Weight loss Challenge: How can obesity be managed?

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Case 1

- Mrs Moly, 43 years
- DM, Hypothyroidism, Obesity, Sleep Apnoea, using Cpap
- Weight 109 kg, BMI 43.7%
- Lab reports: FBG 9.2 mmol/L, HbA1c 8.2%, TSH 7.06 micromole/L
- Semaglutide started on September 2024, gradually increased the dose to maximum

Follow up

September 2024	December 2024	February 2025
Weight 109 kg FBG 9.2 mmol/L, HbA1c 8.2% TSH 7.06 micromole/L	Weight 105 kg HbA1c 6.4% TSH 3.4 mmol/L	Weight 97 kg HbA1c 5.3% TSH 4.4 mmol/L No need of Cpap now

Case 2

- Mrs Nova, 35 years
- DM, HTN, Obesity, OA knee joint, MASLD, on Insulin
- Gaining weight
- Weight 110 kg, BMI 44.1
- FBG 17.3 mmol/L, HbA1c 13.5%
- SGPT 128 mu/l
- Dulaglutide started along with Insulin and Metformin on December 2024

Follow up

December 2024	March 2025	June 2025
Weight 110 kg FBG 17. 3 mmol/L HbA1c 13.5% SGPT 128 mu/l	Weight 97 kg FBG 6.2 mmol/l HbA1c 6.4% SGPT 50 u/L Insulin dose decreased at least 16 unit	Weight 89 kg FBG 5.8 mmol/L HbA1c 6.2% SGPT 44 u/L Insulin stopped, on Metformin, Empagliflozine and Dulaglutide She started walking

Case 3

- Mrs Sabrina, 37 years
- DM, Obesity, Subfertilty, took treatment for subfertility and gaining more weight
- FBG 10 mmol/L, HbA1c 9.3%
- Tirzepetide started with Metformin on 21.03.24

Follow up

21.03.24	10.08.24	12.12.24
Weight 97kg HbA1c 9.3%	Weight 78 kg HbA1c 6.2% Tirzepetide stopped, on metformin 2 gm	Pregnancy test positive Weight 75 kg HbA1c 6.1% Insulin started

Is obesity a disease?

OBESITY

Not Just A Body Shape

But a Silent Chronic Disease!!!

Obesity

- Obesity is a complex, multifactorial, chronic and relapsing disease
- Disorder of energy homeostasis
- ABCD: Adiposity Based Chronic Disease
- Multifactorial: epigenetic, genetic and environmental factors
- Genetic factors may contribute 50-70% of the cause

Obesity: Rising epidemic

- In 2022, over 890 million adults were living with obesity worldwide
- Projected estimates in adults is nearly 3.3 billion in next 10 years
- In Bangladesh approximately 18% of men aged 18 years and older, and more than 32% women aged 15–49 years were overweight or obese

(According to the Bangladesh Demographic and Health Survey (BDHS) 2017–2018 report)

Pathophysiology of Obesity

- Genes and environment interact in a complex system to regulate energy balance
- Two sets of neurons in the hypothalamic arcuate nucleus are inhibited or excited by circulating neuropeptide hormones control energy balance
- Hunger and satiety signals from adipose tissue (leptin), the pancreas (insulin), and the gastrointestinal tract (cholecystokinin (CCK), glucagon-like peptide-I (GLP-1), peptide YY3-36 (PYY3-36), and ghrelin) are involved

Hormones involved in energy balance

- **Leptin**: from adipose tissue, anorexigenic, increase lipolysis, decrease lipogenesis
- **Insulin**: from pancreas, visceral fat negatively corelated with insulin resistance
- **Ghrelin**: from stomach, increases food intake by both peripheral and central mechanisms involving stomach, the HPAL, and the hypophysis
- **GLP1**: co-released with PYY from the distal intestinal L-cells after a meal, stimulate glucose-dependent insulin secretion, enhance β-cell growth and survival, inhibit glucagon release, and suppress food intake
- **PYY**: after food ingestion, released from the L-cells in the distal segment of the small gut, reduces intestinal motility and gallbladder and gastric emptying and therefore decreases appetite and augments satiety
- **Cholecystokinin (CCK)**: endogenous peptide hormone present in the gut and the brain, helps control appetite, ingestive behavior, and gastric emptying

