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# Original Article

# Revised definition of obesity in Asian Indians living in India



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#### ABSTRACT

*Aim*: The prevailing guidelines for obesity in Asian Indians, published in 2009, relied solely on body mass index (BMI) criteria. Recognizing the limitations of BMI in accurately diagnosing obesity and the emergence of new research revealing the association between generalized and abdominal adiposity in Asian Indians and early-onset co-morbid diseases, a comprehensive redefinition was needed.

Method: In a Delphi process focused on obesity in India, experts were invited via email to participate in five rounds. The survey questions were administered through Google Form to gather insights from the selected experts.

Results: In Stage 1 Obesity, individuals exhibit increased adiposity (BMI>23 kg/m²) without discernible effects on organ functions or daily activities. Stage 2 Obesity denotes a more advanced state characterized by heightened adiposity (generalized and abdominal), impacting both physical and organ functions, resulting in functional limitations during day-to-day activities, and contributing to co-morbid diseases. The criteria for Stage 2 Obesity include a mandatory BMI exceeding 23 kg/m² and at least one of the following: excess waist circumference or waist-to-height ratio. Additionally, the presence of one or more symptoms indicative of limitations in daily activities or one or more obesity-related comorbid conditions/diseases are needed to support the stage 2 obesity. Conclusion: This refined framework seeks to enhance precision in identifying obesity and its associated health risks among Asian Indians living in India, and facilitation of rational management, and aligns with worldwide initiative of new definition of obesity.

#### 1. Introduction

Obesity rates in India are on the rise, mirroring a global trend [1,2]. While the increase in obesity was initially observed in urban areas and major metropolitan cities, it is now extending to smaller towns, suburban and rural regions as well. The COVID-19 pandemic has further contributed to sedentary lifestyle and weight gain [3]. This upward trajectory of obesity is accompanied by a simultaneous rise in people with prediabetes and type 2 diabetes (T2D) [4]. Furthermore, there is a notable surge in other obesity-related conditions and diseases, including dyslipidemia, cardiovascular diseases, non-alcoholic fatty liver disease, and obstructive sleep apnea [1]. The escalating prevalence of obesity poses significant challenges in terms of diagnosis, management, and treatment of associated diseases, particularly among Asian Indians [4].

#### 2. Background

An essential and continued consideration revolves around the threshold of obesity (according to whichever criteria are employed) at which the risk of various diseases escalates. Extensive research has been conducted in this realm, with much of it synthesized in our previous publication from 2009, which proposed revised cut-offs for body mass index (BMI) and waist circumference (WC) to define obesity within the Indian population [5]. This publication has emerged as a vital point of reference for physicians, researchers, and even the general population in India, and other countries with an Asian Indian diaspora. Within this document, we examined the applicability of the globally accepted BMI definition in the context of the Indian population, drawing from available Indian data.

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**Table 1**Obesity as defined by various organizations globally.

Organizations	Definition	Parameters
Obesity Canada (2020) [136]  European Guidelines Obesity Management (2015) [137]	Obesity is a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications and reduces lifespan.  Obesity is a chronic disease characterised by an increase	<ul> <li>Healthcare providers can measure height, weight, and calculate body mass index (BMI) in all adults.</li> <li>Measure waist circumference (WC) in individuals with a BMI of 25–35 kg/m<sup>2</sup></li> <li>In adults (age over 18 years) obesity is defined by a BMI</li> </ul>
	in body fat stores.	of 30 kg/m <sup>2</sup> and overweight (also termed pre-obesity) by a BMI between 25 and 29.9 kg/m <sup>2</sup> .  • The amount of abdominal fat can be assessed by WC which highly correlates with intra-abdominal fat content.
American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity (2016) [138]	Obesity is a complex, adiposity-based chronic disease, where management targets both weight-related complications and adiposity to improve overall health and quality of life.	<ul> <li>BMI should be used to confirm an excessive degree of adiposity and to classify individuals as having overweight (BMI 25-29.9 kg/m²) or obesity (BMI≥30 kg/m²).</li> <li>Other measurements of adiposity (e.g., bioelectric impedance, air/water displacement plethysmography, or dual-energy x-ray absorptiometry) may be considered.</li> <li>WC should be measured in all patients with BMI &lt;35 kg/m²</li> </ul>
American Diabetes Association (2023) [133]	Obesity is a chronic and often progressive disease with numerous medical, physical, and psychosocial complications, including a substantially increased risk for type 2 diabetes.	Obesity is frequently subdivided into categories:  • Class 1: BMI of 30 to <35 kg/m <sup>2</sup> • Class 2: BMI of 35 to <40 kg/m <sup>2</sup> • Class 3: BMI of 40 kg/m <sup>2</sup>
World Health Organization (2002) [139]	Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a health risk.	A BMI over $25 \text{ kg/m}^2$ is considered overweight, and over $30 \text{ kg/m}^2$ is obese
North American Association for the Study of Obesity (NAASO) and the National Heart, Lung, and Blood Institute (NHLBI) (1998)[42]	Obesity is a complex, multifactorial disease that develops from the interaction between genotype and the environment	• BMI • WC
Centre for Disease Control and Prevention (2023) [140] (assessed on 9/9/23)	Overweight and obesity are both labels for ranges of weight that are greater than what is generally considered healthy for a given height. Behavior, environment, and genetic factors can affect whether a person is overweight or obese.	25.0 to <30, Kg/m² overweight Obesity is subdivided into categories: •Class 1: BMI of 30 to <35 kg/m² •Class 2: BMI of 35 to <40 kg/m² •Class 3: BMI of 40 kg/m² or higher.
Edmonton Obesity Staging System (2009) [14]	The Edmonton Obesity Staging System (EOSS) is a five- stage system of obesity classification.	It considers the metabolic, physical, and psychological parameters to determine the optimal obesity treatment

# 3. Pitfalls of previous consultation and way ahead

The basic premise for previous consultation [5] was twofold.

- Body fat in Asian Indians is high relative to BMI [6,7], an issue which becomes more discernible upon comparison with other ethnic groups, and
- 2. Comorbidities, specifically T2D, are evident at lower levels of BMI in Asian Indians [7,8] as compared to other populations.

In this context, BMI and mortality data in Indian population were not available in 2009 at the time of the previous publication. Another vital point for consideration was that abdominal obesity is widely prevalent in Asian Indians, and highly correlated to insulin resistance [9]. Further, elevated cardiovascular risk is seen at lower WC in Asian Indians than enunciated by international guidelines [10]. In 2009, based on wide consensus with experts, we devised the following criteria for obesity [5] for Asian Indian population.

- 1. BMI: Between 23 and 24.9 kg/m  $^2$  , defined as overweight and 25 kg/m  $^2$  or more, as obesity
- 2. Waist circumference: 80 cm or more in women, and 90 cm or more in men was defined as abdominal obesity.

As per revised guidelines, the criteria for initiation of lifestyle modifications, pharmacotherapy and bariatric surgery were also changed [5]. All these therapeutic interventions were redesigned to start at lower limits of BMI as compared to international guidelines.

In the subsequent 15-year interval, two additional inquiries surfaced, compelling us to undertake a reassessment of our approach.

# 1. Is the formula for BMI correct for the Indian population?

The basic premise is to adjust the proportion between height and weight, the use of BMI assumes that in each population, weight scales to height squared. This assumption, as well as the thresholds for defining overweight (BMI between 25 and  $<30 \text{ kg/m}^2$ ) or obesity (BMI  $\ge 30 \text{ kg/m}^2$ ) m<sup>2</sup>) have been widely researched and derived from studying the Caucasian population, hence may or may not apply to various other ethnic groups globally. A recent study attempted to answer the following questions [1]: Does weight scale to height square in Asian Indians? and [2] Does the weight-height relationship differ within different Asian populations (i.e., between Asian Indians and South Koreans)? Hood et al. [11] used a dataset of 43,880 adult Asian Indian males aged 15-54 y, including 5549 members of various tribes in India to conclude that weight does scale close to 2 (squared) height in this geographically, socio-economically, culturally, and ethnically diverse population. These authors [11] concluded that BMI, as defined, does normalize weight for height in Asian Indians. In an accompanying editorial Misra and Dhurandhar stated that this study validates the use of BMI to study in Asian Indians [12]. Hence, it would be appropriate to use the current formula for calculation of BMI in the Asian Indian population.

