Involuntary Weight Loss

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- level 1 studies, which meet all of the evidence criteria for that study type;
- level 2 studies, which meet at least one of the evidence criteria for that study type; or
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1. Screening

Screen all patients for IWL. 📜

1.1 Identify patients who meet the criteria for IWL. 📜

Recommendations

- Weigh patient at each visit and compare current with previous weight.
- Identify patients with sustained IWL ≥ 5% of body weight over a 6-month period, or 10% over a 1-year period.

Evidence

- A cohort study of the effect of weight loss in community-dwelling patients with Alzheimer's disease (414 patients with MMSE score between 10 and 26) showed weight loss was associated with rapid cognitive decline in that cohort (1).
- The National Health and Nutrition Examination Survey found that among older women (ages 60 to 74), weight loss was associated with a two-fold increase in the risk for mobility disability compared with weight-stable women. These data were adjusted for age, smoking status, educational level, time to follow-up, and past body mass index (2).
- A cohort study of 247 community-dwelling veterans found a 13% annual incidence of clinically important weight loss. Mortality rates at 2 years were 28% among those participants with IWL and 11% among those without IWL. There was a greater than two-fold risk for death among those participants with IWL when the data were adjusted for age, body mass index, cigarette use, other health status, and laboratory measures (3).
- A summary study of long-term effects of change in body weight on death from all causes included 13 studies from 11 diverse populations, 7 from the U.S., 4 from Europe. The studies suggest that the highest death rates are found in adults who have lost weight or gained excessive weight (4).
- A 2011 cohort study of 3834 men over 7 years found that weight loss was associated with increased all-cause mortality compared with no change in weight (RR, 1.49 [CI, 1.17 to 1.89]) (5).
- A post-hoc analysis of a randomized, controlled trial in 5202 patients with type 2 diabetes found an association between weight loss and increased total and cardiovascular mortality (6).
- A study of 4869 British men aged 56 to 75 drawn from general practices found an increased all-cause mortality risk associated with IWL after adjustment for lifestyle characteristics and preexisting disease (adjusted RR, 1.71 [CI, 1.33 to 2.19]) (7).

Rationale

- IWL is common and is associated with significant illness and death.

1.2 Identify patients with sustained voluntary weight loss. 📜

Recommendations

- Maintain a level of concern for patients who lose and maintain weight loss voluntarily, especially if relative sarcopenia is noted.
- Encourage supervised voluntary weight loss programs for overweight and obese patients.

Evidence

- Studies have been inconclusive in associating voluntary weight loss and increased mortality (6, 8, 9, 10, 11).
- A one-year randomized controlled trial evaluated the effect of voluntary weight loss in the elderly by diet, exercise, or both, and showed significant improvement in physical function and frailty (11).
- The ADAPT study concluded that voluntary weight loss in older adults was not associated with increased mortality and may reduce mortality risk (9).
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- A cohort study of 247 community-dwelling veterans found that the 2-year mortality rate among persons who voluntarily lost weight was 36%. This mortality rate was higher than that experienced by participants with IWL. (3).
- A study of 4869 British men aged 56 to 75 drawn from general practices found an increased all-cause mortality risk associated with IWL after adjustment for lifestyle characteristics and preexisting disease (adjusted RR, 1.71 [CI, 1.33 to 2.19]). However, intentional weight loss in this study was associated with a significant benefit in all-cause mortality (RR, 0.59 [CI, 0.34 to 1.00]), with the benefit most apparent in markedly overweight men with body mass index ≥28 kg/m² (7).

Rationale
- Whether the observed weight loss is voluntary or unintentional is difficult to determine.
- Voluntary weight loss, even if it targets excess fat, may include accelerated muscle loss, which adversely affects functional status in elderly patients.
- Older observational studies suggested an association between voluntary weight loss and an increase in mortality and morbidity, but this finding has not been validated by new studies.

Comments
- The evidence regarding intentional and unintentional weight loss and their physiologic effects is inconsistent and remains an unresolved issue, as it is often difficult to distinguish between intentional and unintentional weight loss in these studies (7; 12; 13; 14; 15). However, more recent studies have shown favorable outcomes of weight loss in the elderly.
2. Diagnosis

Confirm the diagnosis of IWL and understand the likelihood before evaluation of specific causes; then perform a careful history and physical exam to identify the cause.

