

ABSTRACT

The prevalence of obesity is increasing. It is associated with conditions such as type 2 diabetes mellitus, hypertension, dyslipidaemia and non-alcoholic fatty liver disease and together with its co-morbidities, obesity has become a fast-growing public health concern and health burden. However, weight loss has been shown to reduce the development and improve these conditions. This paper looks at the epidemiology, obesity-related co-morbidities, in particular pre-diabetes, and the various strategies that can be implemented to prevent and treat this looming problem.

Keywords: Obesity; Weight loss; Pre-diabetes; Co-morbidities; Prevent

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INTRODUCTION

With overweight and obesity increasingly contributing to greater healthcare burden and costs especially through its related co-morbidities, the primary healthcare professional plays a pivotal role in its management, including obesity prevention starting even before the start of life (i.e. pre-pregnancy). In this article, we aim to provide a basic overview on the epidemiology, co-morbidities and clinical management of obesity, with a special focus on prevention.

Epidemiology

Obesity is a chronic disease that is increasing in prevalence worldwide. Between 1980 and 2008, mean body mass index (BMI) worldwide increased by 0.4 kg/m² per decade for men and 0.5 kg/m² per decade for women. It was estimated that in 2008, there were 1.46 billion adults worldwide that were overweight; of these 502 million were obese¹. A worrisome

trend is a similar rise in obesity prevalence in childhood and adolescence. Not only is this associated with severe obesity in adulthood², increased BMI in childhood leads to development of hypertension, dyslipidemia, and type 2 diabetes mellitus (T2DM) and increases risk of premature death^{3,4}.

Locally, 10.8% or 1 in 9 Singaporeans were found to be obese in 2010 compared to a prevalence of 6.9% a short 6 years ago. This increasing trend is expected to continue and represents a serious public health concern. Even more worrying would be the observation that for a given BMI, Asians, including Singaporeans, generally have a higher percentage of body fat than do Caucasians. It has also been shown that Asians tend to have an elevated risk of T2DM, hypertension, and dyslipidemia at a relatively low level of BMI^{5,6,7}. In view of this, the BMI cut-off levels for Singaporeans have been revised such that a BMI 23 kg/m² or higher marks a moderate increase in risk while a BMI 27.5 kg/m² or more represents high risk for diabetes and cardiovascular diseases⁸.

Co-Morbidities of Obesity

Since the time of Hippocrates, it has been known that excess weight is associated with disease and premature mortality. In the last 3 decades, many studies worldwide have observed and confirmed undoubtedly that an increased BMI is associated with higher all-cause mortality, coronary heart disease (CHD), and type 2 diabetes (T2DM), with the risk deflection starting as low as BMI 20 kg/m² in some series. Regardless of baseline BMI, a weight gain of ≥ 10 kg in adulthood is also associated with increased mortality, CHD and T2DM⁹.

The co-morbidities of excess weight can be broadly categorized into those which are indirectly associated with obesity through metabolic effects (largely mediated through insulin resistance) and those which are direct effects of excess weight (both mechanical and psychosocial). Table 1 illustrates these associations and the relative risks associated.

Strategies for Management of Overweight and Obesity

The natural evolution of obesity starts from weight gain, progressing to development of obesity-related conditions in susceptible individuals, through to increased mortality and morbidity as a complication of these obesity-related diseases in the long-term. Hence, strategies in the management of overweight and obesity should involve prevention of obesity (weight gain prevention) and start earlier than childhood, targeting women in the reproductive age group even before they conceive. Ultimately, the goal on the whole is to reduce the incidence of obesity-related conditions and their sequelae (including increased financial burden).

