Unintentional Weight Loss

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Some definitions

Unintentional weight loss. Clinical entity whereby the patient does not purposefully set out to lose weight for any reason and when weight loss as a consequence of advanced chronic diseases or their treatments (eg diuretics for heart failure) is excluded [1]. Definition criteria were numerical verification of >5% reduction in usual body weight over the preceding 6–12 months, or, for subjects without numerical documentation, at least two of the following: evidence of change in clothing size, corroboration of the reported weight loss by a relative or friend, and ability to give a numerical estimate of the amount of weight loss [4].

Unintentional weight loss of known origin. When a previously reported cause of UWL was identified.

Unexplained unintentional weight loss. When a cause of UWL was not identified after an initial clinical evaluation and workup and it remained unknown 6 months after presentation.

Intentional weight loss. When the patient did purposefully set out to lose weight through dieting, exercise, self-induced vomiting, use of medications (eg anorexigenic drugs, diuretics, or laxatives), or following bariatric surgery [14].

Cachexia syndrome. Clinical entity whereby the patient has lost >5% of weight in <12 months, has an advanced chronic illness (heart failure, respiratory disease [mainly chronic obstructive pulmonary disease and interstitial lung disease], and kidney disease), and has at least three of the following: anorexia, fatigue, decreased muscle strength, low fat-free mass index, and abnormal laboratory tests including increased inflammatory markers, low serum albumin, and anemia [43].

Bosch et al. 2017

Is weight loss clinically important?

- **Definition**
  - Clinically important weight loss can be defined as loss of >**5 kg,** or **>5%** of usual weight over a period of 3 months, or >**10%** loss in 6 months

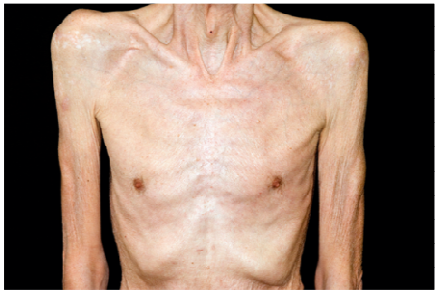
- **Why is it important ?**
  - Unintentional weight loss may reflect ***disease severity of a chronic illness or a yet undiagnosed illness.***
  - Even after adjusting for the comorbidities, weight loss of 5% or more of body weight is associated with ***increased mortality*** (approx. RR: 1.6)

Unintentional Weight Loss: prognosis

Studies on the effect of unintentional weight loss in patients 65 years and older

Study	Country	Study design	No. of patients	Definition of weight loss	Outcomes	Relative risk (95% CI)
Cornoni-Huntley et al, 1991[6]	United States	National multiphase surveys	14 407	> 10% over 10 yr	Increased mortality risk	Men: 1.5 (1.2–2.0) Women: 1.8 (1.4–2.5)
Deeg et al, 1990[15]	The Netherlands	Prospective cohort	512	≥ 10% over 5 yr	Increased mortality risk, worsening overall health	Not reported
Losonczy et al, 1995[16]	United States	Prospective cohort	6 387	> 10% after age 50	Increased mortality risk	Men: 1.69 (1.45–1.97) Women: 1.62 (1.38–1.90)
Wallace et al, 1995[17]	United States	Prospective cohort	247	≥ 4% over 1 yr	Increased mortality	2.43 (1.34–4.41)

Note: CI = confidence interval.



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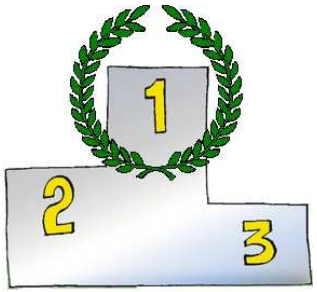
Unintentional Weight Loss

- ***Prevalence*** estimates of weight loss are quite variable:
  - **15-20%** of elderly patients experience weight loss (defined as loss of >5 kg or 5% body weight over 5-10 years)
  - The prevalence can be as high as **25%** in high-risk populations such as the **Frail Elders**
- ***Incidence:*** of weight loss in clinical studies of adults seeking health care is quite variable
  - Depending on the setting and definition it varies from 1.5% to 8%

What are the common causes of unintentional weight loss?

- Causes of unintentional weight loss can classified into 3 broad groups:
  - 1. Organic
  - 2. Psychosocial
  - 3. Idiopathic (up to 10-35% of cases)

1. Organic causes of unintentional weight loss



Organic Causes: the top three

- **Malignancy** (16-36%)
  - Usually it's clear from the history, physical, or routine lab data that malignancy is a potential cause
- **Gastrointestinal** (most common non-malignant organic cause (6-19%)
  - Peptic ulcer, IBD, hepatobiliary/pancreatic disease, oral problems, celiac disease
- **Endocrine** (4-11%)
  - Diabetes, **thyroid disease**, adrenal insufficiency

