWL is a nonspecific condition that may be caused by a multitude of medical and psychiatric disorders. Consequently, its natural history varies considerably depending on the underlying cause.

On the basis of study of Marton et al., 25% of the patients died within 1 year, and another 15% continued to lose weight or deteriorate in function [17].

Most patients who did poorly had advanced cardiopulmonary disease or cancer. In another study 51 of the 104 cancer patients had disseminated disease at diagnosis; median survival of the cancer patients was just 2 months; and only 9 lived longer than 1 year [21].

Most patients without a physical cause of weight loss fared well, survivors do well. Most either maintain or gain weight, but only a minority return to their baseline weight [17, 20, 22].

#### **4. Differential diagnosis of UWL**

The differential diagnosis of the underlying diseases leading to UWL is broad and includes both malignant and benign gastrointestinal (GI) diseases, as well as endocrine, infectious, cardiopulmonary, and psychiatric disorders [20]. GI disorders are commonly associated with

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##### Gastrointestinal diseases

Esophageal ulcer

Moderate/severe esophagitis

Esophageal stricture

Achalasia

Esophageal cancer

Moderate/severe gastritis

Peptic ulcer

Gastric cancer

Gastric lymphoma

Celiac disease

Malabsorption syndromes

Inflammatory bowel disease

Colon cancer

Chronic pancreatitis

Pancreatic cancer

Cholangiocarcinoma

Hepatocellular carcinoma

Endocrine diseases

Diabetes mellitus

Hyperthyroidism

Pheochromocytoma

Infectious diseases

Tuberculosis

Endocarditis

Acquired immunodeficiency syndrome (AIDS)

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Cardiopulmonary diseases
Congestive heart disease
Myocarditis
Chronic lung disease
Lung cancer
Psychiatric disease Depression
Schizophrenia
Anxiety
Hematologic disease Lymphoma
Renal chronic kidney disease
Inflammatory non-infection disease
Connective tissue disease
Vasculitis
Temporal arteritis
Other Medications
Dental and oral health problem
Laryngeal cancer
Pharyngeal cancer
Advanced metastatic cancers
Unknown/idiopathic

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**Table 1.** The most common diseases causing unintentional weight loss.

UWL, with gastric and colon cancer, celiac disease, peptic ulcers, and inflammatory bowel diseases being the leading causes [19].

The list of medications causing weight loss includes a different kinds of medications, which used for treatment of cardiac, neurologic and psychiatric diseases, and tablets used for treatment of diabetes mellitus and pain management can also cause weight loss. Side effects of different medications could include anorexia, dry mouth, dysgeusia, dysphagia, nausea, and vomiting, and the result of these side effects will be lowering the daily oral intake and weight loss [8, 23]. Despite the long list of weight loss causes, in about 5-36% of the patient the cause of the UWL is unknown [2].

However, among elderly patients the 9 Ds could help us to focus of the most common reasons among this group, dementia, depression, disease (acute or chronic), dysphagia, dysgeusia, diarrhea, drug, dentition, and dysfunction (functional disability) [24].

The most common causes of unintentional weight loss are summarized in **Table 1**.

## 5. UWL and cancer

When evaluating patients with UWL, detection of an underlying malignancy is of the greatest concern. A large list of different cancers could cause unintentional weight loss, not only in gastrointestinal cancer but in other malignancies too.

Furthermore, any type of malignant neoplasm can be the cause of weight loss in the advanced metastatic stage. The most common neoplasms causing weight loss are included in **Table 1**.

The reported prevalence of gastrointestinal (GI) malignancies in patients with UWL varies significantly between studies, with rates of 6–38% in different publications [17, 18, 20, 21, 25]. GI malignancy is an important and a feared cause of UWL. Different reports have shown a low GI malignancy rates of 6.6–12% in patients with UWL depending on the diagnostic modality used [20, 26], and another study found 57 (3.7%) and 24 (4.3%) cases of malignancy in the upper and lower GI tract, respectively [27]. Additional study showed that UWL alone was not associated with colorectal cancer among patients who underwent colonoscopy [28].

The differences between malignancy detection rates found in the different studies in the literature are mainly a result of variations in study design, population diversity, and the lack of a standardized definition for what is considered meaningful endoscopic findings in the context of UWL across different studies.

## 6. Diagnostic approach to patients with UWL

Patients with UWL must be investigated, and it poses a diagnostic challenge for the clinician in a large part of the patients because of the broad range of etiologic possibilities. To date, no guidelines have been published for the evaluation and management of patients with UWL; when evaluating patients with UWL, practitioners need to exercise careful judgment in terms of the extent of the initial workup and, if additional investigations are required, in choosing the most appropriate diagnostic modalities. However, the workup should include simple and noninvasive tests in the early investigation stage, and additional invasive tests should be directed to specific organ later. Common practices include detailed medical history, physical examination, laboratory testing, fecal occult blood testing, and imaging as part of the baseline evaluation [2, 23, 24, 29], and endoscopy should be part of the investigation among patients with gastrointestinal symptoms or if the baseline evaluation was normal.

### 6.1. Medical history

Comprehensive detailed medical history is the first and important step. Information regarding other symptoms, particularly gastrointestinal, hematological, and psychiatric symptoms, and symptoms like abdominal pain, rectal bleeding, change of bowel habits, vomiting, anemia, night sweating, and depression should be part of the medical history taking.