Causes of obesity

Lifestyle	Endocrine	Medication	Genetic
Poor dietary habit Sedentary lifestyle Excess screen time Poor sleep hygiene	Hypothyroidism Cushing`s Insulinoma Hypothalamic disorders	Steroids Antipsychotic. Anti depressants Insulin, SU Implant contraceptives Sodium Valproate Pregabalin, Gabapentin	Monogenic Polygenic

Obesity risks start from early life

- Small for gestational age, formula milk, and early introduction of protein in an infant's diet are associated with future weight gain

- Exposure in utero to maternal obesity or gestational diabetes mellitus (GDM) is linked to a high risk for obesity in offspring

Consequences of obesity

CVS	Pulmonary	Endocrine	GIT	MSK	Psychological	Neurological	Cutaneous	Andrology
HTN Dyslipidemia IHD PVD Coagulopathy	Exercise intolerance OSA OHS Asthma	Type 2DM PCOS Subfertility Precocious puberty Hormone related cancers	Gall stone MAFLD GERD Cancer (colon, hepatic, pancreatic)	OA Ankle sprain Gout Flat feet Tibia vera PLID Back pain	Body image disorder Social isolation Stigmatization Depression Poor self esteem	Stroke Idiopathic intracranial hypertension	Intertrigo Hydradenitis suppurativa Acanthosis nigricans Sweating Hirsutism	Low testosterone ED Low sperm quality Prostate cancer

Diagnosis of obesity

- **BMI:** Weight in KG/ height in meter 2

BMI categories	Cut-offs levels
Underweight	<18.5 kg/m^2
Normal	18.5-22.99 kg/m^2
Overweight	23.00-24.99 kg/m^2
Obese	≥25.00-29.99 kg/m^2
Very obese	≥30.00 kg/m^2

