Obesity Treatment

Consequences of obesity and weight loss: a devil's advocate position

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Summary

Obesity is associated with multiple negative health consequences and current weight management guidelines recommend all obese persons to lose weight. However, recent evidence suggests that not all obese persons are negatively affected by their weight and that weight loss does not necessarily always improve health. The purpose of this review is not to trivialize the significant health risks associated with obesity, but to discuss subpopulations of obese people who are not adversely affected, or may even benefit from higher adiposity, and in who weight loss *per se* may not always be the most appropriate recommendation. More specifically, this review will take a devil's advocate position when discussing the consequences of obesity and weight loss for adults with established cardiovascular disease and type 2 diabetes, weight cyclers, metabolically healthy obese adults, youth, older adults and obese individuals who are highly fit.

Keywords: Exercise, metabolically healthy obese, obesity paradox, older adults.

Introduction

Obesity is a major global health challenge. Between 1980 and 2013, the prevalence of worldwide obesity has substantially increased from 28.8% to 36.9% in adult males and from 29.8% to 38.0% in adult females (1). The association between obesity and increased risk for chronic health conditions, such as cardiovascular disease (CVD) and type 2 diabetes (T2D), is well established (2) and obesity is now the fifth leading cause of death worldwide (3). According to national weight management guidelines, all obese adults should be advised to lose weight (4) and a modest weight loss of 5%–10% of body weight has been shown to significantly improve cardiometabolic risk factors (5). However, increasing evidence suggests that there may be subpopulations of obese individuals who are not adversely affected by their increased adiposity, or in whom weight loss may not always result in improved health outcomes, such as adults with established CVD or T2D, weight cyclers, metabolically healthy obese adults, youth, older adults or 'fit and fat' individuals. The purpose of this review is not to convince the reader that obesity is a benign condition or that weight loss cannot be beneficial for health. Rather, this review will attempt to bring light to the fact that obesity is a complex condition that is not always associated with deleterious health outcomes and that weight loss *per se* may not always be the most appropriate recommendation for all obese individuals. A summary of our findings is provided in Table 1.

Individuals with cardiovascular disease and type 2 diabetes

Obesity is clearly an established risk factor for CVD (6) and T2D (7,8) and is associated with increased risk of hypertension, myocardial infarction, coronary artery disease, stroke and heart failure (9). Despite the established association between obesity and risk of CVD, there is a great deal of evidence that an 'obesity paradox' exists in obese individuals with CVD in that they tend to have better prognosis than normal-weight individuals. The obesity paradox has been recognized in patients with heart failure, hypertension,

Table 1 Summary of evidence regarding effect of obesity and/or weight loss in subgroups of obese populations

Obesity subgroup	Summary of evidence
CVD	• Obesity is a significant risk factor for CVD. • 'Obesity paradox' – obese patients with established CVD or heart failure often have a better prognosis than leaner patients, although this may be modified by fitness. • Intentional weight loss via cardiac rehabilitation programmes can result in weight loss and improvements in CVD risk factors. • Effects of intentional weight loss in patients with heart failure are not known.
T2D	• Obesity is a significant risk factor for T2D. • Evidence of an 'obesity paradox' in that obesity at time of diagnosis may be associated with lower mortality risk compared with normal weight. • Intentional weight loss associated with improved glycaemia and cardiometabolic risk factors, but the effect on cardiovascular outcomes and mortality in obese patients with T2D is less clear.
Weight cyclers	• May be associated with adverse body composition, negative cardiometabolic health outcomes and increased mortality risk.
MHO phenotype	• Inconsistent evidence as to whether MHO adults have similar health and mortality risk as metabolically healthy normal-weight adults. • Evidence regarding health outcomes following weight loss in MHO adults is equivocal. • A standardized definition of MHO is needed.
Youth	• Obesity in youth is generally associated with negative cardiometabolic health outcomes that track into adulthood. • MHO children are more likely to retain MHO status as an adult. • Weight loss in obese youth is associated with positive health outcomes but there are currently no clear standardized guidelines for weight loss treatment for obese youth.
Older adults	• Effects of obesity on morbidity and mortality are less clear in older adults than in younger adults. • Intentional weight loss can improve cardiometabolic health and physical function. • An exercise component is critical for weight management in the elderly to preserve or increase muscle mass and strength and to improve physical function.
'Fat and fit' individuals	• Evidence that high cardiorespiratory fitness may be associated with positive metabolic health outcomes and lower mortality risk independent of obesity. • Exercise without weight loss is associated with improved body composition and improved cardiometabolic health.