TAN HONG CHANG, Associate Consultant, Department of Endocrinology, Singapore General Hospital, Obesity and Metabolic Unit, LIFE Centre, Singapore General Hospital

SONALI GANGULY, Consultant, Department of Endocrinology, Singapore General Hospital, Obesity and Metabolic Unit, LIFE Centre, Singapore General Hospital, Assistant Professor, Duke-NUS Graduate Medical School Singapore

THAM KWANG WEI, Consultant, Department of Endocrinology, Singapore General Hospital, Director, Obesity and Metabolic Unit, LIFE Centre, Singapore General Hospital

Table 1. Conditions associated with Obesity.⁹⁻¹²

Associated with Metabolic Effects	Directly Associated with Excess Weight	Relative Risk (RR)
Cancer (breast, endometrial, colon)	Musculoskeletal problems (eg. back pain)	Slightly increased 1-2
Subfertility / Polycystic Ovarian Syndrome	Varicose veins / Cellulitis / Stress incontinence	
Coronary heart disease	Osteoarthritis	Moderately increased 2-3
Stroke	Hernia	
Gout / Hyperuricemia		
T2DM	Obstructive sleep apnoea / Daytime somnolence	Highly increased >3
Hypertension	Asthma	
Dyslipidemia	Social isolation and depression	
Non-alcoholic fatty liver disease (NAFLD)		

a) Prevention: Starting from the Beginning

There is evidence supporting the nutritional programming of obesity, and other chronic diseases, in foetal and early life. The implication is that both under-nutrition and over-nutrition — associated with gestational diabetes, maternal obesity and excessive weight gain — increase the infant’s risk of later fatness and the risk of developing obesity, diabetes, hypertension, and cardiovascular disease in adulthood^{13,14,15}. Children born to mothers with diabetes are at a significantly increased risk of developing IGT even in the pre-adolescent age group¹⁵.

In the US, the Institute of Medicine in the US has made recommendations for weight gain during pregnancy according to a woman’s prepregnancy weight, to avoid too little or excessive weight gain which then predisposes to the problems mentioned above¹⁶. Physicians should perhaps seize the opportune time to counsel women of reproductive age group to attain a healthy weight not just prior but during pregnancy to “safeguard” the next generation.

b) Preventing Obesity-Related Co-Morbidities: Pre-DM as a Classic Example

A modest weight loss of 5-10% from baseline weight has been associated with reduction in the risk of developing obesity-related conditions. This is best illustrated by the reduction in the progression of impaired fasting glycemia (IFG) and/or impaired glucose tolerance (IGT) to T2DM in several diabetes prevention studies^{17,18,19}.

Of all the obesity-related co-morbidities, T2DM displays the greatest risk associated with obesity. In the US Nurses’ Health Study, more than 100,000 healthy nurses were followed up prospectively for 14 years to examine the effects of weight and T2DM development⁹. Even within the normal BMI range of 22.0 – 22.9 kg/m², there is already a 3-fold increase in diabetes compared to women who were <22.0 kg/m². This risk increases to 40-fold in women with BMI ≥ 31.0 kg/m². Weight gain in adulthood was strongly associated with risk for diabetes. Compared with women who gained < 5kg, those who gained between 5.0 – 7.9kg had a nearly 2-fold increase, while those who gained ≥ 20kg had a significantly increased relative

risk of 12.3. A similar trend was observed in men though the risk increase started at a higher BMI of ≥ 24 kg/m² and not was marked as in women¹⁰.

The natural history of development of T2DM in susceptible individuals traverses from completely normal glucose levels through IFG and/or IGT to finally the clinical entity of T2DM. Pre-diabetes broadly refers to the intermediate stage between normoglycemia to overt diabetes.

Pre-diabetes is not only a significant risk factor for progression to T2DM but is also considered a risk factor for macrovascular disease. In the Diabetes Prevention Program (DPP), patients in the standard arm with both IFG and IGT had an annual progression to T2DM of 11%¹⁷. In addition, multiple prospective studies have demonstrated a linear increase in cardiovascular events with 2-hour glucose following an OGTT at levels well below the diagnostic cut-off for T2DM²⁰. On the other hand, the salutary benefits of weight loss are best illustrated in individuals afflicted with pre-diabetes and T2DM.

