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Philosophical determinants of obesity as a disease

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Summary

Is obesity a disease? Much ink has been spilled over this debate and for good reasons. The global prevalence of obesity has more than doubled since the 1980s and is now of pandemic proportions. Whether obesity is a disease has consequences for what kind of treatments are appropriate, as well as how we ought to allocate funding and access to healthcare resources. In most cases, there is no dispute over the medical facts, yet disagreement persists. This is because whether obesity is a disease is not determined by medical facts alone; the issue is, in part, conceptual. Science relies on careful argumentation and conceptual analysis as part of its armamentarium. In this review, we will examine the two concepts of disease most often employed in the philosophy of medicine: the naturalistic and constructivist. We will argue that, whichever definition of a disease is used, obesity fits the criteria for disease definition. Those seeking to meet the challenge of managing obesity will, therefore, need to embrace chronic disease models of care suited to addressing the lifelong challenge posed by this disease and its associated complications.

Keywords: disease, obesity, philosophical analysis.

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; GLP-1, glucagon-like peptide-1; MHO, metabolically healthy obesity; OR, odds ratio; T2DM, type 2 diabetes mellitus.

Introduction

Medical professionals deal with a range of conditions in the course of their work. Diseases form an important class of these conditions, and determining whether a condition is in fact a disease is more than mere conceptual bookkeeping. It can have wide-ranging moral, social and economic implications, as well as affecting clinical treatment.

Obesity is a health problem of pandemic proportions. Globally, its prevalence has more than doubled since 1980 (1). Obesity correlates with morbidity and mortality. It drives up rates of coronary heart disease, ischemic stroke (2) and type 2 diabetes mellitus (T2DM) (3). It increases the risk of cancer of the breast, colon, prostate, endometrium, kidney and gall bladder (4). A body mass index (BMI) above 40 kg m^{-2} reduces life expectancy by 10 years (5). The costs of obesity extend beyond the individual; in addition to the health burden, financial costs of managing obesity and its complications are rising exponentially. In 2005, total direct cost for overweight and obesity in Australia was AUD21bn (AUD6.5bn for overweight and AUD14.5bn for obesity). Indirect costs amount to AUD35.6bn per year, giving an overall total annual cost of AUD56.6bn (6). By 2015, a decade later, estimates of the total cost of obesity had increased to AUD132.7bn (7). But is obesity a disease? We will argue that it is.

Two broad concepts of disease are employed in the philosophy of medicine. According to naturalist accounts, the best concept of disease is grounded in biological facts about malfunction, as well as normative judgements about whether or not the resultant condition negatively impacts upon quality of life. The constructivist account of disease, by contrast, is normative through and through. On this view, we identify undesirable conditions (conditions we deem to be diseases)

and then look for underlying biological causes. One can be a naturalist about some diseases and a constructivist about others. We will demonstrate that, using either definition, obesity satisfies the definition of disease.

The question we are concerned with is 'is obesity a disease?'. This question is related to, but importantly distinct from, the nearby question, 'should we consider obesity a disease?' Clarity concerning this distinction is important but underappreciated in current literature. Many authors confuse the two questions, assuming that whether or not obesity is a disease depends entirely on the practical outcome of such classification (8). Other authors have noted the distinction but concluded that only the second question can be legitimately answered. Allison *et al*. (9), for instance, write that, although the question of whether or not obesity is a disease is "*a seemingly empirical question that should (in principle) yield to scientific inquiry*", it is "*ill posed in that its sensibility is based on premises that are not true. It is therefore insensible and unanswerable*". The crucial objection here seems to be that, because there is no agreement in the medical community about what constitutes disease, it "*makes no sense, from a strictly scientific point of view, to ask whether obesity is a disease*". This, however, is incorrect. It may be true that the empirical facts alone do not settle the matter of what constitutes a disease. However, appeals to bald empirical facts do not exhaust our resources for settling disputes. Science has always involved careful argumentation and conceptual analysis that goes beyond the observed data.

The accounts of disease advanced by various theorists are not arbitrary. They are carefully constructed theories that admit counter-argument. That is to say, there can be good theoretical (i.e. non-empirical) reasons for choosing one concept of disease over another and that part of the business of conceptual analysis is to advance and evaluate those reasons. Data on the concept of disease possessed by the medical community can help fix the subject of analysis, but the question of whether or not this is the best way to carve up the conceptual landscape, however, is an activity that takes place in the proverbial armchair.

