

A proposed algorithm for the prevention of obesity-related disability

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ABSTRACT: Obesity is commonly characterized as a condition where body mass index (BMI) has reached 30 kg/m². However, this is only one stage in the progress of a disease whose basic characteristic is the accumulation of excess body fat in adult life. Obesity is the most prevalent disease worldwide. It is also increasing more rapidly than any other disease in the world and it is responsible for more pathology, distress and disability than any other disease in the world. Stroke is just one of many medical consequences of obesity, but it is an important one because it is potentially, and often it actually is, an irreversible development. Hemorrhagic stroke is primarily mediated by hypertension that is increased by obesity, thrombotic strokes are mediated by the same processes causing coronary heart disease and most importantly dyslipidemia, impaired glucose tolerance or diabetes, hypertension, smoking and chronic inflammation. These, with the exception of smoking, are all metabolic syndrome characteristics, presumably a genetic condition whose phenotypic expression is revealed by weight gain. Many features of metabolic syndrome develop before BMI reaches 30 kg/m². The management of obesity is all to do with prevention. This includes primary prevention of weight gain, the secondary prevention of further weight gain and in those who are already overweight, and the prevention of complications. In the background, there is a theoretical possibility or primordial prevention of the whole disease process by manipulation of an obesogenic environment. Evidence from very large clinical trials has now demonstrated major health benefits from a 5-10% weight loss and a limitation in regaining weight over 4 yrs, with a 58% reduction in cases of new diabetes. Drug trials using orlistat and sibutramine have shown benefits for all cardiovascular risk factors (this can be limited for blood pressure (BP) reduction in the use of sibutramine). A 4-yr randomized clinical trial of orlistat has shown an additional 30% reduction in diabetes from a 3 kg augmentation of weight loss. The literature indicates that modest weight loss can be achieved by many routes bringing major medical benefits. Patients need to be aware of the risks and be sufficiently aware of these benefits to motivate their maintenance of a weight loss of 5-10 kg. (RINPE 2004; 22: 237-42)

KEY WORDS: Obesity, Disability, Prevention, Metabolic syndrome

PAROLE CHIAVE: Obesità, Disabilità, Prevenzione, Sindrome metabolica

INTRODUCTION

Chronic disability comes in many forms – physical, mental and social. Obesity causes, and aggravates, all of these types of disability. Often they occur together. Obesity is seldom the only cause of a medical problem causing disability, but its contribution may be very large, and either unrecognised or ignored. Because obesity is, in principle, totally preventable, the opportunity for prevention of disability is very great from quite modest interven-

tions. Disability becomes more frequent, more troublesome, and more costly to care services with increasing age. Overweight and obesity conspire with age. As they grow older, people with obesity grow fatter, disabilities proliferate and many are simply ascribed to aging. Doctors often treat each symptomatic problem as it presents, without tackling the root causes. Sustained approaches to prevention are largely lacking, partly because healthcare professionals have in the past misunderstood the nature of obesity and have set unrealistic targets.

Evidence-based guidelines are now in place and are being informed by more focussed recent research. Our conceptual base has had to change.

- Obesity is no longer to be considered a self-induced problem but a complex genetic-environmental interaction
- Obesity is no longer simply the state of having a BMI > 30 kg/m², but the disease-process of excess body fat accumulation, with multiple pathological consequences. BMI > 30 kg/m² is still a useful epidemiological cut-point, above which people have excess fat.
- The health consequences of obesity relate importantly to central, intra-abdominal, fat accumulation. Thus waist circumference is a more powerful indicator than BMI.
- The treatment of obesity is no longer just weight loss, but a correction of the disease process i.e. stopping weight gain. Weight loss remains a valuable short-term measure for people who have reached unacceptable or disabling levels of body fat.
- The primary target for management is no longer ideal body weight (BMI 21 kg/m²) or to achieve normal body weight (BMI 18.5 to 25 kg/m²). Instead, success criteria involve
 - (1) restriction of weight gain below the average of about 0.5 kg / year
 - (2) weight loss of 5-10% body weight
 - (3) effective treatment of coexisting cardiovascular risk factors.