Dietary intervention, exercise and pharmacologic therapy are interventions that have been used to prevent T2DM and reduce the risk of progression from pre-diabetes to overt T2DM. More than 80% of cases of T2DM can be attributed to obesity and it is therefore not surprising that diabetes prevention correlated the most with weight loss (16% reduction for every kg weight loss)²¹.

Intensive lifestyle intervention confers the greatest benefit in the prevention of T2DM. This was illustrated in the DPP where a lifestyle-modification program with the goals of at least a 7% weight loss through a reduced fat intake (to <25% of total calories) and at least 150 minutes per week of moderate physical activity proved to be more effective in reducing the incidence of T2DM than a standardized lifestyle program (which adopted the National Cholesterol Education Program Step 1 diet and 150 minutes a week of an activity but with less intense monitoring) with metformin therapy or placebo (58% vs. 31%)²². Similar findings were found in the Da Qing Diabetes Prevention Study where diet and/or exercise interventions led to a significant decrease in the incidence of

T2DM in IGT subjects¹⁸. This effect is seen as early as 3½ years after intervention and is durable to as long as 10-20 years, even after weight regain has occurred in many^{23,24}.

With lifestyle modification as the mainstay of treatment, metformin can be considered in those at highest risk, such as those with multiple risk factors, especially if they demonstrate a progression of hyperglycemia²⁵. Locally, the Pre-diabetes Intervention Program (PIP) initiated by the Health Promotion Board, under the Nurse Educator Program (NEP) aims to empower individuals with the knowledge and skills to adopt lifestyle changes (healthy living and regular physical activity) to reduce the risk of developing type 2 diabetes.

c) Treating Obesity in the Treatment of Established Obesity-Related Co-morbidities

When obesity-related conditions have developed, the main focus should be to reduce the severity and control these co-morbidities through lifestyle modification in weight reduction, with the aim to reduce mortality risks.

In the currently ongoing Look AHEAD trial, supported by the NHLBI, the long-term effects of modest weight loss (of 7%) with intensive lifestyle intervention (ILI), similar to that of DPP, on cardiovascular mortality and morbidity in about 5,000 overweight T2DM subjects will be examined. At one year, the mean weight loss in the ILI arm was 8.6% (versus 0.7% in conventional arm) with a reduction in HbA1c from 7.3% to 6.6%²⁶. 264 of these patients were further examined for the effects of weight loss on obstructive sleep apnoea (OSA). After 1 year, the ILI group had lost 10.1 kg more than the conventional group and the number who had total remission of their OSA was 3 times more in the ILI than those in the conventional group. Moreover, the subjects in the conventional arm saw a worsening of their OSA²⁷.

Bariatric surgery can result in remission of T2DM in up to 95% of patients 2 years after surgery²⁸. In the Swedish Obesity Study, which prospectively examined the effects of more drastic weight loss through bariatric surgery compared with conventional treatment, there was a dramatic reduction on overall mortality (by 40%), particularly that related to cancer, coronary artery disease (by 62%) and T2DM (by 62%, 64% and 90% respectively)^{29,30}.

d) Strategies for Weight Loss

The fundamentals in the treatment of obesity lie in creating an overall energy deficit. Ideally, the treatment paradigm should involve combined modalities of dietary restriction with a balanced diet, increased physical activity (PA) with reduction in sedentary time and behavioural modification with or without pharmacotherapy.

In general, a reduced calorie diet (creating a 500 kcal/day deficit) without increased activity will result in a 0.5kg/week weight loss. Coupling this with exercise will hence create a greater energy deficit and reap the benefits of exercise on cardiovascular health like a reduction in blood pressure³¹.

In the last 2 decades, there have been a slew of diets manipulating the macronutrient marketed to tackle the rising issue of obesity, be it the low-carbohydrate diet or the very-low fat diet. Several studies have shown that the low-carbohydrate diets result in greater weight loss at 6 months but not 12 months compared to the restricted fat diets, with greater improvements in the HDL-cholesterol and triglyceride levels. However, these are generally not sustainable and there are no long-term studies to prove its safety and efficacy in the long-term^{32,33,34,35}.