Elders oral problems = malnutrition

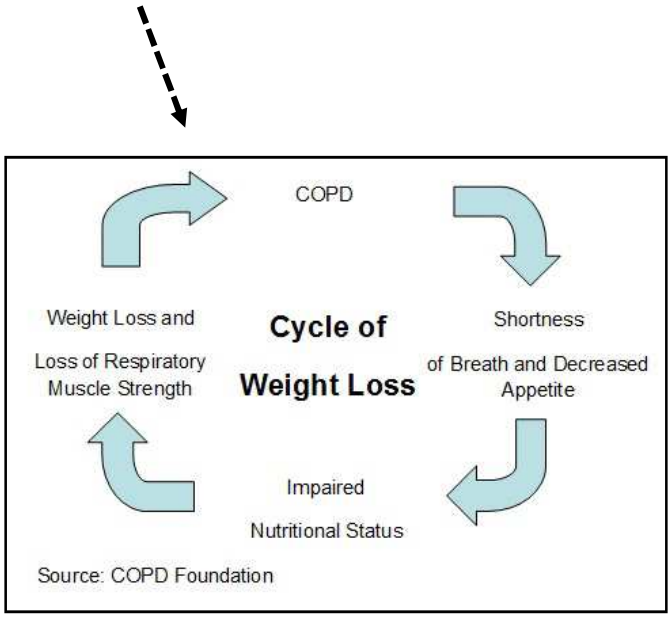
Disease	Treatment considerations
Oral cancer	Surgery, chemotherapy, radiation therapy
Traumatic lesions	Oral rinses (viscous lidocaine HCl 2%, diphenhydramine elixir 12.5 mg/5 Ml, dyclonine HCl 1%, sucralfate), systemic medications (penicillin, amoxicillin, erythromycin 500 mg qid)
Candidiasis	Topical agents (clotrimazole troches 10 mg 5 times daily, nystatin oral suspension 500,000 units, nystatin pastilles 100,000 units), systemic agents (fluconazole 100 mg, itraconazole oral suspension 10 mg/ml, ketoconazole 200–400 mg daily)
Xerostomia	Preventive therapy (topical fluorides, maintenance oral hygiene), salivary substitutes (increased intake of water, oral rinses and gels, use of artificial saliva), salivary stimulants (chewing sugarless gums or mints, electrical stimulation, use of drugs like pilocarpine hydrochloride, bromhexidine and cevimeline)
Oral vesiculobullous and erosive diseases	Pain control measures: 2% viscous lidocaine (swish and spit out 5 ml, 4–5 times a day), liquid diphenhydramine (swish and spit out 5 ml, 4–5 times a day), combination of viscous lidocaine, diphenhydramine, and a covering agent (such as kaopectate or Maalox) in 1:1:1 ratio, 0.1% diclonine hydrochloride benzydamine, systemic analgesia) Supportive care (hydration, ice chips or popsicles, soft bland diet, antipyretics such as ibuprofen, as needed) Systemic medications (prednisolone 5 mg dose or maintenance dose, azathioprine 50 mg 1–2 tabs)
Periodontal diseases	Daily tooth brushing and flossing after every meal, electric toothbrushes, floss holders, pulsed jet water irrigators, 0.12% chlorhexidine antimicrobial rinses, systemic antimicrobial therapy (metronidazole, tetracycline, clindamycin), surgical periodontal therapy
Edentulousness	Prevention of total tooth loss is recommended, fabrication of prostheses with adequate retention, occlusion, esthetics and margin extensions, endosseous dentoalveolar implants, regular assessments to reduce the risks of denture stomatitis, traumatic ulcers or hyperplastic tissue reactions
Neuropathic pain like burning mouth syndrome	Antidepressants (amitriptyline, trazodone, paroxetne), anticonvulsants (conazepam, gabapentin), C-fiber nociceptor desensitizer (capsaicin), antioxidant (alpha-lipoic acid), alternative therapies (electroconvulsive therapy, cognitive behavioral therapy, mind–body interactions, dietary and lifestyle changes)

