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REVIEW ARTICLE

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Practical strategies to manage obesity in type 2 diabetes

Helena W. Rodbard MD[1] | Katharine Barnard-Kelly PhD[2,3,4] | Andreas F. H. Pfeiffer MD[5] | Carina Mauersberger PhD[6] | Oliver Schnell MD[6,7] | Francesco Giorgino MD[8]

[1]Endocrine and Metabolic Consultants, Rockville, Maryland, USA

[2]Southern Health NHS Foundation Trust, Southampton, UK

[3]BHR Limited, Portsmouth, UK

[4]Spotlight Consultations, Fareham, UK

[5]Department of Endocrinology, Diabetes and Nutrition, Campus Benjamin Franklin, Charité Universitätsmedizin Berlin, Berlin, Germany

[6]Sciarc GmbH, Baierbrunn, Germany

[7]Forschergruppe Diabetes eV at the Helmholtz Centre, Munich-Neuherberg, Germany

[8]Section of Internal Medicine, Endocrinology, Andrology and Metabolic Diseases, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari Aldo Moro, Bari, Italy

Correspondence
Helena W. Rodbard, Endocrine and Metabolic Consultants, Rockville, MD, USA.
Email: hrodbard@comcast.net

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Abstract

The rising phenomenon of obesity, a major risk factor for the development and progression of type 2 diabetes, is a complex and multifaceted issue that requires a comprehensive and coordinated approach to be prevented and managed. Although novel pharmacological measures to combat obesity have achieved unprecedented efficacy, a healthy lifestyle remains essential for the long-term success of any therapeutic intervention. However, this requires a high level of intrinsic motivation and continued behavioural changes in the face of multiple metabolic, psychological and environmental factors promoting weight gain, particularly in the context of type 2 diabetes. This review is intended to provide practical recommendations in the context of a holistic, person-centred approach to weight management, including evidence-based and expert recommendations addressing supportive communication, shared decision-making, as well as nutritional and pharmacological therapeutic approaches to achieve sustained weight loss.

KEYWORDS
behavioural interventions, communication, nutrition, obesity, person-centred approach, psychological barriers, type 2 diabetes

1 | INTRODUCTION

Type 2 diabetes (T2D) and obesity are global epidemics of increasing prevalence. While in 2021, 537 million people were estimated to have T2D, it is projected that the number will rise to 783 million by 2045.[1] Alarmingly, this also includes an increasing rate of T2D among children and adolescents,[2] while up to 44.7% of adults with T2D are estimated to be unaware of their disease.[1] Similarly, the global prevalence of obesity has more than tripled since 1975, and in 2020, more than 2.6 billion adults were overweight, of whom 988 million were obese.[3] Both T2D and obesity pose major public health challenges, as they are strongly interconnected and associated with an increased risk of multiple long-term medical complications and mortality.[4,5]

T2D and obesity are not independent phenomena. The increased release of saturated fatty acids, hormones, proinflammatory cytokines and other regulatory factors from adipose tissue promotes insulin resistance and β-cell dysfunction, making obesity the key modifiable risk factor for T2D.[6] Approximately 90% of T2D cases are linked to excess weight,[7] and the relative risk of developing T2D is approximately three-fold higher in overweight subjects and seven-fold higher in subjects with obesity compared with those with normal a body mass index (BMI).[8] It is evident that a high degree of weight loss (e.g. >20% vs. baseline) can lead to the restoration of β-cell function.[9] This has been impressively shown for a significant proportion of individuals with T2D and obesity following bariatric surgery, as well as intensive lifestyle interventions resulting in substantial weight loss.[10–12] Consequently, weight management has been established as a central pillar of T2D therapy by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD).[13]

Yet, as our arsenal of increasingly effective pharmacological options for weight management grows, it is important to acknowledge

that T2D and obesity not only affect physical health but also strongly impact an individual on a psychological and socio-environmental level.[14] These are major determinants of a person's external behaviour in terms of weight outcomes, but they are often downplayed or ignored in the treatment of people with T2D and obesity. Therefore, we here provide practical strategies to support weight management in people with T2D, focusing on person-centred communication, shared decision-making (SDM) and targeted nutritional recommendations.

2 | CLINICALLY TARGETABLE BARRIERS TO THE MANAGEMENT OF OBESITY WITH IMPLICATIONS FOR PEOPLE WITH TYPE 2 DIABETES

Overweight and obesity are the result of a long-term imbalance between energy input and expenditure.[15] However, while maintaining a balanced energy input-to-expenditure ratio is highly effective in preventing obesity, once obesity has ensued, its treatment is considerably more complicated, particularly in individuals with T2D.[16] Counterregulatory neurological and metabolic mechanisms, as well as genetic, psychological and socio-environmental influences, can be massive barriers to weight loss (Figure 1).

It is broadly recognized that socio-environmental influences are particularly powerful drivers of the current 'diabesity' pandemics, largely because of an increasingly sedentary lifestyle paralleled by the rise of a global food industry that makes highly palatable, energy-dense foods easily available. There is broad consensus that these developments are the main causes of the global increase in obesity prevalence over the past 50 years.[17] A direct influential factor is the better availability and affordability of fast food compared with healthy meals rich in fibre, vegetables and healthy fats in many high-income countries.[18] In contrast, physical activity is no longer a regular part of transportation and daily work routines for many people, and leisure entertainment is becoming increasingly dependent on information technology.[19] According to the World Health Organization, more than 80% of adolescents worldwide are physically inactive.[20] Based on UK Biobank findings, low physical activity is particularly prevalent in people with overweight or obesity and probably contributes to a greater risk of obesity.[21] There is also evidence for an important impact of neighbourhood surroundings on both obesity and diabetes risk,[22,23] which, apart from a higher density of unhealthy food restaurants, are influenced by a higher exposure to air pollution and poorer access to greenspace.[24,25]

Understanding these influences is vital for successfully managing obesity, both in people without and possibly even more in those with T2D. The rising global prevalence of obesity is a clear sign that health care providers (HCPs) and insurers in the past failed to recognize obesity as a disease that poses significant physical and mental health risks. Given the profound socio-environmental impact on the development of obesity worldwide, this underscores the need for immediate and greatly expanded disease prevention and education programmes. Public health efforts can be a powerful tool to address the increasing prevalence of both diseases, particularly regarding prevention. The long-term success of anti-smoking policies could be a model for strengthening educational campaigns, taxes and advertising bans on related products.[26] Although the success of many recent public health campaigns needs to be awaited, there is evidence that, for example, taxes on sugar-sweetened beverages can reduce their consumption[27] and restrictions on public advertising of products high in fat, salt and sugar may reduce obesity prevalence in the long term.[28,29]

While these approaches are based on broader health policy decisions, there is a growing toolkit for HCPs to address obesity in an affected individual in the clinical setting. As this review aims to provide a practical guide for HCPs, we therefore focus on those influences and factors that are directly approachable in clinical practice.

