

Obesity and periodontal disease

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Definition and current prevalence

Classification

Obesity is an excess amount of body fat in proportion to lean body mass, to the extent that health is impaired (3). The most commonly used measure of body fat is the body mass index, which is defined as a person's weight, in kilograms, divided by the square of his/her height in meters. The World Health Organization and the National Heart, Lung and Blood Institute (NHLBI) define overweight as a body mass index of 25–29.9 and obesity as a body mass index of ≥ 30 (50, 80). Childhood obesity is defined as a body mass index for age and gender that is greater than the 95th percentile (6). The full classification for overweight and obesity, developed by the National Institutes of Health through an expert panel that reviewed data from approximately 394 studies, is shown in Table 1.

Waist circumference is also an important indicator of visceral abdominal fat. Evidence suggests that abdominal fat carries a higher health risk than peripheral fat, and that the visceral fat component has the strongest correlation with increased risk. A high-risk waist circumference is considered to be ≥ 88 cm for women and ≥ 102 cm for men (50).

Prevalence and trends

Over the period 1960–1980, the prevalence of overweight and obesity among adults, and of overweight among children, was relatively constant. About 13% of adults were obese and 5% of children were overweight. However, data from the National Health and Nutrition Examination Survey III (1988–1991) showed that obesity in adults and overweight in children had markedly increased from the previous survey (38, 74). Those trends continued such that approximately 31% (59 million) of American adults now meet the criterion for obesity. More than 65% of the United States adult population have a body mass index of ≥ 25 kg/m²; and 15.8% of children aged 6–11 years,

and 16.1% of adolescents aged 12–19 years, are overweight (49). Thus, in a relatively short time period, the prevalence of obesity among adults has doubled, and the prevalence of overweight among children and adolescents has tripled.

With the exception of sub-Saharan Africa, trends internationally have mirrored those seen in the U.S.A. The International Obesity Task Force estimates that over 1 billion adults are overweight, including 312 million who are obese. Because Asians experience obesity-related disease complications at lower body mass indices, new criteria for Asians delineate overweight as a body mass index of ≥ 23 . Using this criteria, the number of adults globally who are overweight is closer to 1.7 billion (34).

Twin studies (71), and other longitudinal data (8, 19), clearly demonstrate a genetic component in human obesity. However, recent increases in obesity prevalence cannot be solely explained by changes in the gene pool. Predisposition to obesity is probably influenced by numerous susceptibility genes, accounting for variations in energy needs, fuel utilization, metabolic characteristics, and taste preferences. Although influenced by genetic variability, the three factors believed to contribute most to the etiology of obesity are metabolic factors, diet, and physical inactivity. Metabolic factors, such as resting energy expenditure (the number of calories burned at rest) and the thermic effect of food (energy expended during digestion, transport, metabolism and storage of food), vary among individuals but do not appear to be a major component in explaining risk for developing obesity (68). Large portion sizes, high fat intakes, and easy access to calorically sweetened beverages, all play a role in the development of obesity (25, 30). Longitudinal data suggests a particularly important role of reduced physical activity. In a 5-year prospective study of over 12,000 Finnish adults, sedentary individuals were almost twice as likely to experience substantial weight gain as physically active men and women (66). For children, decreased participation in organized sports, changes in

Table 1. Classifications for body mass index (BMI)

Classification	BMI
Underweight	<18.5
Normal	18.5–24.9
Overweight	25.0–29.9
Obesity class I	30.0–34.9
Obesity class II	35.0–39.9
Obesity class III	40+

school physical education policies, parental rules restricting activity as a result of safety and convenience, and environmental barriers to physical activity, all contribute to decreased energy expenditure (15).

Obesity and inflammation

For many years, adipose tissue was considered as an inert organ that stored triglycerides. It is now clear that adipose tissue is a complex and metabolically active endocrine organ that secretes numerous immunomodulatory factors and plays a major role in regulating metabolic and vascular biology. Adipose cells, which include adipocytes, preadipocytes, and macrophages, secrete more than 50 bioactive molecules, known collectively as adipokines. Some of these adipokines act locally, whereas others are released into the systemic circulation where they act as signaling molecules to the liver, muscle, and endothelium (73). Adipokines play a number of different roles, such as hormone-like proteins (e.g. leptin and adiponectin), classical cytokines (e.g. tumor necrosis factor- α , interleukin-6), proteins involved in vascular hemostasis (e.g. plasminogen activator inhibitor-1, tissue factor), regulators of blood pressure (angiotensinogen), promoters of angiogenesis (e.g. vascular endothelial growth factor), and acute-phase respondents (e.g. C-reactive peptide).