Although we will be agnostic as to the correct concept of disease, we proceed on the assumption that the question 'is obesity a disease?' is intelligible and important.

The naturalist account of disease

Central to a naturalistic concept of disease is the idea that the human body comprises systems that naturally function in certain ways. When these systems malfunction, they may do so in ways that are harmless, or even beneficial, or may do so in a way that that is undesirable. The undesirable malfunctions are diseases. Naturalists believe that whether or not a condition involves biological malfunction is something that can be objectively determined by science (10). Determining whether or not something is a disease thus involves both mind-independent facts about the world and the normative judgement that a malfunction is an undesirable one. Some naturalists (11) have also argued that whether or not a malfunction negatively impacts upon well-being is an objective matter, but the tendency in recent literature has been to recognize an indispensable role for normative judgements (12). This bipartite analysis is supposed to help us exclude instances of bodily dysfunction that we do not recognize as disease, such as vaccination, surgical incision or male pattern alopecia. It also allows for differing cultural considerations, such as among the Hmong people, to whom epilepsy is considered a sign of spiritual gifts and affords higher social status (13).

As noted above, obesity can lead to significantly shorter life spans (14), is associated with a range of other diseases (15) and negatively impacts upon quality of life (16). Individuals with obesity are also subject to various forms of discrimination (discussed in more detail below). Because obesity is clearly undesirable, it satisfies the normative component of a naturalist concept of disease.

Furthermore, obesity involves a malfunction of the organism.[1] Contrary to long-held perceptions, obesity is not simply a product of gluttony and sloth, but the result of complex pathological adaptations of the arcuate nucleus in response to an obesogenic environment. Disruption of the orexigenic (appetite-increasing) and anorexigenic (appetite-suppressing) neuronal homeostatic mechanisms results in a chronic, sustained and well-defended shift (increase) in energy intake and consequent weight gain (17). Among the well-demonstrated and documented malfunctions in satiety signalling is central insulin and leptin resistance. In addition, secretion of glucagon-like peptide-1 (GLP-1), an important satiety hormone (18), is attenuated in obesity, with higher GLP-1 responses associated with a lesser degree of obesity (19). The pathology involving these three important satiety hormones are only some of the mechanisms by which energy dysregulation and resultant obesity occur.

The human body naturally resists and defends attempted weight loss (Fig. 1), with counter-regulatory responses driving hunger, for example, by reducing levels of hunger-suppressing hormones. In addition, there is slowing of the metabolic rate and a reduction in non-purposeful movement, leading to a reduction in energy expenditure (20). These changes are physiological and, in individuals without

[1]A central challenge for proponents of a naturalist account of disease is to spell out exactly what counts as 'malfunction'. However, for our purposes, our intuitive understanding of malfunction will suffice. This is because any theory of malfunction must respect our pre-existing classificatory practices. To fail to do so would simply be to change the subject from what we care about when we talk about malfunction.

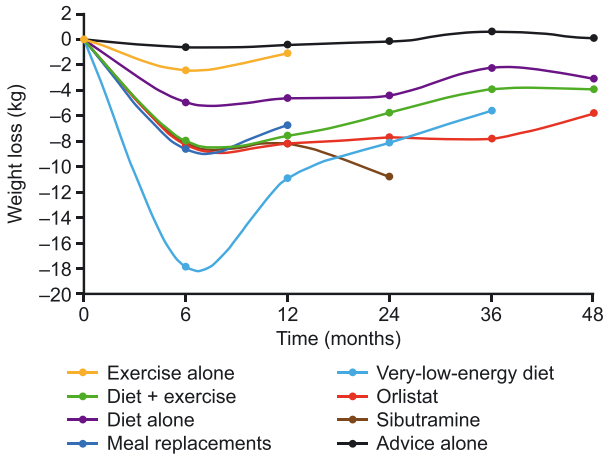

Figure 1 Regain of weight following a 6-month weight loss intervention (62). Reprinted from Journal of the American Dietetic Association, 107, Franz MJ et al., Weight loss outcomes: a systematic review and meta-analysis of weight loss clinical trials with a minimum 1-year follow-up, 1755–1767, Copyright 2007, with permission from Elsevier. [Colour figure can be viewed at wileyonlinelibrary.com]

obesity, confer a survival benefit during periods of food insecurity/shortage. However, in individuals with obesity, the weight that is defended is in the unhealthy weight range. Rather than protecting the organism against starvation or deprivation, these counter-regulatory mechanisms perpetuate and sustain an unhealthy level of adiposity resulting in long-term risk of morbidity and mortality (21).