CVD, cardiovascular disease; T2D, type 2 diabetes; MHO, metabolically healthy obese.

coronary artery disease and in those who have undergone cardiac revascularization (10–15). Several studies have demonstrated that obese adults with heart failure may have a similar or even lower mortality risk compared with normal-weight individuals (16–20). There is also evidence that obese persons who undergo coronary revascularization have a lower in-hospital mortality risk or risk of adverse cardiac events (21–24) and a significantly lower mortality risk compared with normal-weight patients (25). Recently, it has been suggested that an obesity paradox may also be present for adults with T2D (26), in that adults who have normal weight when diagnosed with T2D have a higher mortality risk than adults who are obese at the time of diagnosis (27) regardless if they have a history of CVD or not (28). As well, obese adults with both CVD and T2D have also been reported to have a lower mortality risk compared with normal-weight adults (29). Thus, although obesity is a significant risk factor for these conditions, once the disease is present obesity may in fact improve survival. However, some studies suggest that this obesity paradox may only exist in individuals with low cardiorespiratory fitness as there is no difference in mortality rates by obesity in individuals with high cardiorespiratory fitness (30,31).

Although the underlying mechanisms of the obesity paradox are unknown, there are several hypotheses. Because heart failure is considered a catabolic state, obese individuals with heart failure may have more metabolic reserve (32). Obesity is a common primary contributor to the development of heart failure in obese individuals and therefore normal-weight or lean persons who develop CVD or heart failure may have a greater genetic predisposition for CVD or be resistant to medical interventions (33). Further, adults with obesity may experience less unintentional weight loss and cachexia, may take more protective CVD medications and may have increased muscle mass than lean adults (11). In adults with T2D, it has been suggested that having normal weight at the time of diagnosis may imply a different patho-physiology of T2D than in those who are obese (34) and that it may actually be a sign of latent autoimmune diabetes in adults (27). As well, differences in lean mass (35) or in types of diabetes medications that are typically prescribed to lean versus obese individuals have also been suggested to play a role (36). Clearly, the mechanisms that are associated with better survival in obese patients with CVD or T2D requires further investigation.

The effects of weight loss in patients with CVD or T2D are also not clear. Several studies have demonstrated that intentional weight loss that is achieved through a cardiac rehabilitation programme (10,37,38) is associated with improved cardiovascular risk factors in obese patients with CVD. Conversely, weight loss in CVD patients that is achieved through other modalities, such as liquid protein diets or very-low-calorie diets, have been associated with arrhythmias, ventricular tachycardia and in some cases

death (39). There is also evidence that body mass index (BMI) alone is not a good indicator of mortality risk following a cardiovascular event and that total weight loss may be associated with increased mortality risk, whereas fat loss is associated with lower mortality risk (40). However, this is in contrast to evidence that a higher body fat percentage is the strongest predictor of event-free survival in patients with heart failure (41). Further, there is little evidence for the effects of intentional weight loss on long-term prognosis in patients with heart failure, and thus more research in this area is needed (11,12). Thus, the relationship between adiposity and weight loss with mortality risk in CVD patients requires further investigation.

In obese adults with T2D, there is considerable evidence to suggest that intentional weight loss markedly improves glycaemia and other cardiometabolic risk factors (42–45). Some observational studies suggest that intentional weight loss is associated with decreased mortality risk in adults with T2D (46–48), although this is not a consistent finding (49). Recently, the Look AHEAD trial, the only trial to randomize overweight and obese adults with T2D to an intensive lifestyle intervention or usual care, was stopped prematurely because of a lack of evidence that the lifestyle treatment group experienced less CVD deaths or events than the control group, despite losing more weight and improving on most CVD risk factors (50). Furthermore, one study reported that among adults with CVD and T2D, weight loss but not weight gain was predictive of a higher risk of hospitalization, myocardial infarction, stroke and death (29).

Therefore, although obesity is an established risk factor for CVD and T2D, there is considerable evidence that an obesity paradox exists in obese individuals with CVD, and recently, there have been reports that this phenomenon may also exist in patients with T2D. However, the biological mechanisms for this paradox are unclear. Evidence regarding the effect of purposeful weight loss on obese individuals with either disease is not clear cut and more research in this area is warranted.

Weight cyclers

The prevalence of US adults who are obese and attempting weight loss is estimated to be 56% in men and 64% in women (51). Even when attempts at weight loss are successful, only about 20% of obese adults are able to maintain weight loss after 1 year (52). This can lead to a pattern of repeated episodes of weight loss followed by weight gain, referred to as weight cycling. Studies that have investigated the prevalence or the health effects of weight cycling show inconsistent results, possibly because of the different definitions used to describe weight cycling. Weight cycling has been defined as losing ≥20 pounds at least three times (53), gaining and losing ≥5% of body weight (54), losing

and regaining ≥5 kg one or more times (55) and losing and regaining ≥5 kg five or more times (56).