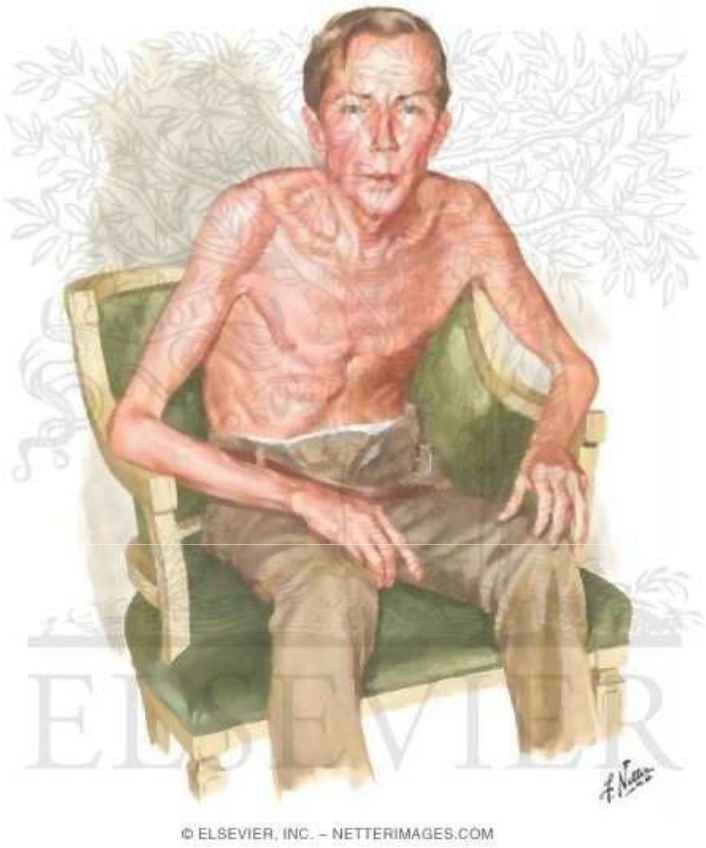
Older oral problems

1. Organic causes of unintentional weight loss

Organic causes (less common):

- Cardiovascular disease - CHF (2-9%)
- Respiratory disease (~6% - COPD)
- Renal disease (~4%)
- Neurologic disorder (2-7%)
- Chronic infections (2-5%)
- Drugs side effects (~2%)





Pink Puffer

2. Psycosocial causes of unintentional weight loss

Psychosocial Causes

- Psychiatric disorder (9-42%)
  - ***Depression, anxiety***
- Dementia (2-5%)
- Poor nutritional intake
  - Due to poverty or inadequate access to meals (e.g. ***disability in IADLs and ADLs***)

2. Psycosocial causes of unintentional weight loss

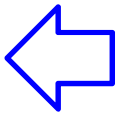
Psychosocial Causes

- Depression and dementia are poorly recognized in clinical practice
- All elderly patients with weight loss should undergo screening for:
  - dementia with the **MMSE**
  - depression with the Geriatric Depression Scal (**GDS**)
- Screen for malnutrition with **MNA** or one validated tools (ENS or SCREEN)

Depression diagnosis

MODIFYING *DSM-IV* CRITERIA

- Hopelessness, helplessness, not caring anymore
- Loss of interest particularly in people
- Feeling bad about oneself, not one's situation; feeling that illness is a punishment for wrongdoing
- Diminished ability to think or concentrate not easily explained by delirium, dementia, physical illness, or treatments
- Recurrent thoughts of death – not related to wishing to be dead to end physical suffering, but temporally related to affective and cognitive symptoms of depression
- Vegetative changes (significant weight/sleep/appetite changes; anergia) not easily explained by physical illness, treatments, or hospital environment
- Psychomotor agitation or retardation not easily explained by delirium, dementia, physical illness, or treatments
- Assessment of the patient's sphere of functioning extended to include participation in medical care. The point is not participating in medical care in spite of his or her ability to do so, not progressing despite improved medical condition, and/or is functioning at a lower level than the medical condition warrants.



Rao M. *Primary Psychiatry.* Vol 15, No 9. 2008.

Unintentional Weight Loss

ETIOLOGIES (% OF PATIENTS)	MARTON	RABINOVITZ	THOMPSON	LEDUC	HUERTA	
Cancer	19	36	16	1	10	
Organic (Other than Cancer)	50	30	40	28	38	%
GI disorders	14	17	11	--	--	
Cardiovascular	9	0	0	--	--	
Alcohol	8	0	0	--	--	
Pulmonary	6	0	0	--	--	
Endocrine	4	4	9	--	--	
Infectious	3	4	2	--	--	
Inflammatory	2	1	0	--	--	
Renal	0	4	0	--	--	
Neurologic	0	0	7	--	--	
Psychiatric	9	10	20	60	42	
Unknown	26	23	24	11	10	%

Unintentional Weight Loss

Medical

Increased metabolism-hyperthyroidism, pheochromocytoma , parkinson disease

Anorexia-drugs , abdominal ischemia , cancer , hyperparathyroidism

Swallowing problem-dysphagia, cerebrovascular accident

Malabsorption-gluten enteropathy

Increased metabolism and anorexia-COPD, cardiac cachexia

Age-Related

Impaired olfactory sensitivity

Appetite suppression

Impaired taste sensitivity

Unintentional Weight Loss

" D's " of weight loss in the elderly patient

Dentition	Depression
Dysgeusia	Dementia
Dysphagia	Dysfunction
Diarrhea	Drugs
Disease (chronic)	Don't Know

Unintentional Weight Loss

In the absence of localizing symptoms or signs or findings on the laboratory work listed above, routine screening test for cancer is indicated, as recommended by American Cancer Society[15]:

1-Flexible sigmoidscopy (if fecal occult blood negative and age≥50)