Leptin

Leptin is secreted almost exclusively by adipocytes. Leptin signals through the central nervous system and peripheral pathways to suppress appetite and increase energy expenditure. Leptin mimics some of the actions of insulin by increasing glucose uptake in muscle and adipose tissue and by lowering hepatic glucose production (45). Most obese individuals have elevated leptin levels that do not suppress appetite.

Many consider this leptin resistance to be one of the features contributing to obesity's pathology. In obese patients with leptin resistance, leptin may elevate blood pressure and contribute to atherosclerosis and cardiovascular disease (12, 62).

Adiponectin

Adiponectin is produced primarily by adipocytes, but surprisingly is decreased in obese subjects, especially those with abdominal obesity. Clinical studies demonstrate inverse associations between adiponectin and serum markers of inflammation (54). Adiponectin has anti-atherogenic properties and appears to play a protective role in cardiomyopathy. Low levels of adiponectin are associated with an increased risk of coronary artery disease and other features of the metabolic syndrome (39).

Tumor necrosis factor- α

Obesity-associated tumor necrosis factor- α is primarily secreted from macrophages accumulated in abdominal (as opposed to peripheral) adipose tissue (75). Although studies have not shown completely consistent results, it is thought that increased circulating tumor necrosis factor- α from adipose tissue contributes to poor health outcomes by increasing insulin resistance and by inducing C-reactive peptide production and general systemic inflammation (7). It also facilitates monocyte recruitment into developing atherosclerotic lesions (52, 63). Tumor necrosis factor- α is a potent inhibitor of adiponectin, an important anti-inflammatory adipokine (69).

Interleukin-6

Interleukin-6 is secreted by human adipose tissue and is produced in greater amounts by deep abdominal (or visceral) fat than by subcutaneous fat. It is a pro-coagulant cytokine and increases plasma concentrations of fibrinogen, plasminogen activator inhibitor-1, and C-reactive peptide (65). Elevated levels of interleukin-6 are associated with increased risk of cardiovascular events in healthy men (64). Despite its association with cardiovascular disease states, data also demonstrate its roles in inducing lipolysis and decreasing appetite and weight gain (7).

Plasminogen activator inhibitor-1

Plasminogen activator inhibitor-1 is a regulatory protein of the coagulation cascade. It prevents the

dissolution of clots by inhibiting extracellular matrix degradation and fibrinolysis. Plasminogen activator inhibitor-1 is produced both by adipocytes and stromal cells surrounding the adipocytes. The levels of plasminogen activator inhibitor-1 are raised with increased accumulation of adipose tissue, especially in the abdominal area (46). Plasminogen activator inhibitor-1 is thought to contribute directly to obesity complications, including the development of type 2 diabetes and coronary thrombi (14).

Angiotensinogen

Angiotensinogen is secreted from adipose tissue, mostly from abdominal fat stores. Increased levels are seen in obesity (9). Angiotensinogen has many effects on blood vessels, including the well-known vasoconstrictive effects and contribution to hypertension (18).

Vascular endothelial growth factor

Obesity is associated with increased levels of the angiogenic factor, vascular endothelial growth factor, which also plays a role in hypertension and atherogenesis (48). Although vascular endothelial growth factor is necessary for vascular remodeling after angioplasty and for the development of collaterals in diabetic peripheral vascular disease, vascular endothelial growth factor also contributes to the initial development of atheromatous changes and post-catheterization restenosis (16).

C-reactive peptide

Elevated C-reactive peptide levels are associated both with obesity and with increased risk of cardiovascular disease. Elevated C-reactive peptide levels in obese patients predict both the development of cardiovascular disease and the risk of progression to type 2 diabetes mellitus (58).

Health consequences

Mortality

In younger and middle-aged, but not older, women and men, mortality risks appear to be directly related to body mass index (24). Although the mortality risk associated with being overweight (a body mass index of 24.9–30) is less clear, most studies consistently demonstrate increased mortality among

young and middle-aged adults who are obese. In Flegal's study of National Health and Nutrition Examination Survey data, relative to the normal weight category (body mass index 18.5 to <25) obesity was associated with 111,909 excess deaths in the year 2000 (22).