METABOLIC SYNDROME AND CARDIOVASCULAR RISKS

This review will look at one aspect of obesity and disability, the Metabolic Syndrome. This is the very common (20-40%) genetic predisposition to accelerated cardiovascular disease, indicated by having coexisting major risk factors (IGT / type 2 diabetes, hypertension, and dyslipidaemia). It also includes a range of other me-

diators in the processes of cardiovascular disease, including raised inflammatory markers, microalbuminuria and hypercoagulability. The Metabolic Syndrome commonly occurs in families, and is more frequent in certain ethnic groups – particularly Asians. The phenotypic expression of the syndrome depends very heavily on weight gain. Features of Metabolic Syndrome are very rare at ideal body weight (BMI 21 kg/m²) and increase with BMI above 23 kg/m². They start to become common with BMI above 25 kg/m² and the epidemiological cut-point of BMI > 30 kg/m² is associated with a very high prevalence.

Metabolic Syndrome results in chronic disability as a result of the clinical manifestations of cardiovascular disease, heart failure and angina, from vascular dementia and from catastrophic sudden strokes. These are all common. Cardiovascular disease kills, mainly by myocardial infarction and stroke. It is the major cause of premature death in most countries, but it is also a major source of chronic disability. In the Scottish Health Survey (1), for example, 20% of all adults have already developed symptomatic cardiovascular disease. The proportion increases with age (Tab. I). Similar relationships can be found worldwide.

The major risk factors for cardiovascular disease, IGT (2) / type 2 diabetes (3), hypertension (4) and dyslipidaemia (5) all increase with BMI, and at levels of BMI found in large proportions of the population.

Impaired Glucose Tolerance / Type 2 diabetes

Type 2 diabetes is vanishingly rare at ideal body weight (BMI 21 kg/m²) but is already increased 5-fold by a BMI of 25 kg/m² (3). The median BMI at clinical diagnosis of diabetes is 18-19 kg/m² in UK (6) but higher and at a younger age in USA, where more young people are obese (7) (Fig. 1). Diabetes is also diagnosed younger, but at a lower BMI in South Asians. Impaired Glucose Tolerance (IGT), an earlier stage in the process of developing diabetes, follows the same pattern. Its im-

TABLE I - PREVALENCE OF ANY CARDIOVASCULAR DISORDER, BY RISK FACTORS, AGE AND SEX (SCOTTISH HEALTH SURVEY 1995)

Body Mass Index (kg/m ²)	Men		Body Mass Index (kg/m ²)	Women	
	16-44 %	45-64 %		16-44 %	45-64 %
20 or under	6.6	[6]	20 or under	9.9	13.8
Over 20 - 25	7.2	24.8	Over 20 - 25	10.9	26.2
Over 25 - 30	10.7	33.5	Over 25 - 30	13.6	29.9
Over 30	24.4	51.0	Over 30	20.8	53.0

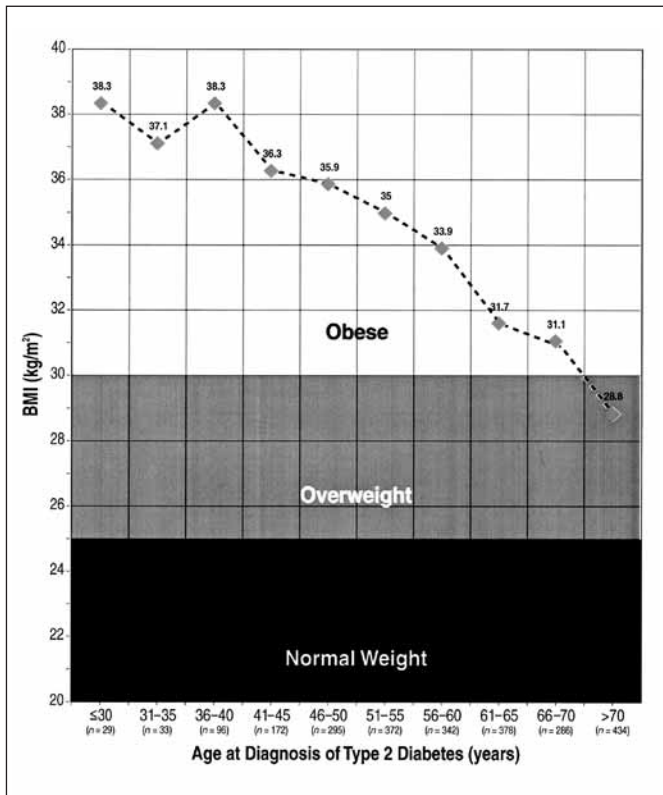


Fig. 1 - Relation of BMI and age at diagnosis among people with newly diagnosed type 2 diabetes. *P* for trend <math><0.0001</math>, based on linear regression of BMI on age at diagnosis (see Ref. 7).

portance is that the high cardiovascular risks associated with type 2 diabetes are already elevated by IGT. The diagnostic threshold of Fasting Plasma Glucose for diabetes is important for the development of micro-vascular complications, but the main clinical consequence of diabetes is cardiovascular disease. It happens with lower plasma glucose, at younger age, and at lower BMI than micro-vascular complications and before the current diagnostic criteria for diabetes are reached (Fig. 2).