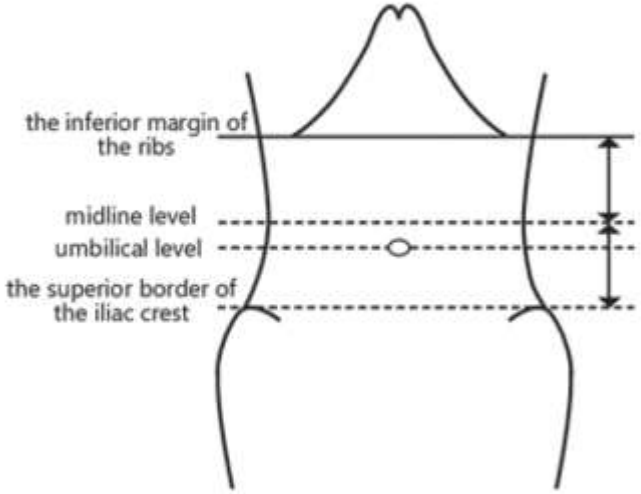
Diagnosis of obesity

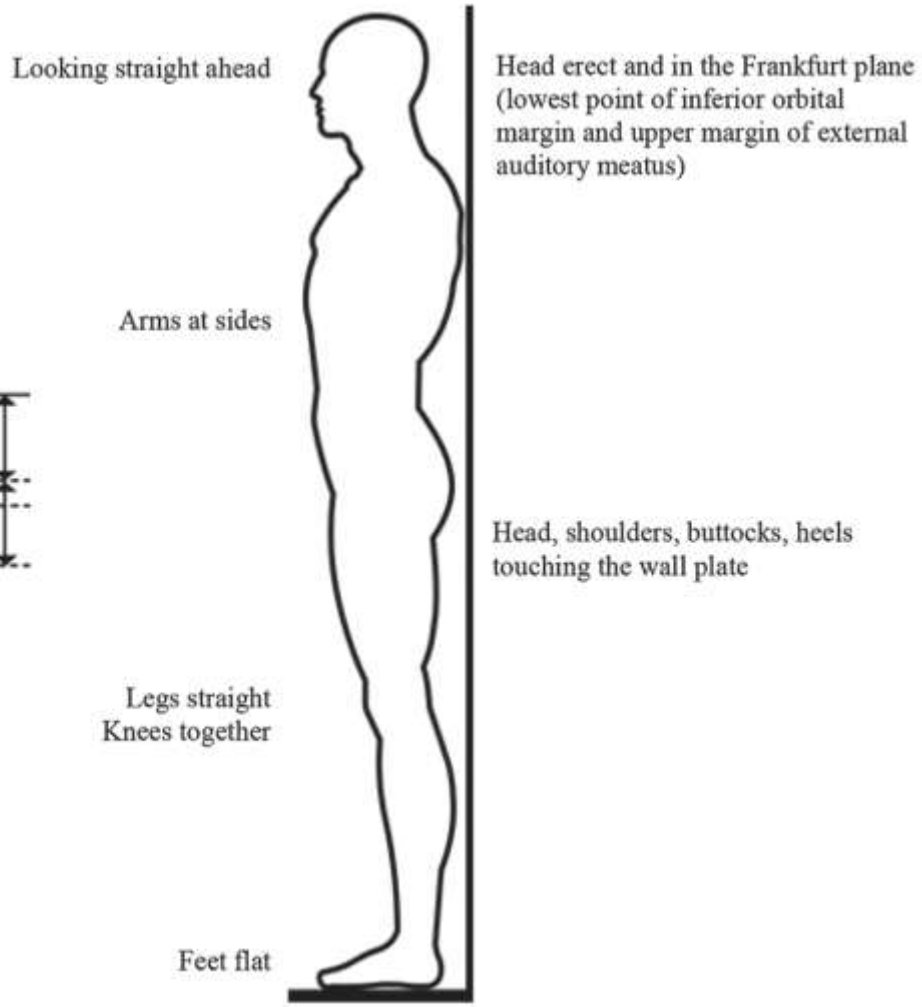
Waist circumference: WC is a measure of abdominal obesity and is directly associated with increased metabolic risk

Category	Waist circumference (cm)		Waist-Hip Ratio	
	Male	Female	Male	Female
Normal	<90	< 80	<0.95	< 0.8
At-risk	≥90	≥80	≥0.95	≥0.8

Source: WHO, 2004

Measurement of BMI and WC





Management of Obesity

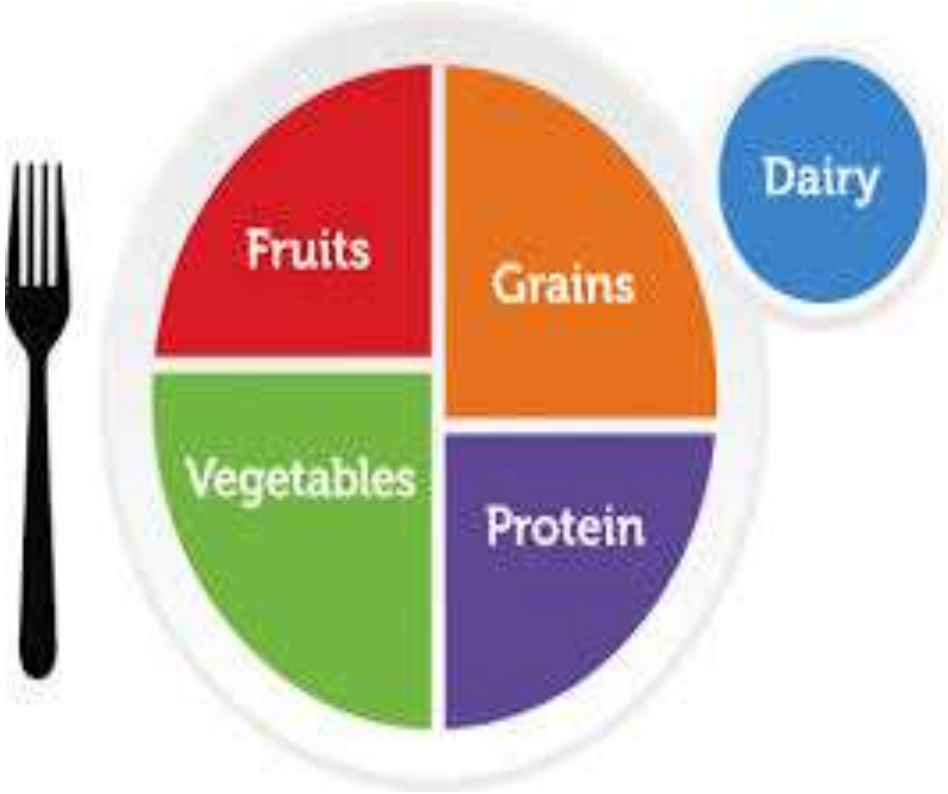
Multidisciplinary team should include:

- Nutritionist
- Endocrinologist
- Educator
- Psychiatrist
- Hepatologist
- Pulmonologist

Nutrition modification

What To do:

- Fat: <30%, take mono and poly unsaturated fat, avoid saturated/transfat
- Protein: 25-35%, include lean meat, fish, eggs, poultry without skin, low fat dairy, legumes
- CHO: 45-55%, switch to whole grain, avoid refined CHO
- Five portions of fruits and vegetables
- Fiber 20-35 g/day
- Salt: <6g/day



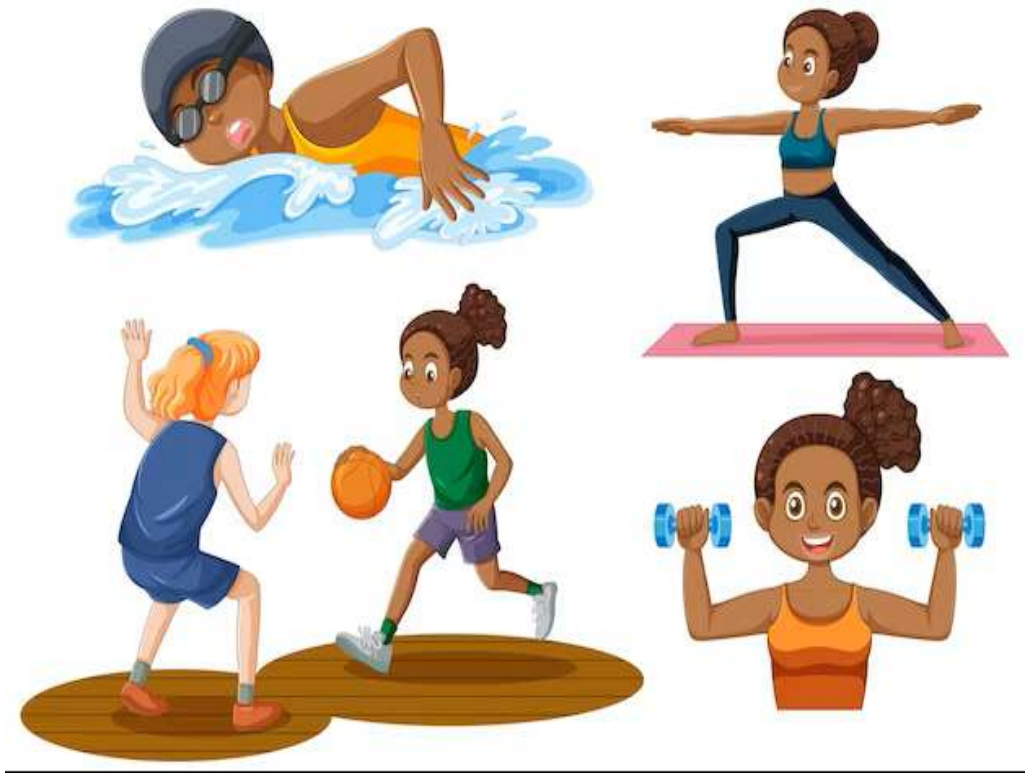
Nutrition modification

Not to do

- Snacking
- emotional eating
- eating out or ordering in
- Skipping meals especially breakfast
- media during meals
- eating hidden carbohydrate and fast food

Physical activity

- 150 min/week of moderate intensity aerobic or endurance exercise
- This means 30 min sessions, 5 days a week
- The examples of aerobic exercise are brisk walking or jogging, yard work, dancing, swimming, biking, playing tennis or basketball
- Moderate intensity exercise increases the heart rate by 56%–70%



