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Beyond BMI – Phenotyping the Obesities

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BMI – Help or Hindrance?

For more than a decade, researchers in the field of obesity have debated the value of the BMI as the most common and convenient index for classifying the obese condition. The implications of using BMI are profound. The cut-off points of BMI of <18.5 kg/m^2, 18.5–24.9 kg/m^2, 25.0–29.9 kg/m^2, 30.0–34.9 kg/m^2, 35.0–39.9 kg/m^2 and 40.0+ kg/m^2 define categories usually referred to as underweight, normal weight, overweight (pre-obese) and obese (grades I, II and III). These cut-off points therefore define the number of individuals falling into each category which, in turn, tells us the prevalence of obesity on the planet. However, the essence of obesity is adipose tissue in the body (not a relationship of height and weight), so the BMI can only serve as an indirect estimate of obesity. Obesity is defined as an excess accumulation of body fat, and this excess fat is normally conceived as an indicator of poor health and, in turn, constitutes a risk factor for a range of diseases including diabetes, ischaemic heart disease, hyperlipidaemia, sleep apnoea, arthritis and others [1]. The BMI is therefore a measure of the number of people in the world who are in poor health, and who possess a condition that is threatening to their longevity or their quality of life. This has implications for who should be concerned (about themselves) and who should be a candidate for treatment (by others). Since the risk of early death or a life of disease prompts actions by public health authorities or medical agencies, the economic consequences are profound. If BMI provides a faulty quantification of who is at risk, then the personal, social and economic consequences are serious.

However, BMI is an anthropometric concept and therefore serves only as a surrogate measure for fatness. Although BMI correlates with percentage body fat, the correlation between both parameters is not sufficiently accurate to truthfully reflect the amount of fat in

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the body in a particular subject. Therefore if fatness is the true risk factor for longevity and health, then BMI is only an approximation and is therefore inadequate.

For several years some reviewers have argued for the adoption of direct measures of body fat [2–4]. The advantages arising from accurate measures of fat itself should be evident in research, prevention and management of obesity-dependent co-morbidities, and should result in more truthful and valid relationships underlying the aetiology of obesity and its physical and social consequences. What are the major problems associated with the continued use of BMI?

Definitions of Obesity

Clearly the BMI categories (defined by the cut-off boundaries noted above) can only be approximate indications of the characteristics of individuals contained by these categories. However, for years there have always been advocates of using other indices to identify obesity, such as skin-fold thickness, waist circumference and waist-to-hip ratio (WHR). Indeed the WHR has been used to identify the so-called android and gynoid morphological types and their relationship with obesity-related co-morbidities. With the development of devices and equipment to more accurately measure body fat, including DEXA, air-displacement plethysmography (BodPod), bioimpedance and body scanning procedures – replacing the cumbersome underwater weighing –, it has become possible to more easily classify individuals according to the degree of bodily adipose tissue and to measure the consequences independently of BMI. This approach has also drawn attention to the function of non-adipose tissue – that is, fat-free mass or lean mass – and the contribution made by fat-free mass to physiological functioning, pathology and well-being.

Should we persist with BMI (because of its convenience) when there now exist more accurate measures of fatness and fat distribution? Decisions concerning the adoption of particular BMI cut-off points (for defining obesity) appear to have been established on the basis of data collected by the Metropolitan Life Insurance Company more than 50 years ago. These statistical tables apparently showed that health began to deteriorate at a BMI above 25 kg/m^2. Therefore this BMI value came to be regarded as the upper level for 'normal weight' based on associated markers of health. This decision has implications for the absolute numbers of people considered to be at risk of ill health or premature death as well as on the development of preventive and therapeutic strategies both at individual and collective level.

Obesity, Mortality and Ill Health

One good reason to replace BMI with alternative measures would be if the BMI failed to accurately reflect the likelihood of early death or vulnerability to various diseases. One area of investigation in which BMI has retained its value is epidemiology; for the obvious reason that height and weight are easy (sometimes deceptively easy) measures to take when participant numbers are usually in the hundreds and may reach several thousands of individuals. However, accuracy cannot be guaranteed when self-measurement is employed rather than uniform standardised procedures carried out by trained staff. Nevertheless, the use of BMI (and BMI cut-off points to define obese categories) has given rise to controversial and hotly debated associations between categories of BMI and mortality [5]. For many years (since the adoption of the Metropolitan Life Insurance Company data) it has been assumed that the risk of death conforms to a U-shaped function with normal BMI (18.5–24.9 kg/m^2) representing the lowest risk. A lower BMI (<18.5 kg/m^2) carries a larger risk similar to categories of BMI