2.1 Use objective measures of weight loss to confirm the diagnosis.

Recommendations
- Use documented weights or objective evidence of weight loss, such as change in fit of clothes or corroboration by trusted observer, before pursuing a work-up of IWL.
- Screen at-risk patients for adequate caloric intake by using a screening tool like the Mini Nutritional Assessment-Short Form.
- Body mass index can be limited by error in height measurement because of kyphosis, which is common in the elderly.

Evidence
- Almost one-half of patients initially enrolled in a cohort study of IWL had not lost weight (16).
- Early screening has the potential to identify either nutritional risk or nutritional decline in older adults (17; 18).

Rationale
- Many patients who report IWL in fact have not lost weight.
- The cause may simply be inadequate caloric intake for social reasons, which invalidates the need for comprehensive investigations.

2.2 Confirm that changes in total body water are not the cause of IWL.

Recommendations
- Evaluate volume status and weight serially.
- Be attentive to muscle mass, and look for loss of muscle mass in obese patients with intentional weight loss.

Evidence
- Consensus.

Rationale
- Dramatic weight changes can occur with gain or loss of total body water. These changes often occur more quickly and erratically than changes in lean body mass, which is often gradual and sustained.
- Obesity can mask the development of loss of muscle mass (sarcopenia), which has a negative effect on functional status.

Comments
- The assessment of weight change due to gain or loss of total body water will often be made on clinical grounds such as in a patient with congestive heart failure and recent increase in diuretic dose or a patient with diabetes and uncontrolled blood glucose levels experiencing significant osmotic diuresis.

2.3 Understand the likelihood of IWL in specific settings before evaluating its cause.

Recommendations
- Understand the common causes of IWL, which are in four major categories:
Involuntary Weight Loss

- Psychiatric diseases including depression, which may be the cause in 10% to 20% of patients
- Malignancy
- Chronic inflammatory conditions or infections
- Metabolic causes, commonly hyperthyroidism or uncontrolled diabetes

**Ask about:**
- Substance abuse and smoking, which may be associated with a physical cause of unintentional weight loss
- Gastrointestinal symptoms such as nausea or vomiting, diarrhea, dysphagia, or bleeding
- Oral health
- A general medical history to look for new or worsening chronic illnesses and signs of potential malignancy
- Current and recent medication use
- Symptoms suggesting dementia in older patients
- Endocrine symptoms, including menstrual irregularities

- Take a careful social history, since social isolation, poverty, and immobility can lead to IWL.
- Perform a complete physical exam, looking for signs of malignancy, and consider screening for depression or dementia.
- See table **Differential Diagnosis of Involuntary Weight Loss.**
- See table **Studies of Involuntary Weight Loss: Basic Patient Characteristics and Causes.**

**Evidence**

- The most common causes belong to four major categories: malignancy; chronic infections or inflammation, especially gastrointestinal; metabolic, such as hyperthyroidism; and psychiatric. Other causes are drugs, social factors, and age-related (19).
- In some patients, more than one of these causes is responsible (19).
- A small prospective study of patients with unintentional weight loss found that the following factors were associated with a physical cause of IWL: fatigue, smoking (>20 pack-year history), nausea or vomiting, change in cough, and increased appetite (16).
- Cancer is the most common physical cause of IWL and gastrointestinal causes are the second most common physical cause (16, 20, 21).
- Many medicines can cause IWL by inducing anorexia, dysgeusia, gastrointestinal symptoms, dry mouth, confusion or inattention, or a movement disorder. These can be caused by antibiotics, anticholinergic agents, antiparkinsonian agents, digoxin, iron supplements, NSAIDs, opiates, potassium supplements, SSRIs, theophylline preparations, and thyroid hormone supplementation (22; 23).
- A study of 100 VA patients evaluated on a geriatric rehabilitation unit found that the number of general oral problems was the best predictor of IWL within 1 year of admission (24). A study of 563 community-dwelling adults aged 70 and older found that approximately one-third lost 4% or more of their body weight. Edentulousness, female gender, and advanced age were independently associated with IWL (25).
- Social isolation, poverty, and immobility are associated with functional IWL (26), and insomnia has been associated with weight loss (27).
- Ask about memory loss, aphasia, apraxia, anomia, and problems with executive function. IWL is associated with dementia and may precede diagnosis of the dementia (28).