2.1 | Neurometabolic barriers

The gut-brain axis has been identified as a critical driver in the pathophysiology of obesity.[30] The hypothalamic-melanocortin pathway is the central regulator of energy homeostasis and appetite and consists of two main populations of opposing neurons: the anorexigenic pro-opiomelanocortin neurons and the orexigenic agouti-related peptide/neuropeptide Y neurons.[31] They either activate or inhibit melanocortin 4 receptors in the paraventricular nucleus of the hypothalamus, resulting in either appetite stimulation or inhibition. These brain neurons are strongly influenced by peripheral hormones, including anorexigenic cholecystokinin, glucagon-like peptide-1 (GLP-1),

FIGURE 1 Obesity is the result of a complex interplay of genetic, environmental, neurometabolic and psychological factors. The impact of these various factors on risk of obesity development can vary from person to person, but each of them can make successful and sustained weight loss significantly more difficult, particularly in people with type 2 diabetes.

peptide tyrosine tyrosine (PYY), orexigenic ghrelin and the adipocyte hormone leptin.[32] The hormones are secreted in the gastrointestinal tract in response to the composition and quantity of ingested nutrients, whereas leptin is constitutively released in proportion to the amount of adipose tissue.[31] This pathway appears to be severely disturbed in people with obesity, regarding GLP-1, PYY and ghrelin levels,[33] but also leptin, which is unable to exert its anorexigenic effect because of central leptin resistance, similar to insulin resistance in T2D.[34] Likewise, expression of gut hormone receptors at vagal afferents and other sites was found to be lower in individuals with obesity.[35] There is also growing evidence that the gut microbiome, which is strongly influenced by dietary composition, influences intestinal absorption of nutrients and feeding behaviour, for example, by secreting short-chain fatty acids and hormone-like structures that may directly affect the gut-brain axis.[36] Although further research is needed, it seems probable that individuals with overweight or obesity have an altered microbiome composition, which may also influence the success of weight-loss interventions.

Recent evidence also indicates the existence of altered responses to peptides regulating food intake and energy expenditure in the central nervous system, particularly the corticolimbic pathway, which may strongly influence or even override the homeostatic control mechanisms of the melanocortin pathway.[37] This brain system mediates the so-called hedonic response to eating, influencing eating behaviour beyond biological necessity. Hedonic eating is strongly related to the activation of dopaminergic reward systems but also multiple other brain regions throughout the corticolimbic system, involving endogenous opioids, cannabinoids and serotonin.[35,38] Hedonic eating is particularly triggered by highly palatable foods, that is, foods containing a high amount of sugar or fat.[39] In people with obesity, this reward response is significantly altered compared with normal-weight individuals and persists even in a satiated state.[40,41] Individuals with obesity also show hyperactivity of the visual and attentional control regions and lower activity of the cognitive control regions.[42] This finding was correlated with an impaired ability to respond to negative outcome learning, which has an important influence on the adjustment of behaviour towards optimal outcomes.[43,44] At the same time, the corticolimbic system is involved in the central insulin resistance observed in obesity, which may impair the beneficial effects of brain insulin action on body fat distribution as well as peripheral insulin effects such as suppression of hepatic glucose production and stimulation of glucose uptake.[45] As a result, people with obesity show a dysregulated response to food cues and are prone to maladaptive behaviours that increase the motivation to eat beyond biological needs, in addition to altered neurometabolic signalling. This can not only predict future weight gain[46,47] but also the efficacy of weight-loss interventions.[48]

Strikingly, when people with obesity engage in dietary restriction, this biological misalignment has a paradoxical effect: despite the overabundance of energy, it may trigger evolutionarily ingrained weight-protecting mechanisms associated with starvation. Thereby, circulating levels of ghrelin remain elevated and the release of anorexigenic peptides such as leptin, cholecystokinin and PYY is reduced, leading to a counter-regulatory increase in appetite and a reduced degree of satiety.[49] On the other hand, in addition to the lower energy requirements associated with the loss of body mass, energy expenditure is decreased because of a reduced resting metabolic rate.[50] This effect, known as adaptive thermogenesis, significantly decreases a person's calorie demand during weight-loss interventions.[51] Remarkably, several studies suggest that these effects may last for years, even beyond the weight-loss period.[49,52,53]

Individuals with both obesity and T2D are even less likely to respond to weight-loss interventions than those with obesity alone.[54,55] Beyond diabetes medications promoting weight gain, such as insulin, sulphonylureas and pioglitazone, and probably the higher genetic burden of these individuals, T2D-related effects on gut-brain signalling may play a role.[56] Indeed, parasympathetic activity is often reduced in people with T2D because of diabetic neuropathy,[57] which may also interfere with vagal feedback to the corticolimbic system. Moreover, T2D is associated with an increased risk of cognitive impairment, affecting learning and memory.[58,59] It is hypothesized, that this may be closely related to hyperglycaemia-induced neurotoxicity and inflammation.[60] In addition, insulin resistance was found to be correlated with food craving in people with obesity[61] and may potentiate obesity-associated effects on corticolimbic and hypothalamic control of eating. We should therefore be even more sensitive to the disease-related gut-brain abnormalities that people with both obesity and T2D need to overcome to lose weight, although further research on the underlying mechanisms is needed.

