Obesity

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Objectives

- Definition
- Pathogenesis of obesity
- Factors predisposing to obesity
- Complications of obesity
- Assessment and screening of obesity
- Management of obesity

What is Obesity?

- Obesity means excess accumulation of fat in the body
- 20% or more over an individual's ideal body weight

- Once it develops it is difficult to 'cure' and usually persists throughout life

- Obesity is usually diagnosed on the basis of calculation of
  - Body mass index
  - Measurement of waist-hip ratio

Obesity Classification-BMI

- BMI Calculation (kg/m2):

$$\frac{\text{Weight (Kg)}}{\text{Height squared (meters)}}$$

Table 6. Classification of Overweight and Obesity by BMI and Waist Circumference (31 [EL 4; NE])

Classification	BMI		Waist	
	BMI (kg/m^2)	Comorbidity Risk	Waist Circumference and Comorbidity Risk	
			Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >35 in (88 cm)
Underweight	<18.5	Low but other problems		
Normal weight	18.5–24.9	Average		
Overweight	25–29.9	Increased	Increased	High
Obese class I	30–34.9	Moderate	High	Very high
Obese class II	35–39.9	Severe	Very high	Very high
Obese class III	≥40	Very severe	Extremely high	Extremely high

Abbreviations: BMI = body mass index; in = inches.

Obesity...we

Table 7. Waist Circumference Thresholds for Abdominal Obesity (32 [EL4; NE])

POPULATION	ORGANIZATION	MEN	WOMEN
Europid	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Caucasian	WHO	≥94 cm (↑ risk) ≥37 inches ≥102 cm (↑↑ risk) ≥40 inches	≥80 cm (↑ risk) ≥31 inches ≥88 cm (↑↑ risk) ≥35 inches
United States	AHA/NHLBI (ATPIII)	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Canada	Health Canada	≥102 cm ≥40 inches	≥88 cm ≥35 inches
European	European Cardiovasc. Societies	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Asian (including Japanese)	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Asian	WHO	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Japanese	Japanese Obesity Society	≥85 cm ≥33 inches	≥90 cm ≥35 inches
China	Cooperative Task Force	≥85 cm ≥33 inches	≥80 cm ≥31 inches
Middle East, Mediterranean	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Sub-Saharan African	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Ethnic Central and South American	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches

Abbreviations: AHA = American Heart Association; ATPIII = Adult Treatment Panel III; IDF = International Diabetes Federation; WHO = World Health Organization.

Classification of obesity as per fat distribution

Android (or abdominal or central, males)

-Collection of fat mostly in the abdomen (above the waist)

-apple-shaped

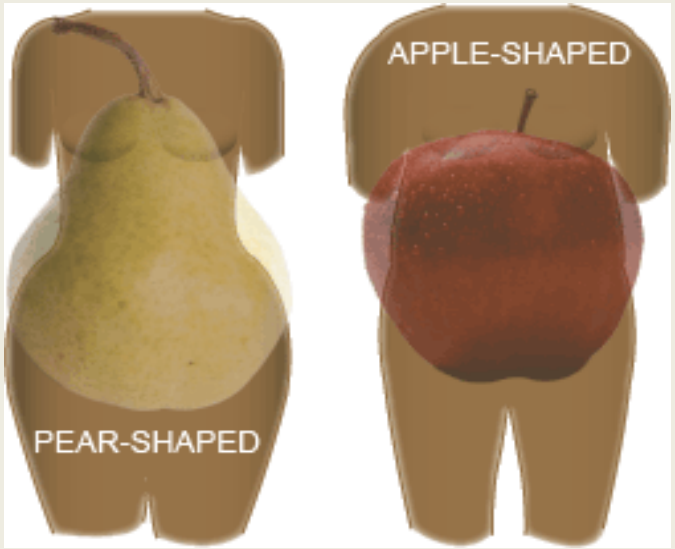
-Associated with insulin resistance and heart disease

Gynoid (below the waist, females)

- Collection of fat on hips and buttocks

-pear-shaped

-Associated with mechanical problems



Obesity-prevalence

- Well recognized as a serious and growing public health problem
- WHO estimates that over 1.7 billion people around the world are overweight, 310 million are obese
- Rates of obesity have tripled in the last 20 years in the developing world
- In US, 33.3 % of men and 35 % of women are obese in 2007

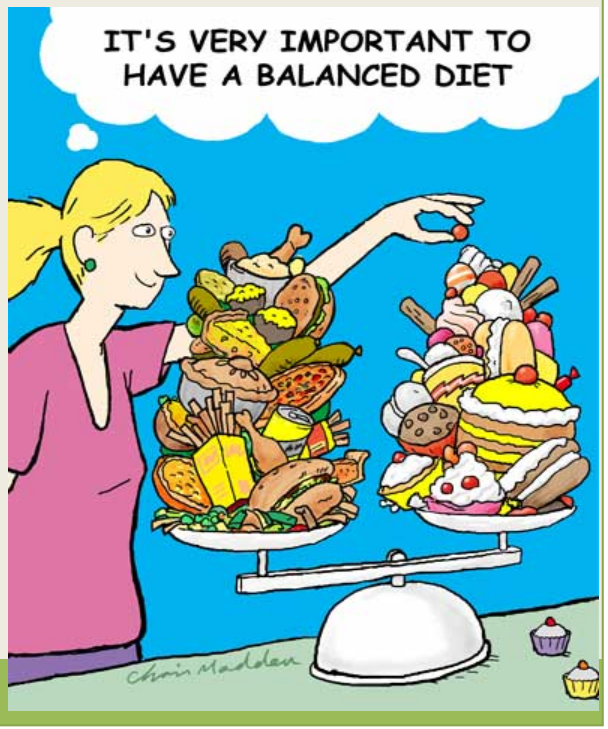
Obesity-prevalence

- 15-25 % of American children are obese
- In SA: study done between 1995-2000 in age group between 30-70 on 17000 subjects
- Prevalence of overweight: 36.9 % : 42% male, 31.8 % female
- Prevalence of obesity: 35.5 % , severe obesity 3.2 % with female of 44 %, male 26.4 %
- The prevalence of overweight and obesity was higher amongst a group of married women than among a group of single women in Saudi Arabia

Saudi Med J. 2005 May;26(5):824-9
International Journal of Obesity (2003) **27**, 134–139.

Mechanism of Obesity

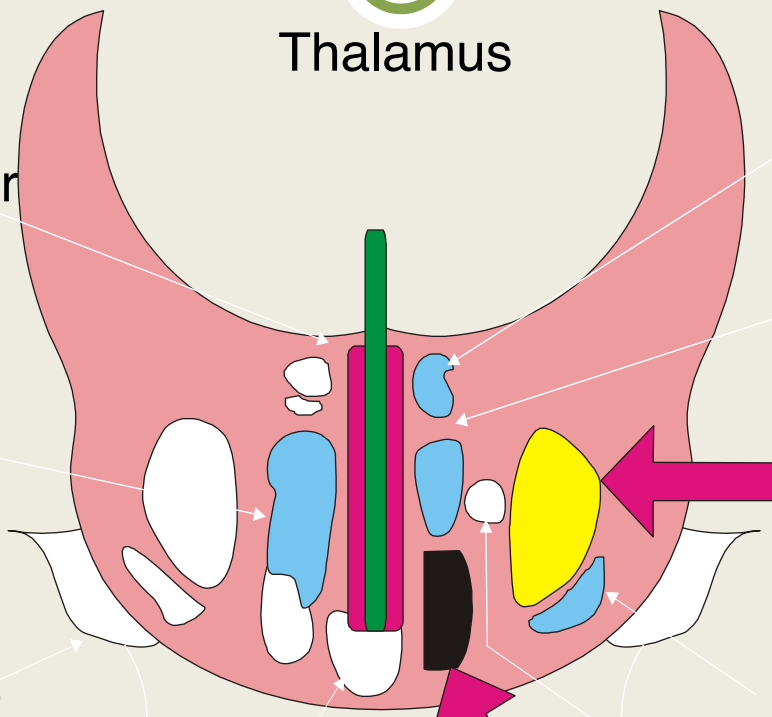
- Food intake and utilization is regulated:
  - Hormones
  - Neurotransmitters
  - Central nervous system



Mechanism of obesity

- Signals from peripheries are carried out by neurotransmitters and hormones to CNS in presence or absence of food
- Signal from fat by hormone leptin to hypothalamus to reduce food intake and increase sympathetic activity and energy expenditure
- Gastric distension and contraction send signal for satiety and hunger
- Fall in blood sugar send signals to CNS for hunger
- Sympathetic activity from food thermogenesis leads to reduce food intake

Role of hypothalamus in mediation of hunger and satiety



Thalamus

Periventricular
Neuroendocrine

Paraventricular
H_2O conserv
Oxytocin rel.