**Rationale**

- There have been few studies on the relative prevalence of various causes of IWL; however, these studies have been consistent in the proportion of patients with various causes.

**Comments**

- Although studies are consistent in distribution of causes for IWL, they are all subject to substantial referral bias. Involuntary weight loss is common among community-dwelling older adults. A community-based study of 563 adults age 70 and older found that approximately one-third of the sample lost 4% or more of their previous total body weight, and 6% of men and 11% of women
lost 10% or more of their body weight. In this sample, dentate status was a strong risk factor for IWL. Such data suggest that in nonselected populations, both other and unknown causes of individual weight loss may be more common than those seen in the previously cited studies (25). In addition, in an analysis of National Health and Nutritional Examination Survey data, 13% of the population reported recent IWL, with 6.9% reporting recent IWL ≥5% (29).

2.4 Understand that the cause of IWL among nursing home residents may be different from the noninstitutionalized population.

Recommendations
- Consider undernutrition, depression, medications, dehydration, and issues related to dementia in the diagnosis of IWL in nursing home residents.

Evidence
- Undernutrition due to inadequate feeding is one of the major causes of weight loss in nursing home residents (30; 31).
- A study of residents in a community nursing home found depression to account for IWL in 60% of residents who stayed in the nursing home for less than 6 months and in 36% of residents who stayed more than 6 months (32).
- A retrospective chart review at a tertiary care VA hospital found that the frequency and degree of weight loss in medically ill elderly patients taking fluoxetine should be studied further (33).
- A review discusses the clinical implications of the aging heart (34).
- The complicated issues associated with IWL in elderly outpatients are outlined in a review (22).
- Common problems causing failure to thrive in the elderly are the focus of this article (23).

Rationale
- These conditions commonly cause IWL in nursing home residents.

Comments
- The study of residents in a community nursing home (32) had certain methodologic flaws; further studies in this area are necessary.

2.5 Limit diagnostic testing to a set of basic studies unless history and physical exam suggest a specific physical cause of IWL requiring additional testing.

Recommendations
- Consider obtaining the following if the cause of the weight loss is not clear:
  - Complete blood count
  - Erythrocyte sedimentation rate or C-reactive protein
  - Serum chemistry tests, including calcium and liver function
  - HIV test
  - Thyroid-stimulating hormone level
  - Urinalysis
  - Chest radiograph
  - Stool occult blood
- In patients with gastrointestinal symptoms, also consider upper gastrointestinal series, abdominal ultrasonography, abdominal CT scan, or esophagogastroduodenoscopy.
- See table Laboratory and Other Studies for Involuntary Weight Loss.

Evidence
• In a study of 45 elderly patients with IWL, 10 CT scans were performed on 5 patients. These CT scans offered no further information except in 1 patient in whom the CT scan localized a malignancy that had been previously suspected on plain radiographs (21).
• In other studies in which a cause of IWL was aggressively pursued, thorough history and physical exam and basic laboratory testing, rather than advanced imaging, provided the diagnosis in nearly all patients (16; 20; 22; 35).
• A study of asymptomatic IWL at a tertiary referral center in Spain found that, among those patients ultimately diagnosed with cancer (n=104), the following were the most useful follow-up tests to make a diagnosis: for patients who had only an isolated abnormality in the CBC (n=39), abdominal CT scan (n=12), abdominal ultrasonography (n=9), and endoscopy (n=8); for patients who had only an isolated abnormality in liver function tests (n=52), abdominal ultrasonography (n=40) and abdominal CT scan (n=9); and for patients who had normal liver function tests and CBC (n=13), upper endoscopy (n=5), and abdominal CT scan (n=5) (36).

Rationale
• Body imaging of the thorax and abdomen with CT or MRI in the absence of historical information or physical exam findings pointing to the thorax or abdomen has not been shown to help determine the cause of IWL.