2.2 | Psychological barriers

Despite significant genetic and environmental influences on responsiveness to food cues, individual behaviour also has a fundamental impact on overweight and obesity risk. A recent study in humans confirmed that, in line with previous evidence from rodent studies, brain reward circuits can be rewired by repeated exposure to high-fat/high-sugar snacks and significantly decrease preference for low-fat food, even before weight gain.[62] Unhealthy food preferences can be ingrained very early in childhood and thus pave the way for harmful eating behaviours that may persist throughout life.[63] Habitually overeating and excess consumption of unhealthy foods not only psychologically reinforces this behaviour over the long term but also negatively influences the gut microbiome.[42] In contrast, low-fat diets are associated with reduced hedonic hunger in people with overweight or obesity and T2D.[64] Therefore, food choices not only have a direct metabolic impact but also affect eating behaviour in the future. This reveals a striking parallel to drug abuse, which similarly alters brain signalling and leads to consolidation of behaviour that reinforces its intake and induces cravings for the particular stimulus in its absence.[42,65,66]

Other effectors can also rewire central circuits and impact eating behaviour. Chronic stress is associated with an increased intake of unhealthy foods, even in children.[67,68] This may be because of down-regulated executive control mechanisms that increase reward-driven eating behaviour.[69] In people with obesity, responses to stress cues

were found to be strongly correlated with food cue-induced craving. Both stimuli led to an increased activation of corticolimbic and hypothalamic brain regions, which was not observed in lean individuals.[61] In the absence of hunger, stress-induced food cravings result in a higher caloric intake in individuals with a high BMI.[70] Consequently, psychological stress is associated with increased weight gain in individuals who are overweight.[71,72] Thus, for many people with obesity, eating appears to be a learned strategy for coping with stress. However, there is considerable heterogeneity in the management of stress and its effects on eating behaviour,[67] which may also be rooted in individual personality traits such as 'neuroticism' or 'impulsivity'.[73]

It is important to acknowledge that social stigmatization can also cause significant psychological distress in individuals with obesity.[74] This distress includes symptoms of depression and anxiety and is associated with self-isolation, which impedes effective weight management. One study found an up to 60% increased mortality in people who were affected by weight discrimination, independent of other physical and psychological risk factors.[75] Consequently, weight stigma, which includes not only perceived stigma but also self-stigma, is associated with weight gain and negative health outcomes rather than, as sometimes assumed, having a motivational function.[74] At the same time, compensatory eating, distress and neurological disorders, such as depression, can trigger neurological circuits that epigenetically promote excess weight gain.[76] Beyond the detrimental influence of weight stigma on mental wellbeing, obesity-associated low-grade inflammation and the intake of high-fat or high-sugar foods leading to neuroinflammation are reported to have a negative psychological impact.[77] Interestingly, there is evidence from a mouse study for a direct link between obesity-associated cell senescence and anxiety.[75] As a result, people with obesity were found to be 32% and 40% more likely to have depression and anxiety symptoms, respectively, than those with a normal weight.[78,79]

Likewise, people with diabetes experience stigmatization that is strongly related to psychological distress and associated with negative health outcomes.[80,81] Furthermore, people with T2D are more likely to experience weight stigma than the general population, suggesting that this population may be more affected by stigmatization than individuals with either T2D or obesity.[82] To conclude, neurometabolic and psychological influences significantly alter reactivity to food signals and food reward responses in people with obesity, leading to a higher psychological evaluation of food and an increased risk of overeating. This vicious cycle is also fuelled by public and self-stigmatization and resultant obesity- and diabetes-related psychological distress.

2.3 | Iatrogenic barriers and clinical inertia

In view of the increasing burden of preventable metabolic diseases such as obesity and T2D on our health care systems, it should be a primary goal of HCPs to (a) educate about the benefits of a healthy lifestyle, and (b) provide individuals with effective strategies to actively manage overweight or obesity. Unfortunately, structural problems, including lack of time and resources, as well as gaps in HCP education, are major barriers to this approach.[83,84] While acknowledging that behavioural changes towards a healthy lifestyle are a fundamental pillar of weight management, many HCPs do not feel confident in providing nutritional counselling.[85] Educational gaps may also lead to the common misconception that individuals can fully control their body weight through lifestyle interventions without external assistance, disregarding the multifaceted aetiology and pathophysiology of obesity.[86] There is also some lack of willingness to address these barriers in primary care settings, as many primary care physicians see their role in weight management as one of awareness raising and signposting rather than proactive prevention or weight monitoring.[87]

At the same time, HCPs are not immune from weight-related stigma, as people with obesity often face negative judgements from HCPs.[88] The combination of implicit and explicit negative obesity attitudes can undermine person-centred communication, which is linked to a significantly higher risk of non-adherence, lower trust and health care avoidance, and ultimately poorer weight-loss and mental health outcomes.[89,90] When people with T2D experience weight stigmatization from their physicians, they display greater diabetes-specific distress and reduced diabetes-specific self-care behaviours.[91] This can affect the quality of communication between providers and patients and may negatively influence treatment decisions.[92,93] As a result, people with obesity often do not receive the medical care they need to delay or prevent complications such as T2D.[94,95] This may particularly affect younger people and first-degree relatives of individuals with T2D, despite their high potential for prevention.[96] Furthermore, the importance of weight management for people with T2D has long been underrecognized. Despite increasing awareness of recent clinical guidelines, there is considerable therapeutic inertia in the treatment of T2D in general,[16] jeopardizing both the achievement of glycaemic and weight goals.[97]

Likewise, there are important iatrogenic barriers to weight management. These are based in large part on the frequent selection of inappropriate or ineffective medications for people with overweight and obesity. According to the National Health and Nutrition Examination Survey 2017-2018, one in five adults in the United States has been prescribed at least one obesogenic medication, most commonly β-blockers, insulin or oral antidiabetic agents such as sulphonylureas and pioglitazone.[98] Beyond its anabolic effect, peripheral insulin may also lead to defensive eating in many people with diabetes because of a fear of hypoglycaemia.[99] In addition, many psychotropic medications, particularly amitriptyline, citalopram and mirtazapine, have negative effects on body weight.[100] This is a very important yet under-discussed issue, given the elevated risk of depression in people with obesity.

3 | PRACTICAL STRATEGIES FOR WEIGHT MANAGEMENT IN TYPE 2 DIABETES

As reported, many people with obesity and T2D are strongly tied to their disease by powerful neurometabolic as well as psychological mechanisms, which they can hardly control in the given obesogenic environment. These forces must be taken into account when initiating

weight-loss interventions. The steps to take to overcome these barriers will be discussed in the following sections.