Hypertension

Hypertension is a particularly important factor in causing disability through strokes and heart failure. Not all hypertension is attributable to weight gain or obesity. Data from NHANES suggests a prevalence of about 20% in thin Americans, but this rises to 60% with BMI > 35 kg/m². Because so many Americans are overweight, it is estimated that 55% of all hypertension is currently attributable to obesity (4), and thus potentially preventable.

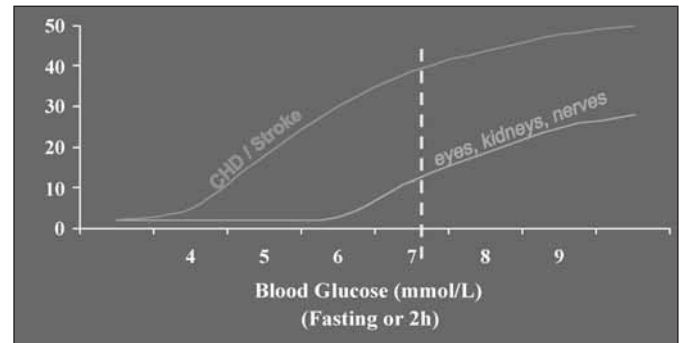


Fig. 2 - Clinical Consequences of Impaired Glucose Tolerance/Diabetes Mellitus.

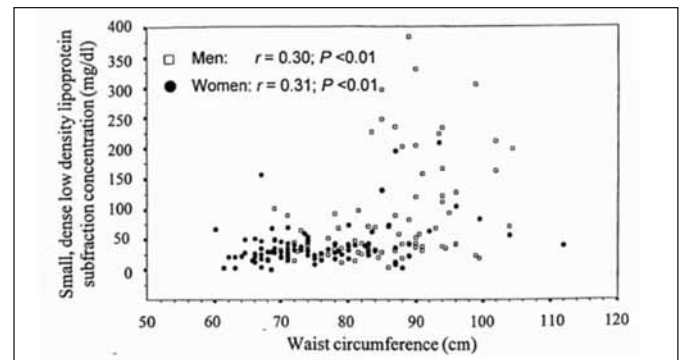


Fig. 3 - Relationship between small, dense low density lipoprotein and waist circumference in 93 men and 98 women. Correlation coefficients are controlled for age and cigarette smoking.

Dyslipidaemia

Obesity does increase total serum cholesterol, and LDL cholesterol, but to a relatively small degree, probably related to the higher saturated fat consumption of the obese, and in part due to the change in LDL particle composition to smaller, denser, more atherogenic species. Such smaller LDL particles contain less cholesterol so in fact LDL-C can decline beyond above a certain threshold for insulin resistance (8). The major effect on blood lipids, however is the elevation of serum triglycerides, with a reduction in HDL cholesterol, and a consequent increase in the small-dense-LDL fraction (Fig. 3).

It has been recognised for some years now that the major risk factors for CVD commonly coexist (9, 10). The unifying feature is to do with insulin resistance (11). As people gain body fat, insulin sensitivity declines, and this effect assessed by clamping studies, or by elevated insulin / glucose ratios, is most marked in people who develop clinical features of Metabolic Syndrome. These individuals are also identifiable by their predisposition to accumulating fat in intra-abdominal

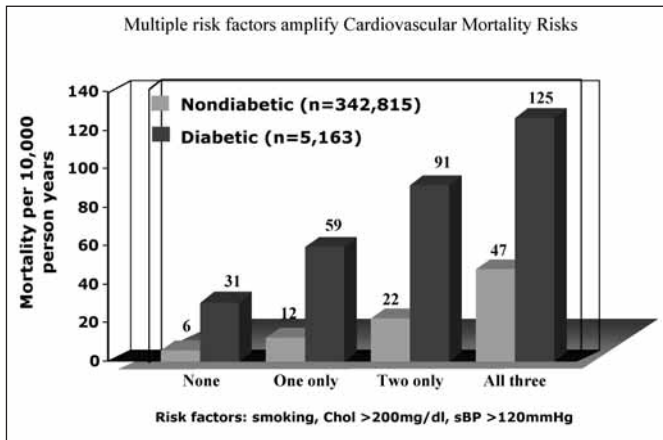


Fig. 4 - Multiple risk factors amplify Cardiovascular Mortality Risks (see Ref. 13).