Comments
• The work-up should be tailored to the needs and status of the individual patient.

2.6 Recognize the broad differential diagnosis underlying IWL. 

Recommendations
• Recognize the pretest likelihood of different causes of IWL, and use the clinical evaluation and selected laboratory studies to narrow the differential diagnoses.
• See table Differential Diagnosis of Involuntary Weight Loss.

Evidence
• The most common physical cause of IWL is malignancy. The second most common physical cause is benign gastrointestinal disease. A broad spectrum of conditions accounts for the remainder of physical causes (16; 20; 21; 36; 38).
• Although these studies are consistent in distribution of causes of IWL, they are all subject to substantial referral bias. A community-based study of 563 adults age 70 and older found that approximately one third of the sample lost 4% or more of their previous total body weight, and 6% of men and 11% of women lost 10% or more of their body weight. In this sample, dentate status was a strong risk factor for IWL. Such data suggest that in nonselected populations, both other and unknown causes of IWL may be more common than those seen in the studies cited above (25).

Rationale
• Although certain causes are more common, it is often difficult to establish a definitive diagnosis.
3. Consultation

Consider consultation for diagnosis based on the specific findings. Consider consultation to address management of the underlying cause of IWL. [B C]

3.1 Refer patients to appropriate specialists for evaluation only when specific clinical problems underlying weight loss are identified. [E]

Recommendations

- Refer patients with abnormal findings on oral exam to a dentist.
- Consider consultation when a specific cause is clear, such as oncology in the patient with cancer or gastroenterology in the patient with a gastrointestinal cause requiring specific diagnostic testing or management.
- Conduct a careful follow-up with repeated careful history, physical exam, and basic laboratory work-up for patients in whom a cause for IWL cannot be determined by an initial work-up.

Evidence

- Studies suggest that if a physical cause of IWL is to be diagnosed after initial work-up, it will become apparent within 6 months of the initial evaluation (16).

Rationale

- Approximately 25% of patients will not have a discernable cause found after appropriate work-up and long-term follow-up.

3.2 Obtain consultation for help in managing patients with IWL with selected problems. [E]

Recommendations

- When appropriate, consider:
  - Dental consultation for all patients with oral problems such as loose teeth, caries, or poorly fitting or painful dentures
  - Oncology and gastrointestinal specialty consultation to manage specific causes of IWL
  - Psychiatric consultation for patients with depression or anxiety disorders not amenable to treatment by their primary care physician
  - Social work consultation for social issues related to IWL
  - Occupational or physical therapy to address functional issues related to IWL
  - Geriatrics medicine consultation for older persons with IWL

Evidence

- Mainly consensus.
- With regard to dental consultation, a study of older community-dwelling adults found that edentulosity was independently associated with IWL. Although there are no specific data to prove that improving dental care will alleviate IWL, it is reasonable to attempt to correct dental problems (25).

Rationale

- Certain causes of IWL may require subspecialty management.
4. Hospitalization

Recognize that hospitalization for IWL is rarely required except for certain underlying causes.

4.1 Hospitalize patients who are volume-depleted and who cannot consume fluids or for reasons related to the primary condition.

Recommendations
- Hospitalize patients who are volume depleted and unable to consume oral fluids or for whom treatment of the primary condition may result in improved ability to take fluids and food.

Evidence
- Consensus.

Rationale
- Given the broad differential diagnosis for IWL and the fact that a specific condition may not always be apparent, decisions about hospitalization must be made on an individual basis.
5. Therapy

Direct therapy for involuntary weight loss at its underlying cause.

5.1 Treat the presumed cause of IWL.

Recommendations
- Once a presumed specific diagnosis of the cause of IWL is made, anticipate that treatment of that condition should, in most patients, alleviate the IWL.
- If the patient continues to lose weight involuntarily, recognize that the presumed diagnosis may not be related to IWL.

Evidence
- Consensus.

Rationale
- Involuntary weight loss may or may not necessarily be related to an identifiable underlying disease process.