2-Cervical Pap smear in women

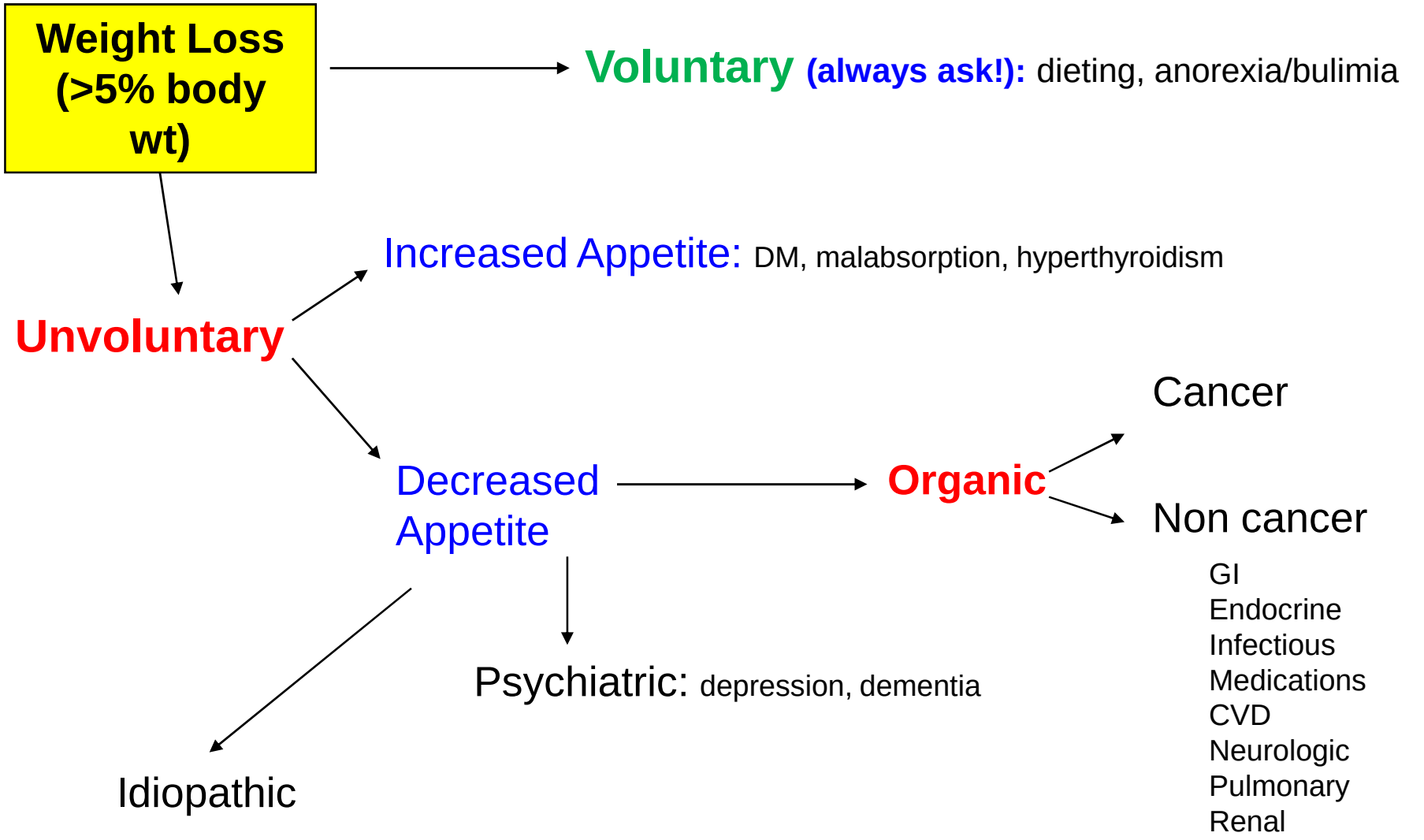
3-Mammography in women aged≥40 years

4-Prostate-specific antigen in men aged ≥50 years

Unintentional Weight Loss

- Several concepts emerge from etiologic studies of unintentional weight loss:
  - Among organic causes ***Cancer*** is most common
  - Etiology of weight loss is evident without extensive evaluation in most of patients
  - ***Psychiatric illness*** and non-diagnostic evaluations are common
  - Remember ***drugs*** side effects !

Approach to Weight Loss



Common causes of unintentional weight loss in elderly patients (with approximate range of occurrence)

- Malignant disease (16%–36%)
- Psychiatric disorder (especially depression) (9%–42%)
- Gastrointestinal disease (6%–19%)
- Endocrine disorder (especially hyperthyroidism) (4%–11%)
- Cardiovascular disease (2%–9%)
- Nutritional disorders or alcoholism (4%–8%)
- Respiratory disease (~6%)
- Neurologic disorder (2%–7%)
- Chronic infection (2%–5%)
- Renal disease (~4%)
- Connective tissue disease (2%–4%)
- Drug-induced weight loss (medication side effects) (~2%)
- *Unknown (10%–36%)*

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"Meals on Wheels": a mnemonic for common treatable causes of unintentional weight loss in the elderly

M Medication effects
E Emotional problems, especially depression
A Anorexia tardive (nervosa), alcoholism
L Late-life paranoia
S Swallowing disorders

O Oral factors (e.g., poorly fitting dentures, cavities)
N No money

W Wandering and other dementia-related behaviours
H Hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoadrenalism
E Enteric problems (e.g., malabsorption)
E Eating problems (e.g., inability to feed self)
L Low-salt, low-cholesterol diets
S Social problems (e.g., isolation, inability to obtain preferred foods), gallstones