Dorsomedial
GI stimuli

Anterior
hypothalamic
Body temp

Lateral hypothalamic
Hunger, thirst

Optic tract

Supraoptic
Vasopresin rel.

Arcuate
Neuroendocrine

Ventromedial
Satiety

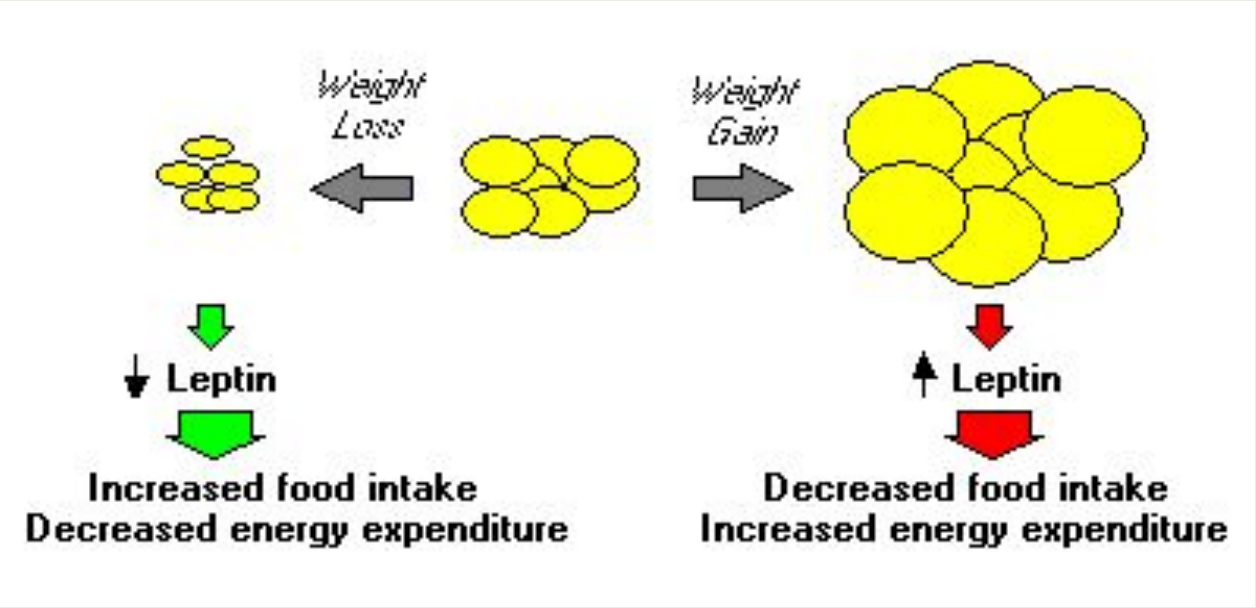
Fornix
Rage,
Hunger

Obesity-Pathogenesis

- More in and less out = weight gain
- More out and less in = weight loss
- Hypothalamus:
  - Control center for hunger and satiety
- Endocrine disorders:
  - Where are the hormones?

Hormones

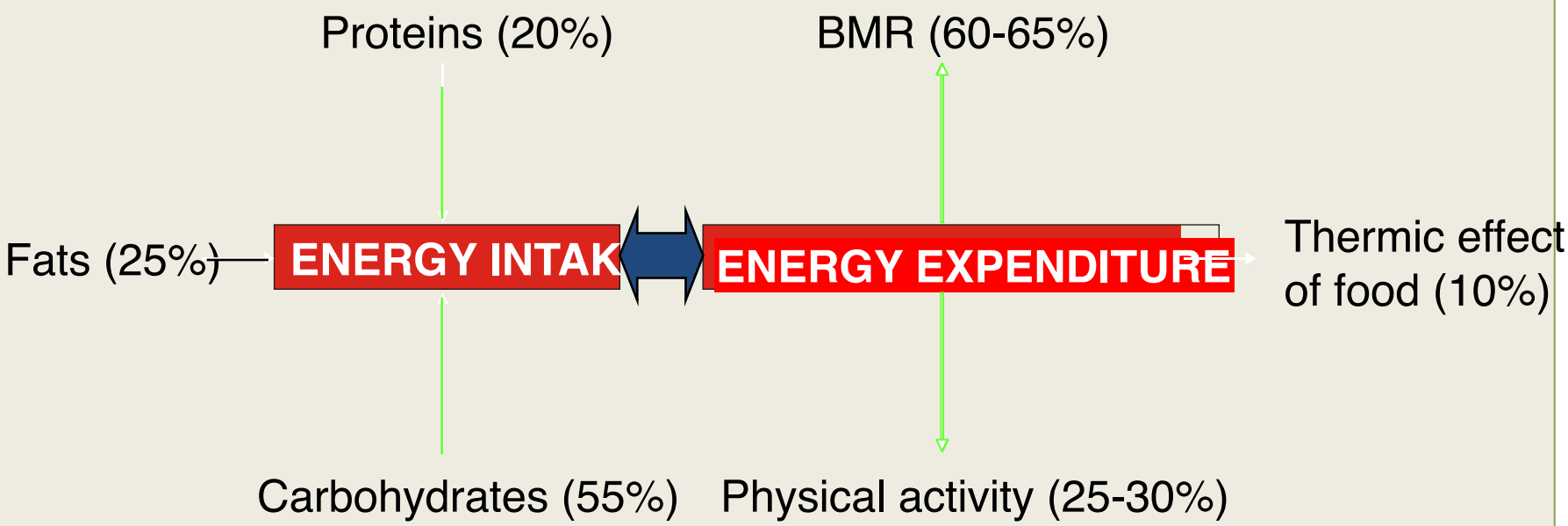
- Leptin from adipocytes
- Acts on hypothalamus to decrease food intake and stimulate energy expenditure



Hormones

- Ghrelin:
  - Secreted in the stomach
  - Acts on hypothalamus to stimulate appetite
  - Peak before meal and decrease after

Obesity – An imbalance in energy intake and energy expenditure



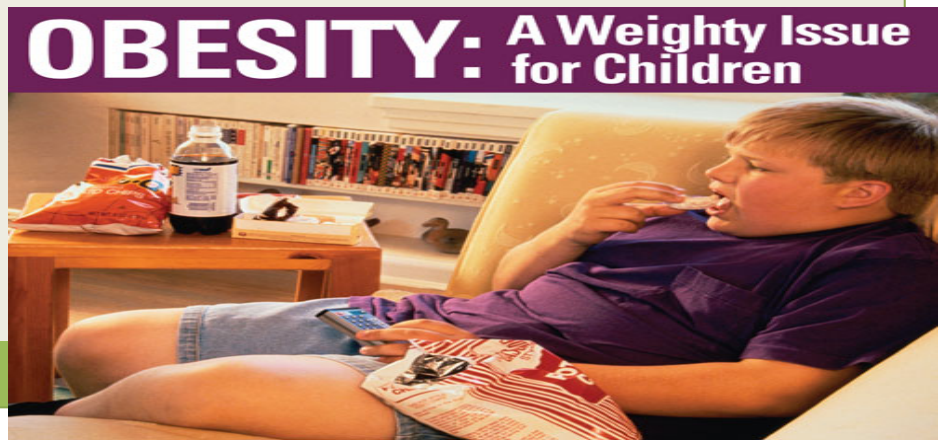
Obesity: How does it happen?