2. Is definition of obesity based on BMI and WC adequate to separate "obesity without pathological consequences vs. Obesity with pathological consequences"?

A debatable question is whether obesity is just a condition or a disease. This question was not considered in the previous consultation [5]. International guidelines from multiple organizations have taken varied approaches to address this question, as reflected in Table 1. The WHO, in its obesity consultation [13] did not approach this question of whether

obesity should be considered as a "disease". However, in the last few years, this has been considered by other agencies/scientific groups, the best example being the Edmonton Obesity Staging System (EOSS) [14]. In this staging system, obesity is graded from stage 0 to stage 4, depending on scoring on the following four domains: metabolic, mechanical, mental and milieu. Overall, this seems to be a rational approach, but is it practical? For example, diagnosing stage 2 obesity by EOSS method will require blood (blood glucose, and liver transaminases) and other tests (polysomnography), in addition to mental and environmental assessments. These comprehensive assessments are costly and time-consuming, posing challenges for physicians who work in diverse geographic locations and have busy schedules. Consequently, this approach may not be feasible, particularly in low- and middle-income countries with limited resources.

However, despite above mentioned difficulties, the definition of obesity (as defined further in this document) should encompass more than just anthropometric parameters. It is crucial to consider organ dysfunction and symptoms directly associated with obesity. Nevertheless, conducting extensive biochemical and other diagnostic tests can be costly and may not be easily accessible in all locations. Furthermore, the results of these tests are not readily available for immediate assessment. In such situations, a practical and feasible alternative is to promptly assess symptoms and diseases associated with organ dysfunction. This approach can be used for a quick evaluation and help in determining the presence, severity, and significance of obesity-related complications.

Most of the obesity-related symptoms are related to the following organ systems, although several other diseases can cause similar symptoms. These are counted when they occur during activities of daily living. The following symptoms and diseases can be recorded to broadly assess organ dysfunction due to obesity.

- Respiratory: Shortness of breath due to restriction of lung or cardiac afflictions.
- 2. Cardiovascular: Palpitations, due to poor exercise tolerance, lung, or heart problems.
- 3. Musculoskeletal: Limitation of movements mostly due to osteoarthritis of knees and hip, or prolapse intervertebral disc.
- 4. Mental: Depression and anxiety, arising due to physical condition.
- 5. Obesity-linked co-morbid disease (see later).

For quick diagnostic consideration of obesity, the most common symptoms and presence of co-morbid diseases could be taken.

In this consultation and narrative review, we shall discuss these points in detail and take help from Delphi-based opinions to arrive at a reasonable diagnosis of obesity. We shall also describe the clinical workup of obesity and briefly illustrate its management. Some of the ideas discussed and developed in this Consensus are cross fertilisation from discussions from The Lancet Obesity Commission (AM is a member of the commission) [15,16].

# 4. Diagnosis and definition

Obesity is characterized by an abnormal or excessive accumulation of body fat that poses a health risk [17]. While this definition is based on body fat, its measurement is done by an apparatus (Bioelectrical Impedance, Dual Energy X Ray Absorptiometry etc), which is not easily available in clinics and could be costly. While obese individuals differ in the amount of excess fat they store, the regional body distribution of this fat within the body predominantly results in associated risks and diseases [18,19]. There is evidence to believe that excessive abdominal fat poses a greater risk of disease than excess body fat elsewhere in the body [20,21]. It is useful to distinguish between those at higher risk due to 'android obesity' caused by abdominal fat distribution and those with the 'gynoid' fat distribution, which is more evenly and peripherally distributed adiposity, and may lead to lesser metabolic consequences vs. former [22].

Different measures of obesity, such as BMI, waist-hip circumference ratio [W-HR], and WC, are increasingly linked with high cardiometabolic risk in both cross-sectional and prospective studies [23-26]. An investigation that evaluated the pooled data from 11 prospective cohort studies concluded that in white adults, larger WC was associated with higher mortality at all levels of BMI ranging from 20 kg/m<sup>2</sup> to 50 kg/m<sup>2</sup> [27]. Similarly, in the European population, indicators of abdominal obesity such as WC, W-HR, and waist-to-height ratio (W-HtR) were stronger predictors for CVD mortality than BMI alone [28]. The heterogeneity of abdominal tissues, such as adipose tissue and skeletal muscle, and their varying composition across different ethnic groups, and their location-specific characteristics and varying associations with metabolic and cardiovascular risk factors, present considerable challenges in formulating a universally applicable and concise definition of abdominal obesity [29,30]. Asian Indians, in particular, have higher morbidity rates at lower WC cutoff points than white Caucasians [30].

# 5. Clinical measurements of generalised and abdominal obesity

#### 5.1. Body mass index (BMI)

The BMI is calculated as the ratio of weight to height squared (kg/ m<sup>2</sup>). BMI is a simple and inexpensive method for measuring body fat, and it provides standard cutoff points for defining overweight and obesity. BMI is correlated with levels of body fat [1]. In a large South Asian population-based study, BMI was shown to be a strong determinant of blood pressure and T2D, both of which are strongly associated with cardiovascular mortality [24]. Further, the association of BMI with all-cause mortality follows a U-shaped or J-shaped curve, and higher mortality is seen among people with very low BMI (<18.5 kg/m<sup>2</sup>) and very high BMI (>40 kg/m<sup>2</sup>) as compared to those within normal range BMI in South Asians/Asian Indians [24,31]. A sample from MON-ICA/KORA (MONItoring of trends and determinants in CArdiovascular disease/Cooperative Health Research in the Region of Augsburg) study, comprising 3055 men and 2957 women aged 35-74 years at baseline was used to assess the association of BMI with the incident T2D [32]. These authors reported, after adjusting for various covariates (including age, education qualification, family history of diabetes, physical activity status, alcohol intake, dyslipidaemia, and smoking status) that as the BMI increases, i.e., BMI greater than equal to 25.1 kg/m<sup>2</sup> in men and BMI greater than equal to 23.4 kg/m<sup>2</sup> in women, the hazard ratios for incidence of T2D also increase in both genders [32].

Another study was carried out on a Japanese population with 16,829 men and 8370 women aged 30–59 years at baseline to assess the association between BMI and incidence of T2D [33]. These authors reported that the hazard ratios for incident T2D increase with every 1 kg/m² rise in the BMI in both genders. The authors concluded that with every 1 kg/m² increase in the BMI, the risk of developing T2D increases by 25% [33]. In other studies, high BMI was shown to be associated with kidney diseases [34]. Specifically, mortality associated with kidney diseases increases by 60% for every 5 kg/m² increase in BMI [35]. Finally, grade 2 and 3 obesity (BMI more than 35 kg/m²) significantly increases all-cause mortality [36].

Data regarding BMI threshold and morbidities in the Asian Indian population have emerged in a couple of publications after our last consultation in 2009 [37,38]. A recent study [38] showed that in overweight and obese Asian Indians, each unit increase in BMI increases the probability of T2D by about 1.5% vs. 0.5% in non-overweight individuals [38]. Luke and colleagues carried out a study to test the association between BMI status and diabetes in the Indian population using the household data from the India Human Development Survey (IHDS), a nationally representative data of 1,50,000 observations on metabolic diseases such as diabetes, hypertension, and cardiovascular diseases. In addition, the 2015–2016 round of the Demographic Health Survey (DHS) including 770,000 adults was also used to obtain

Table 2 Clinical and laboratory workup\*.