While not all studies have shown detrimental effects of weight cycling (57–61), many have reported that weight cycling may be associated with a higher BMI, body fat percentage, waist circumference, greater fat mass distribution to the upper body, lower resting metabolic rate, increased risk of hypertension, decreased glucose tolerance and higher prevalence of low high-density lipoprotein cholesterol (HDL) compared with non-weight cyclers (62–67). It has also been reported that weight cycling is associated with lower self-esteem, a higher prevalence of binge eating, more frequent visits to the doctor and poorer perceived self-health (55,62,68–70). During a weight loss intervention, weight cyclers lose less fat and more lean mass than non-weight cyclers (71) and when weight is regained, a greater proportion of fat is regained than lean mass (72). Further, there are many studies that have demonstrated a higher mortality risk in individuals with a history of weight cycling, although this is not always observed (53,73–80). However, one study reported that only when weight was gained during young or middle age, but not old age, was weight cycling associated with increased mortality risk (54). In summary, there is some evidence that weight cycling is associated with multiple negative health outcomes, including increased mortality risk. However, whether or not losing weight and regaining it is safer or more dangerous than remaining obese and not attempting weight loss remains to be elucidated.

Metabolically healthy obese phenotype

Metabolically healthy obese (MHO) persons are a subset of obese individuals typically defined as having excess body fat, but are insulin sensitive, normotensive, have a favourable lipid profile and have less visceral fat than the typical individual with obesity-related comorbidities (81–84). Currently, there is no standardized definition of MHO and the underlying mechanisms of this phenotype are not clear. It has been suggested that a preserved insulin sensitivity (85), as well as high levels of physical activity and physical fitness (86–88) may differentiate metabolically healthy from unhealthy obese adults, although this is not always a consistent finding.

There is evidence that MHO adults are not at an elevated risk for CVD (89,90), myocardial infarction (91) and do not have excess mortality risk (92–94) compared with metabolically healthy normal weight adults. This is in contrast to others who have reported that MHO individuals are still at a higher risk for premature mortality (83,95), as well as T2D (89,96,97), heart failure (91) and subclinical atherosclerosis (98). However, it is important to note that the majority of the aforementioned studies defined MHO as the presence of ≤1 or ≤2 metabolic risk factors.

Therefore, the majority of individuals defined as MHO in these studies were likely not truly metabolically healthy, which may explain the inconsistent findings regarding MHO and health risk. This may be due to the fact that a true MHO phenotype, defined as no clinical or subclinical metabolic risk factors, is quite rare and may only represent 3–6% of adults with obesity (83,99).

Whether or not weight loss improves cardiometabolic risk factors in MHO individuals is of interest. Several studies have reported that following weight loss, MHO individuals significantly improved body composition and cardiometabolic risk factors (100–102), as well as physical fitness (102). However, other studies have failed to show improvements in metabolic risk factors in MHO adults despite significant loss of body weight (103–105). Interestingly, weight loss in MHO adults may even have a detrimental effect on health, as after 6 months of caloric restriction, insulin sensitivity improved in at-risk obese women, but actually decreased by 13% in MHO women (106). Furthermore, some studies report that when obese adults who do not have comorbidities intentionally lose weight, they have a higher mortality risk compared with those who remain weight stable (46,47,107).

Given the existence of the MHO phenotype, the question becomes if all obese individuals should be advised to lose weight as the guidelines suggest and how obese people with no morbidities should be medically counselled. The Edmonton Obesity Staging System (EOSS) is a clinical staging system that was recently developed to evaluate the metabolic, psychological and physical health of obese patients and recommend treatment according to severity of health risk (108). The stages range from 0 to 4, indicating no obesity-related risk factors to severe end-stage disease. Individuals in stage 0 or 1 have no established obesity-related chronic diseases and it is recommended that they engage in lifestyle modification to prevent further weight gain, but not to necessarily lose weight. Conversely, only persons in stages 2–4 have established obesity-related disease and are counselled to lose weight. Because EOSS is a relatively new model, the clinical utility of EOSS is not yet established. However, given the inconclusive evidence that MHO individuals benefit from weight loss, EOSS may prove to be a valuable clinical tool in terms of better assessment and treatment of obese persons.

In summary, although there is evidence of an MHO phenotype, it may represent a rare subgroup of obese individuals. More research is needed to elucidate the mechanisms underlying the MHO phenotype and the effect of weight loss on cardiometabolic health and mortality in this population.

