

# In the Era of Budgetary Constraints, Cost-Effective Management of Metabolic Syndrome, Type 2 Diabetes, and Obesity is Essential

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## Abstract

The incidence and prevalence of type 2 diabetes, obesity, and metabolic syndrome have escalated in recent years, with skyrocketing associated management costs. Insufficient mass education on importance of healthy diet, adequate physical activities, and the lack of preventative measures are the most common reasons for this. In most countries, departments of health carry the financial burden. However, in western, industrialized countries, the cost is shared in varied proportions by the governments and insurance companies. Although the aforementioned entities pay these bills, costs eventually trickle down to consumers and taxpayers. The current approach of standardized care, a one-treatment-fits-all model, is inefficient in achieving the desired goal of preventing long-term complications and adds to the cost of managing these common diseases. A cause-driven, individualized approach may seem time consuming but likely to be the most cost-effective in the long run in controlling these diseases and containing costs through the prevention of long-term complications.

**Keywords:** Type 2 diabetes; Obesity; Metabolic syndrome

**Abbreviations:** T2D: Type 2 Diabetes; CVD: Cardiovascular Disease; NASH: Non-Alcoholic Steatohepatitis; BMI: Body Mass Index

## Introduction

Obesity is more than simply a thermodynamic, genetic, epigenetic, or a metabolic problem of handling calories. It is also an inflammatory and neurohormonal disease and a behavioral disorder that is significantly influenced by environment. These ailments in various combinations lead to derangements of metabolism and affect the energy balance in favor of caloric retention and thus weight gain. Based on underlying vulnerabilities and genetics, this leads in an accumulation of visceral fat, resulting in insulin resistance, the development of

type 2 diabetes (T2D), and serious long-term complications.

### **Obesity is not only a lifestyle entity but also a disease**

From an energy balance standpoint, obesity results from an imbalance of energy intake and energy expenditure. Weight gain is influenced by excessive caloric intake; less-than-appropriate physical activity; socio-economic status; social, cultural, and behavioral factors; and other factors [1]. For many, the stigma associated with obesity hinders the successful outcome of treatments [2]. Like many other diseases, obesity is a disorder, but it is a complex disease with certain characteristics (Table 1) [3-13].

**Table 1:** Characterization of obesity as a disease.

Ailment	Characteristics	Reference
Obesity has a causes	Caloric imbalance, availability and abundance of food, and consumption of food with low nutritional value and high-caloric density	[3-5]
Obesity has an identifiable pathology	Adipocyte-mediated excessive production of inflammatory cytokines and hormones Mitochondrial abnormalities Genetic susceptibility	[6-8]
Obesity has complex pathophysiology	An environmentally and psychologically inducible dysregulation of appetite, low activity levels, body fat distribution, psychological issues, and deranged body-weight-controlling mechanisms	[9-11]
Therapies to treat obesity are available	Can be treated with anti-obesity medication or by bariatric surgery	[12,13]

### **Not all obese patients are vulnerable to developing metabolic complications**

There are groups of patients who are more vulnerable than others to becoming obese and experiencing T2D. It is easier and more cost-effective to prevent a person from becoming overweight or obese than to have a person lose weight. Similarly, although almost all obese people eventually experience complications related to weight and body-structure, such as osteoarthritis, snoring, sleep apnea, and hypersomnolence, not all obese people experience serious metabolic consequences [14-16].

Obesity and T2D have become major public health issues [17-19], threatening the well-being of millions of people worldwide in industrialized and emerging economies [20]. In many, these two disorders co-exist and are important public health issues with major health and socioeconomic consequences that require serious attention from all stakeholders. Many of the complications in obesity and T2D are caused by insulin resistance and the consequent metabolic syndrome [17,21]. Thus, the focus of treatment should be on reducing these indices in parallel with healthful lifestyle changes [14]. By doing so, one would directly or indirectly reduce the severity of a number of associated diseases and disorders, including hypertension, glucose intolerance, and hyperlipidemia.

### **Causes of obesity and susceptibilities to the development of complications**

In addition to simple energy imbalance, there are secondary causes leading to weight gain, including aging [22], the menopausal period in women [23], institutionalization [15,24,25], psychiatric disorders that require treatment with anti-psychotic medications [26-29], and medications that are known to cause weight gain [30-32]. Genome-wide association studies have revealed several genes that are associated with weight gain [33,34]. However, this knowledge has not been translated into new drug development.

In those who are genetically susceptible, exposure to an adversarial environment (e.g., smoking, an excessive intake of alcohol, lack of physical activities, excessive intake of energy), intake of energy over and above what is expended, favors weight gain, the development of glucose intolerance, and the subsequent development of T2D and complications [35].

### **Identifying those who are predisposed to developing complications is essential**

However, not all obese patients experience complications such as T2D, cardiovascular disease (CVD), and strokes [36,37]. Nevertheless, in many countries managing diabetes has become one of the most expensive healthcare expenditures. To cost-effectively treat diabetes, it is necessary to identify those who are vulnerable to developing the disorder as early as possible and intervene aggressively to prevent future complications [14].