1	Physical examination	<ul> <li>Height, weight, calculate BMI.</li> <li>Waist circumference.</li> <li>Calculate: Waist circumference-to-hip circumference ratio, and waist circumference-to-height ratio.</li> <li>Blood pressure</li> <li>Estimation of percentage body fat</li> <li>Clinical signs: <ul> <li>Acanthosis nigricans</li> <li>Xanthelasma</li> <li>Excess fat under chin ('Double chin') [60,141]</li> <li>Excess dorsocervical fat, 'buffalo hump' [60,141]</li> <li>Skin tags</li> <li>Hirsutism, acne</li> <li>Abdominal palpation for liver and spleen.</li> </ul> </li> </ul>
2	Laboratory tests	Abdominal palpation for liver and spieen.     75 g oral glucose tolerance test     Glycated hemoglobin (HbA1c)     Fasting lipid panel     Liver function tests     Thyroid function test     Blood urea and serum creatinine     Uric acid     Serum cortisol, other hormones (if indicated)*
3	Other investigations	<ul> <li>Urine microalbuminuria</li> <li>Ultrasound abdomen (liver span, ovarian volume and cysts)</li> <li>FIB-4 index (AST, ALT, platelet count in combination with patient age to assess if an individual is at higher risk for advanced liver fibrosis)</li> <li>Liver elastography</li> <li>ECG, Echocardiography</li> <li>Polysomnography</li> </ul>

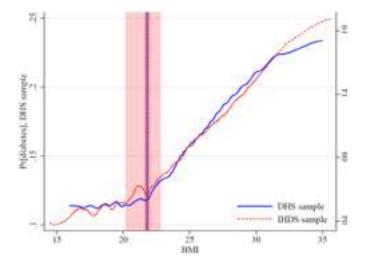
<sup>\*</sup>The investigations need to be applied as per clinical profile and should be individualized.

information about the income level, BMI status, and diabetes. After accounting for factors such as age, gender, caste, area, and survey round, a positive correlation was discovered between BMI and diabetes, beyond a BMI of  $21.8 \text{ kg/m}^2$  [37]. (Fig. 1).

Limitations: BMI is commonly used to diagnose obesity because of its ease, and almost all physicians know about it. However, one of the key limitations of BMI is that it varies with age, sex, ethnicity, and physical conditioning. Further, it cannot distinguish between bone density, muscle mass, and body fat [6]. Moreover, it could be faulty in the elderly. Due to aging, skeletal muscle mass tends to decrease while fat mass tends to increase, yet overall weight may remain roughly the same, resulting in no change to BMI [39,40]. The sensitivity and specificity of BMI vs. body fat have been demonstrated to be inadequate in Asian Indians [6]. Furthermore, the correlation between BMI and body fat percentage is not linear and varies between males and females [40]. As stated previously, in the South Asian population, BMI was found to have little association with vascular mortality despite being linked to increased systolic blood pressure, which is a risk factor for vascular mortality [24].

# 5.2. Waist circumference (WC)

It is the most common method to measure abdominal obesity. The World Health Organization and the International Diabetes Federation (IDF) suggest measuring WC in the horizontal plane midway between the lowest ribs and the iliac crest while standing in normal posture (standing barefoot in a comfortable position with eyes directed straight ahead) [13]. We previously defined WC as follows for simplicity and as per the recommendation of the National Institute of Health, "the subject should be in the fasting state and standing erect and looking straight ahead and the observer should be sitting in front of the subject. WC is measured with a non-stretchable flexible tape in the horizontal position, just above the iliac crest at the end of normal expiration [41,42] (Fig. 2). The latter method is easier to do since it involves the identification of



**Fig. 1.** Association of diabetes and BMI in two Indian cohorts. Source: India Human Development Survey (IHDS), Demographic and Health Survey (DHS), WHO STEPS (Luke *et al.*, 2022) [37].

only one landmark, keeping in mind culturally appropriate lesser exposure of bare skin. It is easy to measure, inexpensive, and is strongly correlated with body fat in adults [32].

Abdominal obesity is an important factor in health, even independent of BMI [21,43,44]. A meta-analysis of 11 prospective cohort studies including white adults aged 20-83 years from Australia, Sweden, and the USA stated that WC is positively associated with all-cause mortality [27]. Coutinho and colleagues carried out a systematic review of cohort studies with adults from the US, Denmark, France, and Korea (n, 14000, suffering from coronary artery disease) and observed that the higher tertiles (second and third) of WC were associated with the higher risk of death even after adjusting for age, gender, smoking, and BMI [45]. Sluik and colleagues carried out a prospective cohort study with over 5000 participants with T2D and observed that the highest tertile for WC was associated with higher risk of death [HR 2.11, 95 % CI 1.23-3.61] [46] after adjusting for T2D duration, insulin treatment, smoking, and BMI. The consensus statement by the International Atherosclerosis Society and International Chair on Cardiometabolic Risk Working Group states that WC is a risk factor for cardiometabolic diseases and, hence, should be evaluated in clinical practice [26].

*Limitations*: The measurement procedure has not been optimally standardized. The measurement of WC may be influenced by posture, respiratory cycle, and prandial status [47]. It may be difficult to measure and is likely to be less accurate in individuals with a BMI of  $35 \text{ kg/m}^2$  or higher. In India, it is sometimes difficult and inaccurate to measure WC on top of clothing in women.

# 5.3. Waist-to-hip circumference ratio (W-HR)

The W-HR is an easy method to assess abdominal obesity and shows a strong correlation with body fat [48]. Several studies have demonstrated its predictive value for cardiometabolic diseases and all-cause mortality [49,50]. A recent meta-analysis reported that each 0.1 unit increase in W-HR is associated with a 20% increase in all-cause mortality risk [49]. In the MacArthur Successful Aging Study, conducted in the USA on a diverse ethnic population of healthy older adults aged 70–79 y, W-HR was found to be a more accurate predictor of all-cause mortality risk than BMI or WC, suggesting its suitability for risk stratification in this population [50]. Furthermore, high W-HR is linked to an elevated risk of developing cardiovascular diseases, particularly among South Asians compared to individuals from other countries [51]. These authors also observed that among women, there was a positively significant association between W-HR and population-attributable risk.



**Fig. 2.** Method of measurement of waist circumference
The subject should be in the fasting state and standing erect and looking straight ahead and the observer should be sitting in front of the subject. Waist circumference is measured with a non-stretchable flexible tape in the horizontal position, just above the iliac crest at the end of normal expiration [41,42].

Limitations: The measurement of W-HR can be prone to errors (see discussion on WC). Additionally, measuring the hip circumference is particularly challenging, especially when it comes to Indian women. Furthermore, interpreting W-HR is more complicated compared to WC alone. An increased W-HR can be the result of either increased abdominal fat or reduced lean muscle mass around the hips, making it harder to determine the underlying factors. Converting the measurements into a ratio may lead to a loss of information since two individuals with significantly different levels of BMI could end up with the same W-HR value. This value may remain unchanged even if both waist and hip circumferences increase by a similar measure over time. Lastly, as for WC, accurately measuring W-HR in individuals with a BMI of 35 kg/m<sup>2</sup> or higher can be challenging.

#### 5.4. Waist circumference-to-height ratio (W-HtR)

Recently, the W-HtR has emerged as an important anthropometric index for the assessment of abdominal adiposity. It is calculated by dividing WC (cm) by height (cm). Compared to BMI, W-HtR is increasingly considered a more sensitive tool for screening health risks and is also easy to measure [52,53]. A systematic review revealed that estimation of W-HtR resulted in a 4–5% and a 1–2% improvement in the discriminatory power over BMI and WC, respectively for adverse



Fig. 3. Acanthosis Nigricans Darkly pigmented and thickened skin, typical of acanthosis nigricans, at the nape of neck in a 42 year old male with BMI 34 kg/m $^2$ , waist circumference 110 cm and prediabetes.

cardiovascular outcomes. Moreover, statistical analysis of the within-study difference in Area Under the Curve indicated that W-HtR was significantly better than WC for the prediction of diabetes, hypertension, dyslipidaemia, CVD, and all outcomes combined for both genders [53]. A recent study reported that with every 0.1 unit increase in W-HtR, the risk of all-cause mortality increased by 20% [49]. The study also reported a J-shaped non-linear response in both males and females, with the lowest all-cause mortality risk at 0.5 and a sharp linear increase after that [49]. Another study concluded that W-HtR is associated with years of life lost and is a better measure than BMI to predict mortality in both men and women [54]. In Asian Indians with a high prevalence of cardiometabolic risk factors, the combination of WC and W-HtR seemed to have greater clinical usefulness than BMI and W-HR for identifying those at risk for cardiometabolic disorders [55,56]. A systematic review and meta-analysis conducted for 30 studies with over 300000 participants from different ethnic groups suggests that W-HtR cutoff of 0.5 can be used in different sex and ethnic groups and that the same cutoff can be applied in children and adults [53]. Despite progress, additional data is required to better understand the correlation between W-HtR, diabetes, and mortality.

*Limitations*: Similar to limitations in measurement of WC (see previous para).