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above 25 kg/m^2. The controversy has arisen since the Centers for Disease Control (CDC) data [5] reported that the overweight BMI category (24.9–29.9 kg/m^2) revealed a lower death rate than the normal-weight category and therefore appears to offer some protection. The significance of these data has been challenged [6–9]. One of the comments is that the demonstrated postponement of death (in the overweight category) does not necessarily imply a longer life free from disease. Indeed when morbidity rather than mortality is the target variable, then increasing BMI above 25 kg/m^2 may confer a disadvantage. In addition the use of BMI to define a person's level of obesity already masks a huge spectrum of individuals varying in body fatness, body shape as well as proportions of neck, thighs, hips, waist and height. The question is whether or not a person's risk of premature death could be better predicted by using an accurate measure of adipose tissue in the body (absolute amount, distribution or incorporation of fat into non-adipose tissues – referred to as ectopic fat).

Further research on health risks in the field of diabetes has indicated that the relationship between BMI and mortality may be paradoxical [10]. In recently diagnosed diabetic patients an inverse relationship between BMI and mortality was found even after controlling for various obvious associated risk factors such as smoking and waist circumference. In addition a 15-year investigation on male diabetics (African American and Caucasian) has reported that BMI was inversely related to mortality [11]. Ahima and Lazar [12] have questioned how it is possible for overweight and obesity to promote survival? The answer possibly lies in the tendency of BMI to combine (in a single number) key biomarkers associated with both health and disease. For example, BMI does not discriminate between fat mass and fat-free mass, or distinguish between visceral and subcutaneous fat, or between eutopic or ectopic fat, and does not reflect body shape. Of particular importance may be the ratio of fat mass to fat-free mass. For example, because skeletal muscle represents the largest glucose buffering system in the body, a large muscle mass is likely to promote insulin sensitivity and protect against metabolic syndrome [13, 14]. In addition the relationship between body composition, energy expenditure and energy intake [15–17] suggests that fat-free mass exerts a regulating action on energy homeostasis with possible associated health benefits.

All these data suggest that obesity evaluation by BMI does not provide the clinician with an assessment good enough to establish the actual presence of obesity and its relation to potential associated diseases, thus reducing the possibilities for an effective therapeutic intervention.

Metabolically Healthy Obese?

A consequence of examining BMI has been that, although obesity (defined by BMI) constitutes a risk factor for several diseases, when body composition is also entered into the analysis, evidence shows that some individuals with a BMI over 30 kg/m^2 and a significant amount of body fat may be metabolically healthy. These so-called metabolically healthy obese (MHO) may have a prevalence of 10–40% depending on the population and on the diagnostic criteria used. In its simplest form MHO can be defined as obesity in the absence of metabolic complications. This can be most readily detected by the absence of a reduction in insulin sensitivity which normally accompanies abdominal fat accumulation. Indeed it has been observed that an obese person who is insulin sensitive has only the same degree of risk of disease as a lean person (with similar insulin sensitivity) [18].

This intriguing notion has yielded explanatory concepts such as the Adipose Tissue Expandability Hypothesis [19] and the Overnutrition Toxicity Syndrome. The current view is that for a particular person there is a finite limit to which adipose tissue can expand to fulfil its role as a storage organ. Above this limit any excess nutrition (energy) must be stored as ectopic fat in sites such as muscle, liver and viscera. It is argued that metabolic consequences

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(reflected by insulin resistance) are associated not with fat mass per se, but occur when fat deposition exceeds the capacity of the natural adipose tissue stores. Among other consequences, this has given rise to the speculation that weight loss could be detrimental to the MHO. However, this should not be used to imply that the MHO are without problems or distress. Indeed it should be noted that there is strong opposition to the idea that 'metabolically healthy' obesity is a viable category. 'Compared with metabolically healthy normal-weight individuals, obese persons are at increased risk for adverse long-term outcomes even in the absence of metabolic abnormalities, suggesting that there is no healthy pattern of increased weight' [20]. It has been further emphasised that 'healthy obesity' is a myth [21].

Considering the temporal dimension, it is worth mentioning that most MHO findings/publications are based on cross-sectional data as opposed to prospective studies. When longitudinal analyses are performed, a cumulative incidence of each metabolic abnormality over time is observed with the duration of obesity being an independent risk factor for adverse health outcomes [22]. This obviously leads to the importance of years of disease and the link to the relevance of childhood obesity. Current epidemiological data on MHO are based on individuals becoming obese as adults and, therefore, have been exposed to the adverse metabolic effects of obesity for a shorter period of time than individuals that have been obese since childhood and might exhibit different morbidity and mortality outcomes. This might be an important aspect to consider given that the metabolic alterations of obesity are already evident in childhood obesity [23–25].