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Medication and Weight Loss

Box 2: Examples of medications that can potentially cause weight loss[2,32]

Cardiac

- Digoxin
- Aspirin
- Angiotensin-converting enzyme inhibitors
- Calcium channel blockers
- Hydralazine
- Loop diuretics
- Hydrochlorothiazides
- Spironolactone
- Statins
- Nitroglycerin

Neurologic and psychiatric

- Selective serotonin reuptake inhibitors
- Tricyclics
- Neuroleptics
- Benzodiazepines
- Anticonvulsants
- Lithium
- Levodopa
- Dopamine agonists
- Donepezil
- Memantine

Bones and joints (including pain medications)

- Bisphosphonates
- Nonsteroidal anti-inflammatory drugs (including COX-2 inhibitors)
- Opiates
- Allopurinol
- Colchicine
- Gold
- Hydroxychloroquine

Endocrine

- Levothyroxine
- Metformin

Other

- Anticholinergics
- Antibiotics
- Decongestants
- Antihistamines
- Iron
- Potassium
- Alcohol
- Nicotine

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Medications weight loss

Side effects of drugs and supplements that can contribute to weight loss[30,40,41]

Side effect	Drug or supplement
Anorexia	Amantadine, amphetamines, antibiotics (e.g., atovaquone), anticonvulsants, benzodiazepines, decongestants, digoxin, gold, levodopa, metformin, neuroleptics, nicotine, opiates, SSRIs, theophylline
Dry mouth	Anticholinergics, antihistamines, clonidine, loop diuretics
Dysgeusia or dysosmia or both	Acetazolamide, alcohol, allopurinol, amphetamines, ACE inhibitors, antibiotics (e.g., atovaquone, ciprofloxacin, clarithromycin, doxycycline, ethambutol, griseofulvin, metronidazole, ofloxacin, pentamidine, rifabutin, tetracycline), anticholinergics, antihistamines, calcium-channel blockers, carbamazepine, chemotherapy agents, chloral hydrate, cocaine, etidronate, gold, hydralazine, hydrochlorothiazide, iron, levodopa, lithium, methimazole, metformin, nasal vasoconstrictors, nitroglycerin, opiates, penicillamine, pergolide, phenytoin, propranolol, selegiline, sodium cromoglycate, spironolactone, statins, terbinafine, tobacco products, triazolam, tricyclics
Dysphagia	Alendronate, antibiotics (e.g., doxycycline), anticholinergics, bisphosphonates, chemotherapeutic agents, corticosteroids, gold, iron, levodopa, NSAIDs, potassium, quinidine, theophylline
Nausea or vomiting or both	Amantadine, antibiotics, bisphosphonates, digoxin, dopamine agonists, hormone replacement therapy, iron, levodopa, metformin, metronidazole, nitroglycerin, opiates, phenytoin, potassium, SSRIs, statins, theophylline, tricyclics

Note: SSRI = serotonin-specific reuptake inhibitor, ACE = angiotensin-converting enzyme, NSAID = nonsteroidal anti-inflammatory drug.

Unintentional Weight Loss

- The diagnostic utility of the medical history and physical examination in identifying the cause of weight loss has not been sistematically evaluated …
- The same about screening investigations

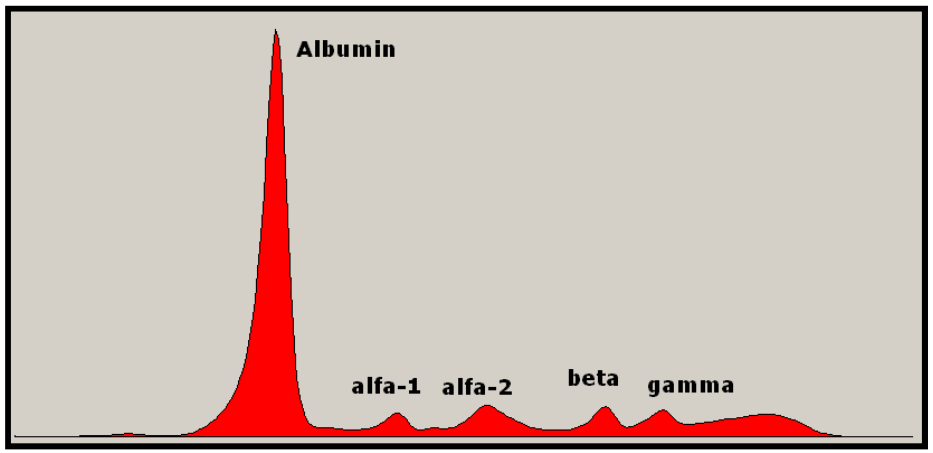
- Despite the lack of systematic evaluation, a complete history, physical examination, and selected “routine” investigations are recommended !