- Calories consumed not equal calories used
- Over along period of time

- Due to combination of several factors:
  - Individual behaviors (10 % to BMI)
  - Social interaction
  - Environmental factors
  - Genetic (40 % to BMI and adiposity)

Factors predispose to obesity

- Lifestyle:
  - Sedentary lifestyle lowers energy expenditure
  - 52 % of Saudi women are inactive, < 19 % doing regular physical activity
  - Prolonged TV watching
- Sleep deprivation:
  - < 7 hours of sleep → obesity
  - ↓ sleep → ↓ leptin, ↑↑ Ghrelin → ↑ appetite and CHO eating at night



Factors predispose to obesity

- Cessation of smoking:
  - Average weight gain is 4 kg
  - Due to nicotine withdrawal
  - Can be prevented by calories restriction and exercise program
- Social influences:
  - Obese parents most likely to have obese children
  - Obese individuals are surrounded by obese friends
- Diet:
  - Overeating, frequency of eating, high fat meal, fast food(> 2 fast food/wk)
  - Night eating syndrome: if > 25 % of intake in the evening

Factors predispose to obesity

Table 1. Causes of Obesity

- Excessive/inappropriate food intake
- Sedentary lifestyle
- Genetic disorders with obesity
  - Prader-Willi syndrome
  - Bardet-Biedl syndrome
  - Carpenter's syndrome (acrocephalopolysyndactyly type II)
  - Cohen syndrome
- Endocrine disorders
  - Cushing's syndrome
  - Hypothalamic tumors/inflammation/trauma
  - Hypothyroidism
  - Polycystic ovary syndrome
  - Insulinoma
- Drugs
  - Antipsychotics, especially atypical agents
  - Tricyclic antidepressants
  - Sulfonylureas
  - Insulin
  - β Blockers
  - Corticosteroids
  - Estrogen
  - Progestins

Health consequences of obesity

- Greater BMI is associated with increased death from all causes and from CVD
- Although overweight associated with decreased survival
- Each 5 kg/m2 increase in BMI was associated with significant increase in mortality related to:
  - IHD and stroke
  - Diabetes and non-neoplastic kidney disease
  - Different types of cancer
  - Respiratory disease

Figure 3. Clinical Component of the Medical Diagnosis of Obesity

Candidates for weight-loss therapy can present with either excess adiposity (ie, the anthropometric component) or weight-related complications (ie, the clinical component)

Patients Present With Overweight or Obesity	Candidates for Weight-Loss Therapy	Patients Present With Weight-Related Disease or Complications	
Patients with BMI ≥25 kg/m² or ≥23 kg/m² in certain ethnicities and excess adiposity	Evaluate for weight-related complications: R9–R29 →	R9, R10	Prediabetes
		R9, R10	Metabolic syndrome
		R11	Type 2 diabetes
		R12	Dyslipidemia
		R13	Hypertension
		R14, R15	Cardiovascular disease
		R16	Nonalcoholic fatty liver disease
		R17	Polycystic ovary syndrome
	← Evaluate for overweight or obesity: R9–R29	R18	Female infertility
		R19, R20	Male hypogonadism
		R21	Obstructive sleep apnea
		R22	Asthma/reactive airway disease
		R23	Osteoarthritis
		R24	Urinary stress incontinence
		R25, R26	Gastroesophageal reflux disease
		R28	Depression

Health consequences of obesity

- Obesity is associated with reduction in life expectancy during adulthood
- Increase in BMI is associated with increase in morbidity and CVD risk factos

Health consequences of obesity

Table 2. Complications Associated with Obesity

Cardiovascular	Coronary artery disease, stroke, congestive heart failure, hypertension, dysrhythmias, pulmonary embolism
Pulmonary	Obstructive sleep apnea and obesity hypoventilation syndrome
Endocrine	Metabolic syndrome, insulin resistance, dyslipidemia, diabetes mellitus type 2, polycystic ovary syndrome
Gastrointestinal	Gallstones, abdominal hernia, nonalcoholic fatty liver disease, gastroesophageal reflux disease
Bone, joint, and skin	Osteoarthritis, low back pain, gout, acanthosis nigricans
Vascular	Venous stasis
Neurologic	Pseudotumor cerebri
Gynecologic/ genitourinary	Stress incontinence, sexual dysfunction, abnormal menses

NOTE: Obesity is also associated with cancer of the esophagus, colon, pancreas, liver, prostate, breast, endometrium, cervix, and ovaries.

Acanthosis nigricans

Classic hyperpigmented axillary lesion in acanthosis nigricans.

Courtesy of Jeffrey Flier, MD.

UpToDate

Health consequences of obesity

- For both men and women, increasing BMI was associated with higher death rates due to the following cancers:
  - Esophagus
  - Colon and rectum
  - Liver
  - Gallbladder
  - Pancreas
  - Kidney
  - Non-Hodgkin lymphoma
  - Multiple myeloma

Health consequences of obesity

- Increase cost rate on obesity
- Increase number of sick leaves for obese subjects
- Increase number of hospitalization
- Early age of retirement
- Increase cost of drugs for DM, CVD, GI disease
- Poor quality of life due to psychosocial issues

Assessment and screening

- screening of adults for obesity is important
- With significant increase in morbidity and mortality
- Although not in routine practice but it should be as a part of periodic health assessment
- Screening:
  - BMI measurement
  - Waist circumference
  - Evaluation of overall medical risks

Assessment and screening

- Is the patient obese or overweight?
- What are his key health issues? Morbidity and mortality-related

Assessment and screening

Height, in or cm	_____
Weight, lb or kg	_____
Calculated BMI, kg/m2	_____
Waist circumference, in or cm	_____
Blood pressure SBP/DBP, mm Hg	_____
Fasting serum triglyceride, mg/dL or mmol/L	_____
Serum Hdl-cholesterol, mg/dL or mmol/L	_____
Fasting blood glucose, mg/dL	_____
Are there symptoms of sleep apnea?	_____
Are there medication(s) that increase body weight?	_____
Is there regular physical activity?	_____
Are there other etiologic factors?	_____

Assessment and screening

- BMI measurement:
  - Reliable, easy, correlated with percentage of body fat
  - Guide for selection of therapy
  - Varies among different races
  - Recent WHO classification applied to whites, hispanics and black
  - Asians are different: overweight BMI 23-24.9 kg/m2 and obesity by BMI > 25 kg/m2

Classification of overweight and obesity by BMI, waist circumference, and associated disease risk

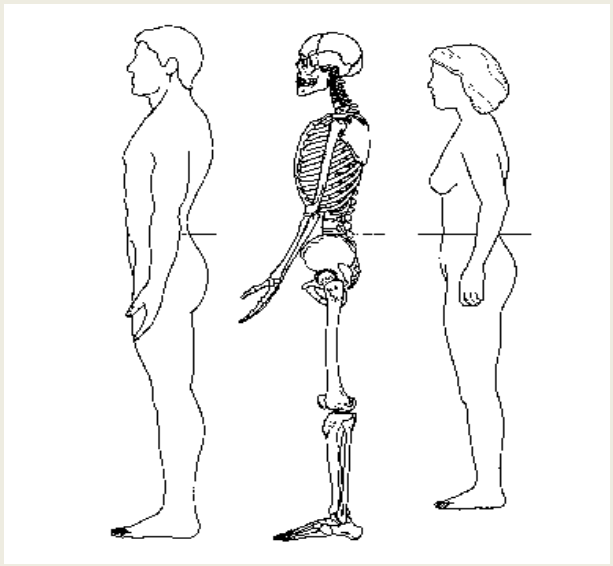
	BMI kg/m^2	Obesity class	Disease risk* relative to normal weight and waist circumference	
			Men ≤102 cm (≤40 in)	>102 cm (>40 in)
			Women ≤88 cm (≤35 in)	>88 cm (>35 in)
Underweight	<18.5		-	-
Normal•	18.5-24.9		-	-
Overweight	25.0-29.9		Increased	High
Obesity	30.0-34.9	I	High	Very High
	35.0-39.9	II	Very High	Very High
Extreme Obesity	≥40	III	Extremely High	Extremely High

* Disease risk for type 2 diabetes, hypertension, and CVD.
• Increased waist circumference can also be a marker for increased risk even in persons of normal weight.
Reproduced from: Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. National Institutes of Health. Obes Res 1998; 6:515.