In addition to mortality risk, obesity continues to be a major risk factor for high blood pressure, cardiovascular disease, osteoarthritis, respiratory disorders, gall bladder disease, nonalcoholic fatty liver, and type 2 diabetes. Obesity markedly increases the years of life lost to illness and diminishes quality of life, especially among younger age and lower socioeconomic level groups (23, 28).

Hypertension

Blood pressure is strongly correlated with body mass index. In a study of 10,000 men and women between 20 and 60 years of age, body mass index was significantly associated with systolic and diastolic blood pressure, independent of age, alcohol intake, and tobacco use (17). Excess weight and adult weight gain substantially increase the risk for developing hypertension. Each 1-kg increase in weight after age 18 years is associated with a 5% increase in risk for hypertension (32). The increase in blood pressure is a result, in part, of the release of angiotensinogen (a precursor of angiotensin that increases blood pressure – see above under the heading 'Angiotensinogen') from adipocytes, an increase in blood volume from increased body mass, and increased blood viscosity (related to the release of plasminogen activator inhibitor-1 from adipocytes).

Diets that predispose individuals to weight gain also increase blood pressure. Saturated fats induce a rise in systolic and diastolic pressures, along with high sugar intakes (2, 59). Reducing the energy density of foods by consuming more fruit and vegetables (as shown by the Dietary Approaches to Stop Hypertension trials) lowers blood pressure (2). Although body weight and diet are both related to hypertension, it is difficult to distinguish whether the effect of weight loss, or the effect of dietary changes leading to weight loss, is more important in blood pressure control (5).

Cardiovascular disease

Obesity remains an independent risk factor for cardiovascular disease (33). In a study of 33 cohort studies, including 310,283 participants, baseline body mass index was associated with increased risks of

ischemic stroke, hemorrhagic stroke, and ischemic heart disease. Each 2 kg/m² lower body mass index was associated with a 12% lower risk of ischemic stroke, an 8% lower risk in hemorrhagic stroke, and an 11% lower risk of ischemic heart disease (4). About 14% of heart failure cases in women and 11% in men are attributable to obesity (36). This is probably the result of a combination of factors, including associated hypertension, diabetes, dyslipidemia, diabetes, and accelerated atherosclerosis, all of which increased with obesity.

Osteoarthritis

Obesity is associated with both knee and hip arthritis, and with arthritis involving the carpometacarpal joints of the hand. Recent studies have proved that being overweight antedates the development of the knee osteoarthritis and increases the risk of radiographic progression (40). In people who are overweight, weight loss can reduce the risk of osteoarthritis. In the Framingham study, women who lost an average of 5 kg decreased their risk of knee osteoarthritis by 50% (20). An increased body mass index is also associated with an increased risk of hip replacement owing to osteoarthritis (35).

Respiratory disorders

Visceral fat accumulation results in restrictive respiratory function with reduced forced vital capacity and expiratory reserve volume (11). Obesity is the major reversible risk factor for obstructive sleep apnea syndrome. The prevalence rises from 2% to 4% in the general population to a prevalence of at least 40% in morbidly obese patients (60). Orofacial findings, typical of obstructive sleep apnea syndrome, include a retrognathic mandible, narrow palate, large neck circumference, long soft palate, tonsillar hypertrophy, nasal septal deviation, and relative macroglossia (43). Waist circumference tends to be a better predictor of obstructive sleep apnea syndrome than body mass index. In a study of male obese patients, those with obstructive sleep apnea syndrome had a greater amount of computed tomography scan-determined visceral adipose tissue in the abdomen than a group of body mass index-matched men without sleep-disordered breathing (76).

Gall bladder disease

Gall bladder disease, or cholelithiasis, is the primary hepatobiliary pathology associated with obesity.

Obese women have at least twice the risk of gall bladder disease compared with women of normal weight. Although not as strong, increased body mass index is also associated with gall bladder disease in men (67). It is thought that this relationship is the result of a higher excretion of cholesterol through the bile in obese patients.

Nonalcoholic fatty liver

Nonalcoholic fatty liver disease is the most common chronic liver disease in the U.S.A. Of individuals with nonalcoholic fatty liver disease, 20–25% progress to cirrhosis and liver-related death within 10 years (47). Contributing factors include obesity, diabetes, hyperlipidemia, and hypertension. The disorder is generally asymptomatic; some patients describe tiredness and abdominal discomfort. The finding of raised concentrations of γ -glutamyl transpeptidase and alanine aminotransferase may be the first indication of nonalcoholic fatty liver disease (31). Currently, liver biopsy is the only method for making a conclusive diagnosis.

