REVIEW ARTICLE

Consensus on Current Landscape and Treatment Trends of Obesity in India for Primary Care Physicians

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Received: 21 April 2023; *Accepted:* 25 May 2023

Abstract

Objectives: The objective of this consensus article was to form a list of expert recommendations and an easily adaptable algorithm for obesity management in India by primary care physicians (PCPs).

Methods: A Delphi-based model was followed to form a list of the consensus recommendations. Consensus statements were created from the results of a literature review that were graded as per the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) criteria. After being evaluated by an expert panel comprising diabetologists, endocrinologists, cardiologists, bariatric surgeons, and gynecologists, the statements were revised and reevaluated by a larger group of practitioners, including PCPs and diabetologists, to arrive at a consensus.

Results: The panel opined that obesity is increasing in prevalence in India and is projected to rise in the coming years. Body mass index and waist circumference were both recommended for better identification of people at risk of obesity-related comorbidities than either of them alone. The Edmonton Obesity Staging System (EOSS) was suggested as being most suitable for the assessment (staging) of obesity. A multidisciplinary team was considered invaluable for assessing and managing patients with obesity. The use of once-a-week semaglutide (2.4 mg) *via* the subcutaneous route was suggested as the first-choice anti-obesity treatment when pharmacotherapy is deemed necessary. An algorithm considering all these aspects was proposed.

Conclusion: Obesity needs to be recognized as a significant contributor to other comorbidities. The diagnosis and management of obesity should be comprehensive and consider patient psychology, the presence or absence of comorbidities, available pharmacologic agents, and long-term outcomes. The proposed algorithm could help clinicians in this aspect and improve the overall outcomes.

Journal of the Association of Physicians of India (2023): 10.59556/japi.71.0349

Introduction

Globally, obesity is a major health issue associated with diseases like type 2 diabetes mellitus (T2DM), fatty liver disease, hypertension, myocardial infarction, stroke, dementia, osteoarthritis, obstructive sleep apnea, and several cancers.[1,2] The stigma and bias associated with obesity may also cause significant economic burdens due to unemployment, social disadvantages, and reduced socioeconomic productivity.[1] Notably, >650 million people live with obesity across the world.[3] It is predicted that by 2030, 20% of women and 14% of men will have obesity [body mass index (BMI) ≥30 kg/m^2]; this means that globally, over 1 billion people will have obesity.[4]

According to a systematic review, >135 million people live with obesity in India.[5] About 38.4% of men and 36.2% of women are living with obesity in India.[6] The economic impact of obesity in India (as per 2019 data) is estimated to be $23 billion [0.8% of gross domestic product (GDP)].[4] Notably, the Asian-Indian phenotype includes a greater fat mass (%), both total and abdominal (including visceral), with less lean mass (skeletal muscle and bone mineral) compared to other ethnic groups—commonly referred to as "thin–fat" Indians.[7,8] This ethnic predilection is one of the important reasons why noncommunicable diseases occur almost 10 years earlier in Asian Indians than in their Western counterparts.

Considering the overall burden of obesity and the recommendation from the World Health Organization, recognizing and managing obesity in India requires the active participation of primary care physicians (PCPs). It is imperative that PCPs are sensitized about the need for recognizing obesity, as a chronic disease, as most patients first visit PCPs for evaluation. India has been ranked 99th in global preparedness for addressing obesity and related issues.[4] We currently have two consensus statements for obesity in India—one from Misra et al. and the other from the Endocrine Society of India (ESI) (obesity guidelines in 2022).[9,10] The 2022 Research Society for the Study of Diabetes in India (RSSDI) clinical guidelines also include a separate section on obesity and T2DM, given the established relationship between the two.[11] Considering the presence of the thin–fat Indian phenotype, customized guidance on when and how to initiate different treatment modalities of obesity care is currently lacking. A simple treatment algorithm that can be easily adapted by PCPs is much needed in the current obesity treatment landscape of India.

Methodology

A Delphi-based model was followed to form a consensus with the following objectives: to evaluate the current burden and assessment process/modalities of obesity in India and identify the treatment gaps; to assess the emerging treatment options for obesity and their applicability in the Indian scenario; to agree upon effective treatment approaches and develop a feasible treatment algorithm for the management of obesity; and suggest a referral (to specialized obesity centers) for PCPs in India. A detailed literature review of related articles available on PubMed was conducted to evaluate the available data. Grading of the evidence was as per the

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How to cite this article: Deshpande NR, Kapoor N, Dalal JJ, *et al.* Consensus on Current Landscape and Treatment Trends of Obesity in India for Primary Care Physicians. J Assoc Physicians India 2023;71(10):69–77.

Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) criteria (see Appendix I for GRADE criteria).[12] An expert panel meeting involving diabetologists, endocrinologists, cardiologists, bariatric surgeons, and gynecologists was then held as the first round of the Delphi consensus to evaluate the statements. Minor modifications were carried out as per the expert evaluation, and the second round of the Delphi consensus meeting, involving a larger group of 20 practitioners, including PCPs and diabetologists, was held to assess the applicability of the statements in the Indian scenario. The consensus statements were finalized based on the agreement during the second meeting.

Results

Obesity Epidemiology and Related Complications

According to a recent nationwide cross-sectional study that evaluated data from 100,531 adults in a randomized cluster sample across India, obesity prevalence in the country is 40.3%, with a higher incidence among women, urban populations, and individuals aged >40 years. Further, the incidence was highest among South Indians (46.51%) and lowest among East Indians (32.96%).[13]

Based on the evaluation of the outcomes noted in the National Family Health Survey (NFHS) 3 and 4, it has been estimated that from 2010 to 2040, the obesity prevalence will triple, whereas the number of overweight people in India between the ages of 20 and 69 years would more than double.[14] Notably, physical inactivity and aging are significantly associated with obesity in India.[13] According to the findings reported in the NFHS-5, the percentage of adults with an increased waist-to-hip ratio (WHR) also increased with age in both women (from 46 to 65%) and men (from 28 to 60%) aged 15–19 and 40–49 years.[15]

The concept of the thin–fat Indian phenotype is well accepted. Notably, the percentage of body fat and abdominal adiposity among Asian Indians is higher at lower BMIs or similar BMIs when compared with Caucasians.[9] According to the Indian Council of Medical Research–India Diabetes (ICMR–INDIAB) phase I study, in India, both abdominal obesity [when waist circumference (WC) is ≥90 cm in men and ≥80 cm in women] and generalized obesity (BMI ≥25 kg/m^2) are highly prevalent. The prevalence rate of abdominal obesity was 16.9–36.3%, and that of generalized obesity was 11.8–31.3%.[16] The prevalence of normal weight obesity (excess body fat among individuals with normal BMI) in the Indian population has been estimated to be about 32% [95% confidence interval (CI): 29.1–34.5].[17]