#### 5.5. Other clinical findings associated with obesity

Besides the anthropometric factors described above, certain clinical findings such as acanthosis nigricans (dark pigmented and thickened skin over the nape of the nexk, and sometimes over face, axillae, and other parts of the body, see Fig. 3) may signify presence of insulin resistance in obese individuals [57]. In a population-based study in South India (n, 986), the prevalence of acanthosis nigricans was found to be 16.1 %, with the highest occurrence in the 30–40 age group. The presence of acanthosis nigricans correlated significantly with female gender, obesity, elevated triglycerides, fasting insulin levels, and diabetes [58]. Additionally, severity of neck acanthosis nigricans showed the strongest correlation with fasting insulin and glucose levels, indicating insulin resistance, compared to acanthosis nigricans in other regions like the axilla and knuckles [59]. Other physical characteristics like skin tags, excess dorsocervical pad ("buffalo hump") and double chin need more data as a marker of cardiovascular risk [60,61].

# 6. Methodology of consensus development process

To establish a consensus on the diagnosis and management of obesity in Asian Indians living in India, our approach involved soliciting opinions from experts in the field. A team of four steering committee members (AM, NV, AG, and PR), each took over one of the four relevant areas of obesity in clinical practice (Definition, diagnosis, clinical workup, and management), formulated relevant questions based on a comprehensive literature search and their own clinical experience. Fifth steering committee member (SG) assisted in all these processes and wrote section on diet.

The consensus-building process utilized the Delphi technique, which has been recognized as a reliable measurement instrument for developing new consensual guidelines [62,63]. The Delphi technique involves gathering the opinions of a panel of experts to assess agreement and resolve disagreements on a particular issue. It has been successfully employed in various subject areas, including obesity and obesity-related behaviours, to establish consensus [2,3]. The consensus-building process consisted of five rounds of Delphi, conducted between September 2022 and April 2023. The following steps were taken.

 Participants, considered to be experts in obesity in India (n, 118), were invited via email to participate in this Delphi survey. Specifically, the expert group consisted of healthcare providers comprising

- physicians, surgeons, physiotherapists, and nutritionists treating Obesity and metabolic disorders in India.
- 2. To complete the Delphi process, participants were required to respond across all rounds. Those who did not respond to Round 1 were not invited to participate in successive rounds.
- 3. Further, the free-text responses from each round were helpful in forming opinions. All surveys were administered using Google Forms and survey links were distributed via email.
- 4. The questions were sent to the expert through the Google Form. The Delphi process comprised of five rounds. (Supplementary file 1, 2, 3, 4 and 5 show Delphi questions). In all rounds the participants were asked to independently rank statements using a 5-point Likert scale ('strongly agree', 'agree', 'neither agree nor disagree', 'disagree', 'strongly disagree') [64]. For a positive response, 67% or more people should state 'agree' or 'strongly agree'. A free-text response was available to participants within each of the surveys.
- 5. Delphi rounds:
  - a. Delphi Round 1 (4<sup>th</sup> October 2022: In the first Delphi round 18 questions were asked about the vital parameters of obesity.
  - Round 2 (31<sup>st</sup> October 2022): In the second round 7 questions were asked regarding diagnostic methods of obesity.
  - c. Round 3 (16<sup>th</sup> December 2022): In this round 12 questions were asked about the cutoffs for various pharmacological and nonpharmacological interventions.
  - d. Round 4 (27<sup>th</sup> February 2023): In this round only one question was asked about what parameters should be taken to diagnose obesity.
  - e. Round 5 (8<sup>th</sup> June 2023): In this final round, participants were asked if classification of obesity by staging is agreeable.

Answers to Delphi rounds were compiled by NV, PR and AG and are presented in Supplementary Table 1.

# 7. Guiding principles for staging of obesity: Recommendations based on Delphi survey

Definition of obesity is subdivided into following two categories. Overall diagnostic algorithm is described in Fig. 4

#### 7.1. Stage 1 obesity

This refers to a state of increased adiposity without impacting organ functions or causing functional limitations in day-to-day activities. The person should have normoglycemia, normal blood pressure, normal lipid profile, and no cardiovascular disease (clinical or on investigations, if performed). In such cases, the focus is on implementing dietary and exercise interventions aimed at weight reduction, with the ultimate goal of preventing the onset of obesity associated comorbid clinical diseases. The following guidelines should be observed.

- a. Body fat is the gold standard for defining obesity. Whenever possible, it should be estimated (optional).
- b. For clinicians and epidemiologists:
  - a. BMI should be used to define generalized obesity i.e., any person having BMI more than 23 kg/m². Rarely, a person may have a BMI below 23 kg/m² but still possess body fat levels exceeding the stipulated limits. In such cases, body fat should be the determining factor for further classification of obesity.
  - b. In addition, WC and W-HtR could be used to define abdominal obesity. The use of these measures is optional but desirable.
  - c. Person with stage 1 obesity should not have:
    - Any symptoms suggestive of limitations of day-to-day activities due to obesity.
    - ii. Any obesity-related comorbid diseases.

#### 7.2. Stage 2 obesity

This pertains to an increase in adiposity (both generalized and abdominal) affecting physical and organ functions, causing functional limitations during day-to-day activities, and resulting in co-morbid diseases. As stated previously, ideally, body fat should be measured, but it is not always possible due to cost and availability. Hence, this criterion of obesity is optional.

Two of the following three criteria are required to diagnose Stage 2 obesity, among them the first statement is mandatory. One more criterion, either 2 or 3 is required.

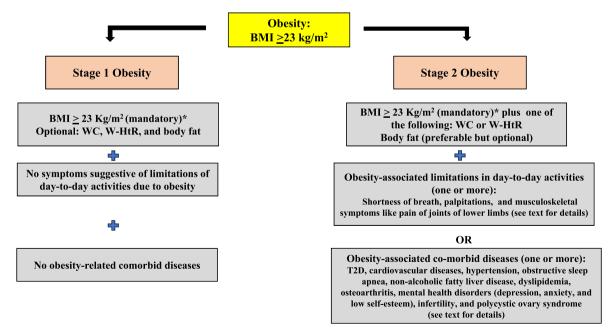


Fig. 4. Diagnostic algorithm for obesity diagnosis among Asian Indians living in India. + indicates "with", \* Rarely, a person may have a BMI below 23 kg/m² but still possess body fat levels exceeding the stipulated limits. In such cases, body fat should be the determining factor for further classification of obesity.

- Two measures of obesity: BMI more than 23 kg/m<sup>2</sup> (mandatory), and one of the following, WC or W-HtR, should be selected. Whenever possible body fat should be done but it is not an essential requirement.
- 2. Symptoms suggestive of limitations of day-to-day activities should be included (see below). One or more sets of symptoms are required.
- 3. If patients are already diagnosed as having obesity-related comorbid conditions/diseases, it should be recorded. One or more of such diseases is required for consideration. If resources permit, diagnosis for these diseases could be initiated.

It is possible that those with higher levels of BMI but qualified as having Stage 1 obesity can convert to Stage 2 obesity faster than with lower BMI levels. However more data are required.

#### 7.3. Obesity-associated limitations in day-to-day activities

Clinical findings such as shortness of breath, palpitations, (indicating obesity related impairment of lungs and heart) and musculoskeletal symptoms like pain of joints of lower limbs (obesity related impairment of weight bearing joints) on doing activities within the house, bathing, dressing, toileting, eating, etc. These differences highlight the significance of their clinical recognition in identifying potential health risks and guiding appropriate interventions [65–67].

#### 7.4. Obesity-associated co-morbid diseases

In addition, the following comorbid conditions/diseases must be taken into consideration; T2D, cardiovascular diseases, obstructive sleep apnea, non-alcoholic fatty liver disease (NAFLD, also termed as Metabolic Dysfunction Associated Fatty Liver Disease), dyslipidemia, hypertension, osteoarthritis (lumbosacral spine and lower limbs), mental health disorders (depression, anxiety, and low self-esteem), infertility, male hypogonadism, lower limb edema, and polycystic ovary syndrome [68]. If resources permit, these should be screened in persons with obesity.