Considering MHO, an unambiguous standard definition is required. Currently, there is a lack of a clear-cut definition for MHO which leads to different published studies applying criteria that allow a diverse degree of unhealthy derangements. In turn this contributes to a confusing use of the term 'healthy' [26] and to a wide spectrum of MHO prevalence values through different studies. Moreover, the role of dietary and lifestyle factors should be considered, especially with respect to healthy eating pattern and physical fitness. Compliance with food pyramid and physical activity recommendations increases the likelihood of MHO [27].

BMI and Ethnicity

The fact that BMI conceals the proportions of fat mass and fat-free mass, and fails to reflect the distribution of fat in body depots and tissues, may have special relevance for comparisons between Caucasians and other ethnic groups. For example when fatness per se is measured accurately, the prevalence of obesity in white and African American males changes so that white men are much more likely to be defined as obese than their African peers. In a comparison of 5 ethnic groups from South Africa and New Zealand [28] the relationship between percentage fat and BMI varied markedly mainly due to central adiposity and muscularity. The implication is that universal BMI cut-off points do not consistently reflect adiposity or fat distribution in different ethnic populations. This situation may be particularly problematic for South Asian groups who display a greater proportion of body fat for a given BMI than Caucasians. In turn South Asians are more susceptible to the development of diabetes [29].

Overlap between Normal Weight and Obesity

When a BMI score is used to define weight categories, individuals of normal weight can be unambiguously distinguished from obese by the adoption of a numerical boundary (a single number). The lack of scientific precision in this strategy can be seen by asking what differences

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would be expected between individuals with BMIs of 24.5 and 25.5 kg/m^2. The categorisation is obviously crude and clearly lacks scientific precision. However, the classification remains problematic even if adiposity is assessed by a direct measure of body fatness. Here some individuals with a high percentage body fat but a normal BMI may possess a greater absolute amount of fat than a person with an 'obese' BMI (because of the impact of fat-free mass on body weight and BMI [30, 31]. This anatomical situation resonates with the observation that some individuals with a normal BMI may be metabolically unhealthy whilst some people with an 'obese' BMI may be metabolically healthy (the MHO). The existence of these patterns poses questions for the understanding and management of obesity as a nomological category. However, it is clear that even using a direct measure of body fat (rather than BMI) does not remove all ambiguity. In certain animal studies large amounts of body fat may be metabolically inert [32] whilst in humans it has been inferred that fat in subcutaneous stores may be relatively non-toxic. A further issue is that body fat is measured with much greater error than body weight and height (the components of BMI). Consequently, this would weaken the relationship between the two variables and explain why any potential superiority of body composition measurements in predicting health risks may sometimes be difficult to demonstrate [33].

Consequently, neither BMI nor total body fat unambiguously reflects the risk to health. It should also be mentioned that other anthropometric indices easy to obtain and related to abdominal fat content such as waist circumference, saggital depth (abdominal height), WHR, waist-to-height ratio (WTHR) may offer better predictors of mortality and morbidity than BMI [34]. Emerging evidence suggests that the accuracy of discriminating health risk based on anthropometry is improved when waist circumference thresholds are stratified by BMI, sex and race/ethnicity [35].

Obesity, Obesities and Phenotypes

The debate about the value of BMI as a marker for obesity has been going on for over a decade. The weaknesses of this unitary metric have been extensively described, universally acknowledged but not necessarily accepted. However, there are now too many anomalies which constitute challenges to our understanding. Is the continuing reliance upon BMI limiting progress? The associations between body physiology and mortality and morbidity require more sensitive analytical tools. Instruments for measuring body composition are now more freely available than they were a decade ago, and permit the possibility of defining phenotypes for research and clinic. The 2008 Foresight Report of the UK government reflected the aetiological complexity by referring to 'obesities' rather than to a single condition. Indeed the individual variability in body composition suggests that a true reflection of the impact of this variability can only be captured by subdividing obesities into specific types with functional properties (phenotypes). This would certainly stimulate research into 'obesities' and open up a fruitful approach to management. Phenotyping beyond BMI should not be limited to physiological or anatomical variables. Biochemical and molecular profiling will also be of help to individualize the potential of obesity mortality. It is clear that BMI can be partitioned using psychometric instruments to yield phenotypes based on traits such as disinhibition and binge eating tendency.

Concern about the fallibility of BMI is no longer of academic interest. There is now a requirement to explain the apparently paradoxical associations between BMI, mortality and morbidity [36]. Obesity is important because of its relationship to health – physically and psychologically – and in turn because of the economic consequences that ensue. Given the stagnation in dealing with the so-called 'obesity epidemic', some radical thinking (and action) is called for. This action should begin with some clear vision and agreement about the fundamental nature of obesity and its diagnostic characterization.

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