Furthermore, as compared to Caucasians, Asian Indians have a higher risk of developing resistance to insulin and cardiovascular problems at lower BMI levels.[9] Higher BMI levels are associated with higher risks of developing asthma, chronic obstructive pulmonary disease, circulatory system diseases, digestive system diseases, multiple sclerosis, musculoskeletal system diseases, T2DM, and malignancies in the digestive system, uterus, kidney, and bladder.[18]

Consensus Statements

- The prevalence of obesity is increasing in India and is projected to rise in the coming years (grade of recommendation: A; level of evidence: 1a).
- Abdominal obesity is very prevalent in Asian Indians and is an important causative reason for the rapid increase in noncommunicable diseases and their outcomes (grade of recommendation: B; level of evidence: 2a).
- Obesity leads to cardiometabolic, mechanical, psychological, and behavioral complications, which need to be identified and managed for a better prognosis (grade of recommendation: A; level of evidence: 1a).

The presence or absence of the following complications should be assessed during obesity evaluation (grade of recommendation: A; level of evidence: 1a):

- Metabolic conditions [prediabetes, metabolic syndrome, T2DM, hypertension, dyslipidemia, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH)]
- Cardiovascular disease risk
- Gynecologic complications [polycystic ovary syndrome (PCOS), infertility]
- Osteoarthritis
- Stress incontinence
- Gastroesophageal reflux disease (GERD)
- Obstructive sleep apnea
- Disability/immobility
- Psychological disorder or stigmatization
- Cancer

Clinical Assessment and Diagnosis of Obesity

One of the critical aspects in diagnosing and managing obesity is addressing the weight bias among practicing clinicians and support staff. Studies have reported that weight bias among medical doctors is as pervasive as in the general population. PCPs, cardiologists, endocrinologists, nurses, and dieticians often feel that individuals with obesity are themselves to be blamed for noncompliance with treatment, lack of willpower, or laziness. Such bias can negatively impact obesity management.[19] Hence, it is important to set up a clinical unit that is accommodating and trained to manage patients with obesity without any bias.

Body mass index (BMI) assessment is one of the most common measures of obesity. However, BMI does not exactly measure/correlate with the total content of body fat; this is because the total content of body fat in two individuals having the same BMI could differ by a factor of two. Assessments of the usefulness of BMI in detecting body adiposity indicate that although BMI cutoff values have high specificity, they lack sensitivity in identifying adiposity (percentage body fat). Also, BMI evaluation is insufficient for identifying individuals with excess body fat percentage in 50% of the cases.[20]

Importantly, BMI assessment alone does not adequately predict associated comorbidities or disease risk, and changes in BMI do not adequately indicate improvements in overall wellness.[21]

According to the consensus guidelines by Misra et al., BMI and WC must be given equal weightage when stratifying population-based clinical, metabolic, and cardiovascular risks.[9] Further, the American Association of Clinical Endocrinologists and the American College of Endocrinology (AACE/ACE) guidelines mention that population and ethnicity-specific threshold values should be considered while making these assessments.[22]

The consensus statement by Misra et al. has proposed the cutoff values for categorizing people based on BMI and WC as mentioned in Table 1.[9]

Other anthropometric parameters, such as waist-to-height ratio (WHtR), neck circumference (NC), and metabolic score for visceral fat (METS-VF), have also been evaluated in Indian settings.[23] According to a recent study by Kapoor et al., WHtR and WHR were higher in those with T2DM than

Table 1: Proposed cutoffs for categorizing people as per BMI and WC values[9]

Category	*Indian guideline (BMI cutoff)*
Normal	18–22.9 kg/m^2
Overweight	23–24.9 kg/m^2
Obesity	>25 kg/m^2
WC-based	
Need lifestyle measures	Men: >78–90 cm; women: >72–80 cm
Need medical attention	Men: >90 cm; women: >80 cm

BMI, body mass index; WC, waist circumference

in those without T2DM, and these measures can be useful for identifying those at risk of developing T2DM.[17] It was found that WC and WHtR were the most reliable factors for predicting metabolic disorders and hypertension, whereas NC values of ≥37 cm in men and ≥34 cm in women were useful predictors of metabolic syndrome. A value of 7.3 in the METS-VF score was sensitive and specific enough to identify those with higher visceral adipose tissue levels.[10] However, these parameters need to be explored further, and these measures are also considered time-consuming; hence, they may not be practical in busy clinical settings. Nevertheless, as the METS-VF test is easily available, reliable, and inexpensive, it may be widely used in lower and middle-income countries in the future.

An approach centered on the management of complications will enable the use of aggressive, targeted, and individualized approaches in patients with complications related to obesity who are more likely to benefit from treatment. This will optimize resource utilization, cost-effectiveness, outcomes for patients, and interventional benefit/risk ratios.[22]

Consensus Statements

- The BMI-centric approach to the diagnosis and management of obesity has limitations (grade of recommendation: B; level of evidence: 2a).
- The combined use of BMI and WC is recommended for better identification of people at risk of obesity-related comorbidities than either of them alone (grade of recommendation: B; level of evidence: 2a).
- Ethnic-based cutoff points for BMI and WC should be used for optimally defining obesity (grade of recommendation: B; level of evidence: 2a).
- Complication-centric obesity management can help individualize management, optimize patient outcomes, and improve the benefit/risk ratio and cost-effectiveness of interventions (grade of recommendation: B; level of evidence: 2a).

Complication-centric Staging

Traditionally, the obesity grade was defined by WC and BMI values. Recent evidence suggests that BMI and/or WC are suboptimal in defining the true health impact of obesity in an individual and that metabolic, functional, and mental comorbidities (staging) when applied to the BMI/WC, can help to define the overall health impact of obesity in a better way.

The Edmonton Obesity Staging System (EOSS) is frequently used (Fig. 1) to optimally categorize an individual's associated health risk of obesity and is also very helpful in defining treatment aggression. The EOSS acknowledges all three (metabolic, functional, and mental) aspects of obesity, thereby helping in creating a well-rounded diagnostic and management system for obesity.[21,24] The EOSS provides options for recording and tracking the progress of risk factors and their severity. This also simplifies the adoption of adequate, timely, and correct therapy changes over time for achieving the desired health outcomes. This system, together with current anthropometric classification systems, forms a simple tool for making decisions in regular clinical practice.[21]

A similar staging framework has also been introduced by the AACE/ACE. This was based on the belief that obesity is caused by multifaceted interactions between biological, environmental, and behavioral factors.[22] However, the staging system suggested by the AACE/ACE is an elaborate staging mechanism, and Indian PCPs may not have adequate time to evaluate all the aspects of their patients' data required by this system. The EOSS is an easier option that uses BMI as a base to identify individuals with obesity and then classify them on the basis of absence/presence of comorbidities. Notably, the BMI values need to be individualized for the Indian population (thin–fat phenotype) as described in the consensus statement by Misra et al.