5.2 Consider medication and lifestyle changes for some patients.

Recommendations
- Change or eliminate medications that may be associated with anorexia or temporally related to the IWL.
- Address issues of social isolation and poor eating environments, if applicable.
- Ensure that the patient's oral health is adequate.
- Ensure the patient has access to food, how the patient gets food, the kind of food chosen, and whether the patient is able to eat it.
- Assist patients who need help with eating by seeking to improve their functional status in order to allow adequate intake of food.
- Eliminate restrictive diets, when appropriate.
- Suggest flavor enhancement of food to help improve dietary intake.
- Consider recommending resistance training in select patients, such as those with AIDS wasting syndrome.

Evidence
- Data in this area are scarce. One trial showed that flavor enhancement of food improves dietary intake and nutritional status of elderly nondemented nursing home residents (39).
- In a small randomized trial of patients with AIDS wasting syndrome, progressive resistance training was associated with improved physical function and quality of life when compared with treatment with oxandrolone or nutrition alone (40).
- Consensus is that these specific recommendations may be helpful, especially in older persons (26).
- In a longitudinal cohort study of community-dwelling elderly individuals, there was a linear relationship between the number of medications used and the risk for weight loss (41).

Rationale
- Simple measures unrelated to any specific underlying disease process may be helpful and are often overlooked.

5.3 Recognize the limited proven benefit of oral nutritional supplementation in patients with IWL.

Recommendations
- Consider oral supplementation, but do not expect it necessarily to reverse IWL.
• Note that nutritional supplementation may be useful for those patients for whom access to calories is an issue because of functional impairments.
• Do not institute enteral feeding, since it provides no survival benefit and may lead to complications.

Evidence
• A meta-analysis of protein and energy supplementation in older persons, not focused on populations with involuntary weight loss, noted the poor quality of most of the trials included in the analysis, particularly with regard to blinding. With those caveats, the analysis found that mortality was reduced with protein and energy supplementation, although the decrease was of borderline statistical significance, and that this was limited to patients given oral supplementation in the hospital and possibly in long-term care, but not in the community. However, effects on mortality and morbidity cannot be generalized for all older patients and care settings (42).
• There are a number of studies of the effects of nutritional supplementation in frail older persons and nursing home patients. The provision of an oral protein/calorie liquid supplement is a common strategy in these studies. Results have been inconsistent. Modest weight gain is shown in some studies (43), while weight loss or no change in weight is shown in others (44; 45).
• A randomized controlled trial examined the effect of nutritional supplementation in frail older adults (age 70 or above) without IWL in the long-term care setting who could walk more than 6 meters at baseline. Nutritional supplementation of 360 kcal/d resulted in a small weight gain (mean 0.8 kg) compared with placebo. The nutritional supplementation blunted normal eating. There was no effect on mobility, muscle strength, or physical activity (46).
• Flavor enhancement of food may be associated with modest gains in body weight in older nursing home patients (39). This strategy has not been studied in patients with IWL.
• Nutritional supplementation provided by enteral feeding tubes provides no survival benefit (47).

Rationale
• Reversal of IWL most often depends on treatment of a true underlying cause.

Comments
• There are no controlled data on nutritional supplementation in patients with IWL per se.

5.4 Recognize that appetite stimulants are of limited benefit for patients with IWL who do not respond to treatment of the primary cause or is of unknown cause.

Recommendations
• Avoid prescribing appetite stimulants for patients with IWL.
• Recognize that studies of both megestrol acetate, usually at a dose of 800 mg/day, and thalidomide, which is restricted in the U.S., have not shown benefit, and both drugs are associated with substantial side effects.
• Consider using mirtazapine to treat depression in patients with depression and weight loss.

Evidence
• Appetite stimulant therapy for IWL has been studied mainly in patients with AIDS or cancer cachexia. In these patients, certain agents have been shown to promote weight gain; however, a survival advantage has not been shown (48; 49; 50; 51; 52; 53; 54; 55; 56; 57; 58; 59; 60; 61), and in some trials, in patients who received such agents, there may have been an increased death rate (48; 49).
• A review of 15 trials of megestrol showed that appetite was improved in most trials, and that quality of life improved in only 2 of 11 trials (62).
• In a randomized, controlled trial of 50 patients with inoperable pancreatic cancer, patients treated with thalidomide lost 0.06 kg compared with 3.62 kg in the placebo group. There were no differences in survival, functional status, or quality of life among the patients taking thalidomide. However, there were significant side effects in the treatment group, including peripheral neuropathy, somnolence, and rash (61).
• While mirtazapine results in weight gain in patients with depression, it has not been studied in nondepressed patients and should not be used to treat weight loss in the absence of depression (63).