# 7.5. Diagnostic cut-offs and other measurements

- 1. Body fat: Body fat percent cutoffs to define obesity: >25.5% for men and >38% for women [69].
- 2. Grades of BMI [5]:
  - a. Normal: 18.5–22.99 kg/m<sup>2</sup>
  - b. Grade I: 23–24.9 kg/m<sup>2</sup>
  - c. Grade II:  $25-27.5 \text{ kg/m}^2$
  - d. Grade III: 27.6–32.4 kg/m<sup>2</sup>
  - e. Grade IV:  $\geq 32.5 \text{ kg/m}^2$
- Abdominal obesity: The best measure to determine abdominal obesity is WC. Additionally, W-HtR may be useful to indicate abdominal obesity and should be preferred over waist-to-hip ratio (W-HR).
  - a. WC Cutoffs level: WC  $\geq$  90 cm in men and  $\geq$  80 cm in women [10]. b. W-HtR cutoff level: >0.5 [70].
- 4. Functional symptoms: In addition, an assessment of functional symptoms should also be performed. The presence of these symptoms during day-to-day activity should be noted. Although there are many such symptoms, those mentioned in 7.3 should be considered.
- 5. Obesity-related co-morbid diseases: One or more, as defined previously (see 7.4).
- A further way to classify is to include grade of BMI after stage of obesity, e.g. a person with BMI 26.5 kg/m<sup>2</sup> without any comorbid or limitations of day-to-day activities can be classified as having Stage 1 Obesity with Grade 2 BMI.

# 8. Management

A proper evaluation of a person with obesity includes careful history, physical examination, and appropriate investigations to exclude secondary obesity and to assess co-morbid diseases (Table 2).

#### 8.1. Management for stage 1 obesity

Lifestyle-related interventions like individualized medical nutrition therapy, physical activity and behavioural intervention should be initiated for obviating risk as seen in stage 2 obesity. In people with stage 1 obesity these measures would usually be sufficient.

Pharmacotherapy could be an option for the following.

- 1. People with stage 1 obesity, who are at risk for converting to stage 2 obesity e.g., a person is at risk for the development of co-morbid diseases like diabetes, CVD etc. (e.g., those with a strong family history of these diseases).
- 2. Substantial weight gain (>10%) is occurring despite optimal application of lifestyle measures.
- 3. People with BMI  $\geq$ 27.5 kg/m<sup>2</sup>.

#### 8.2. Management for stage 2 obesity

- 1. Lifestyle interventions must be consistently and aggressively applied.
- 2. Pharmacotherapy for obesity management should be initiated early.
- 3. Drugs and Injectable Therapies:
  - Persons with obesity, and without diabetes: Orlistat is the recommended drug.
  - In persons with T2D:
    - Glucagon-like peptide-1 (GLP-1) receptor analogues are recommended as the first line of treatment to reduce weight especially in people with higher grade of BMI and in presence of T2D, atherosclerotic CVD and NAFLD.
    - Sodium glucose co-transporters (SGLT2) inhibitors could be used for mild/moderate weight loss. These drugs are especially useful in people with heart failure and renal dysfunction.
    - SGLT2 inhibitor and GLP-1 receptor analogue combination should be used appropriately to maximize weight loss.
    - Orlistat could be used as appropriate.

# 8.3. Dietary management

In the following discussion, we shall discuss the principles of various weight loss diets. Details of these diets are not given here but can be found in appropriate references [71].

# 8.3.1. Principles

- Techniques for a dietary change include a decrease in energy intake, and creating a negative energy balance, which is the foundation for treating overweight and obesity.
- 2. A daily calorie deficit of roughly 500 kcal is advised for weight loss by reducing energy intake and increasing physical exercise.
- 3. These dietary efforts need to be continued long-term. A person under treatment must be advised of the possibility of weight regain after stopping diet, exercise and pharmacotherapy.

# 8.3.2. Dietary approaches for weight loss: recommendations

1. Calorie-restrictive diets: These have been conventionally used, and based on the premise that daily restriction of calories while maintaining balance in macronutrients would lead to weight loss [72].

- Other diets (see below) have been compared with this diet for long-term weight loss data.
- Carbohydrate-based Interventions: Carbohydrate consumption in Asian Indians is high. Various diets, like low carbohydrate and ketogenic diets, have been used for short-term weight loss.
- 3. Protein-based dietary interventions: Increasing protein in diets and replacing meals with protein drinks have been popular approaches. In the Indian population, this may mean supplementing poor protein nutrition as well [73–75].
- 4. Fat-based dietary interventions: High-fat diets (classic ketogenic diets), have been proposed as an approach for weight loss. Such diets automatically have a low carbohydrate load [76,77].
- 5. Other types of diets: Recently popular intermittent fasting has been shown to cause weight loss but its advantage over long-term *vs.* calorie-restrictive diets is doubtful [78.79].

Any dietary intervention should be based on a detailed nutritional assessment, including an evaluation of personal values, preferences, and social determinants of eating habits. Dietary interventions should be flexible, and person centered. Any weight loss diet designed for weight loss sustainability in the long term, with no harm, would be the most durable diet.

#### 8.4. Physical activity

For individuals with overweight/obesity and associated conditions (neuro-muscular, cardiac/pulmonary etc.), the decision to participate in the physical activity must be recommended by a qualified physiotherapist or exercise professional. It is important to select the exercises of an optimal intensity and duration after detailed evaluation by the exercise therapist. This will ensure to achieve the desired results with minimal chances of injury.

A weight loss rate of 0.5–1 kg per week is widely accepted as a safe and effective approach [80,81]. However, achieving weight loss at this recommended rate necessitates maintaining a negative energy balance of approximately 500–1000 kcal/day over an extended duration [82]. Such a substantial energy deficit is challenging to attain solely through energy intake reduction (dietary control). Additionally, significant reductions in caloric intake may give rise to nutritional deficiencies and the loss of lean mass, subsequently leading to a decrease in metabolic rate [83]. Moreover, adhering to such an extreme caloric restriction level for prolonged periods is arduous and enhances the likelihood of relapse and compensatory weight regain. By increasing Lean Body Mass (LBM) in proportion to fat, physical activity helps counterbalance the loss of LBM and the reduction of Resting Metabolic Rate that typically occurs with intentional weight reduction [84].

During the phase of active weight loss, both aerobic and resistance exercise play a crucial role in preserving lean tissue, with the volume of exercise performed over the weight-loss period being a key determinant [85]. Integrating a program that combines caloric restriction with both aerobic and resistance training typically yields superior weight loss outcomes and enhanced overall health compared to a program that incorporates caloric restriction with only aerobic exercise [86]. Furthermore, physical activity has positive effects on cardiovascular health, insulin sensitivity, and energy expenditure [87].

The Physical Activity and Sedentary Behavior Guidelines by the World Health Organization (WHO) suggest that adults engage in 150–300 min per week of moderate-intensity physical activity (such as brisk walking) or 75–150 min per week of vigorous-intensity activity to prevent excessive weight gain, cardiovascular and metabolic diseases, and functional decline. The guidelines also recommend incorporating muscle strengthening exercises at least two days per week. While specific recommendations for sedentary behaviour have not been established, the evidence linking prolonged sedentary time to increased morbidity and all-cause mortality is steadily growing [88].

#### 8.4.1. Principles

- Physical activity has beneficial effects on body composition and helps maintain healthy weight as well as weight loss along with nutritional therapy.
- 2. The benefits of physical activity are dependent on the amount of activity undertaken rather than the type of activity.
- A combination of different types of physical activity (aerobic and resistance exercises) is important for achieving weight loss, maintaining lean body mass and prevention of weight gain.

#### 8.4.2. Recommendations

- 1. A minimum of 60 min of daily physical activity per day is recommended for weight loss and management [89].
- 2. It is recommended that adults reduce their sedentary behaviour and strive to engage in physical activity of any intensity, including lightintensity activities, as a means of promoting health and well-being. Replacing sedentary time with physical activity, regardless of intensity, has been shown to yield significant health benefits [88].
- 3. Engaging in approximately 45–60 min of moderate-intensity activity per day is associated with transitioning from being overweight to normal weight. Moreover, a minimum of 60 min or more of daily moderate-intensity activity may be necessary to facilitate the transition from obesity [90,91]. Physical activity can be accumulated throughout the day in blocks if feasible.
- Resistance exercise or muscle strengthening exercises should be incorporated into the exercise regimen, ideally on all days, but at least 3 days a week.
- The exercise prescription should be individualized with gradual increase in the duration and the intensity.
- 6. A pre-exercise evaluation is indicated to identify co-existing cardiac and other problems which may be exacerbated by the exercise.