Consensus Statements

- The EOSS is most suitable for the assessment (staging) of obesity and is very helpful in treatment planning in primary care settings (grade of recommendation: B; level of evidence: 2a).

Multidisciplinary Approach and Setting Realistic Goals in Obesity Management

A multidisciplinary team involving different specialties is vital for ensuring that diagnosing and managing obesity and its associated complications are based on reliable evidence. This team should be customized as per the availability of specialists and the hospital setting (urban or rural). Underlying comorbidities and medication history must be evaluated and noted to record their influence on obesity and should be appropriately managed first. This should be followed by further evaluation of other risk factors and obesity therapy planning.

The involvement of a multidisciplinary team is a must to ensure holistic support to patients in terms of nutrition, fitness, pharmacotherapy, psychological, and surgical aspects. Additionally, each specialty can ensure the implementation of an evidence-based treatment plan to help patients with obesity achieve desired treatment goals *via* personalized and effective approaches.[25] Shared decision-making, which involves initial assessment by an appropriate team followed by periodic assessment by the multidisciplinary team, along with appropriate customization and modifications in the treatment approach, is essential for optimal and sustained outcomes.

Setting realistic goals is the key to successful obesity management. Very importantly, it improves patient adherence to

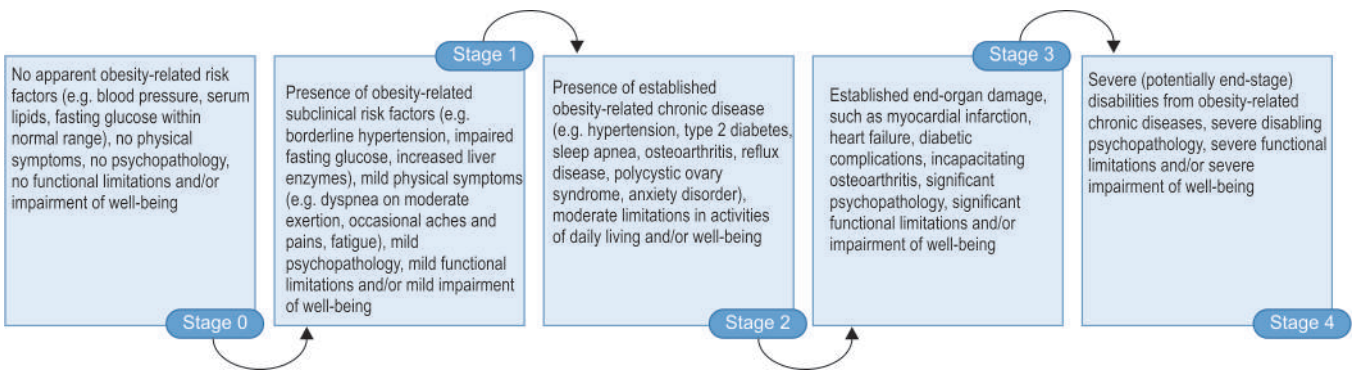


Fig. 1: Edmonton Obesity Staging System (EOSS)[20]

the planned treatment approach. In general, the treatment goals should be realistic and sustainable. The aspects that drive weight gain (such as stress, depression, lack of time, and underlying comorbidities) should always be assessed and addressed appropriately. The treatment success should be evaluated in terms of improvement in all parameters, including metabolic, mental, and functional health.[26]

Realistic goals for metabolic, functional, and mental parameters should follow the Specific–Measurable–Achievable–Rewarding–Timely (SMART) principles. Self-monitoring with a lifestyle (nutrition, fitness, and behavior) journal helps initiate and sustain achieved goals.[26] Successful weight loss achieved has a linear relationship with health outcomes (metabolic, functional, and mental). Greater weight loss is associated with better outcomes; for example, a weight loss of >15% has the potential to remit T2DM, heart failure with preserved ejection fraction (HFpEF), and possibly impact mortality.

Notably, a 2–5% loss in weight led to significant reductions in systolic blood pressure (BP) and serum levels of glucose, glycated hemoglobin (HbA1c), and triglycerides.[27] Furthermore, 5–10% weight loss in individuals with obesity/who are overweight with associated comorbidities can significantly reduce the development of T2DM and improve health outcomes in individuals with dyslipidemia, hyperglycemia, osteoarthritis, stress incontinence, GERD, hypertension, and PCOS.[28] According to the Look AHEAD study (N = 5,145), weight loss in 1 year was highly significantly ($p < 0.0001$) related to lower serum glucose levels, BP, serum triglyceride levels, and serum high-density lipoprotein cholesterol levels.[27]

Consensus Statements

A multidisciplinary team should be involved in the assessment and management of patients with obesity (grade of recommendation: B; level of evidence: 2b).

The following members should be a part of the multidisciplinary team for addressing comorbidities in patients with obesity (grade of recommendation: B; level of evidence: 2b).

- Core team: Physician, dietician, physiotherapist, psychologist, bariatric surgeon, endocrinologist, and gynecologist.
- Others (on call as per comorbidity): Cardiologist, chest physician, orthopedist, gastroenterologist, and psychiatrist.

In individuals with obesity/who are overweight, weight loss is important to prevent or improve control of obesity-related comorbidities (grade of recommendation: A; level of evidence: 1a).

Setting realistic goals is important for the simpler and more effective management of obesity and related complications (grade of recommendation: B; level of evidence: 2b).

The weight loss target should be individualized based on the type of comorbidity (grade of recommendation: B; level of evidence: 2a).

Lifestyle Interventions

The diagnosis of obesity, abdominal obesity, and metabolic syndrome in Asian Indians requires that dietary intake should be planned as follows[9]:

- Carbohydrate intake must be 50–60% of the total energy per day, with a preference for complex carbohydrates and low glycemic index foods.
- Fiber intake must be 25–40 g per day.
- Saturated fats must be <10% of the total energy per day.
- The ratio of essential fatty acids per day must be 1–2% of total energy and must include linolenic acid (LA), 5–8%, and alpha-linolenic acid (ALA), at an optimal ratio of LA/ALA, 5–10%; the cis-monounsaturated fatty acids must make up 10–15%; and trans fatty acids <1% of the total energy.
- Protein consumption must be 10–15% of the total energy per day.
- Salt intake must be 5 gm per day.
- Sugar intake must be <10% of the total energy per day.