Asking about smoking, alcohol abuse, medications, psychosocial factors, dietary history, travel, and sexual risk behavior should be part of taking medical history [2]. Further investigation could be directed by specific symptoms.

### 6.2. Physical examination

Comprehensive whole-body examination should be done and focused on abdominal mass, organomegaly, lymphadenopathy, breast mass, prostate enlargement, sign of wasting, and weight loss. The importance of mouth examination particularly among elderly adults is to exclude dental problem, dry mouth, or other lesions that may interfere chewing and swallowing.

### 6.3. Laboratory testing

Laboratory testing is an important part of the UWL investigation, abnormalities of results could be a direction to the cause of the weight loss and then further specific investigation should be the next step. The important laboratory tests should be included in the baseline investigation are: complete blood count, liver, kidney, thyroid function tests, serum glucose, lactate dehydrogenase, C-reactive protein, electrolytes, albumin, iron studies, urinalysis and fecal occult blood test.

### 6.4. Imaging

Chest radiography and abdominal ultrasonography are included in the baseline investigation on unintentional weight loss. However, there are no published dates regarding the diagnostic yield of computer tomography among patients with UWL. For patients, who underwent baseline investigation, and there is no direction to diagnosis, further investigation with chest, abdominal, and pelvic contrast computer tomography will be appropriate; the advantages of computer tomography are imaging of chest, mediastinum, lymphadenopathy, and better imaging of the abdomen and pelvis including organs like pancreas and the bowel.

### 6.5. Endoscopy

Gastrointestinal disorders may account for up to 25–30% of the cases of UWL [20, 25]. Unfortunately, data on the diagnostic yield of endoscopy in UWL are scant [26, 30]. The role of endoscopic evaluation in this framework remains controversial. Although some authors include esophagogastroduodenoscopy (EGD) as part of the initial workup of all patients with UWL, others argue that it should be reserved for those who initially present with GI symptoms or signs [1, 24]. However, little is known about the diagnostic yield of endoscopy in the context of UWL. A small study from the non-English literature has showed that gastroscopy can lead to a definite diagnosis in more than half of the cases [31]. However, this study was carried out in a small cohort of elderly (mean age, 80 years) in-patients; thus, its conclusions may not be generalizable to the broader population of patients with UWL. Another study found that the yield of endoscopy for the evaluation of UWL was not negligible. Of 2098 procedures performed in 1843 patients, endoscopic findings that could explain weight loss were found in 10% of EGD and 6% of colonoscopies [27]. However, the rate of detection of clinical significant endoscopic finding in both upper and lower endoscopies was significantly lower in patients who had no other indications for endoscopy besides weight loss [27].

Patients, who have gastrointestinal symptoms in addition to the UWL and patients with normal baseline evaluation, should undergo endoscopy.

## 7. Age and UWL

A slow decrease in body mass (0.1–0.2 kg/year) usually occurs in association with normal aging [32]. However, beyond this naturally occurring process, elderly patients are more prone to present with clinically significant weight loss [7, 16]. Accurate diagnosis of the underlying

cause for weight loss in this population is important as the natural history of this condition at an older age is less favorable [33].

Approximately 60% of the patients in both the gastroscopy and colonoscopy cohorts were 65 years of age and older [27]. Furthermore, age older than 65 years or more was strongly associated with detection of any pathologic endoscopic findings, whereas 60% of the clinical significant endoscopic finding by gastroscopy and 50% of those diagnosed by colonoscopy were found in patients in this age group. Different studies showed increased mortality among patients older than age 65 with UWL [16, 34, 35].

## 8. Treatment of UWL

The treatment of UWL should be targeted to the primary disease causing the weight loss. In cases, in which no organic or psychiatric disease was found, the treatment has to be individualized and target patient's nutrition status, risk factors, and social conditions.

Patient's medications must be reviewed and if any medication is suspected to be contributed to the weight loss should be discontinued and replaced by an alternative drug.

Nutritional interventions as a non-pharmacologic treatment were investigated in several studies. The hallmarks of nutritional intervention should include optimizing food intake, oral nutritional supplements, and adding multivitamins. The patients should have been encouraged to eat small and often meals, eating favorite food, avoiding gas-producing foods, and taking multiple vitamins daily. The compliance of patients to the different diets is an important issue.

Consultation, support, and follow-up by a dietician are important parts of the management of patients with UWL.

Physical training has a positive impact of the increasing weight among community-dwelling individual. Regular exercise (particularly resistance training) is also recommended for frail elderly patients because it stimulates appetite and prevents sarcopenia.

Different small trials examined pharmacologic treatment of patients with UWL.

The evidence supporting any pharmacologic agent for the treatment of weight loss is limited to mostly small and uncontrolled studies.

The effect of different appetite stimulants and anabolic medications of UWL was examined. Some of them showed a trend of weight gain; however, most of the medications have significant side effects, particularly in frail elderly people. Megestrol acetate, dronabinol, ornithine oxoglutarate, cyproheptadine, and human growth hormone were examined in few studies.

## 9. Conclusions

Unintentional weight loss is a common health problem with increase mortality with a broad spectrum of differential diagnosis. The diagnostic approach should be targeted according the medical history, physical examination, and laboratory results.

## Conflict of interest

There are no conflicts in interest to be reported.

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