**Rationale**

• Appetite stimulant therapy does not offer a survival advantage.
6. Patient Education

Provide patients with information about their condition, its treatment, and management. ⚫

6.1 Inform patients that IWL requires physician evaluation, that the cause is often detectable and treatable, and that most patients with this condition do not have cancer. ⚫

Recommendations

- Advise patients that:
  - Involuntary weight loss may be associated with many conditions
  - The history and physical exam are the most important aspects of the evaluation and that they need to be especially forthcoming with historical information
  - Laboratory and diagnostic tests may be needed to help diagnose the cause of IWL
  - The use of advanced imaging techniques such as CT scans and MRI in the absence of a specific indication is not appropriate
  - If the initial work-up is unrevealing, close medical follow-up for at least 6 months is required
  - If the initial work-up is normal, it is important to report any new physical or psychiatric symptoms
  - The prognosis for patients in whom a specific cause of IWL is not found is the same as for those without IWL

Evidence

- Based on data from studies of IWL (16; 20; 21).

Rationale

- A basic understanding of IWL will help the patient deal with the condition and may enhance the physician's ability to diagnose and treat the patient's IWL.
7. Follow-up

For patients with IWL in whom a cause could not be determined initially, reevaluate at 3 to 6 months.

7.1 Reevaluate patients with IWL of undetermined cause at 3 to 6 months.

**Recommendations**
- Carefully repeat the history, focusing on any new symptoms that the patient may have.
- Repeat the physical exam, especially those portions dictated by any new history information.

**Evidence**
- In one cohort of patients, physical causes of IWL were always apparent within 6 months of initial evaluation (3; 16).

**Rationale**
- If the initial evaluation is normal, it is reasonable to enter a period of watchful waiting and reevaluate the patient in 3 to 6 months.
- It is unusual for IWL to be due to serious disease that is occult. If serious disease is present, the cause is likely to become evident within 3 to 6 months.
- Repeating the history and physical and targeted laboratory exam may uncover a cause of IWL not apparent at the initial evaluation.

7.2 Identify patients in whom a cause of IWL cannot be determined after appropriate initial and follow-up evaluation at 6 months, and reassure them of a good prognosis.

**Recommendations**
- Reassure patients that their prognosis is good and continue to monitor them.

**Evidence**
- In studies examining the cause of IWL, patients in whom a cause of IWL could not be found after appropriate initial and follow-up evaluation had the same long-term outcomes as patients without IWL (16; 21) and significantly better mortality than those with an established cause of weight loss, independent of whether the cause was malignant or not (38).

**Rationale**
- It is appropriate at this point to reassure a patient that his or her prognosis is good.
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References