Medical nutrition therapy (MNT) is a widely discussed option in the West. It mainly involves nutritional assessment, counseling, advice, and follow-up by a qualified or trained PCP. However, some challenges hinder the initiation of MNT in the Indian population. Some of the key challenges include the nonavailability of insurance coverage, lack of awareness among physicians, inability to individualize MNT, and lack of nutritionists trained in MNT. The MNT is often preferred/opted for by individuals with a busy lifestyle (who find it difficult to plan their regular diet) and those who can afford it.[10] A detailed approach for individualizing MNT among South Asians has been published in the Consensus on Medical Nutrition Therapy for Diabesity by Kapoor et al.[29]

Lifestyle intervention that mainly involves dietary modifications remains important for the successful management of obesity in India. Exercise is vital, along with dietary modifications, to achieve the weight loss targets and control metabolic comorbidities. The intensity and type of activity are to be individualized based on the comorbidities and physical activity levels of patients.

Unlike other care programs, promoting both diet and physical activity lowered T2DM incidence (risk ratio: 0.59), body weight [net change: 2.2% (CI, 2.9–1.4%)], and fasting blood glucose levels (net change: 2.2 mg/dL), and other cardiometabolic risks.[30] A study that analyzed 32 randomized controlled trials (RCTs) demonstrated that an average exercise session of 45 minutes per day and mean exercise frequency of 3.25 days/week significantly decreased HbA1c levels ($p < 0.0001$), fasting blood glucose levels ($p < 0.03$), BMI ($p < 0.04$), and WC ($p < 0.007$) in the exercise group when compared with the group that did not exercise.[31]

Weekly targets for exercise can be set to 75–150 minutes of vigorous exercise or 150–300 minutes of moderate exercise.[10,32] Resistance training is useful as it preserves lean body mass during weight loss regimes and not only helps with fat loss but also improves metabolic and physical function.[33] Combining resistance training with aerobic exercise and restricting calories significantly reduced regional adiposity and body weight in individuals with obesity and overweight, as per a large meta-analysis of 114 trials by Lopez et al which included 4184 participants ($p < 0.001$).[34]

Consensus Statements

- The dietary targets set in the consensus statement by Misra et al.[9] can be followed for obesity management in India (grade of recommendation: B; level of evidence: 2a).
- Physical activity reduces the risk of developing obesity-associated comorbidities and should hence be advocated along with dietary modifications (grade of recommendation: A; level of evidence: 1a).
- Physical activity target for moderate-to-vigorous exercise should be as follows (grade of recommendation: D; level of evidence: 5):
  - About 150–300 minutes of moderate physical activity per week.
  - About 75–150 minutes of vigorous physical activity per week.
- Resistance training is an important aspect of lifestyle interventions for weight management in Asian Indians (grade of recommendation: B; level of evidence: 2a).

Pharmacotherapy

A detailed assessment of the steps taken by patients or PCPs to address obesity is essential before initiating pharmacotherapy for obesity. It must be ensured that patients put in adequate efforts in terms of lifestyle

measures and physical activity. Additionally, the effects of medications being taken by patients with comorbidities need to be assessed. Medications such as antidiabetics, antihypertensives, antipsychotics, antihistamines, and antidepressants are known to cause weight gain. Weight neutrality or the weight loss potential of a drug should be considered when choosing any pharmacotherapy for a patient with obesity. For example, glucagon-like peptide-1 receptor agonists (GLP-1RAs), such as liraglutide, semaglutide or dulaglutide, and sodium–glucose cotransporter-2 inhibitors (SGLT2i), such as dapagliflozin, canagliflozin, or empagliflozin, among patients with T2DM, help in maintaining glycemic control while also promoting a safe and effective loss of weight along with pleiotropic benefits, including end-organ protection.[24]

Among other patients who have been advised only lifestyle interventions (nutrition, fitness, and behavior therapy), there may be a saturation point or set point where further weight loss will not happen. Individuals thereon may start gaining weight again despite these measures, as neurohormonal mechanisms, including reduced resting metabolic rate or increased appetite, are triggered, driving a significant weight gain. Hence, continued management of obesity is important for sustained weight loss, retention of the weight loss, and long-term health benefits. Long-term strategies (such as pharmacotherapy) can positively impact the counter-regulatory mechanism and hence prevent obesity relapse.[35] Pharmacotherapy is also considered essential for bridging the gaps in managing obesity.[36]

According to the consensus statement by Misra et al., pharmacotherapy is advisable for people with BMI ≥27 kg/m^2 and no comorbidities or people with BMI ≥25 kg/m^2 with comorbidities.[9] For initiating pharmacotherapy, WC cutoff values of 80 cm for Asian Indian women and 90 cm for Asian Indian men were unanimously agreed upon. An individualized approach to pharmacotherapy is required; this must include considerations of comorbidities, preferences, insurance coverage, and costs. In addition, combination therapy is less preferable than single weight-loss drugs.[37] Multiple agents may be considered in patients with difficulty in reducing weight. Currently, the approved medications for managing obesity in India include orlistat 120 mg (oral)[38] and semaglutide 2.4 mg[39] (subcutaneous injection). Other medications and their characteristics have been enumerated in Table 2.

Orlistat

Orlistat exerts its action by inhibiting lipases. It bonds covalently with an active site serine residue in gastric lipases and pancreatic lipases and irreversibly inactivates them. It also inhibits triglyceride hydrolysis partially and reduces monoacylglycerides and free fatty acid absorption.[40,41] The XENical in the prevention of Diabetes in Obese Subjects (XENDOS) study was one of the largest RCTs that evaluated the efficacy of orlistat in 3,305 individuals with obesity. The use of orlistat led to a 2.4% net weight loss after 4 years. Notably, this lowered the risk of T2DM development in the group taking orlistat than the placebo group (9 vs 6%, respectively).[42,43] According to a study in India, orlistat was associated with a significant ($p < 0.05$) weight reduction (4.65 kg) compared to a placebo (2.5 kg; Fig. 2) and reductions in WC, BMI, and cholesterol levels.[44]

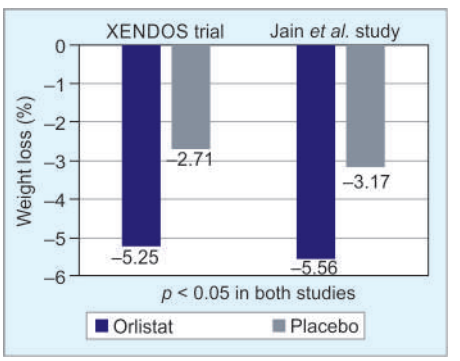


Fig. 2: Weight loss noted with orlistat or placebo[43,44]