3.1 | Psychological approaches

3.1.1 | Strategies for successful communication

Supportive communication is the first step for HCPs to build rapport, trust and motivation with their patients. Influential diabetes associations have devoted their own statement publications to the important aspect of language in diabetes care, and these concepts likewise apply to obesity communication.[101,102] Accordingly, respectful and non-judgemental language that is empathic, empowering, understanding and collaborative is key when talking to individuals with obesity and T2D.[103] This includes avoiding stigmatizing words such as 'fat', 'obese' or 'diabetic' where possible and instead using neutral terms such as 'weight' or 'BMI'.[104] Thus, a good way to begin a conversation about weight management is to first ask permission to discuss the person's weight and allow the person to open up or defer this discussion to another time, rather than confronting him or her directly with this sensitive topic, which can provoke defensiveness.[105,106]

The second, closely related principle of supportive communication is to focus on the person, not the disease. The conversation should be conducted with empathy and an intention to understand the individual's lived experience, which is essential to providing targeted care.[107] Fisher et al. developed a framework for a motivational conversation to promote behaviour changes in people with diabetes.[108] It requires the clinician to (a) shift his or her interactive mindset to an empathic, collaborative, eye-level conversation, and (b) reorient from the role of an information provider to an active listener and collaborator. Subsequently, with this reshaped mindset, clinicians can build a relationship with the individual. This relationship enables them to provide person-centred behavioural and educational support in the next step.[108] Another aspect of a person-centred approach is to put the person before the disease linguistically. For example, speaking of a 'person with obesity' instead of an 'obese person' is less judgemental.[109] At the same time, it is essential to respect personal preferences, as many different perceptions exist among people with obesity regarding obesity-related issues.[110] Table 1 provides examples of motivational interviewing questions.

TABLE 1 Examples of how to integrate supportive and motivational communication when talking to a person with obesity.

1. How could you personally benefit from losing weight?
2. Is there anything holding you back from living a healthier life?
3. What kind of support would be most helpful for you to lose weight?
4. What do you like about healthy eating? What does it mean to you?
5. Is there a type of physical activity that you enjoy or have enjoyed in the past?

Note: Adapted from Durrer Schutz et al.[105]

3.1.2 | Shared decision-making: collaboratively individualizing weight management

Therapeutic decisions should take into account a person's individual circumstances, needs and preferences. This includes two principles that go hand in hand: SDM as a process of involving the individual directly in treatment decisions and personalizing treatment to tailor it optimally to the person for whom it is intended. Both aspects have gained increasing attention in recent clinical guidelines, including the 2024 Standards of Care in Diabetes.[111]

As a first step, it is essential to obtain the comprehensive medical history of an individual, involving active listening. Thereby, HCPs should not only understand potential causes and risk factors of weight gain but also personal preferences, strengths and needs, as well as individual psychological and environmental barriers to weight loss. This information should then be used to develop collaboratively the individual weight-loss goals and interventions with the affected person.[111] Individuals who are more actively engaged in managing their health care have better health outcomes, and providing them with decision aids as part of SDM improves their knowledge and satisfaction.[112] In the setting of diabetes prevention, incorporating face-to-face SDM into usual care was shown to increase significantly the participation in an intensive lifestyle change programme and/or metformin uptake in people with overweight or obesity and prediabetes.[113] Depending on the person's individual situation, it may also be a helpful approach to involve family members or caretakers in this step.

The collaborative deliberation model is another practical example for a person-centred, SDM-based approach in obesity management.[114] It is based on an empathic interpersonal conversation between the HCP and a person with obesity, in a process of collaboratively changing the person's perspectives and beliefs to create a common ground for jointly making optimized health care decisions. SDM is also an important part of the 5A's approach to obesity management, originally developed for smoking cessation.[115] Accordingly, HCPs should (a) ask the person to discuss their weight (see also Section 3.1.1), (b) assess individual risk, current behaviour and readiness for change, (c) advise on appropriate interventions, (d) jointly agree on an individualized goal and intervention plan, and (e) assist with its implementation, including regular follow-up.[116]

Individual weight management also involves individualized assessment of health risks. There is sufficient evidence that surrogate markers such as the waist-to-hip ratio[117] reflecting excess visceral fat or the Edmonton Obesity Staging System[118] can better predict weight-related health risks.[119] The latter not only considers the impact of obesity on comorbidities but also on physical and psychological aspects of health. Accordingly, it is recommended that these additional tools be incorporated into the medical assessment of obesity to obtain a better estimate of individual risk beyond BMI.[111] This approach is highly clinically relevant, as people who appear to be of normal weight by BMI can have an unfavourable accumulation of lipids in the liver with deleterious health consequences.[120] Indeed, those individuals can greatly benefit from weight-loss interventions and even achieve T2D remission.[121]

3.1.3 | Establishing positive health behaviours

A person's behaviour is the result of a complex interplay of multiple different influences, including environmental, social, educational and emotional aspects. Although external factors can be strong drivers, it is always a person's perception of reality, that is, their beliefs and emotions, that shapes motivation and behaviour (Figure 2).[122] Emotions and personal beliefs can be much more powerful drivers of behaviour than hard facts. HCPs should reflect on the emotions that their own behaviour may evoke in the recipient and try to channel them in a positive direction. The power of positive emotions was nicely shown in a cohort study that investigated weight-loss outcomes based on either positive, neutral, or negative emotion-evoking language. The presentation of weight loss as a positive opportunity was associated with increased agreement to and attendance in a weight-loss programme and with improved weight loss in participants with obesity.[123] Related to that, helping the person recognize their own reasons and goals for weight change and thereby evoke associated emotions may be more effective than external pressure, which can cause the person to shut down.[105]

In addition, avoiding sources of negative emotion, such as stigmatizing language, and instead using a respectful and supportive communication style will help maintain a positive relationship and access to the individual. HCPs should strive to create an atmosphere of trust in which the person feels taken seriously. This includes active listening on the part of the HCP, so the individual should be given sufficient time to explain his or her point of view. No equipment should block eye contact and comfortable, non-restrictive chairs and the availability of appropriately sized equipment, such as scales and blood pressure cuffs, are also important means to avoid the feeling of being stigmatized.[124]

It is important to give the individual the feeling that he or she has the ability to achieve an envisaged weight-loss goal.[105,122] HCPs can help a person gain this confidence by breaking down a large, overwhelming goal into several small steps that are realistic and achievable in a person's everyday life. An already moderate weight loss of 3%-7% can improve glycaemia and intermediate cardiovascular risk factors, and every additional kilogram lost is a step towards better outcomes.[111] For example, for children, an effective low-threshold intervention may be extending the duration of family mealtimes. An average of just 10 more minutes can measurably improve a child's diet and eating behaviour.[125]