TABLE II - DIAGNOSIS OF METABOLIC SYNDROME (ATP III 2001)

3 or more of:	
Waist circumference	m > 102 cm (> 40") f > 88 cm (> 35")
Triglycerides	> 1.7 mM
HDL cholesterol	m < 1.0 mM f < 1.3 mM
BP	> 138/85 mmHg
Fasting glucose	> 6.1 mM

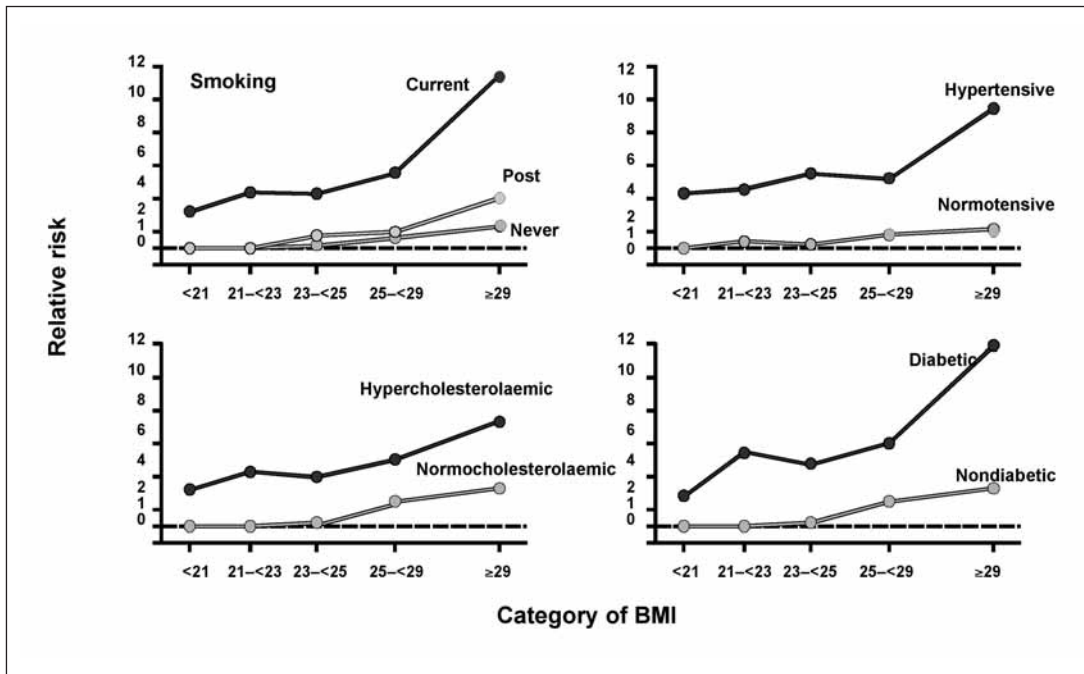


Fig. 5 - Relative risks of myocardial infarction (see Ref. 14).

sites. Intra-abdominal fat is highly metabolically active, being derived from brown adipose tissue, most evident in infancy (12). When intra-abdominal fat mass increases, excess fatty acids are released and impair insulin function in the liver.

Increased intra-abdominal fat is most evident from raised waist circumference, which is an important pointer towards cardiovascular risk. Indeed, the diagnostic criteria for Metabolic Syndrome include waist circumference (Tab. II). The other criteria used in the diagnosis for BP, glucose and lipids are set at rather low levels.

That is because the risk of cardiovascular disease is enormously compounded by having two, or three, elevated risk factors, even at relatively low levels (13) (Fig. 4). The presence of quite modest degrees of overweight and obesity has a striking effect (a doubling by BMI > 29 kg/m²) or risk of myocardial infarction in people without a major risk factor. In people with diabetes, hypertension, hyperlipidaemia or smoking, the risks from being overweight are greatly exaggerated (14) (Fig. 5). In all these associations, using waist, instead of BMI, will show at least equivalent risk. In most cases, rela-

tionships with waist and a little stronger than with BMI, waist reflects both total body fat and also the more hazardous intra-abdominal fat mass (15, 16). Thus, when both are available in population surveys, adding waist circumference increases the predictive power above that of BMI alone (17). Waist circumference defines insulin sensitivity better than BMI (18).