Table 2: Medications for managing obesity

	Orlistat 120 mg	*Naltrexone/ bupropion*	*Phentermine/topiramate 3.75/23 mg and 15/92 mg*	*Liraglutide 3.0 mg*	*Semaglutide 2.4 mg*
MoA	Energy wastage	Appetite suppressant	Appetite suppressant	Appetite suppressant	Appetite suppressant Reduced energy intake
Weight loss (1 year, US label)	3.89% Placebo: 1.27%	5.4/8.1%* Placebo: 1.3/4.9%*	5.1/10.9%† Placebo: 1.6%	7.4% Placebo: 3.0%	16.9% Placebo: 2.4%
Effect on cardiovascular morbidity/mortality	Cardiovascular risk factors lowered: BP and serum lipid levels	Not established	Not established	Liraglutide 1.8 mg CVOT LEADER safety data have been added to the label	SUSTAIN 6 and PIONEER 6 safety data have established cardiovascular safety
Dosing	Three times daily, oral	Two times daily, oral	Once daily, oral	Once daily, subcutaneous injection	Once weekly, subcutaneous injection
Most common AEs (>5%)	Oily spotting, flatus with discharge, fecal urgency, fatty/ oily stool, oily evacuation, increased defecation, and fecal incontinence	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea	Paresthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth	Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, dyspepsia, fatigue, dizziness, and abdominal pain	Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, and abdominal distension
Approval in India	Approved	Not approved	Not approved	Not approved	Approved (not yet available in the Indian market)

*Data from the phase III CONTRAVE obesity research I and II studies, respectively; †Data are for 3.75/23 mg and 15/92 mg doses of phentermine/topiramate, respectively; AEs, adverse events; CVOT, cardiovascular outcome trial; MoA, mechanism of action

The safety assessment of orlistat based on seven multicenter, placebo-controlled, double-blind clinical trials with 1,913 individuals treated with orlistat and 1,466 individuals receiving placebo revealed that 8.8% of patients given orlistat and 5.0% of patients given the placebo discontinued treatment due to adverse events. The most common adverse reactions included oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation, and fecal incontinence.[45]

Semaglutide

A long-acting GLP-1 analog, semaglutide is a native GLP-1 mimic and reduces energy intake, thereby causing loss of weight; it also reduces gastric emptying, increases satiety, reduces hunger, and improves glycemic control.[45,46] Alongside weight loss and blood glucose effectiveness, GLP1-RAs also protect vital organs (heart, liver, kidney, and brain).

In a double-blind trial involving 1,961 adults with obesity, treatment with once-weekly 2.4 mg semaglutide therapy with changes in their lifestyles led to a reduction of 14.9% of their weight at week 68 along with greater improvements in cardiovascular risk compared to treatment with a placebo. The most common adverse events included diarrhea and nausea.[47]

As per the semaglutide treatment effect in people with obesity (STEP) program, a series of five phase III clinical trials measuring the efficacy of subcutaneously administering 2.4 mg of semaglutide once a week for managing weight in people with obesity and with/without T2DM, semaglutide treatment was associated with substantial weight loss across all trials.[48] The comparative mean loss in weight noted in the STEP 1–5 trials has been enumerated in Figure 3.[49–54] However, semaglutide use was associated with gastrointestinal adverse events.

Although injectable semaglutide (2.4 mg) is approved for use in India by the Central Drugs Standard Control Organization for obesity management, it is not yet available in the Indian market.[39]

Consensus Statements

Pharmacotherapy is a vital cog in obesity care for weight loss, long-term weight maintenance, prevention of weight regain, and protection of end organs (grade of recommendation: A; level of evidence: 1b).

Based on the safety, durability, and effectiveness, once-weekly subcutaneous semaglutide 2.4 mg could be the first-choice anti-obesity medication (expert recommendation).

A pharmacotherapeutic approach should be initiated in the following population of Asian Indians (grade of recommendation: D; level of evidence: 5):

- BMI ≥27 kg/m^2 with or without comorbidity.
- Body mass index (BMI) ≥25 kg/m^2 with at least one associated comorbid medical condition, such as hypertension, dyslipidemia, T2DM, and obstructive sleep apnea.

Bariatric surgery

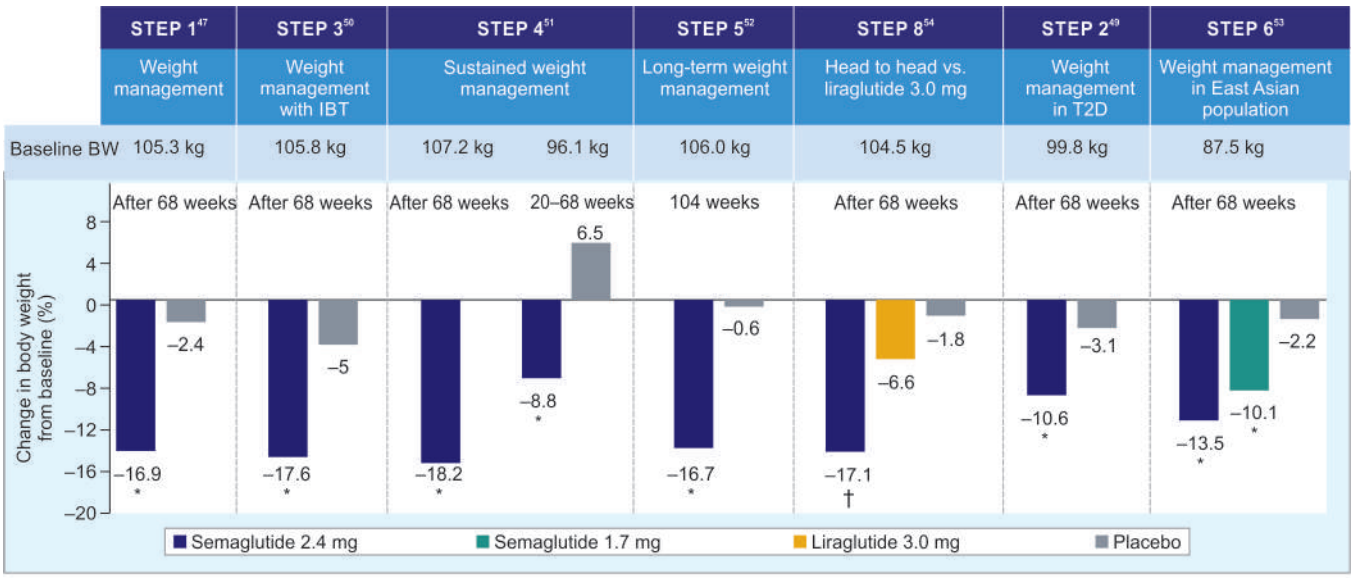
According to the Obesity and Metabolic Surgery Society of India (OSSI) 2020 guidelines, the following population groups are eligible for bariatric surgery[55]:

- BMI ≥35 kg/m^2, with/without any comorbidities related to obesity
- BMI ≥32.5 kg/m^2 with >1 comorbidity related to obesity (OSSI 2013 guidelines)[56]
- BMI ≥30 kg/m^2, with >2 comorbidities related to obesity
- BMI ≥27.5 kg/m^2, having uncontrolled T2DM despite treatment
- Women with WC of ≥80 cm and men with WC of ≥90 cm having comorbidities related to obesity.