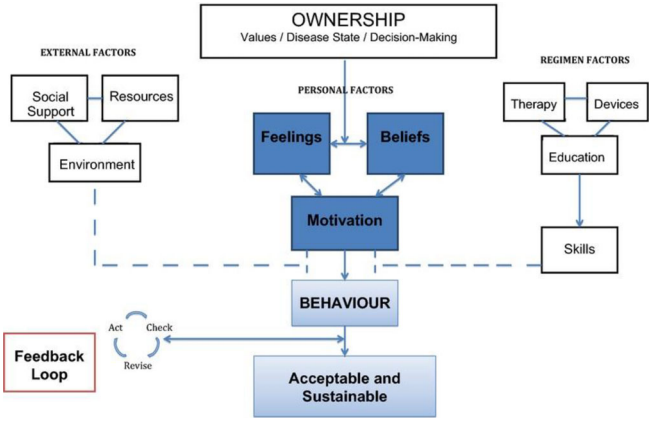

FIGURE 2 Behaviour is impacted by a combination of environmental, clinical and intrinsic factors, unique to each individual. Reused with permission from Barnard et al.[122]

Not only emotions can positively influence a person's behaviour, but also their ingrained beliefs. Increasing cognitive awareness of a largely unconsciously regulated harmful behaviour, for example, pathologically increased food cue reactivity, might be an effective way of shaping a person's perception, beliefs and, thereby, behaviour. As shown from neuroimaging studies, greater recruitment of cognitive control regions during food signal processing is associated with anti-obesogenic behaviour and improved weight loss.[48,126] However, it is still a matter of research to find effective ways to trigger cognitive awareness in the clinical context. Mindful eating approaches, which gained increased interest in recent years, were shown to reduce emotional eating, but thus far, without providing evidence for increasing weight loss.[127,128] In addition, several effective behaviour change techniques implicate increasing cognitive awareness and self-efficacy in weight-loss interventions. Self-monitoring of weight or food intake is firmly associated with sustained weight-loss effects and should therefore be strongly encouraged,[129,130] particularly in a weight-loss maintenance phase, at weekly intervals.[111] Other important drivers of behavioural change that should be supported or implemented by HCPs are action planning, providing clear instructions and showing interventions when possible.[131]

Finally, the positive health outcomes associated with weight-loss interventions can also have a strong impact on a person's motivation to continue. This was reported by participants in the previously cited DiRECT trial. Observing rapid weight-loss outcomes and improved glycaemic control, as well as experiencing enhanced physical and psychological well-being, were important aspects that helped participants sustain their motivation to adhere to the rigorous interventions. As a result, despite the high demand for personal effort, participants reported that adhering to the diet was less difficult than they anticipated.[132]

3.1.4 | Sustainable results through continuous and interdisciplinary support

Professional support and supervision are crucial to the success of weight-loss interventions. People with overweight or obesity and T2D who participated in a lifestyle intervention program rated a high level of professional supervision as the primary driver of weight loss.[133] HCP support and external liability appear to be key elements to sustain a person's motivation to lose weight, which is also reflected in the success of an intervention.[134,135] According to a meta-analysis of primary care-based behavioural weight management interventions, more frequent contacts between patients and HCPs were correlated with greater weight loss.[101] Accordingly, a high frequency of counselling (≥14-16 sessions in 6 months) is recommended in the guidelines.[111,136]

Nevertheless, it is crucial to provide continuous support to individuals not only during initial weight-loss interventions but also during the weight-loss maintenance phase.[137] Preventing weight regain after a successful weight-loss intervention is one of the greatest challenges in weight management, as it often marks a transition from clearly defined behavioural rules and professional supervision to independent meal and exercise planning, which can be overwhelming for an individual.[138] In addition, the neurometabolic circuits that regulate appetite may still be imbalanced.[139] Therefore, it is crucial to support people at this stage with continued monitoring and care, through either face-to-face or virtual contacts.[140] A meta-analysis estimated the effect of extended care on long-term maintenance of weight loss to be 3.2 kg over an assessment period of 18 months.[141] In the recent Maintain Study, a 12-month weight maintenance intervention involving nutritional counselling and physical activity, the mean BMI was significantly reduced and remained reduced at 48 months, although improvements in insulin sensitivity did not persist beyond the intervention period in most participants.[142]

Although basic medical supervision is usually involved in weight-loss interventions,[101] it does not appear to make a difference whether support is provided by medical or non-medical professionals.[101] The most effective techniques to improve behavioural changes in people with T2D involved 'supervised physical activity', 'group sessions', 'contact with an exercise physiologist' and 'contact with an exercise physiologist and a dietitian'.[131] In the DiRECT trial, ongoing support by research dietitians was rated as a key element of the study's success.[143] Besides, multidisciplinary care, involving pharmacists, nurses, diabetes educators, nutritionists and psychologists, was found to be one of the most effective approaches to overcome clinical inertia on glycaemic control in people with T2D.[144] Therefore, it is recommended to involve a multidisciplinary team with an individually tailored structure in the treatment plan to utilize the relevant expertise of different HCPs for the long-term weight management of an individual.

In addition, community resources and digital health tools can also support people with obesity and/or T2D in a weight-loss or weight-loss maintenance programme to overcome barriers such as distance, time and costs. Support from family and friends and from other participants in weight-loss interventions can have a significant impact on weight outcomes.[138] It may also be worthwhile to prescribe commercial weight-loss programmes with peer-reviewed efficacy and safety.[136,145] Although currently based on a few short-term trials, there is also evidence for improved efficacy of weight loss by means of eHealth weight management interventions, including web-, smartphone- or telephone-based support for people with overweight or obesity.[146,147]

In conclusion, continuous support from a variety of sources is vital for preventing weight regain after weight-loss interventions. Individuals should be empowered to adopt healthy eating behaviours in the long run and to receive regular feedback and encouragement from their health care team.

3.2 | Interventional recommendations

3.2.1 | Nutritional interventions

A healthy diet can protect against several chronic diseases, including T2D, cardiovascular diseases and cancer,[148] and serves as the foundation of obesity management in T2D. Although the primary endpoint of reducing cardiovascular events in people with overweight or obesity and T2D was not met in the Look AHEAD study, it showed that long-term weight loss is achievable by a moderate energy restriction diet and physical activity in people with obesity and T2D.[149]