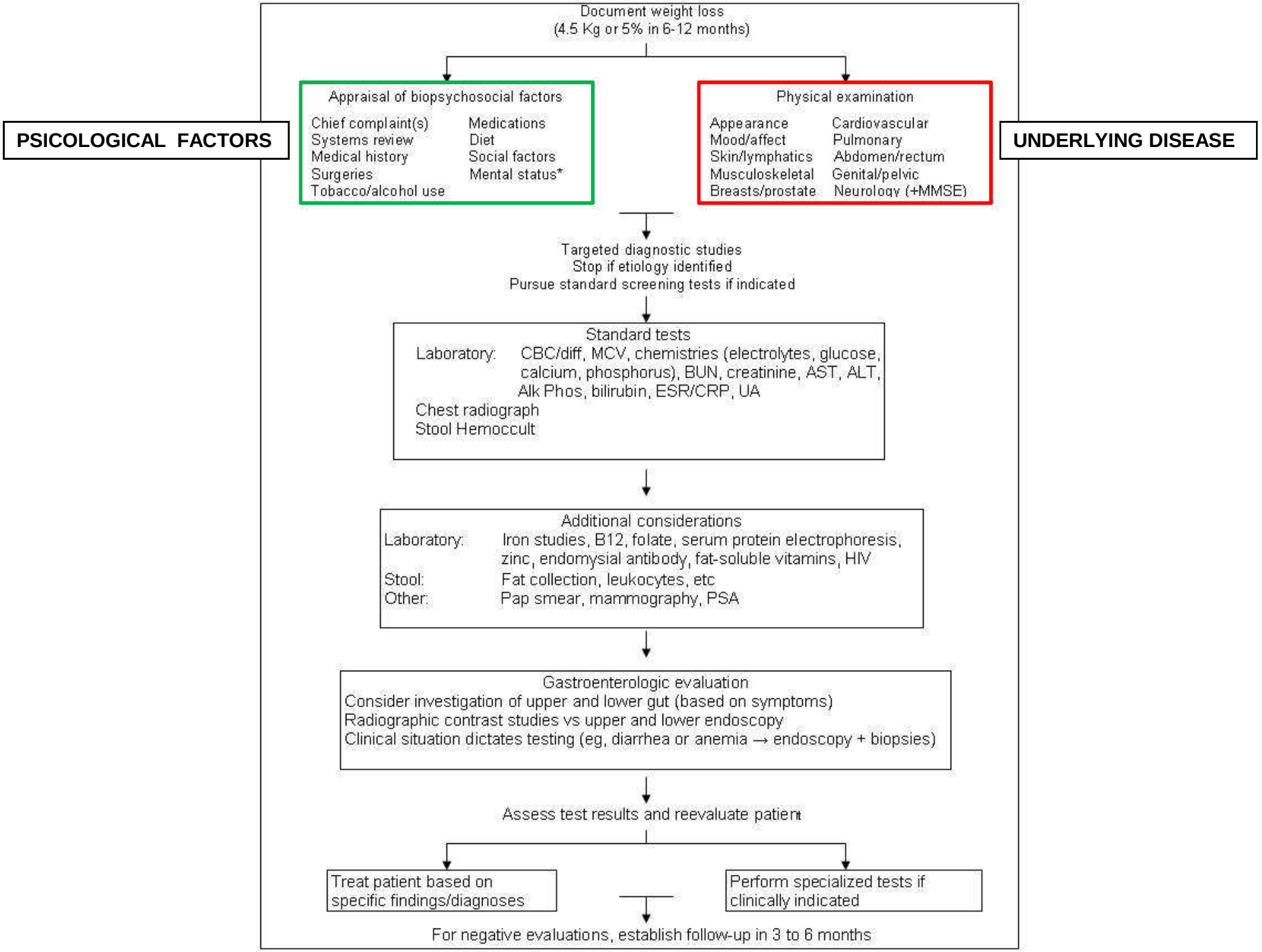
Unintentional Weight Loss

- Routine Investigations
  - CBC
  - Biochemistry (lytes, glucose, Ca, PO4, BUN, CRP, OBR-RSO, celiac test)
  - CXR
  - TSH
  - Liver enzymes
  - Urinalysis

Unintentional Weight Loss

- Additional tests are ordered as clinically indicated:
  - ***Serum Proteins Electrophoresis***
  - ***Mammogram, PSA***
  - ***GI investigations*** (if there are symptoms, microcytic anemia, or abnormal liver enzymes)
    - Gastroscopy or colonoscopy plus biopsies
    - Stool analysis
    - Celiac serology
    - Abdominal imaging
  - **HIV test**