Currently, all bariatric and metabolic surgeries rely on procedures that are restrictive, malabsorptive, or a combination of the two and include one-anastomosis gastric bypass (OAGB), Roux-en-Y gastric bypass, and sleeve gastrectomy (SG).[52] Recently, in India, OAGB surgery is the second most popular procedure after SG due to significantly high weight loss and satisfaction rates, low rates of complications, and a low reversal rate of only 0.2%.[55]

Newer Approaches

New medications, such as tirzepatide, which is a dual gastric inhibitory polypeptide and GLP-1RA, and CagriSema, a combination of cagrilintide (amylin analog) with semaglutide (GLP-1RA), are currently under development.[57] Looking at the promising pipeline of anti-obesity medications, we can expect a change in the treatment landscape for obesity. Patients who are now candidates for bariatric surgery may be managed with newer anti-obesity medications in the future.



*Statistically significant vs. placebo. †Statistically significant vs. liraglutide 3.0 mg
BW: Body weight; IBT: Intensive behavioral therapy, T2D: Type 2 diabetes.

Fig. 3: Weight loss across STEP trials with Semaglutide (Trial product estimand)[47,49–54]

Proposed Obesity Management Algorithm

In India, the following approach has been suggested for diagnosing and managing obesity. A summary of the same has been provided in Figure 4.

Step 1: Anthropometric evaluation

- During the initial visit, anthropometric values including height, weight, BMI, WC, hip circumference, WHtR, and WHR are to be measured.

Step 2: Clinical evaluation (including laboratory tests) for comorbidities and impacts

- Evaluate complications and consequences (including comorbidities and physiological and psychological impacts).

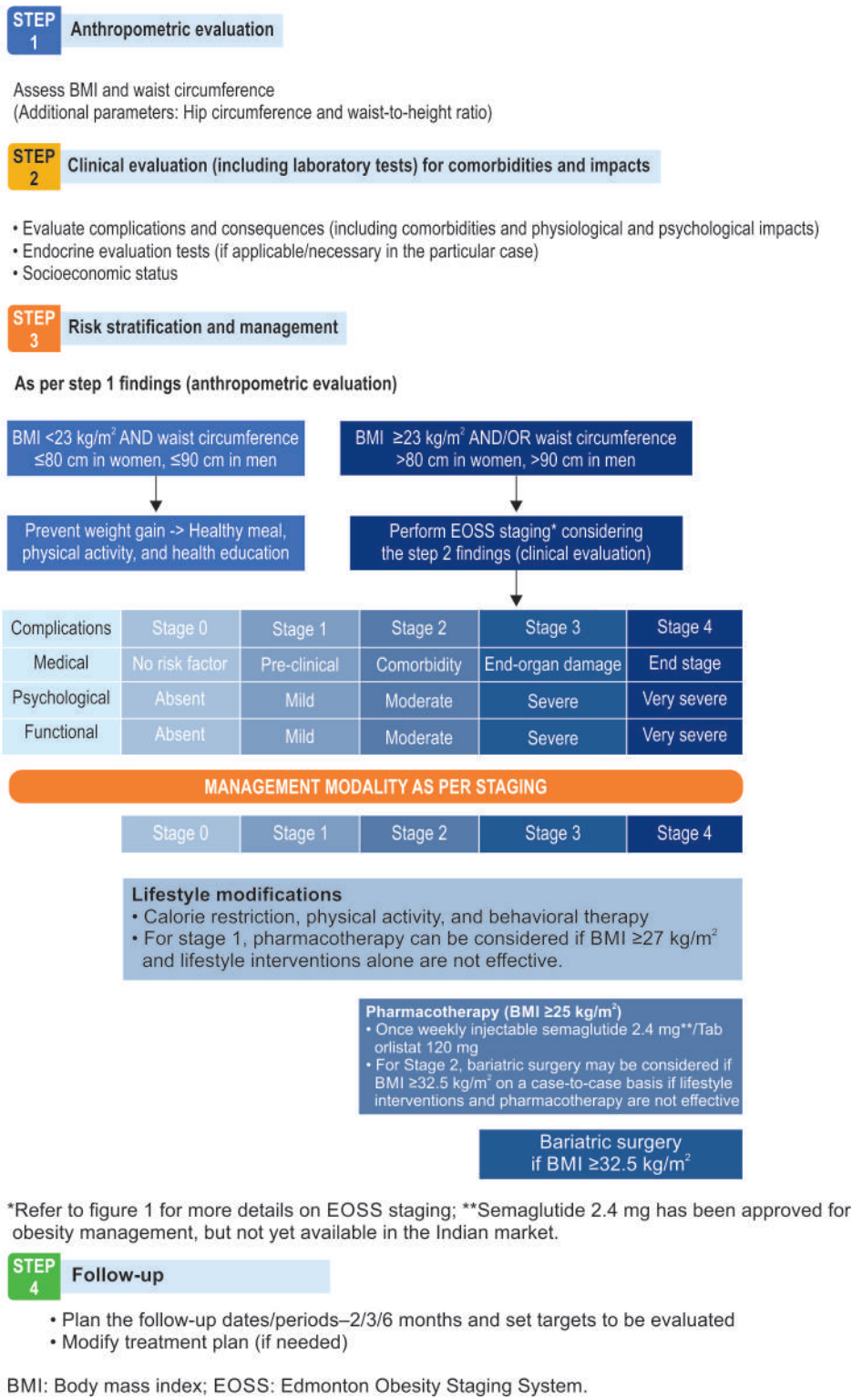


Fig. 4: Proposed diagnosis and management algorithm for obesity

- Endocrine evaluation tests (if applicable/necessary in the particular case).
- Socioeconomic status.