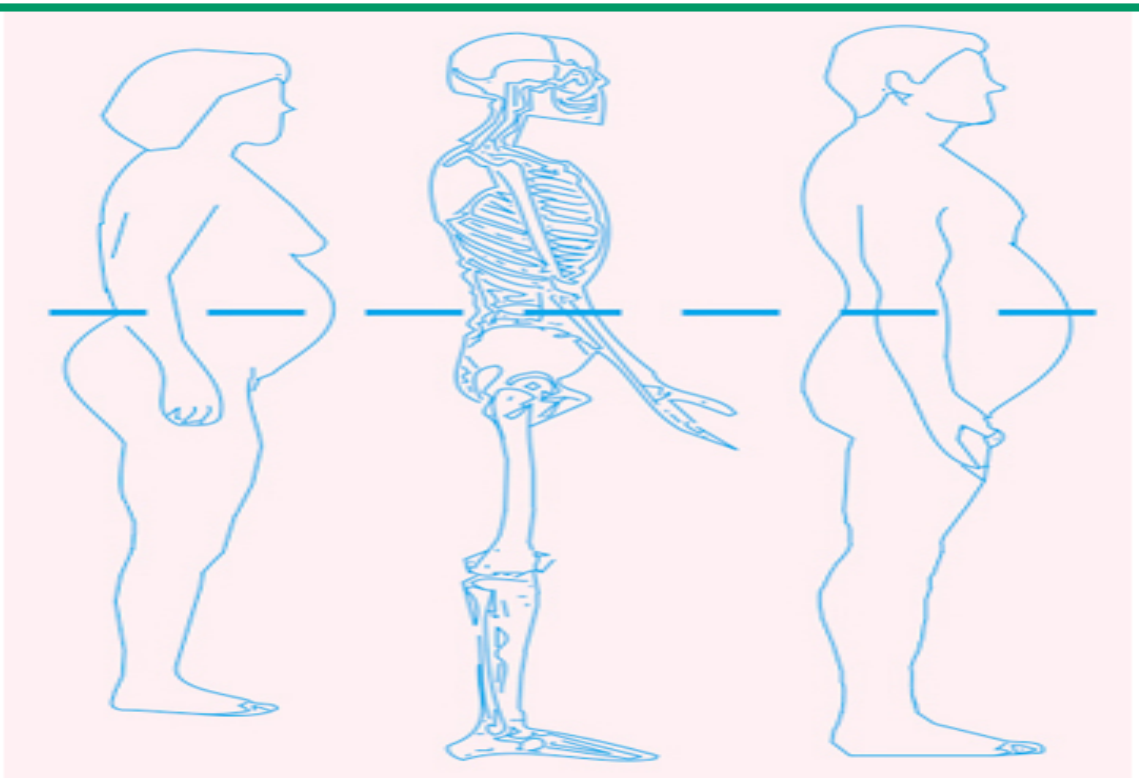
Assessment and screening

- Waist circumference:
  - Measurement of central adiposity
  - Associated with increased risk of morbidity and mortality
  - Reflects visceral adiposity
  - Increase risk of heart disease, DM, hypertension, dyslipidemia
  - Important in identifying the risk in BMI 25-34.9 kg/m2
  - Risk increase with WC > 88 cm in women, 102 cm in men
  - Not useful if BMI > 35 kg/m2
  - In Asian population risk starts with WC > 80 cm in Asian women and > 90 cm in Asian men

Waist circumference



Waist circumference measurement



Measuring-tape position for waist (abdominal) circumference in adults. To measure waist circumference, locate the upper hip bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement is made at the end of a normal expiration.

Reproduced from: National Heart, Lung, and Blood Institute. The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart Lung and Blood Institute, Bethesda, MD, October 2000.

Assessment and screening

- Identify the aetiology:
  - Medical history is important
  - Age at onset of obesity, course of it
  - Eating habits, activity habits
  - Past medical history
  - Medications
  - Cessation of smoking history
  - Ethnic background
  - Family history of obesity

Etiologic classification of obesity

Iatrogenic causes
Drugs that cause weight gain
Hypothalamic surgery
Dietary obesity
Infant feeding practices
Progressive hyperplastic obesity
Frequency of eating
High fat diets
Overeating
Neuroendocrine obesities
Hypothalamic obesity
Seasonal affective disorder
Cushing's syndrome
Polycystic ovary syndrome
Hypogonadism
Growth hormone deficiency
Pseudohypoparathyroidism
Social and behavioral factors
Socioeconomic status
Ethnicity
Psychological factors
Restrained eaters
Night eating syndrome
Binge-eating
Sedentary lifestyle
Enforced inactivity (post-operative)
Aging
Genetic (dysmorphic) obesities
Autosomal recessive traits
Autosomal dominant traits
X-linked traits
Chromosomal abnormalities
Other
Low birth weight

Drugs that cause weight gain and alternatives

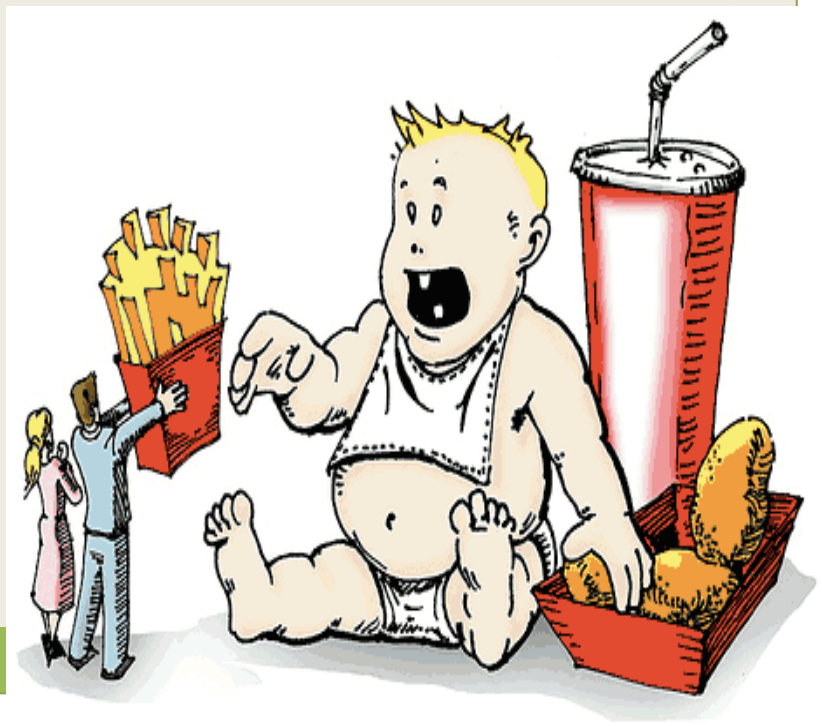
Category	Drugs that cause weight gain	Possible alternatives
Antipsychotics		
Conventional	Thioridazine	Haloperidol
Atypical	Olanzapine, Clozapine, Quetiapine, Risperidone	Ziprasodone, Aripiprazole
Lithium	Lithium carbonate	
Anti-depressants		
Tricyclics	Amitriptyline, Clomipramine, Doxepin, Imipramine, Nortriptyline	Protriptyline
Selective serotonin reuptake inhibitors	Paroxetine	Other SSRIs
Other	Mirtazapine	Bupropion, Nefazadone
Anticonvulsant drugs	Valproate, Carbamazepine, Gabapentin	Topiramate, Lamotrigine, Zonisamide
Antidiabetic drugs	Insulin, Sulfonylureas, Metiglinide, Thiazolidinediones	Metformin, Alpha-glucosidase inhibitors
Serotonin and histamine antagonist	Pizotifen	
Antihistamines	Cyproheptidine	
Beta-adrenergic blockers	Propranolol, Atenolol, Metoprolol	
Steroid hormones	Glucocorticoids	
	Progestins: Megestrol acetate, Medroxyprogesterone acetate	