A more practical approach is a reduced calorie intake using the Mediterranean-type diets. These include a healthy balanced diet, incorporating an increased intake of unsaturated fatty acids, and have been shown to improve cardiovascular risk factors in the metabolic syndrome³⁶. Meal replacements used within a low calorie diet have been proven to be practical, effective in losing weight and also safe and sustainable in the long-term (by to 10 years)³⁷. It is vital to emphasize that the diet adopted needs to be balanced not just in its macronutrients but also meeting the patient's daily requirements for minerals, vitamins and fiber. Locally, the Health Promotion has published a comprehensive guide on healthy eating for all age-groups as well as an online platform with the nutritional information of our local foods. These resources are very helpful both for the primary care physicians to educate their patients and for the public³⁸.

Bariatric surgery should be considered in carefully selected eligible individuals, particularly those with very high BMI, multiple obesity-related co-morbidities not well-controlled with conventional medical treatment and in whom weight loss was successful but with regain. Regardless of whether meal replacements, pharmacotherapy or bariatric surgery is used, the fundamentals of caloric restriction, increased PA and behavioral modification should be reinforced and adopted as these will enhance the weight loss and facilitate weight maintenance^{39,40}.

However, before embarking on any form of treatment, it is important to assess each individual to determine how aggressive treatment should be, based on individual motivation level and readiness for change. In the patient who is not ready for weight loss, maintaining weight and preventing further weight gain is a reasonable goal and may mean reduction in long-term metabolic risks⁴¹. However, those in whom there are established obesity-related co-morbidities, should be encouraged and given appropriate help to increase their motivation and readiness to effect these lifestyle changes. As obesity is a chronic disease like hypertension and T2DM, different strategies may need to be adopted at different stages especially if weight regain occurs. For an example, someone with initial weight loss with dietary modification and exercise but not at targeted goal yet may be started on meal replacements.

Due to the lack of effective pharmacotherapy available that can be used long-term at present, it is important for both the healthcare team and the patient to recognize from the outset that some form of lifestyle change is necessary⁴². Though ideally

this should involve both reduced caloric intake and increased PA, greater emphasis on either one may be necessary as some individuals may prefer - or respond better to - one approach over the other. So varying amounts of either modality need to be tailored according to each patient's needs and/or past experience of which modality worked better.

The Role of the Family Physician

The family physician plays a pivotal role in the care of the patient as he/she walks through the various stages of life with him/her. The interaction with the patient over the years provides an understanding of the patient and what strategies will work best for the patient, while not neglecting the role of the patient's family in supporting him through the weight loss treatment. The goals of treatment should be agreed upon by both the physician and the patient and regularly monitored. Different strategies will often need to be used over the years, providing the best result and care for the patient.

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LEARNING POINTS

- **Obesity has become a fast-growing public health concern and health burden.**
 - **Weight loss has been shown to reduce the development of several obesity related conditions – namely, type 2 diabetes mellitus, hypertension, dyslipidemia, and non-alcoholic fatty liver disease and their co-morbidities.**
 - **Asians tend to have an elevated risk of obesity related conditions at a relatively low level of BMI – and hence the BMI cut-off levels for normal risk is set at 23 kg/m².**
 - **There is also evidence supporting nutritional programming of obesity and other chronic diseases in foetal and early life and this should continue through the whole life span.**
 - **The weight control strategy involves combined modalities of dietary restriction with a balanced diet, increased physical activity (PA), reduction in sedentary time, with or without pharmacotherapy.**
 - **Bariatric surgery should be considered in carefully selected eligible individuals – very high BMI, multiple obesity-related co-morbidities not well controlled with conventional medical treatment and in whom weight loss was successful but with regain.**
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