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Glossary

AIDS
acquired immunodeficiency syndrome

CBC
complete blood count

COPD
chronic obstructive pulmonary disease

CT
computed tomography

EGD
esophagogastroduodenoscopy

ESR
erythrocyte sedimentation rate

GI
gastrointestinal

HIV
human immunodeficiency virus

IWL
involuntary weight loss

MMSE
Mini-Mental State Examination

MRI
magnetic resonance imaging

NSAID
nonsteroidal anti-inflammatory drug

qd
once daily

SSRI
selective serotonin-reuptake inhibitor

tid
three times daily

TSH
thyrotropin

VA
Veterans Affairs
### Laboratory and Other Studies for Involuntary Weight Loss

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td></td>
<td></td>
<td>Abnormal (usually anemia) in 14% with physical cause of weight loss (16).</td>
</tr>
<tr>
<td>Electrolytes, blood urea nitrogen, creatinine, glucose,</td>
<td></td>
<td></td>
<td>In one study, patients with a combination of decreased albumin and elevated alkaline phosphatase had 17% sensitivity and 87% specificity for cancer (20). In another study, 22% patients with physical cause of IWL had abnormal blood chemistry findings (16). Adrenal insufficiency was associated with electrolyte disturbances in 92% of patients (27).</td>
</tr>
<tr>
<td>liver function tests</td>
<td></td>
<td></td>
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<tr>
<td>ESR or CRP</td>
<td></td>
<td></td>
<td>Examined in one study of persons with IWL (20). Increased in patients with neoplasia (mean ESR 49) compared with those with psychiatric (mean ESR 19) and unknown cause (mean ESR 26) of IWL</td>
</tr>
<tr>
<td>Combination of low albumin and elevated alkaline</td>
<td>17</td>
<td>87</td>
<td>This combination was 17% sensitive and 87% specific for neoplasia as a cause of IWL in one study (20).</td>
</tr>
<tr>
<td>phosphatase levels</td>
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<tr>
<td>Thyroid-stimulating hormone</td>
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<td>To look for hyperthyroidism</td>
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<td>Fecal occult blood test</td>
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<tr>
<td>Chest radiography</td>
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<td>Most useful test in one series with 41% abnormal among individuals with a physical cause of IWL (16).</td>
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<tr>
<td>HIV</td>
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<tr>
<td>Upper GI series or EGD</td>
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<td>Upper GI had the highest yield in disclosing a pertinent abnormality among tests beyond basic screening tests—20% with abnormalities among persons with physical cause of weight loss, all with GI symptoms (16).</td>
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<tr>
<td>Abdominal ultrasonography</td>
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<tr>
<td>Abdominal CT scan</td>
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</tbody>
</table>

CBC = complete blood count; CRP = C-reactive protein; CT = computed tomography; EGD = esophagogastroduodenoscopy; ESR = erythrocyte sedimentation rate; GI = gastrointestinal; HIV = human immunodeficiency virus; IWL = involuntary weight loss.
# Differential Diagnosis of Involuntary Weight Loss

<table>
<thead>
<tr>
<th>Disease</th>
<th>Characteristics</th>
</tr>
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<tbody>
<tr>
<td>Cancer</td>
<td>Percent of patients with physical cause of IWL: 30%-55%. Percent of all patients with IWL: 16%-38% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Percent of patients with physical cause of IWL: 22%-25%. Percent of all patients with IWL: 10%-18% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>Percent of patients with physical cause of IWL: 6%-9%. Percent of all patients with IWL: ~5% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>Infections</td>
<td>Percent of patients with physical cause of IWL: 6%-9%. Percent of all patients with IWL: ~5% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>Pulmonary disorders</td>
<td>Percent of patients with physical cause of IWL: 8%. Percent of all patients with IWL: 6% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>Medications</td>
<td>Percent of patients with physical cause of IWL: 3%-18%. Percent of all patients with IWL: 2%-9% (16; 20; 21)</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>Percent of patients with physical cause of IWL: 13%. Percent of all patients with IWL: ~9% (16; 20; 21; 36)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>Percent of patients with physical cause of IWL: 6%. Percent of all patients with IWL: 4% (16; 20; 21)</td>
</tr>
<tr>
<td>Neurologic disease</td>
<td>Percent of patients with physical cause of IWL: 2%-13%. Percent of all patients with IWL: 2%-7% (16; 20; 21; 36)</td>
</tr>
<tr>
<td>Depression</td>
<td>Percent of all patients with IWL: 9%-18% (16; 20; 21; 36; 38)</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>Percent of all patients with IWL: 5%-26% (16; 20; 21; 36; 38)</td>
</tr>
</tbody>
</table>

IWL = involuntary weight loss.
# Studies of Involuntary Weight Loss: Basic Patient Characteristics and Causes

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>Outpatients (%)</th>
<th>Age (y)</th>
<th>Cause (%)</th>
<th>Physical</th>
<th>Psychiatric</th>
<th>Unknown*</th>
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</thead>
<tbody>
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<td>30</td>
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<td>66</td>
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<td>58</td>
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<td>66</td>
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<td>48</td>
<td>42</td>
<td>10</td>
</tr>
</tbody>
</table>

* 'Unknown' refers to patients in whom no cause of involuntary weight loss could be elicited after history and physical exam, appropriate diagnostic work-up, and long-term follow-up. Adapted from 16; 20; 21.