Assessment and screening

- Assessment of risk status
  - Identify risk factors:
    - After BMI and WC, history
    - BP measurement
    - Fasting lipid profile
    - Fasting blood sugar
  - Identify comorbidity:
    - Help to classify the risk of mortality
    - Presence of atherosclerosis, DM2, HTN, dyslipidemia
    - Sleep apnoea
    - GI, osteoarthritis, gout

Assessment and screening

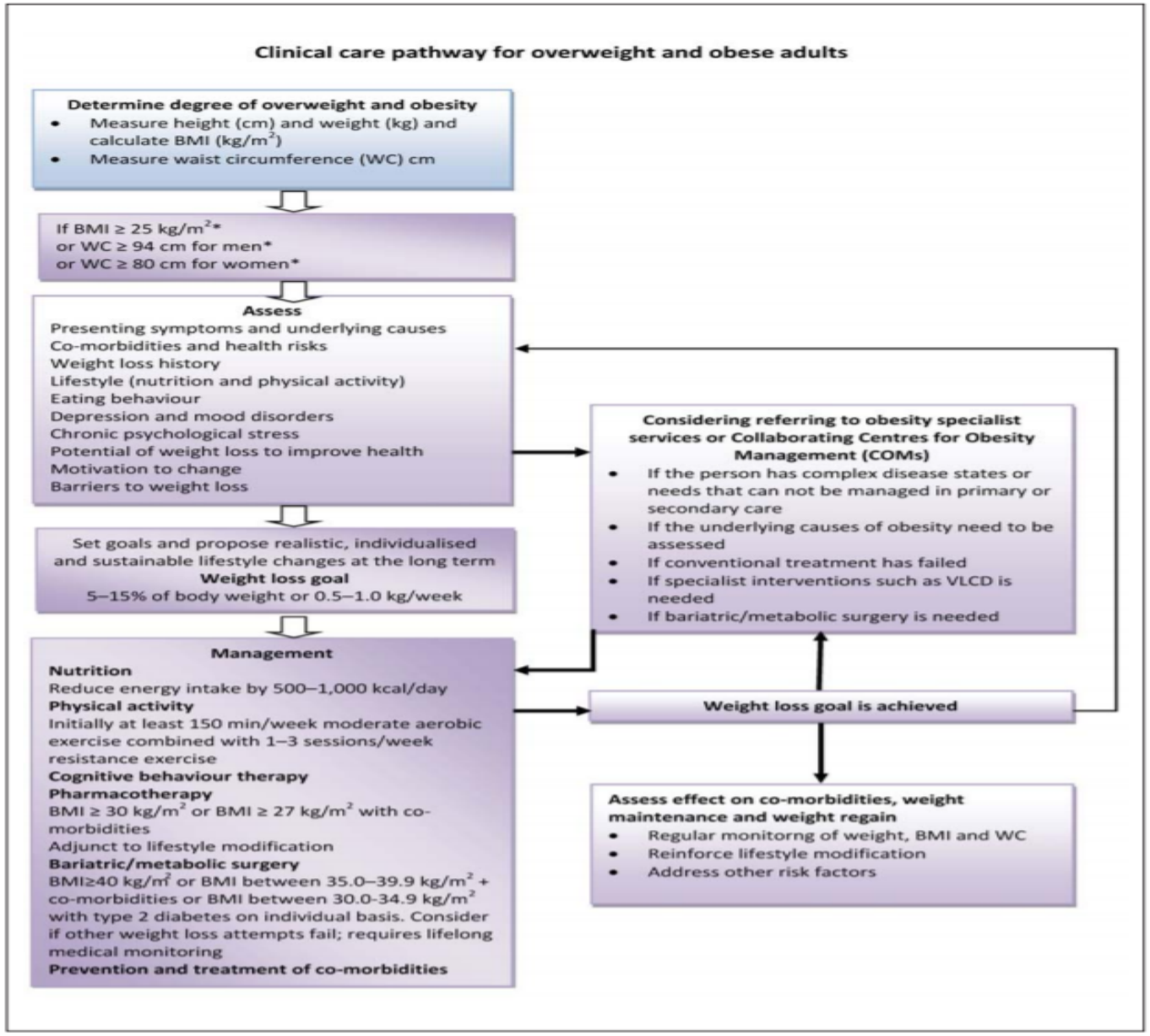
- CVD risk factors that would affect mortality risk:
  - HTN
  - DM2 (fasting blood glucose 110-125 mg/dl)
  - Smoking
  - Dyslipidemia (low HDL < 35 or high LDL> 130)
  - Family history of premature CAD
  - Physical inactivity
- other risk factors:
  - Age of onset of obesity



Assessment and screening

- Why is it important to look at it?
  - It is a common disease with significant morbidity and mortality and without screening many high risk patients may not receive counseling about health risks, lifestyle changes, obesity treatment options, and risk factor reduction.
  - • Screening with BMI, waist circumference, and risk factor assessment is inexpensive and available to nearly all clinicians.
  - • Weight loss is associated with a reduction in obesity-associated morbidity.

- Weight loss of 0.5-9 kg (n=43,457) associated with 53% reduction in cancer-deaths, 44% reduction in diabetes-associated mortality and 20% reduction in total mortality
- Survival increased 3-4 months for every kilogram of weight loss
- Reduced hyperlipidemia, hypertension and insulin resistance
- Improvement in severity of diseases
- Person feels ‘fit’ and mentally more active


Clinical care pathway for overweight and obese adults
Determine degree of overweight and obesity
• Measure height (cm) and weight (kg) and calculate BMI (kg/m²)
• Measure waist circumference (WC) cm
If BMI ≥ 25 kg/m²*
or WC ≥ 94 cm for men*
or WC ≥ 80 cm for women*
Assess
Presenting symptoms and underlying causes
Co-morbidities and health risks
Weight loss history
Lifestyle (nutrition and physical activity)
Eating behaviour
Depression and mood disorders
Chronic psychological stress
Potential of weight loss to improve health
Motivation to change
Barriers to weight loss
Set goals and propose realistic, individualised and sustainable lifestyle changes at the long term
Weight loss goal
5–15% of body weight or 0.5–1.0 kg/week
Management
Nutrition
Reduce energy intake by 500–1,000 kcal/day
Physical activity
Initially at least 150 min/week moderate aerobic exercise combined with 1–3 sessions/week resistance exercise
Cognitive behaviour therapy
Pharmacotherapy
BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with co-morbidities
Adjunct to lifestyle modification
Bariatric/metabolic surgery
BMI≥40 kg/m² or BMI between 35.0–39.9 kg/m² + co-morbidities or BMI between 30.0-34.9 kg/m² with type 2 diabetes on individual basis. Consider if other weight loss attempts fail; requires lifelong medical monitoring
Prevention and treatment of co-morbidities
Considering referring to obesity specialist services or Collaborating Centres for Obesity Management (COMs)
• If the person has complex disease states or needs that can not be managed in primary or secondary care
• If the underlying causes of obesity need to be assessed
• If conventional treatment has failed
• If specialist interventions such as VLCD is needed
• If bariatric/metabolic surgery is needed
Weight loss goal is achieved
Assess effect on co-morbidities, weight maintenance and weight regain
• Regular monitorng of weight, BMI and WC
• Reinforce lifestyle modification
• Address other risk factors

Treatment goals

- Prevention of further weight gain
- Weight loss to achieve a realistic, target BMI
- Long-term maintenance of a lower body-weight

How much weight loss is significant?