# 8.5. Pharmacological management

The pharmacological management of obesity is guided by the stage of obesity and in addition, grade of BMI could be considered. The primary goal of drug therapy for individuals with obesity is to achieve long-term weight reduction and overall health improvement, while closely monitoring for adverse effects. The following is a brief description of pharmacological approaches to weight loss.

#### 8.5.1. Principles

- It is important to counsel patients before initiating pharmacotherapy, informing them that a weight loss plateau is expected after initial progress, and additional strategies may be needed to achieve further weight loss.
- Patients should also be prepared for the likelihood of weight regain once these medications are discontinued.
- 3. When pharmacotherapy is coupled with lifestyle measures, a weight loss of about half kg per week can be expected with a fall of 5–10% body weight below baseline in three to six months.
- 4. A weight reduction of 5–10% can substantially reduce the odds of development of T2D among persons with prediabetes [92–94], and reduce blood pressure and risk factors for cardiovascular disease [95, 96].
- 5. Certain antihyperglycemic, antidepressants, and other drugs [41] are known to cause weight gain and should be avoided or replaced with weight neutral alternatives [97].

# 8.5.2. Drugs for management of obesity in persons without T2D (as available in India)

Various studies have shown that the use of anti-obesity drugs such as orlistat, lorcaserin, naltrexone-bupropion, phentermine-topiramate, or

liraglutide, in conjunction with lifestyle modifications, can lead to weight loss ranging from 5 to 22.5 percent [98–100]. Some of these have been withdrawn due to prohibitive adverse drug reactions. Presently, except GLP-1 receptor agonists (GLP-1 RAs) and orlistat, these are not available in India. Only orlistat is licensed for use as an anti-obesity drug in India.

#### 8.5.3. Orlistat

Orlistat inhibits pancreatic lipases, leading to reduced fat digestion and increased excretion of fecal fat. It is commonly used for weight loss but is less effective compared to therapy with GLP-1 RAs and the combination of phentermine-topiramate. Orlistat has been shown to be safe and effective in promoting weight loss in various randomized trials and meta-analyses [101-103]. Patients taking orlistat, along with a behavioural intervention, experienced weight loss of 5-10 kg (8 percent of baseline weight) over 12 months compared to the control group [104]. Long-term treatment with orlistat maintained weight loss for up to 24–36 months [104]. Orlistat also demonstrated benefits in reducing the incidence of T2D (STOP-NIDDM trial) and improving blood pressure and lipid levels [105,106]. However, the use of orlistat is associated with gastrointestinal side effects such as cramps, flatus, fecal incontinence, and oily spotting in about 7% of cases [107]. It may also affect the absorption of fat-soluble vitamins and increase the risk of oxalate-induced kidney injury. Orlistat is contraindicated in pregnancy, chronic malabsorption, cholestasis, and a history of calcium oxalate stones. The recommended dose is 60-120 mg three times daily during meals.

#### 8.5.4. Drugs for management of obesity in people with T2D

1. Glucagon-like peptide-1 receptor agonists:

The therapeutic utilization of GLP-1RAs is characterized by the

induction of weight loss through mechanisms that intricately modulate intercellular communication between the gastrointestinal tract and the central nervous system. This modulation leads to a reduction in appetite and food cravings, concomitant with an augmentation of thermogenesis within brown adipose tissue. Among its physiological effects, GLP-1RAs impede both gastric and duodenal peristalsis by exerting inhibitory influence upon the vagus nerve, concurrently elevating pyloric pressure to curtail appetite. Furthermore, these agents effectively retard postprandial gastric emptying and attenuate gastric acid secretion. Cumulatively, these multifaceted mechanisms culminate in the observed weight loss outcomes [108].

Several GLP-1RAs have received international approval for weight management in non-diabetic individuals with obesity. However, it is noteworthy that in the Indian context, specific molecules such as liraglutide, dulaglutide, and oral semaglutide have obtained licensure solely for usage in individuals afflicted with T2D.

Many randomised controlled trials (RCTs) have compared the efficacy of weight loss between GLP-1RAs in people with and without T2D [109](Table 3).

A. *Liraglutide*: This molecule has 97 % homology to human GLP-1. It is approved up to 1.8 mg once daily for the treatment of T2D. Weight loss with liraglutide is dose dependant, up to 3 mg once daily [110]. In India 3 mg dosage of liraglutide is not available.

The Satiety and Clinical Adiposity—Liraglutide Evidence (SCALE trials) established the safety and efficacy of liraglutide across different subset of population like individuals with diabetes (6% weight loss) [111], prediabetes (6.1% weight loss) [92], obstructive sleep apnoea (5.7% weight loss) [112], and in people with obesity without diabetes (8.1% weight loss) [113]. The proportion of subjects who lost  $\geq$ 5% of baseline body weight

Table 3
Selected studies of GLP-1Receptor analogues on obesity with/without T2D.

Reference	Population (BMI in kg/m <sup>2</sup> )	Duration	Intervention	Mean Weight Loss from Baseline	Percentage of Subjects Achieving Weight Loss of 5%	Percentage of Subjects Achieving Weight Loss of 10%
Pi-Sunyer <i>et al.</i> (2015) [113]	Individuals without T2D BMI of ≥ 30 or ≥27	56 weeks	Liraglutide 3 mg (n = 2487)	-8.0%	63.2%	33.1%
SCALE Obesity and Prediabetes			Placebo (n = 1244)	-2.6%	27.1%	10.6%
Astrup et al (2009) [142]	Obese individuals without diabetes	56 weeks	Liraglutide 3 mg (n = 93)	-9.2%	73%	
			Placebo (n = 98)	-3.1%	2.8%	
Halawi et al.(2017) [143]	Individuals BMI ≥30 kg/m <sup>2</sup>	16 weeks	Liraglutide 3 mg (n = 19)	−5.3 kg		
			Placebo (n = 20)	-2.5 kg		
Wadden et al. (2013) [144]	Obese individuals without diabetes (BMI $\geqslant$ 30 or $\geqslant$ 27) kg/m <sup>2</sup>	56 weeks	Liraglutide 3 mg (n $= 212$ )	-6.2%	50.5%	
SCALE Maintenance			Placebo (n = 210)	-0.2%	21.8%	
Blackman <i>et al.</i> (2016) [112]	Individuals with obesity OSA without diabetes	32 weeks	Liraglutide 3.0 mg $(n = 180)$	-5.7%	-	
SCALE Sleep Apna			Placebo (n = 179)	-1.6%		
Wadden et al. (2020) [145]	Obese individuals with and without diabetes	56 weeks	Liraglutide 3.0 mg $(n = 142)$	-7.5%	61.5%	30.5%
SCALE Intensive behaviour therapy			Placebo (n = 140)	-4.0%	38.8%	19.8%
Wilding et al. (2021) [99]	Individuals with a BMI of $\geq 30$ or $\geq 27$ kg/m <sup>2</sup> in persons with $\geq 1$ weight-related coexisting condition,	68 weeks	Semaglutide 2.4 mg (n = $1304$ )	-14.9%	86.4%	69.1%
STEP 1	who did not have diabetes		Placebo (n = 655)	-2.4%	31.5%	12.1%
Wadden <i>et al.</i> (2021) [146]	Individuals without diabetes and with either overweight (BMI ≥27kg/m² ) plus at least 1	68 weeks	Semaglutide 2.4 mg ( $n = 407$ )	-16.0%	86.6%	75.3%
STEP 3	comorbidity or obesity (BMI $\geq$ 30kg/m <sup>2</sup> )		Placebo (n = 204)	-5.7%	47.6%	27.0%
Rubino et al.(2022) [147]	Individuals with BMI $\geq$ 30 or $\geq$ 27kg/m <sup>2</sup> with 1 or more weight-related comorbidities, without diabetes	68 weeks	Semaglutide 2.4 $mg (n = 126)$	-15.8%	87.2%	70.9%
STEP 8			Liraglutide 3.0 mg $(n = 127)$	-6.4%	58.1%	25.6%
			Placebo (n = 85)	-1.9%	29.5%	15.4%

across these studies was 54-63%, >10% weight loss 25-33% and >15% weight loss in 14% of population. In a 3-year follow-up of the participants greater weight loss with liraglutide resulted in a >50% reduction in the risk of progression from prediabetes to T2D [92].