Total diet replacement (TDR) interventions are among the most effective dietary approaches to achieving substantial weight loss,[150] involving replacing all or most of the usual food intake with formula products that provide a low-energy, nutritionally complete diet (e.g. 840 kcal/day for 12-20 weeks). The most prominent example of successful TDR use is the DiRECT study. Here, 46% of participants who had been diagnosed with T2D within the previous 6 years achieved T2D remission within 1 year. Strikingly, of those who lost at least 15 kg of body weight, 86% achieved diabetes remission.[10] Similar results come from the DIADEM-I study that enrolled people in Quatar with a shorter history of T2D, reporting diabetes remission in 61% of people after 12 months.[12] In both studies, the TDR intervention was followed by structured food reintroduction and weight-loss maintenance support. Together, these TDR-based interventions resulted in a 54% diabetes remission rate at 12 months and were thereby significantly more effective than programmes that only involved partial meal replacements or a Mediterranean diet.[150] By analogy with T2D remission, resolution of prediabetes can be achieved by even less stringent lifestyle interventional weight-loss programmes and should be considered a prevention approach for people with obesity.[151] Very low-calorie diet interventions were shown to significantly improve insulin sensitivity and β-cell function and reduce hedonic hunger to a similar magnitude as bariatric surgery, at least in the short term.[152,153] However, it is important to consider the potential risks of such strict dietary interventions, including electrolyte abnormalities and cardiac arrhythmias. Thus, very low-calorie diets should only be recommended for selected individuals for a short period of time, and accompanied by close medical monitoring.[111]

An important lesson learned from the POUNDS LOST study is that calorie reduction is the primary driver of weight loss, regardless of the macronutrient composition.[154,155] More evidence comes from a WHO-commissioned meta-analysis on the effect of dietary sugars on body weight. The study could attribute the significant weight loss achieved by a reduction in the intake of added sugars to a decrease in total energy intake rather than the reduction in carbohydrates per se.[156] Although carbohydrate restriction had a direct beneficial effect on glycaemic control in people with T2D, this effect was neither correlated with significant weight loss nor sustained over the long term.[157] Likewise, an umbrella review of current evidence confirmed that overall, low-carbohydrate diets were no better for weight loss than higher-carbohydrate/low-fat diets after 12 months in people with T2D.[150] There was also no significant difference in the reduction

of food cravings between high-protein and isocaloric higher-carbohydrate diets in people with T2D.[64] Another 12-month weight-loss diet study directly compared a high-quality low-fat diet versus a high-quality low-carbohydrate diet in people with overweight or obesity without T2D and did not find a significant difference in weight change, independent of genotype or baseline insulin secretion.[158] Likewise, compared with dietary interventions of similar calorie restriction, evidence from randomized controlled trials does not support the superiority of low-fat diets over other dietary interventions for long-term weight loss.[159] Nevertheless, there is evidence from the DiOGENES Study that in the weight maintenance phase, weight regain may be more effectively prevented by a high-protein, low-glycaemic index diet, particularly in participants with pre-diabetes.[160]

The quality of macronutrients, such as carbohydrates (starchy vs. non-starchy vegetables) and fats (saturated vs. unsaturated), should also be taken into account in nutritional counselling. For example, fibre or micronutrient content may have additional health effects, including on the microbiome, low-density lipoprotein cholesterol levels, and satiety, which influences how well individuals can maintain a certain caloric limit.[158,161] There is increasing research interest in the field of precision nutrition because of the impact of individual genetic factors on the development of obesity and T2D. Although still in its infancy, this research holds promise to better tailor dietary recommendations to individual needs, taking into account an individual's phenotypic, behavioural, genetic and microbiome-based information.[162] In addition, intermittent fasting diets have become very popular in the past few years, as they can significantly promote weight loss. Even though time-restricted eating has no additional benefit over calorie restriction alone,[163] it may be a helpful alternative to conventional dieting approaches.[164,165] Combining intensive calorie restriction with intermittent fasting may also be an efficient approach to achieving diabetes remission.[166,167]

In conclusion, TDR interventions, provided by trained health professionals and followed by long-term support for weight-loss maintenance, are the most effective approaches to achieving significant weight loss and are recommended to induce remission of T2D in carefully selected individuals.[168] Guidelines also recommend that nutritional interventions target a daily caloric deficit of approximately 500-750 kcal.[111] According to current evidence, healthy diets to support the maintenance of weight loss include moderately low carbohydrate intake, high fibre, healthy non-saturated fats, and high vegetable and fruit intake with moderate enrichment of protein. Nevertheless, dietary recommendations should take into account personal preferences and nutritional needs rather than rigid macronutrient ratios.[111] Individuals should receive nutritional and physical activity-based support or get access to long-term weight maintenance programmes following successful weight-loss interventions, when possible.

3.2.2 | Physical activity

Physical activity is another pillar of weight management. It not only positively influences energy balance, but may also be associated with positive changes in food preferences and improved appetite control.[56] A microbiome-dependent gut-brain pathway was recently identified in mice that mediates dopamine release during exercise and thereby influences exercise performance. The gut-brain axis may therefore not only regulate eating but also exercise behaviour.[169]

While caloric restriction is the main driver of weight loss, physical activity can play a crucial role in weight-loss maintenance.[129,170] For instance, without a change in diet, a coached and supervised aerobic exercise intervention during 12 months in people with obesity was recently shown to significantly lower T2D risk sustainably over 10 years of follow-up.[171] This effect was achieved both with vigorous and moderate exercise. In clinical practice, several types of exercise are suitable for people with obesity and T2D, such as swimming, walking, yoga, or dancing. However, it is crucial to consider an individual's capabilities and limitations, particularly for those with comorbidities. Combined exercise approaches, integrating moderate to vigorous aerobic (at least 150 min per week, regularly distributed over several days) and resistance exercise (two to three sessions per week), have been shown to significantly improve glycaemic control and insulin sensitivity and positively influence weight loss. They are therefore recommended by guidelines for people with T2D.[172,173] For weight-loss maintenance, 200-300 min of regular physical activity per week is a recommended goal.[111,174]

There is also evidence that people with T2D may benefit more from exercise performed after a meal than immediately before a meal, and from exercise performed later in the day than in the morning.[175,176] Nevertheless, the overriding premise should always be that an individual engages in physical exercise, rather than how or when. Therefore, people should be encouraged to find and engage in an activity that they enjoy. Group activities with other people with similar medical conditions or at the workplace can facilitate access to physical exercise and integrate it into everyday life.[131,177]

3.2.3 | Integrating pharmacological and other options for weight management in type 2 diabetes