A 5-10% reduction in weight (within 6 months) and

weight maintenance should be stressed in any weight

loss program and contributes significantly to

decreased morbidity

Management of obesity

- 3 main interventions:
  - Lifestyle intervention (diet, exercise)
  - Pharmacotherapy
  - Surgical intervention

Lifestyle

- Diet
- Physical activity
- Behavior change

- Most important recommendation

Figure 4. Lifestyle Therapy

Evidence-based lifestyle therapy for treatment of obesity should include 3 components
Recommendations: R64 through R75

Meal Plan (R64, R65, R66)

- Reduced-calorie healthy meal plan
- ~500–750 kcal daily deficit
- Individualize based on personal and cultural preferences
- Meal plans can include: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian
- Meal replacements
- Very low-calorie diet is an option in selected patients and requires medical supervision

Team member or expertise: dietitian, health educator

Physical Activity (R64, R67, R68, R69, R70, R71)

- Voluntary aerobic physical activity progressing to >150 minutes/week performed on 3–5 separate days per week
- Resistance exercise: single-set repetitions involving major muscle groups, 2–3 times per week
- Reduce sedentary behavior
- Individualize program based on preferences and take into account physical limitations

Team member or expertise: exercise trainer, physical activity coach, physical/occupational therapist

Behavior (R64, R72, R73, R74, R75)

An interventional package that includes any number of the following:

- Self-monitoring (food intake, exercise, weight)
- Goal setting
- Education (face-to-face meetings, group sessions, remote technologies)
- Problem-solving strategies
- Stimulus control
- Behavioral contracting
- Stress reduction
- Psychological evaluation, counseling, and treatment when needed
- Cognitive restructuring
- Motivational interviewing
- Mobilization of social support structures

Team member or expertise: health educator, behaviorist, clinical psychologist, psychiatrist

lifestyle

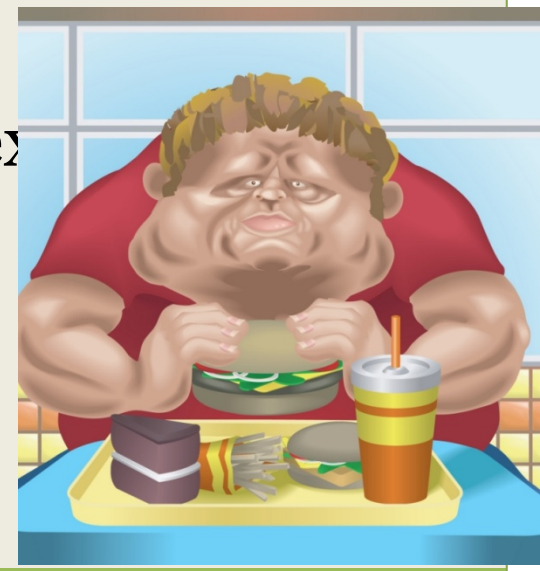
- Initial goal: 10% weight loss
  - Significantly decreases risk factors
- Rate of weight loss:
  - 1-2 pound per week
  - Reduction of calories intake 500-1000 calories/day
- Slow weight loss is preferred approach
  - Rapid weight loss is almost always followed by rapid weight gain
  - Rapid weight loss is associated with gallstones and electrolytes abnormalities

lifestyle

- Aim for 4-6 months for weight loss
- Average is 8-10 kg loss
- After 6 months, weight loss is difficult
  - Ghrelin and leptin effect
  - Energy requirement decreased as weight decreases

- Set goals for weight maintenance for nex

6 months then reassess



Diet therapy

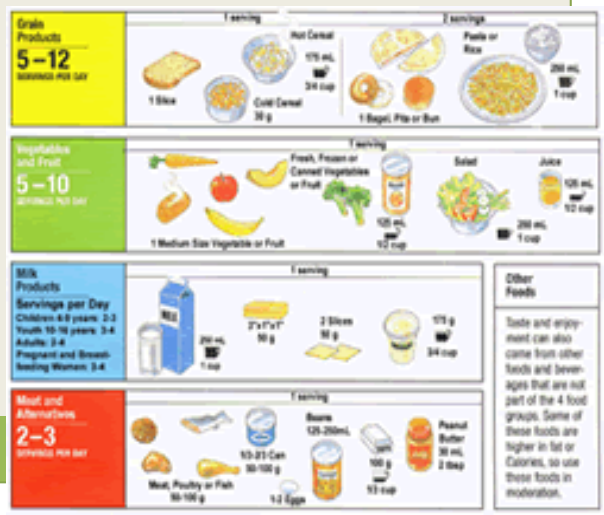
- Indicated for all with BMI > 30 and those with BMI 25- 30 with comorbidities
- Teaching about food composition (fat, CHO, protein)
- Calories contents of food by reading labels
- Type of food to buy and to prepare

The L.E.A.N. Take on Fast Food	Calories	Total Fat (g)	Saturated Fat (g)	Trans Fat (g)
McDonald's				
Big Mac*	540	29	10	1.5
Med Fries	380	19	2.5	2.5
Total	**920**	**48**	**12.5**	**4**
Chipotle				
Chicken Burrito**	1100	51	19.5	0
Chips	570	27	3.5	0
Total	**1670**	**78**	**23**	**0**

* Beef patty, bun, cheese, sauce, lettuce, pickles, onions
** Flour tortilla, cilantro-lime rice, black beans, chicken, cheese, sour cream, guacamole

Diet therapy

- Low calories diet-portion controlled
- Low fat diet
- Low CHO diet
- Meditarrean diet
- Average for women: 1000-1200 kcal/day
- Average for men: 1200-1600 kcal/day
- Adjust based on activity and weight



Diet therapy

- How much is 1200 calories?

- 1 big mac (580)
- 1 small fries (210)
- 1 small shake (430)

Diet therapy

- Then weight maintenance
- How much should people eat?

Male	**Age 20-49**	**2900 kcal/day**
	Age 50 +	2500 Kcal/day
Female	Age 20-49	2300 Kcal/day
	Age 50+	1900 Kcal/day

Physical activiy

- As integral part of weight loss
- Reduce risk of DM, heart disease, hypertension
- Alone is not helping
- Help to prevent weight regain

Table 9. Association of Eating Patterns and Macronutrient Composition on Weight-Loss Efficacy

Eating Pattern or Macronutrient Change	Effect	Reference [EL]
Low glycemic index/load	• ⬆ Endothelial function • ⬇ Glycemic variability • Effects on energy expenditure • Decreased adipocyte diameter • No incremental effect on weight loss[1]	33 [EL 1; RCT], 34 [EL 1; RCT], 35 [EL 1; RCT, small N=13], 36 [EL 1; RCT]
Low carbohydrate	• Improved glycemic status and lipids • Improved other cardio-metabolic risk factors • Improved renal function • No incremental effect on weight loss (some studies show more short-term weight loss)[2]	37 [EL 4; NE], 38 [EL 1; RCT], 39 [EL 1; RCT], 40 [EL 1; RCT], 41 [EL 1; RCT], 42 [EL 1; RCT], 43 [EL 2; NRCT], 44 [EL 1; RCT], 45 [EL 1; RCT], 46 [EL 1; RCT], 47 [EL 1; RCT]
High protein	• Longer benefit on WC, %fat • Improved cardio-metabolic risk factors • Decreased adipocyte diameter • Animal (not plant) proteins associated with markers of inflammation • Less relative loss of muscle mass • No incremental effect on weight loss	33 [EL 1; RCT], 38 [EL 1; RCT], 45 [EL 1; RCT], 48 [EL 1; RCT], 49 [EL 1; RCT], 50 [EL 1; RCT], 51 [EL 1; RCT], 52 [EL 1; RCT], 53 [EL 1; RCT]
Moderate carbohydrate – moderate protein	• Improved body composition, lipid, ppINS • No incremental effect on weight loss	37 [EL 4; NE]. 54 [EL 1; RCT]
Low fat	• Beneficial effects on lipids • Benefits on lipids replacing with unsaturated fat • Improved renal function • No incremental effect on weight loss	37 [EL 4; NE], 41 [EL 1; RCT], 47 [EL 1; RCT], 55 [EL 1; RCT], 56 [EL 1; RCT]
High fat	• With lactation: when hypocaloric, great weight loss compared with hypocaloric low-carbohydrate diet	57 [EL 2; PCS]
Mediterranean-style	• Decreased risk certain cancers • EVOO supplementation – no effect on weight • Reduces cardio-metabolic risk factors and MetS • Reduces markers of inflammation • Improves hepatic steatosis and insulin sensitivity • Improves renal function • No incremental effect on weight loss	40 [EL 1; RCT], 58 [EL 1; RCT, post-hoc analysis], 59 [EL 2; PCS, post-hoc analysis], 60 [EL 1; RCT, secondary analysis], 61 [EL 2; PCS], 62 [EL 1; RCT], 63 [EL 1; RCT], 64 [EL 2; PCS], 65 [EL 2; PCS], 66 [EL 1; RCT]

Abbreviations: EL = evidence level; EVOO = extra-virgin olive oil; MetS = metabolic syndrome; ppINS = postprandial insulin response; WC = waist circumference.