The slowed metabolic rate in individuals with obesity who have successfully lost weight can persist for at least 6 years (22). In addition to reduced energy expenditure, levels of the hunger hormone ghrelin are raised (23), while satiety hormones such as amylin, PYY and cholecystokinin are suppressed (24).

There are three objections to this picture of the naturalistic definition of obesity as a disease that must be considered. The first is that, far from being a disease, obesity represents necessary biological adaptation and that it is, on occasion, associated with better health outcomes. This is sometimes referred to as the 'obesity paradox'. This, as we will show, is generally unsupported by the empirical facts. The second argument, often offered during a retreat from the first, is based on the apparent observation that some individuals with obesity may not show any signs of illness. If it were possible to have obesity yet not exhibit any signs of bodily malfunction, then obesity would not satisfy the naturalist's concept of disease. The last objection we consider is that the classification of obesity as a BMI ≥30 involves no reference to illness or malfunction. It is therefore, by definition, merely a risk factor for disease and not a disease itself. We address each of these arguments in turn.

Obesity as adaptation

Some have argued that obesity is not a malfunction of the organism, but a necessary biological adaptation. It has been suggested that obesity is a homeostatic adaptation ensuring maintenance and protection of the organism. One example of this is Hervey's ponderostat hypothesis, which suggests that central adiposity is mediated by glucocorticoids (steroid stress hormones) and is thus a physiological response to stress and the resultant increased activity of the hypothalamic pituitary axis. Visceral fat, by virtue of its higher density of glucocorticoid receptors than subcutaneous fat, functions to increase the clearance of stress-mediated hormones (25).

There are animal and human data indicating that resetting the ponderostat results in the accumulation and retention of excess adiposity (26). Indeed, attempts at weight loss invoke counter-regulatory mechanisms that vigorously defend the state of overweight or obesity, making sustained, meaningful weight loss difficult in the extreme. Obesity, rather than being a physiological, protective response by the organism, represents maladaptation in response to abnormal stressors. These stressors may occur throughout life and can begin *in utero*, setting the trajectory for increased weight gain through the early and middle years of life, whether these stressors persist or not.

Other defenders of the obesity-as-adaptation argument point towards the apparent obesity paradox: the observation that obesity may be protective and associated with greater survival in certain groups, such as the elderly and those suffering from certain chronic diseases. First described in 1999 in patients undergoing haemodialysis (27), the obesity paradox has been observed in those with heart failure (28–30), myocardial infarction (31), the elderly (32) and those with chronic obstructive pulmonary disease (33).

The obesity paradox, then, is a juxtaposition of two seemingly inconsistent outcomes. The association between obesity and conditions such as T2DM, hypertension, cardiovascular disease (CVD) and certain types of cancer is well established. This relationship has been shown to have a typically U-shaped association with lowest risk in the BMI 20–30 kg m^{-2} range, with an increased risk in both the low and high weight zones (<20 and >30). However, contrary to this widely held tenet, there are extensive data supporting the notion of an obesity paradox. The paradox thus arises from observations that, in conditions closely associated with obesity, obesity may be simultaneously both causative/contributory and protective.

However, others dispute this, suggesting that studies purporting the obesity paradox suffer from methodological limitations:

1 The majority are retrospective analyses or observational studies.
2 The majority were not specifically designed to study the obesity paradox as a primary goal.

3 Studies have data on preceding unintentional versus intentional weight loss, resulting in selection bias due to reverse causality. When one takes measures to eliminate reverse causality, such as in this study, where peak lifetime BMI is used rather than BMI at survey, confounders are removed and the obesity paradox disappears (34).
4 When weight loss is intentional, multiple benefits have been demonstrated, with the greatest benefits achieved with 5–10% loss of body weight. Conversely, unintentional weight loss can often signal end-stage disease with unfavourable or poor prognosis. In other words, high weight generally causes health problems, while low weight is caused by health problems (35,36).
5 Others suggest that the measurement/unit of obesity, BMI, and the somewhat arbitrary 5-unit divisions for healthy weight, overweight, obesity and so on fail to capture the true measure of adiposity. A more sensitive test is required to clarify the existence of the obesity paradox, and hence an improved measure.