Screen time and sleep

- Less than 2 hours screen time
- Sitting breaks
- Not less than 6 hrs and not more than 8 hrs sleep
- Be early bird, not night owl
- Good quality sleep
- Maintain sleep hygiene

Pharmacotherapy

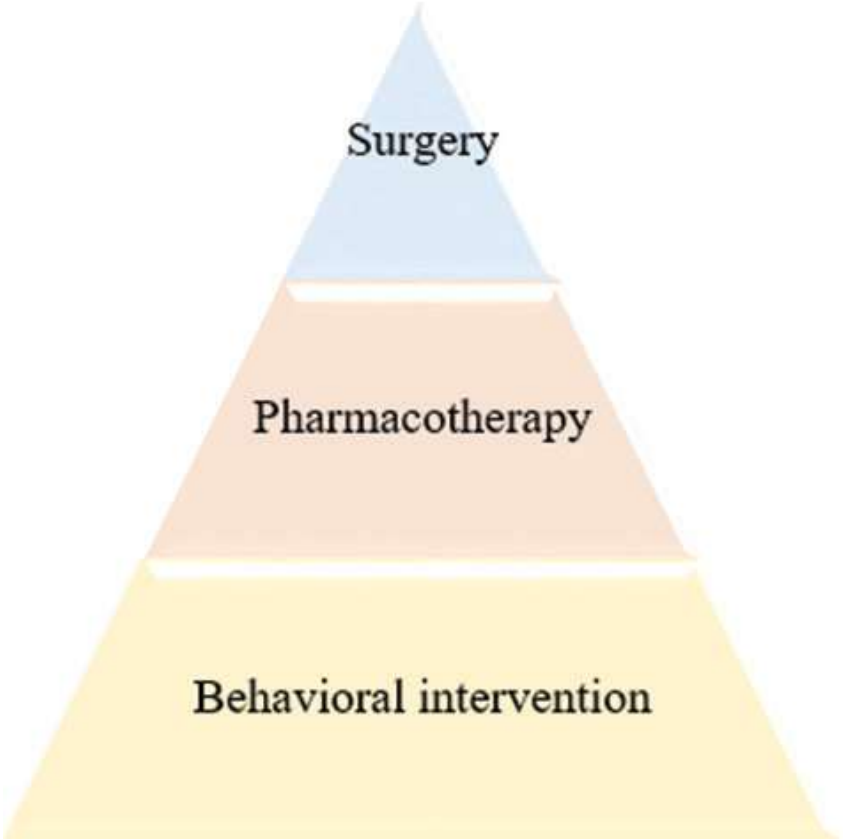
International obesity societies and guidelines recommend initiating pharmacotherapy in adults:

- with BMI ≥30 kg/m_2 without comorbidities, and
- with BMI ≥27 kg/m_2 with at least one weight-related condition (such as hypertension, dyslipidemia, type 2 DM, obstructive sleep apnea, or CVD) who have failed to achieve ≥5% weight loss after 6 months of lifestyle interventions
- However, anti-obesity medication can be started concurrently with lifestyle measures if a person has weight-related complications that can be reduced by weight loss

Pharmacotherapy

- A 2009 consensus statement proposed a BMI of >25 kg/m2 with comorbidity and >27 kg/m2 without comorbidity for initiation of pharmacotherapy in South Asian population
- This was based on an expert meet of over 100 specialists from all over India
- The ADA recommends commencing anti-obesity pharmacotherapy at a BMI cutoff of 25 kg/m2 in Asian Americans with type 2 diabetes mellitus

Pharmacotherapy (proposed by BES)



	Comorbidity	
	present	absent
BMI	≥ 27 kg/m^2	≥ 35 kg/m^2

	Comorbidity	
	present	absent
BMI	≥ 25 kg/m^2	≥ 27 kg/m^2

All

Pharmacotherapy

- Orlistat
- Liraglutide, Semaglutide (GLP-1 receptor agonists)
- Tirzepatide (glucose-dependent insulinotropic polypeptide receptor agonist and GLP-1 receptor agonist)