[1] Incremental effect in comparison to a isocaloric control diet does not occur or is inconsistent.

[2] Short-term is <1 year.

Physical activity

- Start slowly
  - Change of daily living activities
  - Avoid injury
- Increase intensity and duration gradually
- Long –term goal:
  - 30-45 min or more of physical activity daily
  - 5 or more days per week
  - Burn 1000+ calories per week

Behavioral strategies

- Keep agenda of diet and activity
  - Set specific goals regarding: diet, activity related behavior
  - Reminder system
  - Reward yourself
  - Don't deprive yourself, watch portion
- Track improvement:
  - Weight measurement on regular basis

Pharmacotherapy

- Indicated in:
  - BMI > 30
  - BMI 27-30 with comorbidities
  - Should not be used for cosmetic weight loss
  - Used only when 6 months trial if weight and exercise fail to achieve weight loss

Pharmacotherapy

- Sympathomimetics:
  - Stimulate release of norepinephrine or inhibits its reuptake by nerve terminals
  - Block serotonin and NE reuptake (sibutramine)
  - Directly act upon adrenergic receptor
  - Reduced appetite by early satiety
- Pancreatic lipase inhibitor:
  - Orlistat: inhibits fat absorption
- Antidepressant
- Antiepileptic
- Diabetic drugs: metformin

Drugs approved by the FDA for treatment of obesity

Drug	Trade names	Dosage	DEA schedule
Pancreatic Lipase inhibitor approved for long-term use			
Orlistat	Xenical	120 mg three times daily before meals	-
Norepinephrine-serotonin reuptake inhibitor approved for long-term use			
Sibutramine	Meridia	5 to 15 mg/day	IV
	Reductil		
Noradrenergic drugs approved for short-term use			
Diethylpropion	Tenuate	25 mg three times daily	IV
	Tenuate Dospan	75 mg every morning	
Phentermine	Adipex	15 to 37.5 mg/day	IV
	Ionamin Slow Release	15 to 30 mg/day	
Benzphetamine	Didrex	25 to 50 mg three times daily	III
Phendimetrazine	Bontril	17.5 to 70 mg three times daily	III
	Prelu-2	105 mg daily	

Recommendation for use of drugs listed in the American College of Physicians guidelines

Drug	Net weight loss (kg) (statisticians view)	Gross weight loss (kg) (patients view)	Recommendation
Orlistat	-2.75	-8.25	Approved for long term use
Sibutramine	-4.45	-9.95	Approved for use up to two years
Phentermine	-3.6	-9.1	Approved for short term use (12 weeks)
Diethylpropion	-3.0	-8.5	Approved for short term use (12 weeks)
Fluoxetine	-14.5 to + 0.4	-21 to -5.6	Not recommended
Bupropion	-2.77	-8.27	Not recommended

Net weight loss assumes an average weight loss of 5.5 kg with placebo. The 5.5 kg is then subtracted from the gross weight loss achieved with drug therapy.
With permission from: George Bray, MD. Data adapted from Li Z, Maglione M, Tu W, et al. Ann Intern Med 2005; 142:532. Snow, V, Barry, P, Fitterman, N, et al. Ann Intern Med 2005; 142:525.

CLINICAL CHARACTERISTICS OR COEXISTING DISEASES		MEDICATIONS FOR CHRONIC WEIGHT MANAGEMENT				
		Orlistat	Lorcaserin	Phentermine/ topiramate ER	Naltrexone ER/ bupropion ER	Liraglutide 3 mg
Diabetes Prevention (metabolic syndrome, prediabetes)			Insufficient data		Insufficient data	
Type 2 Diabetes Mellitus						
Hypertension				Monitor heart rate	Monitor BP and heart rate.	Monitor heart rate
					Contraindicated in uncontrolled HTN	
Cardiovascular Disease	CAD			Monitor heart rate	Monitor heart rate, BP	Monitor heart rate
	Arrhythmia			Monitor heart rate, rhythm	Monitor heart rate, rhythm, BP	Monitor heart rate, rhythm
	CHF	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Chronic Kidney Disease	Mild (50–79 mL/min)					
	Moderate (30–49 mL/min)			Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg bid	
	Severe (<30 mL/min)	Watch for oxalate nephropathy	Urinary clearance of drug metabolites	Urinary clearance of drug	Urinary clearance of drug	Avoid vomiting and volume depletion
Nephrolithiasis		Calcium oxalate stones		Calcium phosphate stones		
Hepatic Impairment	Mild-Moderate (Child-Pugh 5–9)	Watch for cholelithiasis	Hepatic metabolism of drug	Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg in AM	Watch for cholelithiasis
	Severe (Child-Pugh >9)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Depression			Insufficient safety data	Avoid maximum dose: 15 mg/92 mg per day	Insufficient safety data	
			Avoid combinations of serotonergic drugs		Avoid in adolescents and young adults	
Anxiety				Avoid max dose: 15 mg/92 mg per day		
Psychoses		Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Binge Eating Disorder			Insufficient data. Possible benefit based on reduction in food cravings	Insufficient data. Possible benefit based on studies with topiramate	Insufficient data. Possible benefit based on studies with bupropion	Insufficient data
					Avoid in patients with purging or bulimia nervosa	
Glaucoma				Contraindicated, may trigger angle closure	May trigger angle closure	
Seizure Disorder				If discontinued, taper slowly	Bupropion lowers seizure threshold	
Pancreatitis		Monitor for symptoms				Monitor for symptoms
						Avoid if prior or current disease
Opioid Use					Will antagonize opioids and opiates	
Women of Reproductive Potential	Pregnancy	Use contraception and discontinue orlistat should pregnancy occur	Use contraception and discontinue lorcaserin should pregnancy occur	Use contraception and discontinue phentermine/topiramate should pregnancy occur (perform monthly pregnacy checks to identify early pregnancy; risk of cleft lip/palate)	Use contraception and discontinue naltrexone ER/bupropion ER should pregnancy occur	Use contraception and discontinue liraglutide should pregnancy occur
	Breast-feeding	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Age ≥65 years *		Limited data available	Insufficient data	Limited data available	Insufficient data	Limited data available
Alcoholism/ Addiction			Might have abuse potential due to euphoria at high doses	Insufficient data. Topiramate might exert therapeutic benefits	Avoid due to seizure risk and lower seizure threshold on bupropion	
Post-Bariatric Surgery		Insufficient data	Insufficient data	Limited data available	Insufficient data	Data available at 1.8 – 3.0 mg/day

* Use medications only with clear health-related goals in mind; assess patient for osteoporosis and sarcopenia.

Abbreviations: BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; HTN = hypertension.