Such a focused treatment approach not only would curtail costs dramatically by preventing long-term serious complications but also would improve the quality and duration of lives of millions of people.

### **Blanket approach would not help all patients**

The use of unmitigated approach to obesity, including treating those who are unlikely to experience metabolic complication or waiting until complications develop (the complications-driven approach to obesity) before initiating interventions, is not cost-effective. The currently available biochemical methods are not specific enough to distinguish those who are at risk from those who are unlikely to experience obesity-associated metabolic complications [38,39].

Without such distinction, millions of obese people will be subjected to expensive therapies with little benefit. In obese persons, the worse health risks are associated with accumulation of intra-abdominal/visceral fat [40]. Visceral obesity is linked with insulin resistance and metabolic syndrome [41,42], and patients with excess visceral adipose tissue have the worst metabolic profiles and highest risks for complications [43,44]. In addition to multiple metabolic abnormalities, many of those who are obese may have mitochondria dysfunction, which plays a major role in energy metabolism and handling [45]. Insulin resistance positively correlates with visceral fat content [38,46], and visceral adiposity is a common denominator in persons who are at high risk for experiencing complications [14,47]. Nevertheless, expensive testing to quantify visceral fat and lipid fractionations and other specialized testing to identify those who are at high risk of CVD are no better than the measurements of waist circumferences and simple lipid profiles and thus are not cost-effective.

### **Reducing visceral adiposity (key site of generation of inflammatory cytokines) is an essential part of therapy**

Excess visceral adiposity is positively correlated not only with insulin resistance and T2D but also with certain cancers and untimely deaths [48]. An effective strategy is needed for the early identification of cause(s) of obesity in individual persons and preventing individuals from becoming overweight. Identification of causes and risk factors in a given patient is important so that healthcare workers can meaningfully intervene with individualized care for their patients who are obese and/or have T2D. Effective treatments will minimize long-term complications, improve patient quality of life, and substantially decrease the cost of management of complications [14].

Adipose tissue can be considered as an endocrine organ; it produces mostly inflammatory cytokines and certain hormones that activate a pathological, metabolic vicious cycle [49]. Compared with subcutaneous fat cells, visceral adipocytes are not only inflammatory but also released excessive amounts

of fat (hyperlipolytic) state and are less sensitive to insulin, [47,50]. The liver receives high concentrations of inflammatory cytokines and free and fatty acids through the portal vein from the visceral (omental) fat [51,52].

This enhances hepatic inflammation, the formation of fatty liver and non-alcoholic steatohepatitis (NASH) [53,54]. It also impairs hepatic uptake of insulin, exacerbates hyperinsulinemia, and increases gluconeogenesis [55], the excessive production of apolipoprotein B-containing triglyceride-rich lipoproteins. This metabolic derangement causes hyperinsulinemia, hyperglycemia, hypertriglyceridemia, and increased apolipoprotein B, leading to glucotoxicity and lipotoxicity in target tissues [21,47,56,57].

### Identification of visceral adiposity using anthropometry

The use of anthropometric measurements, such as the waist circumference or waist-to-hip ratio, and basic blood lipid profiles are as effective as using expensive imaging and biochemical assignments in identifying those with metabolic risks and monitoring their conditions [58,59] and are available at a fraction of the cost. Although the body mass index (BMI) alone is somewhat useful (even though is not specific) in white Caucasians for identifying those who are at risk for CVD [60], BMI is not a useful tool in many other ethnic groups, including Asians, Hispanics, and Pacific Islanders [15,61].

Consequently, screening and diagnostic efforts are hampered by the lack of cost-effective, specific, and sensitive markers (and tests) for identifying those who are vulnerable to developing complications [14]. Nevertheless, the sensitivity of BMI is improved when it is used in combination with an anthropometric measurements related to visceral adiposity such as abdominal girth. Expensive imaging techniques are available to quantify the visceral fat content, but none of those are cost-effective.

### Identifying causes leading to weight gain is essential in metabolically at-risk individuals

In addition to the underlying genetic susceptibilities, the causes and risk factors for excess fat accumulation, the development of T2D, and obesity vary from person to person [38,62]. Thus, to be effective in the management of obesity and T2D, treatment plans need be personalized; one plan will not work for everyone [58]. Although such personalization of care may be an added burden for healthcare workers, it would markedly reduce management costs.

To achieve this, one needs to identify root causes for weight gain and T2D in a given patient [45]. Such identifications of a specific cause in those with high risks for future complications would make interventions and treatments cost-effective. Nevertheless, the treatment strategies need to be acceptable and affordable, and patients must be able to adhere to the treatment plan.

Because there is a strong relationship between insulin resistance and cardiovascular risk, it is logical to categorize those with insulin resistance and other risk factors as a “metabolically at risk” group. This would aid unraveling those who have higher risks for CVD from those who do not [63,64]. In addition to metabolic-related complications, obesity also causes many other diseases and disorders [65], such as hypertension, sleep apnea, osteoarthritis, depression, and CVD [38,39,46,62]. Thus, the key focuses of cost-effective management of obesity need to include the prevention of obesity, minimizing associated complications, and focusing management on the prevention of complications [66].