Orlistat

- Blocks lipase activity in gut
- Side effects: steatorrhea, gas discharge, bowel urgency, fecal incontinence
- May hamper fat soluble vitamin absorption
- The mean weight loss in patients by the end of 6 months of orlistat use is approximately 5.6 kg
- Can be given in children aged 12 years and older

GLP 1 receptor agonist

- Stimulates insulin release
- Suppress Glucagon secretion
- Delays gastric emptying
- Regulates appetite and promotes satiety
- Enhance Beta cell function

GLP 1 receptor agonist

- Promote the differentiation towards BAT and WAT browning, accelerating human metabolism and limiting weight gain
- Significantly reduce macrophage activity in adipose tissue and decrease the levels of inflammatory mediators IL-6, TNF-a and NF-kB together with JNK activation
- play crucial role in the regulation of hunger, satiety and feeding behavior to reduce energy intake, mediated by direct GLP-1 stimulation of the anorexigenic (satiety inducers) POMC and CART neurons along with indirect inhibition of orexigenic neurons (appetite inducers) neuropeptide Y and agouti-related peptide (AgRP)

Dosing schedule

- **Liraglutide**: once daily s/c injection, escalate every 4 weeks

  0.6 mg> 1.2 mg>1.8 mg> 3 mg
- **Semaglutide**: once weekly s/c injection, escalate every 4 weeks

  0.25 mg> 0.5 mg>1 mg>1.7 mg>2.4 mg
- Continue maximum tolerated dose
- If higher dose not tolerated, down titrate and maintain lower dose
- Missed dose: If more than 5 days have passed, the dose should be skipped, and dosing resumed on the scheduled day

GLP 1 receptor agonist

- 2.4 mg semaglutide provided substantial weight loss of 14.9% in a 68 week trial in 2539 obese patients without diabetes mellitus

- No dosage adjustment is necessary in mild to severe impairment renal impairment and dialysis for GLP-1 receptor agonists

- Contraindicated in pregnancy, lactation, allergy to GLP-1 receptor agonists, patients with history of pancreatitis, and in patients with a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia 2A or 2B

Adverse Effects

- GI effects: nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM
- Possible increased risk of thyroid cancer
- Pancreatitis, gallbladder disease, acute kidney injury, suicidal thoughts, and serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) are rarely reported
- Due to delayed gastric emptying, hold 7 days before surgery
- Monitor retinopathy

Tirzepetide

- Dual agonist: glucagon-like peptide-1 (GLP-1) and for glucose-dependent insulinotropic polypeptide (GIP)
- 15 mg tirzepatide showed 21% weight loss at 72 weeks
- Adverse effects and Contraindications: similar
- limited data on tirzepatide in patients with eGFR <30

Dose Schedule

- Once weekly s/c dose, escalate every 4 weeks
- 2.5 mg>5 mg>7.5 mg>10 mg>12.5 mg>15 mg

Monitoring

- Patients should monitor their weight weekly with a weight machine at home
- Follow-up should be every 3 months to monitor weight, other vital signs (heart rate and blood pressure), and address side effects
- Patients who are tolerating a therapeutic dose of medication and are losing weight can have less frequent follow-up
- At least 5%–10% weight loss is expected in the first 6 months

Benefits

- A weight loss of 5%–10% causes reduction of blood pressure, improvement of serum cholesterol, and HbA1c
- Weight loss of 10%–15% is required for diabetes remission and improvement in steatohepatitis, OSA, subfertility, osteoarthritis, and gastroeosophageal reflux
- In case of failure to respond to treatment (weight loss less than 5% after 12 weeks of maximum tolerated dose), reassess poor compliance and secondary cause

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Assessing The Efficacy of Semaglutide on Glycaemia Control and Weight Reduction among Patients with Type 2 Diabetes at the Outpatient Department of Teaching Hospital

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Result

- The data indicates a significant association between Semaglutide use and weight reduction, with the proportion of participants experiencing weight loss increasing from 16.1% to 83.9% (+67.8%, $p < 0.001$)

- The Pearson correlation coefficient ($r = 0.62$) suggests a moderate-to-strong positive correlation between glycemic control and weight reduction. Patients who experienced weight loss were more likely to have improved glycemic control


MILESTONE