Table 3. Pharmacotherapy for obesity in Europe (November 2015) [71–74, 80]

Drugs	Status	Mechanism	Dosing	Response evaluation	Warnings	Contraindications	Side-effects
Orlistat	FDA & EMA approved	pancreatic, gastric lipase inhibitor	120 mg tid 60 mg tid (OTC)	2.9–3.4% 1 year	hepatitis, liver failure (rare), concomitant multivitamin advised	pregnancy, breast feeding, chronic malabsorption syndrome, cholestasis	decreased absorption of fat soluble vitamins, steatorrhoea, faecal urgency
Lorcaserin	FDA approved	5HT2c R agonist	10 bid	3.6% 1 year stop if <%5 weight loss at 12 weeks	serotonin syndrome, cognitive impairment, depression, valvulopathy hypoglycaemia, priapism	pregnancy, breast feeding, use with caution: MAOIs, SSRIs, SNRIs	headache, nausea dry mouth, dizziness fatigue, constipation
Phentermine/ topiramate	FDA approved	NE release (P) GABA modulation (T)	starting dose: 3.75/23 qd recommended dose: 7.5/46 qd *high dose: 15/92 qd	6.6% (recommended dose) 1 year 8.6% (high dose) 1 year stop if <%5 weight loss at 12 weeks	fetal toxicity, acute myopia, cognitive dysfunction, metabolic acidosis, hypoglycaemia	pregnancy, breast feeding, glaucoma, hyperthyroidism, use with caution: MAOIs	insomnia, dry mouth constipation, paresthesia, dizziness, dysgeusia
Bupropione/ naltrexone	FDA & EMA approved	DA/NE reuptake inhibitor(B) opioid antagonist (N)	8/90 mg tb 2 tb bid	4.8% 1 year stop if <%5 weight loss at 12 weeks	fetal toxicity, increased seizure risk, glaucoma, hepatoxicity	uncontrolled hypertension, seizure, anorexia nervosa / bulimia, drug or alcohol withdrawal, use with caution: MAO inhibitors	nausea, constipation, headache, vomiting, dizziness
Liraglutide	FDA & EMA approved	GLP-1 agonist	3 mg sc	5.8 kg 1 year stop if <%4 weight loss at 14 wks	acute pancreatitis, acute gall bladder disease	medullary thyroid cancer history, MEN type 2 history	nausea, vomiting, pancreatitis

FDA = Food & Drug Administration; EMA= European Medicinal Agency; OTC = over the counter; 5HT2c-R = 5 hydroxytryptamine 2c receptor; MAOI = monoamino oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor; NE = norepinephrine; GABA = gamma amino butyric acid; DA = dopamine; GLP-1 = glucagon-like peptide-1; MEN = multiple endocrine neoplasia.

*Careful observation.

Weight loss Surgical therapy

- Indicated in:
  - Well-infomed and motivated patients
  - Have BMI > 40
  - Acceptable risk of surgery
  - Failed previous non-surgical method
  - BMI > 35 with comorbidities like diabetes, sleep apneoa, osteoarthritis, cardiomyopathy
  - BMI 25-29.9 with WC > 102 cm in male and 88 cm in women
  - Age 18-60
  - Psychologically stable

Weight loss Surgical therapy(bariatric surgery)

- Restrictive-type of surgery:
  - Vertical banded-gastroplasy
  - Gastric banding
- Malabsorptive and restrictive:
  - Roux-en-Y gastric bypass
  - Biliopancreatic diversion
- Follow up is crutial

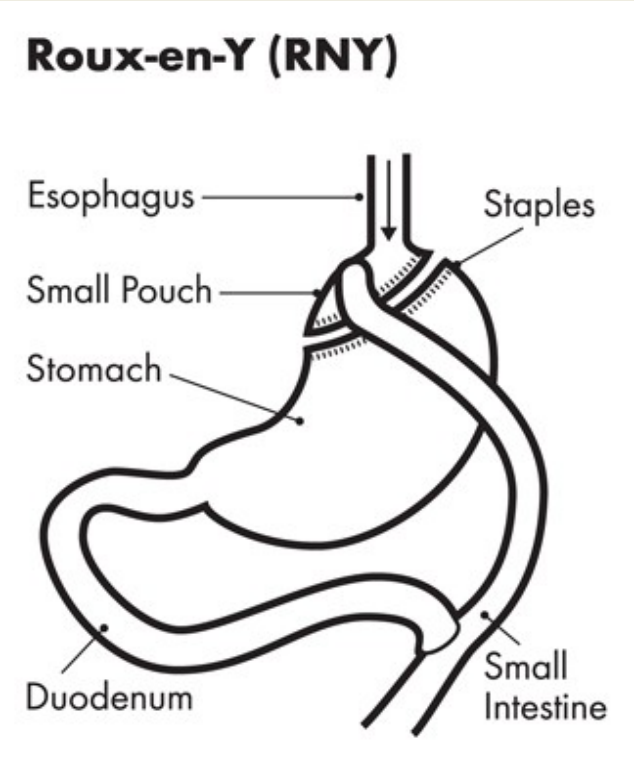


Table 8: Treatment Goals Based on Diagnosis in the Medical Management of Patients With Obesity

	DIAGNOSIS		TREATMENT GOALS		
	Anthropometric Component	Clinical Component	Intervention/ Weight-Loss Goal	Clinical Goals	Qs & Rs
PRIMARY PREVENTION					
Primordial Prevention	BMI ≤25 (≤23 in certain ethnicities)	Obesogenic environment	• Public education • Built environment • Access to healthy foods	Decreased incidence of overweight/ obesity in populations	Q1,R2
Primary Prevention	BMI ≤25 (≤23 in certain ethnicities)	High-risk individuals or subgroups based on individual or cultural behaviors, ethnicity, family history, biomarkers, or genetics	• Annual BMI screening • Healthy meal plan • Increased physical activity	Decreased incidence of overweight/ obesity in high-risk individuals or identifiable subgroups	Q1,R2 Q2,R3
SECONDARY PREVENTION					
Overweight	BMI 25–29.9	No clinically significant or detectable weight-related complications	• Prevent progressive weight gain or • Weight loss	• Prevent progression to obesity • Prevent the development of weight-related complications	Q1,R2 Q4,R29
Obesity	BMI ≥30 (≥23 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Weight loss or • Prevent progressive weight gain	Prevent the development of weight-related complications	Q1,R2 Q4,R29
TERTIARY PREVENTION					
Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome	10%	Prevention of T2DM	Q3.1,R9,R10 Q5.1,R30,R31
		Prediabetes	10%	Prevention of T2DM	Q3.1,R9,R10 Q5.1,R30,R31
		T2DM	5% to ≥15%	• Reduction in A1C • Reduction in number and/or doses of glucose lowering medications	Q3.2,R11 Q5.2,R33,R34
		Dyslipidemia	5% to ≥15%	• Lower triglycerides • Higher HDL-c • Lower non-HDL-c	Q3.3,R12 Q5.3,R37,R38
		Hypertension	5% to ≥15%	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications	Q3.4,R13 Q5.4,R39,R40
		Nonalcoholic fatty liver disease – Steatosis	5% or more	Reduction in intrahepatocellular lipid	Q3.6,R16 Q5.6,R45,R46
		Nonalcoholic fatty liver disease – Steatohepatitis	10% to 40%	Reduction in inflammation and fibrosis	Q3.6,R16 Q5.6,R45,R46
		Polycystic ovary syndrome	5% to 15% or more	• Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels	Q3.7,R17 Q5.7,R48,R49
		Female infertility	10% or more	• Ovulation • Pregnancy	Q3.8,R18 Q5.8,R51
		Male hypogonadism	5% to 10% or more	Increase in serum testosterone	Q3.9,R19,R20 Q5.9,R52
		Obstructive sleep apnea	7% to 11% or more	• Improved symptomatology • Decreased apnea-hypopnea index	Q3.10,R21 Q5.10,R55
		Asthma/reactive airway disease	7% to 8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology	Q3.11,R22 Q5.11,R56
		Osteoarthritis	• ≥10% • 5% to 10% or more when coupled with exercise	• Improvement in symptomatology • Increased function	Q3.12,R23 Q5.12,R57, R58
		Urinary stress incontinence	5% to 10% or more	Reduced frequency of incontinence episodes	Q3.13,R24 Q5.13,R59
		Gastroesophageal reflux disease	10% or more	Reduced symptom frequency and severity	Q3.14,R25, Q15.5,R60
		Depression	Uncertain	• Reduction in depression symptomatology • Improvement in depression scores	Q3.15,R28 Q5.15,R63

Abbreviations: A1C = hemoglobin A1c; BMI = body mass index; BP = blood pressure; HDL-c = high-density lipoprotein cholesterol; T2DM = type 2 diabetes mellitus.

Questions????