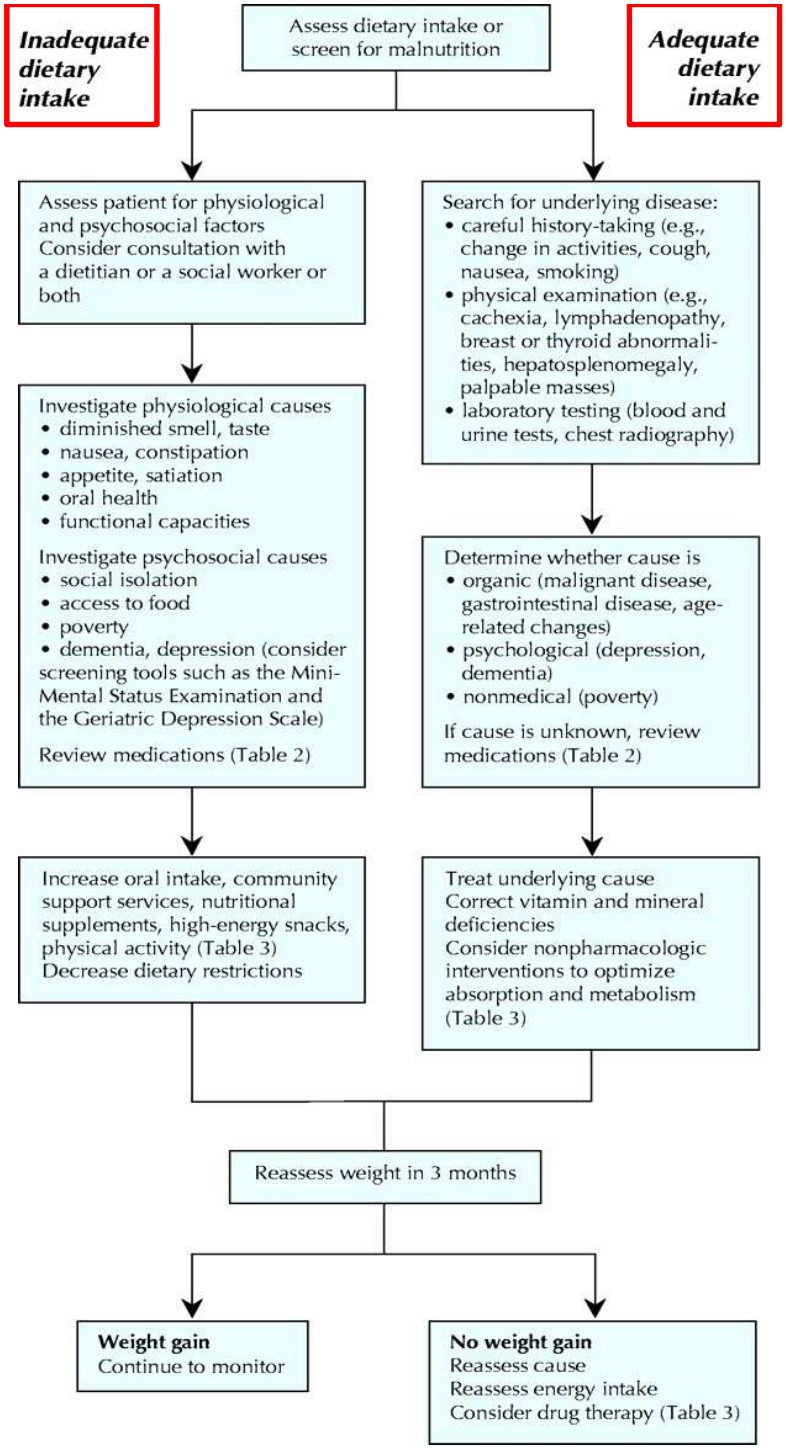

PSICOLOGICAL FACTORS
UNDERLYING DISEASE
Document weight loss
(4.5 Kg or 5% in 6-12 months)
Appraisal of biopsychosocial factors
Chief complaint(s)
Systems review
Medical history
Surgeries
Tobacco/alcohol use
Medications
Diet
Social factors
Mental status*
Physical examination
Appearance
Mood/affect
Skin/lymphatics
Musculoskeletal
Breasts/prostate
Cardiovascular
Pulmonary
Abdomen/rectum
Genital/pelvic
Neurology (+MMSE)
Targeted diagnostic studies
Stop if etiology identified
Pursue standard screening tests if indicated
Standard tests
Laboratory: CBC/diff, MCV, chemistries (electrolytes, glucose, calcium, phosphorus), BUN, creatinine, AST, ALT, Alk Phos, bilirubin, ESR/CRP, UA
Chest radiograph
Stool Hemoccult
Additional considerations
Laboratory: Iron studies, B12, folate, serum protein electrophoresis, zinc, endomysial antibody, fat-soluble vitamins, HIV
Stool: Fat collection, leukocytes, etc
Other: Pap smear, mammography, PSA
Gastroenterologic evaluation
Consider investigation of upper and lower gut (based on symptoms)
Radiographic contrast studies vs upper and lower endoscopy
Clinical situation dictates testing (eg, diarrhea or anemia → endoscopy + biopsies)
Assess test results and reevaluate patient
Treat patient based on specific findings/diagnoses
Perform specialized tests if clinically indicated
For negative evaluations, establish follow-up in 3 to 6 months

Unintentional Weight Loss

Reassess weight after 2-3 months

- If it remains stable or goes up: further assessment is not necessary
- If she/he is continuing to lose weight: repeat the evaluation process, with emphasis on searching for an **organic** or **psychosocial cause**