More research is needed to determine whether, and to what extent, the obesity paradox exists but, in the end, it may turn out to be immaterial; recall that all the naturalist needs for obesity to count as a disease is that it (i) involves malfunction of the organism and (ii) negatively impacts upon quality of life. Obesity may, under certain circumstances, be protective. However, as discussed above, the condition results from a malfunction of the body's energy systems and significantly reduces quality of life.

Obesity without malfunction

The phenotype of metabolic obesity in the absence of any metabolic abnormalities or comorbidities has given rise to the concept of metabolically healthy obesity (MHO). If it were possible for an individual to have obesity yet not exhibit any signs of bodily malfunction, then obesity would not satisfy the naturalist's concept of disease.

However, several studies have shown that the MHO phenotype is predictive of increased mortality, CVD, T2DM and non-alcoholic fatty liver disease. In a prospective cohort study of 22,654 individuals between the ages of 20 and 59 years (average duration, 13.4 years), the mortality risk of subjects with metabolically healthy abdominal obesity was approximately 40% higher than that of individuals without metabolically healthy abdominal obesity: hazard ratio: 1.43; 95% confidence interval (CI): 1.00; 2.04. The hazard ratio for metabolically unhealthy abdominally obesity was 1.99 (95% CI: 1.62; 2.43), greater than the MHO cohort but not reaching statistical significance (37). The prospective longitudinal Pizarra study of 1051 participants found that, while the risk of developing T2DM after 11-year follow-up was higher in non-healthy subjects with obesity (odds ratio [OR]: 8.20; CI: 2.72; 24.72; $p < 0.0001$), it was still significant in MHO subjects (OR: 3.13; CI: 1.07; 9.17; $p = 0.02$). Furthermore, the association between MHO phenotype and T2DM incidence disappeared in those who lost weight during the course of the study (38).

These studies suggest that, when followed up for adequate durations, MHO has been demonstrated to be not a benign phenotype, but rather the early stages of a disease, yet to manifest harm (39). Obesity is not unusual in this regard. For example, T2DM, which is strongly associated with obesity, generally has no associated end-organ damage or complications during the early phase of its trajectory. This does not invalidate the recognition of T2DM as a disease requiring long-term, progressive management. The same holds true in the case of obesity.

Non-disease by definition

The third argument that obesity is not a disease runs thusly: an individual is classified as having obesity if they have a BMI ≥30. This definition of obesity involves no reference to malfunction. Therefore, obesity is merely a risk factor for other diseases and not a disease itself.[2]

Although it sounds similar, this argument is subtly different from the preceding one. Whereas the preceding argument hinged on empirical facts about whether obesity involved malfunction, here the suggestion is that the presence or absence of malfunction is simply irrelevant to the presence or absence of obesity. Even if there was a perfect correlation between obesity and bodily malfunction, it would be the malfunction that counts as the disease and not obesity, because obesity is just a BMI of ≥30.

Another way to animate this objection is as follows: consider the fictional case of Oscar Bese. Oscar is an individual with obesity (BMI >30). Eager to improve his health, he embarks on a series of interventions that help him lose weight, such that his BMI drops below the threshold for obesity. Intuitively, Mr O. Bese no longer 'suffers' from obesity despite the continued dysregulation of his physiological energy regulation systems.

The problem with this argument is that BMI is merely a tool for measuring and diagnosing obesity[3] and not a

[2]Some write in a way that seems to imply that obesity is a risk factor and therefore can't be a disease. Of course, it's entirely possible that it could be both. The UK National Institute for Health and Care Excellence guidelines state that obesity is both a disease and a risk factor for other diseases. This is entirely consistent with other chronic disease states such as diabetes. Diabetes is a disease in its own right but is also a significant risk factor for a multitude of other diseases such as CVD, neuropathy, retinopathy, chronic kidney disease, and cancer.

[3]And an imperfect one at that. Notably, most professional bodybuilders will fall into the BMI range associated with obesity despite having significantly lower levels of body fat than the general population.

definition of the condition. We are only just beginning to understand the aetiology of obesity, but, as we do, we will be better placed to describe obesity in terms of the underlying physiological malfunction. While BMI is still a starting point for the definition of obesity, recently there has been a move to characterize obesity through full health assessments such as the Edmonton Obesity Staging System (40). More widespread use of these assessments would aid with both prognosis and treatment indications, as well as bringing the management of obesity in line with the staged management of other chronic diseases.