B. Semaglutide: This molecule has 94% homology to human GLP-1. It is available in both injectable and oral forms. Oral semaglutide is modified by the addition of the absorption enhancer sodium N-(8-[2-hydroxybenzoyl] amino) caprylate. Oral and injectable forms are approved for treatment of T2D and only injectable are approved for treatment of obesity without diabetes.

SUSTAIN (Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes), PIONEER (Peptide Innovation for Early Diabetes Treatment), and STEP (Semaglutide Treatment Effect in People with Obesity) trials are three main sets of trials for injectable once weekly semaglutide 1 mg, oral semaglutide 3,7 and 14 mg in diabetes and once weekly semaglutide 2.4 mg respectively. Throughout SUSTAIN trials injectable 1 mg semaglutide was found to be superior in achieving glycemic control and reduction of body weight when compared with placebo and active comparators. When compared with liraglutide 1.2 mg, semaglutide 1 mg achieved superior weight loss with 53% population achieving more than 5% weight loss. In PIONEER trials, a decrease in both HA1c and body weight was significantly greater with oral semaglutide when compared with a placebo, other active comparators and other GLP-1RAs (dulaglutide and liraglutide). After these trials STEP trials were designed to study the effect of 2.4 mg once weekly semaglutide as weight loss medication. When compared to placebo it caused 14.9% weight loss. Further, 86.4%, 69% and 50% of population achieved 5%, 10% and 15% weight loss. (STEP1). In the extension of the STEP-1 trial, 11.6 % of weight was regained after stopping semaglutide for a year. This indicates that ongoing treatment is required for obesity treatment.

Semaglutide Effects on Heart Disease and Stroke in Patients with Overweight or Obesity (SELECT) trial, a randomised double-blind trial included 17,604 patients (aged  $\geq\!45$  years, BMI  $\geq\!27$  kg/m²) from 41 countries who were overweight or obese with established cardiovascular disease and no history of diabetes subcutaneous once weekly semaglutide 2.4 mg was associated with a statistically significant 20% reduction in major adverse cardiovascular events (MACE) compared with placebo in an unpublished study [114].

2. Gastric inhibitory polypeptide receptor (GIPR)/Glucagon-like peptide-1 receptor (GLP-1RA) dual agonists

Tirzepatide is a once-weekly subcutaneous injectable peptide engineered from the native GIP sequence, with agonist activity at both the GIP and GLP-1 receptors. It was recently approved by the FDA for treating T2D. Five clinical trials (SURPASS 1–5 trials) [115] conducted in patients with T2D showed that tirzepatide at dose of 5–15 mg per week reduced body weight substantially (5.4–11.7 kg, 5–10% of body weight) and glycemic goal was achieved in majority of participants on tirzepatide. Weight loss is dose dependant with the use of this drug [116]. In a SURMOUNT-1 trial in adults with obesity and T2D, once-weekly tirzepatide 10 mg and 15 mg provided –12-8% and –14-7%, weight loss respectively in 72 weeks [117]. Participants in SURMOUNT-3, achieved a total mean weight loss of 26.6% over 84 weeks and in SURMOUNT-4 achieved a total mean weight loss of 26.0% over 88 weeks [118].

- 3. New trials and Drugs in Pipeline:
  - A. Oral semaglutide 50 mg: In the most recent trial published in adults with overweight or obesity without T2D, oral semaglutide 50 mg once per day led to a superior and clinically meaningful decrease in body weight compared with placebo (15.1% vs. 2.4%) [119].

- B. Retatrutide (LY3437943): is an agonist of the glucose-dependent insulinotropic polypeptide, GLP-1, and glucagon receptors. In 24 weeks, the mean percentage change in body weight was -7.2% in the 1-mg group, -12.9% in the 4-mg group, -17.3% in the 8-mg group, and -17.5% in the 12-mg group. At 48 weeks, a weight reduction of 5% or more, 10% or more, and 15% or more had occurred in 92%, 75%, and 60%, respectively, of the participants who received 4 mg of retatrutide; 100%, 91%, and 75% of those who received 8 mg; 100 %, 93%, and 83% of those who received 12 mg [120].
- C. Survodutide: It is a dual GLP-1 and glucagon receptor agonist, leading to weight loss in a phase II dosing trial in people with overweight/obesity but without T2D. About 40% of people who were taking the highest dose lost 20% or more of their starting weight at 46 weeks. This drug was also evaluated in a phase II study in adults with non-alcoholic steatohepatitis and liver fibrosis (stages F1/F2/F3) with and without T2D for which it received US FDA Fast Track Designation [121,122].
- D. Orforglipron: It is a nonpeptide GLP-1RA, once-daily oral therapy for weight reduction in adults with obesity. In phase II, randomized, double-blind trial at week 26, the mean change from baseline in body weight ranged from -8.6% to -12.6% across the orforglipron dose cohorts and was -2.0% in the placebo group. At week 36, the mean change ranged from -9.4% to -14.7% with orforglipron and was -2.3% with placebo. About 10% weight loss by 36 weeks was recorded in 50–70% of the participants on this drug.
- E. Cagrilintide and its fixed dose combination with semaglutide (CagriSema): Cagrilintide is an ultralong acting amylin analogue administered subcutaneously. Its fixed dose combination has been found to have a good glycaemic efficacy with nearly 8% weight loss from baseline in people living with diabesity in a recently published randomised controlled trial [123].
- F. Other Novel Drugs: A few other drugs undergoing various phase II/III trials are danuglipron, pemvidutide, and mazdutide.
- 4. Sodium-glucose Co-transporter 2 (SGLT2) inhibitors

SGLT2 inhibitors cause body weight loss via glucose excretion which causes calorie loss (about 60–100 g of glucose per day, amounting to loss of 240–400 kcal/day). Further, under conditions of reduced portal insulin-to-glucagon ratio, lipolysis increases in adipose tissue and releases non-esterified fatty acids which are converted to ketone bodies in the liver through mitochondrial beta oxidation and ketogenesis, resulting in a metabolic condition resembling a prolonged fast [124].

The use of SGLT2 inhibitors in individuals with T2D has demonstrated weight loss, both as monotherapy and as an add-on therapy. Network meta-analyses have revealed consistent reductions in body weight (approximately 1.5-2 kg) compared to placebo across various SGLT2 inhibitor treatments, and these effects have shown a dose-dependent relationship [125]. In a real-world study conducted in India, individuals with T2D who received SGLT2 inhibitors exhibited a weight reduction of 3.45 kg over a 12-month follow-up period [126]. Additionally, a meta-analysis that included six randomized controlled trials involving 872 obese individuals without diabetes showed that the SGLT2 inhibitors, compared to the placebo, achieved statistically significant reductions in absolute changes in body weight (mean difference: -1.42 kg, 95 % CI: -1.70 to -1.14; p < 0.00001) and BMI (mean difference:  $-0.47 \text{ kg/m}^2$ , 95 % CI: -0.63to -0.31; p < 0.00001), although no significant changes were observed in WC [127].

5. Combination of SGLT2-inhibitors with GLP-1RAs

A limited body of research has thus far investigated the impact of concurrent administration of GLP-1RAs and SGLT2 inhibitors in the context of weight loss. When these agents are administered concomitantly, a reduction in body weight of approximately 4.5 kg is observed after a treatment period of 24 weeks. Notably, this weight

loss effect persists over one year, with a sustained reduction of approximately 5.7 kg, particularly evident among obese individuals without a diagnosis of diabetes [128].

A randomized, controlled single blind trial for 24 weeks compared the clinical efficacy of the GLP-1RA Exenatide extended-release 2 mg once weekly and SGLT2 inhibitors, Dapagliflozin 10 mg, in combination and alone, Dapagliflozin and metformin, and the weight loss medication Phentermine/topiramate on metabolic, anthropometric, and hormonal parameters in obese nondiabetic women (n-130) with the polycystic ovarian syndrome. Mean weight loss was 6.9% for those receiving Exenatide extended-release and dapagliflozin therapy and 8% for those receiving phentermine/topiramate extended-release compared with 1.5% for participants receiving only dapagliflozin and 1.7% for those on dapagliflozin and metformin [129].