It is undeniable that behavioural approaches, which incorporate several of the aforementioned critical elements, are effective in achieving significant and sustained weight loss over several years. Yet, it is also evident that only a small percentage of individuals are able to independently achieve weight loss and maintain it beyond the intervention period.[178,179] The use of pharmaceutical weight-loss options is an approach that has been pursued for many years to fill these gaps. However, only with the availability of GLP-1 receptor agonists (GLP-1 RA) in recent years, has the pharmacological approach revealed its true potential. GLP-1 RAs have been developed to mimic the effects of the incretin hormone GLP-1, with its multiple effects not only on the pancreas and gut but also on the brain. Thereby, GLP-1 RA are associated with multiple beneficial functions: increased β-cell insulin secretion and synthesis, enhanced β-cell survival, decreased glucagon secretion and gluconeogenesis, improved peripheral insulin sensitivity and glucose uptake (indirect effects), slowed gastric emptying and

gastrointestinal motility, and dampened food-related reward behaviour and food intake.[32] Semaglutide, the GLP-1 RA with the highest effect on weight loss,[180,181] was associated with an estimated mean body weight loss of 6.2% over placebo in people with obesity and T2D.[182] In the recent SELECT trial, semaglutide was also associated with a 20% reduction in major adverse cardiovascular events during a mean follow-up period of 40 months.[183] It is therefore a favourable option for people with obesity and cardiovascular disease. The most common side effects of GLP-1 RA are gastrointestinal-related, including nausea, vomiting and diarrhoea, with mostly mild to moderate severity.[182,184]

The dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA tirzepatide is based on the positive effects of GLP-1, but with additional GIP-mediated benefits on adipose tissue regarding triglyceride and glucose uptake.[185] Like semaglutide and liraglutide, tirzepatide is approved for glycaemic control in people with T2D and was recently approved for weight loss in people with obesity or a BMI of ≥27 kg/m^2 in the presence of weight-related comorbidities. In the SURMOUNT-2 trial, conducted in people with obesity and T2D, tirzepatide resulted in an estimated treatment difference of −11.6% in mean body weight change versus placebo after 72 weeks of treatment with the maximum approved dose, with adverse effects similar to those seen with GLP-1 RA.[186] According to a recent network meta-analysis, tirzepatide may be more effective than high-dose GLP-1 RA in controlling HbA1c and reducing body weight in people with T2D.[187] There are several additional medications currently in the pipeline, including orforglipron (a non-peptide oral GLP-1 RA),[188] cagrilintide (an amylin analogue) in combination with semaglutide (CagriSema),[189] retatrutide (a tri-agonist of GLP-1, GIP and glucagon receptors)[190] and survodutide (a dual glucagon/GLP-1 RA).[191]

Importantly, while currently available studies show that continuous treatment with GLP-1 RA and GIP/GLP-1 RA can prevent weight regain over 104 and 88 weeks, respectively, withdrawal of the drugs was associated with a substantial weight increase.[192-194] Of note, many of the trials investigating the efficacy and safety of the weight loss medications listed in Table 2 involved lifestyle interventions as an adjunct to treatment. In STEP 3, it was shown that the effect of a more intensive behavioural intervention achieved even higher mean weight-loss results of 16.0% versus 5.7% with semaglutide in people with obesity in the absence of T2D.[215] Similarly, the weight-loss potential of tirzepatide was further enhanced when combined with an intensive lifestyle intervention, resulting in an impressive mean total weight change of −24.3% compared with −4.5% with placebo.[195] This resembles the 1-year weight loss achieved with a sleeve gastrectomy.[196] Therefore, accompanying lifestyle modifications (low-calorie diet, physical activity, professional support and monitoring) can significantly enhance the efficacy of these pharmacological interventions and can thus provide a fundamental basis for successful and sustained treatment effects.

Before semaglutide became available for obesity management, approved drugs (rows 1-4 in body of Table 2) typically resulted in single-digit percentages of body weight loss.[32] Each of the drugs in Table 2 can have a significant beneficial effect on weight loss in people with obesity after individual benefit-risk assessment and in adjunct to behavioural interventions. In addition to potential side effects, the cost of these drugs is also a factor, which is particularly relevant for GLP-1 RA and GIP/GLP-1 RA. However, in people with obesity and T2D, it is an obvious option to exploit the superior potential of semaglutide and tirzepatide to achieve both profound glycaemic and weight benefits.[13] Furthermore, other GLP-1 RA, followed by sodium-glucose cotransporter 2 inhibitors, metformin and amylin mimetics, have beneficial effects on body weight and should be considered when selecting glucose-lowering therapies. In contrast, sulphonylureas, meglitinides and pioglitazone, but also insulin, are associated with weight gain and their use should therefore be carefully reassessed.[111]

Beyond diabetes medications, other drugs are also associated with clinically relevant weight gain (see Section 2.3). Therefore, the use of concomitant medications that negatively influence body

TABLE 2 Overview of current FDA and EMA approved pharmaceutical options for long-term weight management.

INN	Pharmacological class	Maximal dose/ administration	Mean reduction in body weight from baseline (%), placebo/treatment
Orlistat[a,b]	Lipase inhibitor	120 mg, 3× daily, oral	1.2/3.8 (with T2D)[197] 6.1/10.2 (without T2D)[198]
Phentermine/topiramate ER[a]	Sympathomimetic/anticonvulsant	15 mg/92 mg, 1× daily, oral	2.7/9.4 (with T2D)[199] 1.2/9.8 (with ≥2 comorbidities)[200]
Naltrexone SR/bupropion SR[a,b]	Opioid receptor antagonist/dopamine and noradrenaline reuptake inhibitor	32 mg/360 mg, 2× daily, oral	1.8/5.0 (with T2D)[201] 1.3/6.1 (without T2D)[202]
Liraglutide[a,b]	GLP-1 RA	3.0 mg, 1× daily, s.c. injection	2.0/6.0 (with T2D)[203] 2.6/8.0 (without T2D)[204]
Semaglutide[a,b]	GLP-1 RA	2.4 mg, 1× weekly, s.c. injection	3.4/9.6 (with T2D)[182] 2.4/14.9 (without T2D)[184]
Tirzepatide[a,b]	Dual GIP/GLP-1 RA	15 mg, 1× weekly, s.c. injection	3.2/14.7 (with T2D)[186] 3.1/20.9 (without T2D)[205]

Abbreviations: ER, extended release; s.c., subcutaneous; SR, sustained release.
Note: [a]FDA- and [b]EMA-approved pharmaceutical options for long-term weight management. Adapted from Blüher et al.[16] and Müller et al.[32]

weight, including some antipsychotic and antidepressant medications and β-blockers, should be minimized to the extent possible.[111]

For the treatment of rare monogenic forms of obesity caused by a deficiency of the leptin receptor, proprotein convertase subtilisin/kexin type 1 (PCSK1) or pro-opiomelanocortin, setmelanotide, a selective melanocortin 4 receptor agonist, is now available as a targeted therapy option.[206] People with the very rare congenital leptin deficiency may also benefit substantially from leptin replacement. However, these approaches are only effective in people with genetic evidence of the above forms of obesity.[207]