Youth

Obesity in children and adolescents is a growing public health concern as there has been a concomitant increase in obesity-related health conditions that is typically observed in adults, such as hyperlipidaemia (109), metabolic syndrome (110), non-alcoholic fatty liver disease (111) and T2D (112). The increased prevalence of childhood obesity is concerning because obese youth are more likely to remain obese as adults (113–121) and cardiometabolic risk factor clustering has been reported to track well from childhood into adulthood (122). Because obese youth will likely live a longer portion of their life as obese and with chronic health conditions, some have predicted that the youth of today will live unhealthier lives and perhaps have a shorter life expectancy than their parents (123).

Despite evidence that obese youth are at a greater risk for cardiometabolic health conditions as adults (120,124,125), several studies have reported that adult BMI is a better predictor of adult CVD and T2D risk factors than childhood BMI (126). Nonetheless, the pattern of obesity may also be important to consider, as individuals who were obese as both children and adults are more likely to develop T2D, hypertension, dyslipidaemia and CVD compared with individuals who remained normal weight as a child and adult (127–129). However, up to 31% of obese youth have been reported to be MHO (130) and there is evidence that MHO youth are more likely to retain their MHO status as an adult and have similar carotid intima-media thickness in adulthood as non-obese children (131). As well, a longer duration of obesity may be associated with greater insulin sensitivity (132). Moreover, although weight loss in obese youth is typically associated with improved metabolic outcomes (133), weight management goals for this age group are more ambiguous than in adults (i.e. 5–10% of body weight). Although some suggest that weight should be maintained or lost until BMI reaches less than the 85th percentile (134), there are currently no clear standardized guidelines for weight loss treatment for obese children and adolescents.

Older adults

Over the past several decades, the proportion of obese older adults in the United States has more than doubled to 35% (135,136). Given that both age and obesity are associated with increased risk for health conditions, a higher prevalence of obese older adults may pose a large threat to the healthcare system. However, the association between obesity and health risk is not as well understood in the elderly as it is in younger adults, and whether or not obese older adults should lose weight is controversial (137,138).

Some have suggested that increased adiposity may be beneficial for elderly individuals. Obesity in older adults has been associated with higher bone mineral density and decreased risk of osteoporosis (139–141), lower probability of serious injury from a fall (142) and lower risk of osteoporotic fracture (143). Although obesity is a risk

factor for CVD and T2D at any age, the association appears to be stronger for younger adults than older adults (144,145). Furthermore, BMI may not be the most useful indicator of obesity-related health risk in the elderly because of the age-related changes in body composition that can occur without a change in BMI, such as increased visceral adiposity, and decreased lean mass (146). Indeed, high waist circumference has been associated with increased morbidity and mortality risk in older adults independent of BMI (147–149). Conversely, others have reported that obese older adults have a similar (150–152) or lower (153–155) mortality risk compared with normal-weight older adults, regardless if obesity is defined as high BMI, waist circumference, waist-to-hip ratio or body fat percentage (156,157).

Increasing evidence suggests that the length of time that an individual is obese is important to consider, as individuals who are obese throughout adulthood are at a higher risk for hip and knee osteoarthritis (158), low cognition scores (159) and disability (160) during old age compared with those who remain normal weight. Conversely, one study reported that longer duration of obesity was associated with *greater* insulin sensitivity in obese non-diabetic adults (132). Furthermore, the pattern of weight gain may also be important to consider as individuals who gain weight during young and middle adulthood have been reported to have a higher mortality risk compared with persons who only gain weight during old age (54,161).

Whether or not obese older adults should attempt weight loss is also a controversial issue (162). Some intervention studies suggest that weight loss in older adults results in improvements in osteoarthritis, physical functioning, T2D and coronary heart disease (163). However, weight loss in the elderly is often associated with loss of lean mass (164–167), loss of bone mass (166,168,169) and may be associated with risk of fractures (170). A recent systematic review concluded that adding an exercise component to energy restriction during weight loss interventions in obese elderly is critical for improvements in cardiovascular fitness, muscle strength, increasing fat mass and preserving lean mass (171). When exercise is added to a hypocaloric diet in obese older adults, there is evidence that they lose similar amounts of body weight as the diet-only group, but generally lose less lean mass, bone mineral density and bone mass, experience greater increases in muscle strength and insulin sensitivity and have a greater reduction in cardiometabolic risk factors compared with diet-only groups (164–166,169,172–174). Even exercise without weight loss can have beneficial effects in the obese elderly and has been associated with stable or increased bone mineral density (175,176), increases in lean mass and significant decreases in markers of inflammation (177). However, whether or not weight loss is more beneficial than exercise without weight loss is unclear. Thus, it is

suggested that treatment goals for obese older adults should not necessarily focus on weight loss *per se*, but on lifestyle changes that improve physical function status and quality of life and that maintain or increase lean mass and muscular strength (138).