Step 3: Risk stratification and management
All patients must be first broadly categorized based on step 1 findings (anthropometric evaluation) as "normal weight" OR "overweight/obesity." The normal-weight patients can be managed with preventive care while the patients who are classified under overweight/obesity (as per Asian BMI and WC cut-offs) need to be further subclassified using the EOSS to evaluate the clinical stage based on the findings in step 2 of the algorithm. The management of the patients can be individualized accordingly. Lifestyle modification will apply to patients in all stages, while pharmacotherapy needs to be initiated in patients categorized as stage 1 and with BMI ≥27 kg/m^2, if lifestyle interventions alone are not effective in achieving the target weight.[9,38,39,44] Pharmacotherapy will be required in all patients categorized as stage 2 and above (BMI ≥25 and with one or more comorbidities). Bariatric surgery may be considered if BMI ≥32.5 kg/m^2, on a case-to–case basis depending on the clinical scenario in patients categorized as stage 2, and in all patients categorized to be in stages 3 and 4.

The management options should be finalized based on the SMART principle along with short-term and long-term goals for each patient. Pharmacotherapy may need to be continued as part of long-term goals for sustained weight management or prevention of weight gain.

Step 4: Follow-up
The follow-up dates/periods (2/3/6 months) need to be individualized based on the stage and the type of treatment approach planned. The treatment plan may be continued or modified based on the outcomes noted during the follow-up. In general, long-term follow-up is needed in all patients.

Conclusion

Obesity management in India needs to be stepped up with the need to recognize obesity as a significant contributor to other comorbidities. The treatment for obesity needs to be individualized, considering factors such as patient psychology, presence/absence of comorbidities, available pharmacologic agents, and long-term outcomes. The use of appropriate staging criteria, such as the EOSS, after adapting it to the Indian population, can help optimize the treatment strategy and improve treatment outcomes.

Acknowledgments

We extend our heartfelt appreciation to Dr Ashok Kumar Das, Dr Mithun Bhartia, Dr Tejas Shah, Dr Supriyaa Bhakthavatchalam, Dr Arjun BS, Dr Pranjali Shah, Dr Abhijith Jawanjal, Dr Sagar Sourav, Dr Amit Basu, Dr Hrishikesh Bora, Dr Sharad Bedi, Dr Sudharsan Narayanamoorthy, Dr Ranjit Mohan, Dr Anusha, Dr Sharath Hegde, Dr Vishnupriya Reddy, Dr Sagar Sourabh, Dr Karthik, Dr Abdul Raqeeb, Dr Srinath K Bhat, Dr Malay Parekh, Dr Kiran Deep Kamal, Dr S Pawan Kumar Sharma, Dr Amit Bhatnagar, Dr Meghana Reddy, and Dr Saran M S for their valuable contributions and unwavering support throughout this endeavor. We would also like to thank BioQuest Solutions for the editorial assistance.

Author Contributions

All authors have contributed equally to the conception, design drafting, review, and finalization of the manuscript.

Funding

The manuscript has been supported by NovoNordisk under independent publication support to Dr Neeta Deshpande.

Appendix

Appendix 1: Grade criteria

Grade of recommendation	*Level of evidence*	*Type of study*
A	1a	Systematic review of (homogeneous) randomized controlled trials
A	1b	Individual randomized controlled trials (with narrow confidence intervals)
B	2a	Systematic review of (homogeneous) cohort studies of "exposed" and "unexposed" subjects
B	2b	Individual cohort study/low-quality randomized control studies
B	3a	Systematic review of (homogeneous) case-control studies
B	3b	Individuals case-control studies
C	4	Case series, low-quality cohort or case-control studies
C	5	Expert opinions based on non-systematic reviews of results or mechanistic studies

Source: Schünemann H, Brożek J, Guyatt G, Oxman A. (eds). Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Available at: https://gdt.gradepro.org/app/handbook/handbook.html Updated: October 2013. Accessed: 02 Feb 2023

References

1. Blüher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol 2019;15(5):288–298.
2. Ramasamy S, Joseph M, Jiwanmall SA, et al. Obesity indicators and health-related quality of life - insights from a cohort of morbidly obese, middle-aged South Indian women. Eur Endocrinol 2020;16(2):148–151.
3. World Health Organization. Obesity and overweight. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed February 2, 2023
4. World Obesity Federation. World Obesity Atlas 2022. Available at: https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2022. Accessed February 2, 2023
5. Ahirwar R, Mondal PR. Prevalence of obesity in India: a systematic review. Diabetes Metab Syndr 2019;13(1):318–321.
6. Verma M, Das M, Sharma P, et al. Epidemiology of overweight and obesity in Indian adults - a secondary data analysis of the National Family Health Surveys. Diabetes Metab Syndr 2021;15(4):102166.
7. Deepa R, Sandeep S, Mohan V. Abdominal obesity, visceral fat, and type 2 diabetes-"Asian Indian Phenotype." In: Mohan V, Gundu Rao, eds. Type 2 diabetes in South Asians; Epidemiology, Risk factors and Prevention. New Delhi: Jaypee Medical Publishers; 2006. pp. 138-152.
8. Kapoor N, Furler J, Paul TV, et al. Normal weight obesity: an underrecognized problem in individuals of South Asian descent. Clin Ther 2019;41(8):1638–1642.
9. Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India 2009;57:163–170.
10. S V M, Nitin K, Sambit D, et al. ESI Clinical Practice Guidelines for the evaluation and management of obesity in India. Indian J Endocrinol Metab 2022;26(4):295–318.
11. RSSDI clinical practice recommendations for the management of type 2 diabetes mellitus 2022. Int J Diabetes Dev Ctries 2022;42(Suppl 1):S1–S143.
12. Schünemann H, Brożek J, Guyatt G, Oxman A (eds). Handbook for grading the quality of evidence and