We believe that a better way to describe Oscar Bese's case is to say that, even after his weight loss, he still suffers from obesity. He is, rather, successfully managing his condition and thus not exhibiting all the signs and symptoms associated with the state of obesity. This is commensurate with the way we talk about other disease states: a person diagnosed with T2DM due to irregular blood sugar continues to have the disease even if they can successfully manage the condition and maintain healthy blood sugar levels. Adding a simple detail to the story above can help nudge our intuitions in the right direction: Once Oscar ceases treatment, he quickly regains the weight he lost.

Another problem with this argument is that it can be used to define most diseases out of existence. For example, we might argue that because T2DM is diagnosed as dysglycemia utilizing cut points such as an HbA_{1c} blood test result of 6.5% (48 mmol mol^{-1}), and because those diagnostic criteria make no reference to malfunction, T2DM is therefore not a disease. This, of course, is absurd.

The constructivist account of disease

The constructivist concept of disease turns the two-step process of the naturalist account on its head. Instead of starting from some objective set of facts about whether or not an organism is malfunctioning, constructivists assert that we begin by identifying some behaviour or condition we deem to be undesirable and then explain that condition in terms of bodily processes. According to the constructivist, these bodily states are not objective malfunctions but judged by us to be deviant because they depart from our cultural values. As Murphy writes (12), "*the crucial difference between the positions then is that for naturalists, diseases are objectively malfunctioning biological processes that cause harms. For constructivists, diseases are harms that we blame on some biological process because it causes the harm, not because it is objectively dysfunctional*".

Constructivists about disease also tend to be revisionists about our concepts of health and disease. Per this view, understanding the historical and cultural origins of our concepts provides us with the opportunity to reform them in service of other goals, such as reducing stigma or oppression. Constructivist thinkers, for instance, argued against the view, dominant in psychiatry until the 1970s, that homosexuality is a mental illness. The classification of homosexuality as disease was made for offensive moral reasons, not medical ones, and the decision to change that was the result of lobbying on moral grounds and not the discovery of new medical facts. For the constructivist then, whether or not obesity is a disease is informed by the related question mentioned above; should we (i.e. do we have moral reasons to) classify obesity as a disease?

There are at least two moral reasons to endorse the reclassification of obesity as a disease. The first is to reduce social stigma. The second is to improve patient outcomes. Persons with obesity are subject to severe societal discrimination in ways that those with other chronic diseases, such as multiple sclerosis, asthma or hypertension, are not. For example, individuals with obesity are less likely to be accepted as tenants by landlords, are less likely to be offered jobs than equally qualified applicants and are looked down upon by educators and healthcare professionals (9).

The medicalization of obesity could reduce social discrimination by highlighting that many causes of obesity are outside individual control (41). We live in an obesogenic environment (42). Additionally, obesity is now understood to be intergenerational as a consequence of epigenetic changes due to the intrauterine environment and early feeding (43).

Patients hold some degree of responsibility for many conditions (e.g. infections acquired during travel, piercings or tattoos, injuries from extreme sports, etc.). Despite this, they routinely receive medical treatment without being questioned about their lifestyles in the same way (44). Discrimination of the kind faced by individuals with obesity is unjustifiable. Reclassifying obesity as a disease may, therefore, advance the rights of people with obesity, and stigma among medical professionals may be reduced by a better understanding of its aetiology (45).

Dealing with the discrimination and stigma faced by individuals with obesity may also be essential to improving patient outcomes. Reclassifying something as a disease can legitimize the mobilization of medical resources to manage the condition. For instance, a study in Denmark found that attitudes to the treatment of obesity were best predicted by the belief that individuals are personally responsible for their own obesity (46). Another study found a high correlation between the statements '(This state of being) is a disease' and '(This state of being) should be treated with public tax revenue' in both healthcare professionals and lay people (47). In countries where health services are funded through insurance schemes, classification of obesity as a disease may allow patients greater access to payments for treatment (48).