Therefore, the association between obesity and health risk in the elderly is still not fully understood. In older adults, obesity may impose less of a risk for morbidity and mortality compared with younger adults. Obese elderly adults who are prescribed to lose weight should be carefully monitored because of the loss of lean mass and bone mass that often accompanies weight loss, although adding an exercise component may partially ameliorate these effects.

'Fit and fat' individuals

There is a growing body of literature that has shown that physical fitness is a predictor of morbidity and mortality risk independently of BMI (86,178–180) and that adults who are obese and fit may have a comparable mortality risk as normal-weight and fit adults (179,181). This may be in part due to lower overall and visceral adiposity in fit individuals for a given BMI. Further, it is demonstrated that men with high cardiorespiratory fitness have been reported to have higher HDL levels, as well as lower triglyceride levels, prevalence of metabolic syndrome, risk of developing CVD risk factors and mortality risk, independent of adiposity (182–184). However, not all studies find that fitness completely ameliorates the negative health effects of obesity, as some have reported that obese and fit individuals are still at a higher mortality risk compared with normal-weight and fit persons (185,186). This is in contrast to a recent meta-analysis that showed that obese and fit individuals had a similar mortality risk as normal-weight and fit adults (187). Further, another study reported that although obese and fit individuals had a lower all-cause and cardiovascular mortality risk compared with normal-weight and unfit individuals, they still had a higher risk of incident T2D and prevalence of cardiovascular and T2D risk factors (188).

Several studies have shown the beneficial effects of exercise on cardiometabolic risk factors even in the absence of weight loss. This is because even one acute bout of exercise can significantly reduce insulin sensitivity, cholesterol, blood pressure, blood glucose and triglycerides transiently post-exercise, with the effects usually being greatest in high risk or diseased populations (189). Further, exercise without weight loss in obese adults is associated with significant increases in skeletal muscle (190), reduced visceral fat (190–194), reduced hepatic fat (195) and improved fitness.

Thus, evidence shows that it is possible to be physically fit despite a high level of adiposity. Although exercise alone is not typically associated with significant weight loss, it

can lead to improved cardiometabolic risk factors and positive changes in body composition (31). Whether obese and fit individuals can attain similar morbidity and mortality risk as normal-weight and fit individuals is still controversial. In obese individuals who struggle to lose or maintain weight, health professionals should consider acknowledging exercise as a plausible method of reducing obesity-related comorbidities and premature mortality risk, regardless of weight loss achieved (31).

In addition to physical activity and having high cardiorespiratory fitness, several factors may influence health independent of obesity and weight loss. For example, diet quality can influence health independent of changes in body weight. A low glycaemic index diet for even a 24-h period is reported to improve glucose and insulin levels by 30% in adults with T2D (196). Furthermore, a short-term high fat diet has been observed to significantly increase liver fat, intramyocellular lipid content and fasting insulin levels and impair insulin sensitivity without a change in body weight in humans (197,198). Bariatric surgery is also reported to have health benefits that go beyond what is expected through weight loss alone that may be related to decreased systemic inflammation, modifications of the gut microbiota, exclusion of nutrients from the duodenum, increased incretin secretion and increases in bile acids (199,200). Thus, there are several situations in which weight loss may not be required to influence health.

Conclusion

In conclusion, obesity is a rapidly growing problem in both children and adults that is associated with numerous negative health outcomes, many of which can be prevented or ameliorated with modest weight loss. Current weight management guidelines recommend weight loss for all obese adults. However, it is evident that not all obese individuals, such as those who are elderly, metabolically healthy or highly fit, are at an increased risk for health problems. Further, whether weight loss is beneficial for all obese individuals is questionable. In fact, weight loss in obese populations with established CVD or T2D has been reported to be detrimental for longevity. As well, due to the low success rate for obese adults attempting weight loss (52), it is questionable whether the benefits of weight loss outweigh the potential negative effects of weight cycling. Therefore, an emphasis on maintaining a healthy lifestyle that includes a high level of physical activity and physical fitness may be a more appropriate recommendation for some obese populations than just focusing on the goal of weight loss alone. Future research should attempt to elucidate the mechanisms underlying the obesity paradox and the MHO phenotype, as well as continue to investigate the potentially differing effects of weight loss on various populations of obese people.

Conflict of interest statement

No conflict of interest was declared.

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