- 6. Combination of SGLT2 inhibitors with other weight loss medications
  - 1. A combination therapy of canagliflozin with phentermine provided statistically superior weight loss from baseline versus placebo at week 26 (least squares mean difference -6.9% [95% CI -8.6 to -5.2]; p < 0.001) [130]. Phentermine is not approved for weight loss in India. This combination has not been researched subsequently.
  - A real world study from India showed that patients on more than 3 drugs (metformin, SGLT2 inhibitor and GLP-1 RA) along with Orlistat resulted in significant weight loss -4 kg over 6 months duration [131].

During weight loss, there is also loss of lean body weight. This may predispose individuals to the development of sarcopenia. Therefore, strategies to prevent or reduce loss of lean mass, like increase in protein intake and resistance exercises should be incorporated in the treatment regimen.

There are a number of recent drug studies in context of weight reduction. Readers should refer to these studies for details.

#### 8.6. Surgical management

Surgical management of obesity is needed in patients with obesity who have not been able to achieve significant and durable weight loss with non-surgical methods (diet, lifestyle changes and pharmacotherapy) (see Table 4). There has been an increase in the number of bariatric procedures by almost ten-fold over the last two decades with increased acceptance of this treatment by patients. In addition to significant weight loss, several metabolic benefits have also been demonstrated with this treatment. Hence, it is frequently also referred to as 'Bariatric and Metabolic Surgery'.

Over the last decade changes have been suggested by various agencies in the cutoffs of BMI at which bariatric surgery may be indicated, particularly for the Asian/South Asian populations. The American

Society for Metabolic and Bariatric Surgery (ASMBS) and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) guidelines recommend that metabolic and bariatric surgery (MBS) should be offered to individuals with a BMI  $\geq$ 27.5 kg/m² [132]. The American Diabetes Association clinical practice guidelines recommend that metabolic surgery should be offered to Asian American individuals with a BMI  $\geq$ 32.5 kg/m², and may be offered to Asian American individuals with a BMI  $\geq$ 27.5 kg/m², who are not able to achieve durable weight loss and control of hyperglycaemia using non-surgical treatment [133].

The Obesity and Metabolic Surgery Society of India (OSSI) recommend bariatric/metabolic surgery for patients with a BMI  $\geq 35~\text{kg/m}^2,$  with or without presence of any comorbidity. Individuals having two or more obesity-related comorbidities and a BMI of  $\geq 30~\text{kg/m}^2$  should be offered bariatric surgery as a treatment option. For patients with T2D, who are uncontrolled despite optimum medical treatment, bariatric surgery should be considered as a non-primary treatment option at a BMI  $\geq 27.5~\text{kg/m}^2$ . These guidelines also recommend that surgery should be considered in centrally obese patients (waist circumference  $\geq 90~\text{a.m.}$  in men and  $\geq 80~\text{cm}$  in women) with T2D and obesity related comorbidities [134].

Recommendations based on the Delphi survey. Staging of obesity, as enunciated previously, has not been incorporated in guidelines predominantly based on BMI cut-offs. Please note that points 2 and 3 below clearly indicate people with stage 2 obesity, while most of individuals included in point 1 would also have stage 2 obesity.

- 1. Bariatric surgery should be considered a treatment option for obese individuals with a BMI of  $\geq$ 35 kg/m<sup>2</sup> irrespective of the presence of any obesity related comorbidity.
- 2. Bariatric surgery should be considered a treatment option for obese individuals with a BMI of  $\geq 30 \text{ kg/m}^2$  with comorbid conditions and who do not achieve durable weight loss and improvement in comorbidities with optimum lifestyle and pharmacological management.
- 3. Bariatric surgery should be considered a treatment option for obese individuals with a BMI of ≥27.5 kg/m² with comorbid conditions and who do not achieve durable weight loss and control of hyperglycemia despite optimum lifestyle and pharmacological management.
- 4. Bariatric surgery should be a treatment of choice in individuals with obesity who are ≥18 and ≤ 65 years of age. In patients >65 years of age, bariatric surgery may be offered if the patient is medically fit.

#### 9. Clinical implications

The guidelines carry significant implications for clinical obesity management. In Stage 1 obesity, clinicians should focus on advising on diet, exercise, and lifestyle modifications to prevent obesity-related comorbid diseases and activity limitations. In contrast, Stage 2 obesity

**Table 4**Brief description of common surgical procedures for weight loss.

Name of Surgery	Description
Roux-en-Y gastric bypass (RYGB)	A small stomach pouch is created by dividing the stomach and attaching it to the small intestine. The capacity of the stomach is reduced leading to early satiety, reduced absorption and decreased release of Ghrelin and an increase in glucagon-like peptide-1 (GLP-1) and cholecystokinin (CCK).
Sleeve gastrectomy (SG)	The expected loss of excess weight is approximately 70 percent after two years of surgery [148]. In SG larger part of the stomach from the greater curvature side is removed and a tubular stomach is created. In comparison to RYGB, SG is technically easier to perform. It does not require multiple anastomoses. Apart from reduced food intake, several hormonal changes occur that include reduced level of Ghrelin and increase in the level of GLP-1 and peptide YY (PYY) levels promoting less hunger. Besides, insulin resistance is also improved leading to improved glycemic control. One can expect loss of 60 percent of excess
Biliopancreatic diversion with duodenal switch (BPD/DS)	body weight or 30 percent total body weight loss after two years of procedure [149].  BPD/DS causes weight loss by restrictive and malabsorptive mechanisms. Ghrelin appears to be suppressed after this procedure. At two years, approximately 70–80 percent of excess body weight or 40 percent total body weight loss can be expected due to this procedure [148].

warrants a more aggressive approach. Clinicians should implement intensive lifestyle changes and consider the potential inclusion of pharmacological therapy or weight loss surgical procedures to address the increased severity of adiposity and associated health risks. These tailored recommendations aim to enhance the effectiveness of clinical interventions based on the specific stage of obesity.

#### 10. Limitations and future directions

There are a number of well recognized problems with Delphi process [135]. The Delphi process for consensus building encounters challenges such as potential selection bias due to reliance on specific experts. Excluding non-respondents after the initial round may skew the sample, compromising the validity of consensus outcomes. The time-intensive nature of multiple rounds may lead to participant disengagement. Additionally, subjective criteria in expert selection may impact the diversity of perspectives, affecting the overall effectiveness of the Delphi process.

Future studies should explore morbidity and mortality trends through longitudinal cohort studies, shedding light on the long-term effects of new classification of obesity. Additionally, there is a need to assess the impact of lifestyle changes and pharmacotherapy across different stages of obesity to refine intervention strategies. Understanding the factors leading to the transition from Stage 1 to Stage 2 obesity is crucial for targeted prevention and management approaches.

#### 11. Conclusions

In our consensus, we successfully redefined obesity guidelines for Asian Indians by acknowledging the limitations of BMI and recognizing the correlation between adiposity and early-onset co-morbid diseases. Employing a Delphi process, the newly developed framework categorizes obesity into two stages based on adiposity, including multiple measures of obesity, accompanying co-morbidities, and performance of physical functions and daily activities. These guidelines are designed to be simple, applicable in all settings, easily understood, and implementable across diverse environments. Importantly, this redefinition enhances precision in identifying obesity through a pathophysiological approach, resetting management objectives, and aligns with global initiatives for a fresh perspective on understanding obesity among Asian Indians.

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#### Disclosure

Dr Anoop Misra is Editor-in-Chief, Dr Naval Vikram is Associate Editor and Dr Amrita Ghosh is Editorial Board member of the Journal and were authors of this article. They were excluded from the peer review process and editorial decisions for this article. Dr Anoop Misra is a member of Lancet Obesity Commission.

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# **Declaration of competing interest**

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Anoop Misra reports a relationship with USV, Astra Zeneca, Eli Lilly, Lupin, Boehringer Ingelheim, Janssen, Cipla, Astra Zeneca, Glenmark, Novo Nordisk, that includes: funding grants, speaking and lecture fees, and travel reimbursement. Amerta Ghosh reports a relationship with Astra Zeneca, Cipla, USV Pharmaceuticals, Lupin that includes: funding grants and speaking and lecture fees. Other lead authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.dsx.2024.102989.

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