### Importance of a personalized approach to the treatment of obesity

The fundamental approach to the prevention and treatment of obesity and T2D is through lifestyle changes: healthy eating and increased physical activity. However, because of the lack of adherence, the overall effectiveness of lifestyle changes or therapies for weight loss is limited. Nevertheless, the set goals can be achieved successfully through encouraging and closely monitoring motivated persons. The latter needs to be a part of comprehensive management of obesity and T2D. Positive lifestyle changes are essential for all patients who are obese or have T2D for longer-term weight maintenance, including obese persons who opt to use pharmacotherapy or bariatric surgery [45,67]. The combination of sustainable lifestyle changes and pharmacotherapy (or bariatric surgery) would maintain a patient's weight at a new, lower physiological set point and minimize the long-term complications [68].

Data from lifestyle intervention studies have demonstrated efficacy in reducing insulin resistance, CVD, heart failure, stroke, diabetes, and all-cause mortality [69,70], but compliance is essential [21]. Patients need guidance on healthy lifestyles and eating habits, educating them on causes leading to weight gain. They need assistance to adhere to a weight-reducing diet and an acceptable physical activity program (30 to 45 minutes per day; e.g., fast walking). Medications and bariatric surgery can be effective but should be reserved for those who are obese or overweight with complications and those who have failed to have a response to lifestyle changes. Even when medications or bariatric surgery are offered, it is essential to adhere to improve lifestyles on a long-term basis [71].

### Discussion

The pro-inflammatory chemicals and cytokines released from visceral adipose tissues, in particular, lead to a metabolically negative vicious cycle. Obesity, T2D, and metabolic syndrome are complex processes that involve an imbalance of chemicals and hormones released from the enteric, cerebral, and neuro-intestinal systems [21]. In most patients, bypassing the stomach and duodenum via bariatric surgery improves insulin resistance, metabolic syndrome, and T2D [41,72]. Therefore, abdominal

fat *per se* may not be the sole cause of metabolic abnormalities [73,74].

Those who are overweight or obese with excess visceral fat and who engage in smoking and drinking excessive amounts of alcohol, are sedentary, and who have an adverse CVD family history are at the highest risk for insulin resistance, T2D, CVD, and premature death [40,75]. In high-risk populations, the effective intervention of reducing initial weight by approximately 10% is known to significantly improve well-being, morbidities, and personal productivity [41,66]. However, tackling T2D, obesity, and metabolic syndrome requires prioritization of resources combined with cause-driven, cost-effective approaches.

Categorizing obesity as a disease is not intended to lead to over diagnosing or over treating with expensive prescription drugs or subjecting patients to bariatric surgery. Instead, it should encourage more people to seek medical assistance, behavioral help, and advice. Rather than relying too much on BMI or weight, clinicians should give greater attention to a patient's physical fitness, family history, and cause and risk factors of obesity. Motivating messages for weight loss that focus on making healthy behavioral changes without reference to body weight or obesity are more effective in reaching goals.

Nevertheless, the adherence to weight reduction interventions is suboptimal. This is in part due to ineffective peer and family support; unavailability of affordable, healthy, nutritious foods; costs; and the stigma of obesity. Modest weight loss can produce major health benefits and reduce future complications. Although weight-loss medications may decrease excess weight, no study has demonstrated the cost-effectiveness of weight-loss medications.

The approach of treating patients aggressively after they experience complications is counter-productive and both socially and economically unwise. Thus, a "cause-driven approach" is superior to a "complication-driven approach" in minimizing negative outcomes and curtailing costs. Moreover, preventative approaches are more effective in health maintenance and enhancing productivity and cost less. When a person has abdominal obesity, hypertension, hyperlipidemia, sleep apnea, NASH, vascular disease, and so forth, aggressively treating one or two of these components would have little effect on long-term outcomes. Each cause leading to weight gain in a given person needs to be tackled effectively to reduce its negative impact on metabolism and overall health.

### Conclusions

In addition to reasonable weight-reduction programs, controlling obesity-associated complications requires coordinated, individualized, cause-driven approaches. Understanding the cause of obesity in patients, improving adherence to healthier lifestyles via education and trust, using affordable and sustainable treatment plans, and individualizing

treatment strategies would greatly facilitate achieving set goals, lead to successful outcomes, and reduce disease-management costs. However, uncommitted lifestyle changes are unlikely to improve the condition of most patients.

There are no shortcuts or magic pills for losing weight or improving metabolic abnormalities of T2D; most people require intensive attention to a healthy lifestyle to achieve meaningful goals. Meanwhile, attention should be given to broader policy implementations related to environmental and population approaches for managing obesity. Considering the escalating incidences of obesity and T2D, it is essential to develop overall cost-effective strategies to tackle these two disorders, not only to prevent associated complications but also to curtail skyrocketing costs and decrease burdens to stakeholders.

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