REDUCING DISABILITY: PREVENTING AND TREATING METABOLIC SYNDROME

Interventions to treat Metabolic Syndrome have traditionally been directed at each risk factor individually. There are more-or-less effective drug treatments for all the major risk factors, and in some cases there is evidence for small effects on clinical outcomes such as myocardial infarction or stroke. It is common to find people treated with two drugs for their diabetes, three from hypertension, and one for dyslipidaemia. But the cumulative effect is small, so cardiovascular disease remains their major cause of death, and a common cause of chronic disability. None of these drug groups (with the possible exception of the thiazolidiones (glitazones) for diabetes are directed towards mechanisms close to the core of Metabolic Syndrome.

Thiazolidiones and several related new drugs in development, activate PPAR systems in adipose tissue to improve insulin sensitivity. They have the effect of reducing blood glucose and also improving the dyslipidaemia of Metabolic Syndrome. There is also some early evidence that may also lower blood pressure but this requires formal randomised trial evidence (19).

Given that Metabolic Syndrome and its clinical consequence are largely revealed by weight gain, leading to obesity, an alternative approach to management is to try to check the disease process by stopping weight gain, and inducing some weight loss where possible. Ideally, action against obesity should be put in place in early adulthood and as near to ideal body weight (BMI 21 kg/m²) as possible. Many people, recognising their propensities for unwanted weight gain, are able to take active measures to maintain high levels of physical activity, and to limit caloric-specifically fat-intake from foods. The two routes to preventing weight gain (without consciously dieting) are (a) minimising physical inactivity – specifically by limiting sedentary time spent watching television etc (20) and (b) limiting fat in foods (21). This combination also tends to improve the major risk factors for cardiovascular disease independent of a reduction in obesity.

Many people do not find it easy to avoid inactivity, or adopt lower-fat eating habits which others regard as

normal, and weight increases. Some are able, with sympathetic guidance, reinforcement and support to exercise cognitive control. Only small changes are needed. For example, measures could include restricting television watching to under 1 hour / day; walking an extra 2000 steps (1 km, 20 minutes) each day; giving up all butter or margarine; giving up all biscuits or other snacks between meals; starting every main meal with a large bowl of salad (undressed); eating two vegetables (green and another colour) with all main meals.

For people who have reached hazardous levels of overweight (BMI 30 kg/m² or waist > 102 cm for men, > 88 cm for women), the same dietary and lifestyle principles apply. There is no magic. To lose weight, it is necessary to under-eat – and go hungry – for a period of months. It is not easy.

RIASSUNTO

L'obesità è definita dalla presenza di valori di BMI pari o superiori a 30 kg/m²; tale valore tuttavia rappresenta solo un elemento che definisce una patologia complessa, la cui caratteristica è definita da un eccesso di massa grassa nell'età adulta. L'aumento di incidenza di obesità è progressivo e rapido in tutto il mondo ed è causa di più patologie nonché di disabilità. L'ictus è una delle conseguenze dell'obesità, ma particolarmente importante per le conseguenze a lungo termine. L'ictus emorragico è principalmente mediato dalla presenza di ipertensione arteriosa, anch'essa conseguenza dell'obesità, l'ictus ischemico riconosce importanti fattori di rischio coinvolti anche nell'eziologia della cardiopatia ischemica: in particolare dislipidemia, alterata tolleranza al glucosio o diabete, fumo, ipertensione, infiammazione cronica. Tali fattori, ad esclusione del fumo, sono tutti caratteristici della sindrome plurimetabolica, condizione presumibilmente genetica la cui manifestazione nel fenotipo è legata all'incremento ponderale. La prevalenza della sindrome plurimetabolica aumenta progressivamente qualora il BMI sia ≥ 30 kg/m². La gestione del fenomeno obesità è principalmente mediata dalla prevenzione; si intende quindi sviluppo di programmi di prevenzione primaria per l'incremento ponderale e secondaria nei soggetti già in soprappeso, nonché la prevenzione delle complicanze. Trial clinici hanno dimostrato che un decremento ponderale del 5-10%, mantenuto nel tempo, è associato ad una riduzione delle complicanze; la letteratura evidenzia che un modesto decremento ponderale è un obiettivo e possibile e raggiungibile con differenti strategie.

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