Obesity, despite its well-documented association with complex comorbidity and premature death, continues to be under-diagnosed and is not seen as a priority by healthcare practitioners. A survey of general practitioners in Australia revealed lack of awareness and lack of action

in this domain, with only 22.2% of adults having a recorded BMI and 4.3% a recorded waist circumference (49). Despite proven clinical and cost-effectiveness, the appropriateness of public funding for bariatric surgery has been questioned on moral grounds: specifically, the self-inflicted and supposed non-disease nature of obesity (45). The vast majority of bariatric surgeries carried out in Australia are privately funded, despite the fact that equal benefit is found in both publicly funded and privately performed procedures (50)

Furthermore, the evidence suggests that healthcare professionals looking to improve health outcomes for patients with obesity ought to use the same strategies that they use to treat other chronic illnesses (51–53). Recognizing obesity as a disease will promote a greater understanding of the pathophysiology and adverse outcomes/impact of this disease state on the patient, society and the health system. In turn, the benefits of managing this chronic condition, utilizing optimal chronic disease models of care and benefits of intervention, will be better appreciated, attracting appropriate funding and resources from governments and healthcare planners (54).

Conclusions

The ground is shifting, with several international professional bodies now recognizing obesity as a chronic disease. The Obesity Society officially declared that it considered obesity as a disease in 2008 (55), followed by the American Medical Association in 2013 (56) and the Canadian Medical Association in 2015 (57). The European Medical Association and World Health Organization also recognize obesity and overweight as disease states (58,59). Most recently, the World Obesity Federation published a position statement recognizing obesity as a 'chronic, relapsing, progressive disease process' (60). Several organizations have now produced chronic disease management algorithms to address various stages of obesity, such as the American Association of Clinical Endocrinologists/American College of Endocrinology algorithm (61). It is being recognized that, as is the case with diabetes, obesity is a heterogeneous condition requiring individualized care.

Recognizing obesity as a disease will allow for policies that better address prevention, treatments, funding and access to treatments. Healthcare professionals confronted with the challenge of managing obesity will need to embrace chronic disease models of care suited to addressing the lifelong challenge posed by this disease and its associated complications. This makes our conception of obesity as disease not only warranted, but a moral imperative.

Conflict of interest statement

DK reports no conflicts of interest. GK reports personal fees from Novo Nordisk, outside the submitted work. He has also carried out speaker engagements and been an advisory board member for Novo Nordisk and iNova (a Valeant company).

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References

1. Ng M, Fleming T, Robinson M *et al*. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384**: 766–781.
2. Chandra A, Neeland IJ, Berry JD *et al*. The relationship of body mass and fat distribution with incident hypertension: observations from the Dallas Heart Study. *J Am Coll Cardiol* 2014; **64**: 997–1002.
3. Mokdad AH, Ford ES, Bowman BA *et al*. Diabetes trends in the U.S.: 1990-1998. *Diabetes Care* 2000; **23**: 1278–1283.
4. Eheman C, Henley SJ, Ballard-Barbash R *et al*. Annual Report to the Nation on the status of cancer, 1975-2008, featuring cancers associated with excess weight and lack of sufficient physical activity. *Cancer* 2012; **118**: 2338–2366.
5. Kitahara CM, Flint AJ, Berrington de Gonzalez A *et al*. Association between class III obesity (BMI of 40-59 kg/m2) and mortality: a pooled analysis of 20 prospective studies. *PLoS Med* 2014; **11**: e1001673.
6. Colagiuri S, Lee CM, Colagiuri R *et al*. The cost of overweight and obesity in Australia. *Med J Aust* 2010; **192**: 260–264.
7. Naughton J. This is what obesity is costing Australia. Huffington Post: Australia, 2016.
8. Stoner L, Cornwall J. Did the American Medical Association make the correct decision classifying obesity as a disease? *Australas Med J* 2014; **7**: 462–464.
9. Allison DB, Downey M, Atkinson RL *et al*. Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of the Obesity Society. *Obesity (Silver Spring)* 2008; **16**: 1161–1177.
10. Kitcher P. The Lives To Come: The Genetic Revolution and Human Possibilities. Simon & Schuster: New York, 1997.
11. Boorse C. A Rebuttal on Health. In: Humber JM, Almeder RF (eds). What Is Disease? Humana Press: Totowa, NJ, 1997, pp. 1–134.
12. Murphy D. Concepts of disease and health. In: The Stanford Encyclopedia of Philosophy, Spring 2015 edn. Metaphysics Research Lab, Stanford University: Stanford, 2015.
13. Fadiman A. The Spirit Catches You and You Fall Down: A Hmong Child, Her American Doctors, and the Collision of Two Cultures. Farrar, Straus, and Giroux: New York, 1997.
14. Di Angelantonio E, Bhupathiraju SN, Wormser D *et al*. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*; **388**: 776–786.
15. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and