To conclude, pharmacological options, particularly GIP/GLP-1 RA and GLP-1 RA, have recently become a central pillar of weight management in people with obesity and T2D. Particularly in this population, potent options that not only robustly reduce body weight but also improve glycaemic control provide a great opportunity to facilitate weight-loss and weight-loss maintenance. Nevertheless, these medications should not be regarded as an alternative but as an adjunct to medical nutrition therapy, physical activity and psychological interventions (Figure 3).[106]

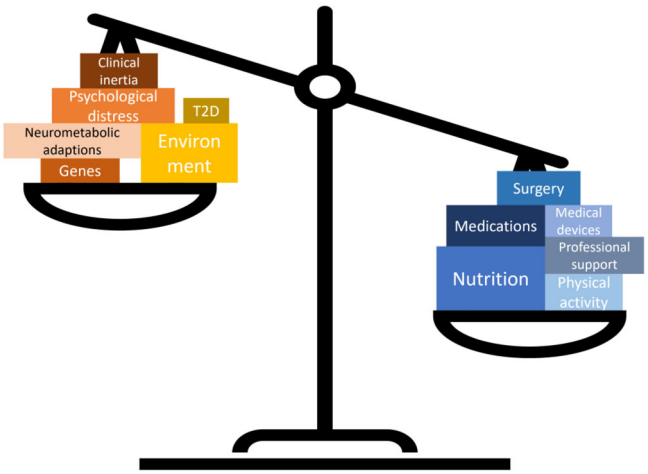

FIGURE 3 Factors influencing body weight in people with obesity and type 2 diabetes (T2D).

Beyond pharmacological treatment options, weight-loss devices are an option to decrease food intake in people by restricting gastric capacity. These include swallowable hydrogels, which can result in a mean weight loss over placebo of <5%,[208,209] and endoscopic bariatric procedures, such as intragastric balloons, which are filled with air or fluid and need to be removed after several months. The expected weight loss, depending on the device and accompanying lifestyle interventions, lies between <5% and >10%.[210-212] Intolerance is very common, leading to the early removal of the device. Associated serious adverse events include gastric outlet obstruction, gastric ulceration and gastric perforation.[212]

Finally, bariatric surgery may be considered an advanced treatment option for individuals who do not respond to conservative weight-loss interventions, despite comprehensive support. Bariatric surgery, particularly Roux-en-Y gastric bypass or sleeve gastrectomy, is a very powerful tool for achieving substantial mean weight loss of up to 30% within 1 year and significantly improving T2D outcomes.[196] However, this invasive intervention should be based on an individualized risk assessment as well as personal motivation and psychological status. It should only be performed in experienced centres (for more information, see Di Lorenzo et al.[213] and Eisenberg et al.[214]).

4 | CONCLUSIONS

There is a pressing need to improve obesity management in clinical practice. It is a most welcome development that drug options are now a highly effective tool in the management of obesity, alongside lifestyle interventions on the one hand and bariatric surgery on the other. However, no one approach can solve the problem of obesity in our society alone, given the complex and influential forces involved in the aetiology of this disease. There are several barriers to obesity management, rooted in the genes, environment, metabolic pathways and

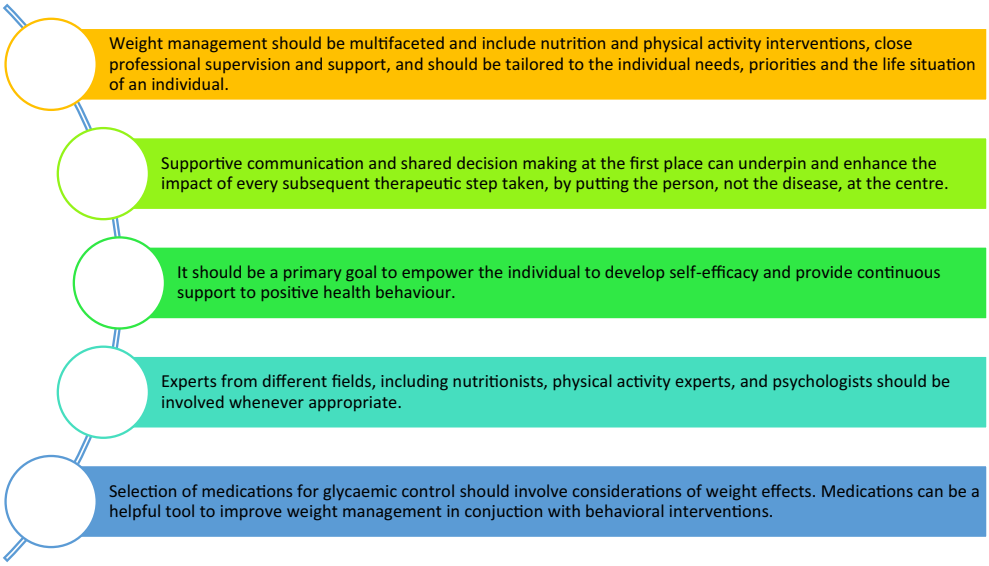

FIGURE 4 Overview of practical strategies and recommendations for obesity management in people with type 2 diabetes.

psychosocial networks of affected individuals, which can counteract the efficacy of treatment approaches. Therefore, we aimed at reviewing and discussing multifactorial practical strategies to target each of these barriers in an evidence-based and up-to-date approach that involves psychological, nutritional, physical activity-based and pharmacological strategies. Individual strategies may not be appropriate for every individual with obesity, so it is important to find the best personalized approach(es) for each person. Early intervention is key to achieving successful weight loss in people with T2D and to preventing fatal complications and premature mortality.

However, it is also clear that only sustained societal behavioural efforts aimed at preventing obesity in the first place will be effective in tackling the problem at its root. Prevention remains the best medicine, and it should be of paramount importance to protect children from this otherwise lifelong battle against obesity and T2D. From a public health perspective, it is also critical to provide HCPs with comprehensive training as well as the time and resources to best address this overarching challenge already in the prevention phase.

In conclusion, weight management in T2D should be understood as a holistic approach of nutritional and lifestyle behavioural changes, psychology and pharmacology, tailored to the individual person (Figure 4).

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DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article, as no new datasets were generated or analyzed in the preparation of this review.

ORCID

Helena W. Rodbard https://orcid.org/0000-0002-6187-8445
Carina Mauersberger https://orcid.org/0000-0003-4241-8854
Oliver Schnell https://orcid.org/0000-0003-4968-2367
Francesco Giorgino https://orcid.org/0000-0001-7372-2678

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