PSICOLOGICAL FACTORS



UNDERLYING DISEASE

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Table 3: Nonpharmacologic interventions and recommendations that may reverse unintentional weight loss in older adults

Intervention or recommendation	Rationale	Evidence
Minimize dietary restrictions[30,56]	Restricted diets are often energy-poor, have poor palatability and are not always medically indicated	Elderly people whose diets are restricted are at increased risk of weight loss[13,57,58]
Optimize energy intake by: • maximizing intake with high-energy foods at the best meal of the day[30,56] • eating smaller meals more often • eating favourite foods and snacks • providing finger foods	May increase total daily energy intake by minimizing gastric distension seen with large meals and increasing the amount of food consumed	Many elderly people consume most of their daily energy intake at breakfast[59,60] Eating favourite foods led to reversal of malnutrition and return of appetite among severely anorectic, malnourished elderly patients[61] Providing finger foods increased food consumption and led to cessation of weight loss in patients with dementia[62]
Optimize and vary dietary texture[63]	Enhancing chewing and palatability of foods may stimulate positive feedback to eat more and minimizes fatigue associated with chewing	In a study involving patients with dementia, altering food texture according to observed patient preferences led to increased food intake and weight maintenance;[63] diversity of food texture was highly valued by adults with congenital anosmia, who may be at high risk of weight loss[64]
Avoid gas-producing foods[56]	May lead to gastric distension with air and earlier satiety	
Ensure adequate oral health[47,56]	Poor oral hygiene and dry mouth are risk factors for decreased oral intake through altered taste sensation and difficulty in chewing and swallowing	Improved ability to detect sweet and salty tastes was found after professional oral hygiene therapy 3 times weekly for 5 wk[65]
Take high-energy and nutritionally dense supplements or add fats or oils to usual foods	Increased energy intake may increase weight; nutrient-dense food (more energy per gram) may avoid satiety-related limitations in intake	Daily energy intake and weight gain significantly increased within 3–6 wk in malnourished elderly patients[66–69] and number of falls decreased;[66] oral supplements were associated with lower mortality and shorter length of hospital stay but not lower risk of complications;[70] studies were not restricted to elderly patients with weight loss
Take supplements between meals	May minimize appetite suppression and compensatory decreased intake of foods	Providing liquid supplements at least 60 min before a meal was associated with less appetite suppression and greater overall energy intake than when supplements were provided immediately before a meal in healthy older subjects[71]
Eat in company or with assistance[47,56]	May lead to enhanced enjoyment of meals and increased energy intake; many older adults need assistance with taking their meals because of physical or cognitive disabilities	
Use flavour enhancers	May counteract age-related increase in smell and taste thresholds (components of anorexia of aging)	Intake of most enhanced foods was increased and immune function and grip strength improved;[72] hunger increased and energy intake and weight gain improved;[73] studies were not restricted to patients with weight loss
Participate in regular exercise	Promotes muscle hypertrophy and gain in lean-body mass and may stimulate appetite	Improvements were seen in strength and muscle volume, especially with resistance exercises;[74] increased energy intake or weight gain or both occurred[68,75,76]
Take a multiple vitamin supplement daily[56]	Most older patients with weight loss have 1 or more nutritional deficiencies	Equivocal evidence showed association between multivitamin supplementation and reduced infections[77]
Use community nutritional support services[47,78]	Functional limitations related to supply, preparation and consumption of food greatly reduce the capacity of elderly people to have access to sufficient food of good quality	Meals-on-Wheels programs improved dietary intake of older recipients[79]

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Weight Loss: pharmacologic intervention

Recommended Pharmacotherapy Interventions	
Agent	**Side Effects/Comments**
Megestrol acetate	Pulmonary embolism, thrombophlebitis, cardiomyopathy, leukopenia, edema, constipation, delirium, hypogonadism, hyperglycemia, adrenal suppression, and impotence. Should not be used in immobilized patients.
Tetrahydrocannabinol/ dronabinol	Dizziness, confusion, somnolence, difficulty concentrating, mood disturbances, anxiety, dry mouth, and ataxia
Oxandrolone	Hepatic necrosis, liver failure, hepatic tumors, congestive heart failure, severe edema, and polycythemia
Mirtazapine	Confusion, somnolence, dizziness, nausea, dry mouth, constipation, flu syndrome, edema, abnormal thinking or dreams, hypo/hypertension, elevated cholesterol or triglycerides, and asthenia. Use with caution in elderly patients.
Human growth hormone/ somatotropin	Intracranial hypertension, pancreatitis, hypothyroidism, generalized edema, glucose intolerance, carpal tunnel syndrome, headache, arthralgias, myalgias, and gynecomastia

Unintentional Weight Loss: Summary

- Unintentional weight loss is a ***common concern especially in the elderly***
- Common causes can be grouped into 3 categories: ***organic, psychosocial or idiopathic***
- Psychosocial causes are often *under-appreciated by clinicians*
- Extensive investigations are not always necessary
- Exclude medication side effects and voluntary weight loss!