overweight: a systematic review and meta-analysis. *BMC Public Health* 2009; **9**: 88.
16. Fontaine KR, Barofsky I. Obesity and health-related quality of life. *Obes Rev* 2001; **2**: 173–182.
17. Williams LM. Hypothalamic dysfunction in obesity. *Proc Nutr Soc* 2012; **71**: 521–533.
18. Matikainen N, Bogl LH, Hakkarainen A *et al*. GLP-1 responses are heritable and blunted in acquired obesity with high liver fat and insulin resistance. *Diabetes Care* 2014; **37**: 242–251.
19. Faerch K, Torekov SS, Vistisen D *et al*. GLP-1 response to oral glucose is reduced in prediabetes, screen-detected type 2 diabetes, and obesity and influenced by sex: the ADDITION-PRO study. *Diabetes* 2015; **64**: 2513–2525.
20. MacLean PS, Bergouignan A, Cornier M-A, Jackman MR. Biology's response to dieting: the impetus for weight regain. *Am J Physiol Regul Integr Comp Physiol* 2011; **301**: R581–R600.
21. Greenway FL. Physiological adaptations to weight loss and factors favouring weight regain. *Int J Obes (Lond)* 2015; **39**: 1188–1196.
22. Fothergill E, Guo J, Howard L *et al*. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. *Obesity (Silver Spring)* 2016; **24**: 1612–1619.
23. Cummings DE, Weigle DS, Frayo RS *et al*. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *N Engl J Med* 2002; **346**: 1623–1630.
24. Sumithran P, Prendergast LA, Delbridge E *et al*. Long-term persistence of hormonal adaptations to weight loss. *N Eng J Med* 2011; **365**: 1597–1604.
25. Alemany M. Steroid hormones interrelationships in the metabolic syndrome: an introduction to the ponderostat hypothesis. *Hormones (Athens)* 2012; **11**: 272–289.
26. Adan C, Cabot C, Vila R *et al*. Oleoyl-estrone treatment affects the ponderostat setting differently in lean and obese Zucker rats. *Int J Obes Relat Metab Disord* 1999; **23**: 366–373.
27. Schmidt DS, Salahudeen AK. Obesity-survival paradox—still a controversy? *Semin Dial* 2007; **20**: 486–492.
28. Kalantar-Zadeh K, Block G, Horwich T, Fonarow GC. Reverse epidemiology of conventional cardiovascular risk factors in patients with chronic heart failure. *J Am Coll Cardiol* 2004; **43**: 1439–1444.
29. Sharma A, Lavie CJ, Borer JS *et al*. Meta-analysis of the relation of body mass index to all-cause and cardiovascular mortality and hospitalization in patients with chronic heart failure. *Am J Cardiol* 2015; **115**: 1428–1434.
30. Padwal R, McAlister FA, McMurray JJ *et al*. The obesity paradox in heart failure patients with preserved versus reduced ejection fraction: a meta-analysis of individual patient data. *Int J Obes (Lond)* 2014; **38**: 1110–1114.
31. Wang L, Liu W, He X *et al*. Association of overweight and obesity with patient mortality after acute myocardial infarction: a meta-analysis of prospective studies. *Int J Obes (Lond)* 2016; **40**: 220–228.
32. Veronese N, Cereda E, Solmi M *et al*. Inverse relationship between body mass index and mortality in older nursing home residents: a meta-analysis of 19,538 elderly subjects. *Obes Rev* 2015; **16**: 1001–1015.
33. Cao C, Wang R, Wang J, Bunjhoo H, Xu Y, Xiong W. Body mass index and mortality in chronic obstructive pulmonary disease: a meta-analysis. *PLoS One* 2012; **7**: e43892.
34. Stokes A. Using maximum weight to redefine body mass index categories in studies of the mortality risks of obesity. *Popul Health Metr* 2014; **12**: 6.
35. Zaccardi F, Dhalwani NN, Papamargaritis D *et al*. Nonlinear association of BMI with all-cause and cardiovascular mortality in type 2 diabetes mellitus: a systematic review and meta-analysis of 414,587 participants in prospective studies. *Diabetologia* 2017; **60**: 240–248.
36. Lechi A. The obesity paradox: is it really a paradox? Hypertension. *Eat Weight Disord* 2016; **22**: 43–48.
37. van der AD, Nooyens AC, van Duijnhoven FJ, Verschuren MM, Boer JM. All-cause mortality risk of metabolically healthy abdominal obese individuals: the EPIC-MORGEN study. *Obesity (Silver Spring)* 2014; **22**: 557–564.