the strength of recommendations using the GRADE approach. [Internet] 2013. Available at: https://gdt.gradepro.org/app/handbook/handbook.html. Accessed February 2, 2023.
13. Venkatrao M, Nagarathna R, Majumdar V, et al. Prevalence of obesity in India and its neurological implications: a multifactor analysis of a nationwide cross-sectional study. Ann Neurosci 2020;27(3-4):153–161.
14. Luhar S, Timæus IM, Jones R, et al. Forecasting the prevalence of overweight and obesity in India to 2040. PLoS One 2020;15(2):e0229438.
15. National Family Health Survey-5: Ministry of Health & Family Welfare, India. International Institute of Population Sciences; 2019-21.
16. Pradeepa R, Anjana RM, Joshi SR, et al. Prevalence of generalized & abdominal obesity in urban & rural India–the ICMR-INDIAB Study (Phase-I) [ICMR- NDIAB-3]. Indian J Med Res 2015;142(2):139–150.
17. Kapoor N, Lotfaliany M, Sathish T, et al. Prevalence of normal weight obesity and its associated cardio-metabolic risk factors - Results from the baseline data of the Kerala Diabetes Prevention Program (KDPP). PLoS One 2020;15(8):e0237974.
18. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med 2021;19(1):320.
19. Puhl RM, Phelan SM, Nadglowski J, et al. Overcoming weight bias in the management of patients with diabetes and obesity. Clin Diabetes 2016;34(1):44–50.
20. Okorodudu DO, Jumean MF, Montori VM, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: A systematic review and meta-analysis. Int J Obes (Lond) 2010;34(5):791–799.
21. Sharma AM, Kushner RF. A proposed clinical staging system for obesity. Int J Obes (Lond) 2009;33(3):289–295.
22. Garvey WT, Garber AJ, Mechanick JI, et al. American Association of Clinical Endocrinologists and American College of Endocrinology position statement on the 2014 advanced framework for a new diagnosis of obesity as a chronic disease. Endocr Pract 2014;20(9):977–989.
23. Kapoor N, Jiwanmall SA, Nandyal MB, et al. Metabolic Score for Visceral Fat (METS-VF) estimation - a novel cost-effective obesity indicator for visceral adipose tissue estimation. Diabetes Metab Syndr Obes 2020;13:3261–3267.
24. Kalra S, Kapoor N, Bhattacharya S, et al. Barocrinology: The endocrinology of obesity from bench to bedside. Med Sci (Basel) 2020;8(4):51.
25. Foster D, Sanchez-Collins S, Cheskin LJ. Multidisciplinary team-based obesity treatment in patients with diabetes: Current practices and the state of the science. Diabetes Spectr 2017;30(4):244–249.
26. Wharton S, Lau DCW, Vallis M, et al. Obesity in adults: a clinical practice guideline. CMAJ 2020;192(31):E875–E891.
27. Wing RR, Lang W, Wadden TA, et al. Look AHEAD research group. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. Diabetes Care 2011;34(7):1481–1486.
28. Cefalu WT, Bray GA, Home PD, et al. Advances in the science, treatment, and prevention of the disease of obesity: reflections from a Diabetes Care Editors' Expert Forum. Diabetes Care 2015;38(8):1567–1582.
29. Kapoor N, Sahay R, Kalra S, et al. Consensus on Medical Nutrition Therapy for Diabesity (CoMeND) in adults: a South Asian perspective. Diabetes Metab Syndr Obes 2021;14:1703–1728.
30. Balk EM, Earley A, Raman G, et al. Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: A systematic review for the Community Preventive Services Task Force. Ann Intern Med 2015;163(6):437–451.
31. Shah SZA, Karam JA, Zeb A, et al. Movement is improvement: the therapeutic effects of exercise and general physical activity on glycemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Diabetes Ther 2021;12(3):707–732.
32. Niemiro GM, Rewane A, Algotar AM. Exercise and fitness effect on obesity. [Updated 2022 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK539893/. Accessed February 1, 2023.
33. Stone T, DiPietro L, Stachenfeld NS. Exercise treatment of obesity. [Updated 2021 May 15]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK278961/. Accessed February 2, 2023.
34. Lopez P, Taaffe DR, Galvão DA, et al. Resistance training effectiveness on body composition and body weight outcomes in individuals with overweight and obesity across the lifespan: a systematic review and meta-analysis. Obes Rev 2022;23(5):e13428.
35. James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. Lancet 2000;356(9248):2119–2125.
36. Tchang BG, Aras M, Wu A, et al. Long-term weight loss maintenance with obesity pharmacotherapy: a retrospective cohort study. Obes Sci Pract 2021;8(3):320–327.
37. Sombra LRS, Anastasopoulou C. Pharmacologic therapy for obesity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
38. Central Drugs Standard Control Organisation (CDSCO). List of drugs during 2004. Available at: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadApprovalMarketingFDC/LIST%20OF%20DRUGS%20DURING%202004.pdf. Accessed March 27, 2023.
39. Central Drugs Standard Control Organisation (CDSCO). Recommendations of the SEC. Available at: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadCommitteeFiles/Endo-%20Recommend%2024-08-2021,%2025-08-2021.pdf. Accessed March 27, 2023.
40. FDA. Orlistat. Prescribing Information. Available at: www.fda.gov/downloads/UCM205349.pdf. Accessed February 1, 2023.
41. Guerciolini R. Mode of action of orlistat. Int J Obes Relat Metab Disord 1997;21(Suppl 3): S12–S23.
42. Tak YJ, Lee SY. Long-term efficacy and safety of anti-obesity treatment: where do we stand? Curr Obes Rep 2021;10(1):14–30.
43. Torgerson JS, Hauptman J, Boldrin MN, et al. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004;27(1):155–161.
44. Jain SS, Ramanand SJ, Ramanand JB, et al. Evaluation of efficacy and safety of orlistat in obese patients. Indian J Endocrinol Metab 2011;15(2):99–104.
45. Xenical (orlistat) Prescribing Information. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2015/020766s035lbl.pdf. Accessed February 1, 2023.
46. Knudsen LB, Lau J. The discovery and development of liraglutide and semaglutide. Front Endocrinol (Lausanne) 2019;10:155.
47. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021;384(11):989–1002.
48. Kushner RF, Calanna S, Davies M, et al. Semaglutide 2.4 mg for the treatment of obesity: key elements of the STEP Trials 1 to 5. Obesity (Silver Spring) 2020;28(6):1050–1061.
49. Davies M, Færch L, Jeppesen OK, et al. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): A randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet 2021;397(10278):971–984.
50. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. JAMA 2021;325(14):1403–1413.
51. Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. JAMA 2021;325(14):1414–1425.
52. Garvey WT, Batterham RL, Bhatta M, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nat Med 2022;28(10):2083–2091.
53. Kadowaki T, Chin R, Ozeki A, et al. Safety and efficacy of tirzepatide as an add-on to single oral antihyperglycaemic medication in patients with type 2 diabetes in Japan (SURPASS J-combo): A multicentre, randomised, open-label, parallel-group, phase 3 trial. Lancet Diabetes Endocrinol 2022;10(9):634–644.
54. Rubino DM, Greenway FL, Khalid U, et al. STEP 8 Investigators. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. JAMA 2022;327(2):138–150.
55. Bhasker AG, Prasad A, Raj PP, et al. OSSI (Obesity and Metabolic Surgery Society of India) Guidelines for Patient and Procedure Selection for Bariatric and Metabolic Surgery. Obes Surg 2020;30(6):2362–2368.
56. Obesity and Metabolic Surgery Society of India. Guidelines. Available at: https://www.theossi.com/guidelines-obesity-surgery. html. [Last accessed on 2023 01st February].
57. Garvey WT. New Horizons. A new paradigm for treating to target with secondgeneration obesity medications. J Clin Endocrinol Metab 2022;107(4):e1339–e1347.