38. Soriguer F, Gutierrez-Repiso C, Rubio-Martin E *et al*. Metabolically healthy but obese, a matter of time? Findings from the prospective Pizarra study. *J Clin Endocrinol Metab* 2013; **98**: 2318–2325.
39. Bluher M. Are metabolically healthy obese individuals really healthy? *Eur J Endocrinol* 2014; **171**: R209–R219.
40. Sharma AM, Campbell-Scherer DL. Redefining obesity: beyond the numbers. *Obesity* 2017; **25**: 660–661.
41. Puhl RM, Heuer CA. The stigma of obesity: a review and update. *Obesity (Silver Spring)* 2009; **17**: 941–964.
42. Sallis JF, Glanz K. Physical activity and food environments: solutions to the obesity epidemic. *Milbank Q* 2009; **87**: 123–154.
43. van Dijk SJ, Tellam RL, Morrison JL, Muhlhausler BS, Molloy PL. Recent developments on the role of epigenetics in obesity and metabolic disease. *Clin Epigenetics* 2015; **7**: 66.
44. Blackburn GL. Medicalizing obesity: individual, economic, and medical consequences. *Virtual Mentor* 2011; **13**: 890–895.
45. Saarni SI, Anttila H, Saarni SE *et al*. Ethical issues of obesity surgery—a health technology assessment. *Obes Surg* 2011; **21**: 1469–1476.
46. Lund TB, Sandoe P, Lassen J. Attitudes to publicly funded obesity treatment and prevention. *Obesity (Silver Spring)* 2011; **19**: 1580–1585.
47. Tikkinen KAO, Leinonen JS, Guyatt GH, Ebrahim S, Järvinen TLN. What is a disease? Perspectives of the public, health professionals and legislators. *BMJ Open* 2012; **2**: pii: e001632.
48. Lobstein T, Brinsden H, Gill T, Kumanyika S, Swinburn B. Comment: obesity as a disease—some implications for the World Obesity Federation's advocacy and public health activities. *Obes Rev* 2017; **18**: 724–726.
49. Turner LR, Harris MF, Mazza D. Obesity management in general practice: does current practice match guideline recommendations? *Med J Aust* 2015; **202**: 370–372.
50. Lukas N, Franklin J, Lee CM *et al*. The efficacy of bariatric surgery performed in the public sector for obese patients with comorbid conditions. *Med J Aust* 2014; **201**: 218–222.
51. Wright F, Boyle S, Baxter K *et al*. Understanding the relationship between weight loss, emotional well-being and health-related quality of life in patients attending a specialist obesity weight management service. *J Health Psychol* 2013; **18**: 574–586.
52. Cefalu WT, Bray GA, Home PD *et al*. Advances in the science, treatment, and prevention of the disease of obesity: reflections from a Diabetes Care Editors' Expert Forum. *Diabetes Care* 2015; **38**: 1567–1582.
53. Jung RT. Obesity as a disease. *Br Med Bull* 1997; **53**: 307–321.
54. Kopelman PG, Finer N. Reply: is obesity a disease? *Int J Obes Relat Metab Disord* 2001; **25**: 1405–1406.
55. Society CotO. Obesity as a disease: the Obesity Society Council resolution. *Obesity (Silver Spring)* 2008; **16**: 1151.
56. AMA. Resolution 4202013. [WWW document]. URL http://www.npr.org/documents/2013/jun/ama-resolution-obesity.pdf. Accessed 27 April 2017.
57. RichP.CMA recognizes obesity as a disease2015. [WWW document]. URL https://www.cma.ca/En/Pages/cma-recognizes-obesity-as-a-disease.aspx. Accessed 27 April 2017.

58. EMA. Guideline on clinical evaluation of medicinal products used in weight management2016. [WWW document]. URL http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500209942.pdf. Accessed 27 April 2017.
59. WHO. Obesity: preventing and managing a global epidemic2000.
60. Bray GA, Kim KK, Wilding JPH. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev* 2017; **18**: 715–723.
61. AACE/ACE. Algorithm for the Medical Care of Patients with Obesity 2016. [WWW document]. URL https://www.aace.com/files/guidelines/ObesityAlgorithm.pdf. Accessed 27 April 2017.
62. Franz MJ, VanWormer JJ, Crain AL *et al*. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc*; **107**: 1755–1767.