Type 2 diabetes

Around 90% of individuals who develop type 2 diabetes have a body mass index higher than 23.0 kg/m². The relative risk for an obese person to develop type 2 diabetes is 10-fold for women and 11.2-fold for men (21). Diabetes risk is significantly increased by early weight gain, especially in childhood and in people with a family history of diabetes, with abdominal obesity, or whose mothers who had gestational diabetes (77).

Metabolic syndrome

Metabolic syndrome is a clustering of inter-related risk factors that identify individuals at risk for type 2 diabetes and cardiovascular disease. Insulin resistance is considered to be the major underlying abnormality (61). Several definitions and criteria have been put forth by organizations, including the World Health Organization, The American Association of Endocrinologists, and the National Cholesterol Education Program Adult Treatment Panel III. The most clinically straightforward criteria are those crafted by the National Cholesterol Education Program Adult Treatment Panel III (Table 2). When three or more of the five listed criteria are present, the diagnosis of metabolic syndrome can be made (29).

Table 2. Criteria for the diagnosis of metabolic syndrome

Elevated waist circumference	
Men	≥ 40 inches (102 cm)
Women	≥ 35 inches (88 cm)
Elevated triglycerides	≥ 150 mg/dl
Reduced HDL ('good') cholesterol	
Men	<40 mg/dl
Women	<50 mg/dl
Elevated blood pressure	≥ 130/85 mmHg
Elevated fasting glucose	≥ 100 mg/dl

When three or more of the five listed criteria are present, the diagnosis of metabolic syndrome can be made (29). HDL, high-density lipoprotein.

Obesity and oral health

Periodontal disease and obesity

The immunologic activity of adipose tissue may play an important role both in the development of insulin resistance and in periodontal disease. Several decades ago, obesity was noted to contribute to the severity of periodontal disease in rats (56). Several recent studies have suggested a relationship between periodontal disease and obesity. In Saito's study of Japanese adults, increasing body mass index and waist:hip ratio was associated with increasing risk of periodontitis. Al-Zharani et al. analyzed data from the Third National Health and Nutrition Examination Survey and reported a significant association between measures of body fat and periodontal disease among younger adults, but not among middle-aged or older adults (1). Using the same database as Al-Zharani et al., Wood et al. evaluated the relationship between different measures of adiposity and periodontal disease (79). Instead of waist circumference used by Al-Zharani et al., Wood et al. noted correlations between body mass index, waist:hip ratio, and various periodontal measures, including mean periodontal attachment loss, mean pocket depth, mean gingival bleeding index, and mean calculus index (79). Lundin et al. recently noted a correlation between tumor necrosis factor- α in the gingival crevice fluid and body mass index (42). Given recent evidence regarding adipose tissue serving as a reservoir for inflammatory cytokines, it is possible that increasing body fat increases the likelihood of an active host inflammatory response in periodontal disease (27). However, these studies have all been cross-sectional, and may be limited by sig-

nificant residual confounding. Longitudinal studies with more precise measures of adiposity will provide better insights into the relationship between periodontal disease and obesity.

Impact of obesity on oral health

In addition to the potentially negative effects that obesity may have on the periodontium, obesity may also negatively affect the safety of intravenous sedation and the effectiveness of regional anesthetic blockade. Assessment of lung function and comorbidities are essential before engaging in any form of anesthesia.

Prevention and treatment of obesity

Pediatric obesity

Some studies suggest that intrauterine overnutrition predicts lifelong obesity. High maternal glucose, free fatty acid, and amino acid plasma concentrations may result in overnutrition of the fetus which, in turn, may lead to permanent changes in appetite and satiety, neuroendocrine functioning, or energy metabolism in the developing fetus, leading to obesity in later life (78). A few studies suggest that breast feeding may be beneficial in preventing obesity, but a recent systematic review and meta-analysis concluded that although mean body mass index in later life was lower among breast-fed subjects, the difference was small and might have been influenced by publication bias and confounding factors (55). Most studies also have not found combined promotion of healthy eating and physical activity to be effective at preventing childhood obesity (72). Clearly, this is an area where much more research is needed. Because no clear evidence-based overweight-prevention guidelines exist, the American Academy of Pediatrics Committee on Nutrition published recommendations to promote children's health, including: yearly calculation and plotting of body mass index in children and adolescents; identification of excess weight relative to linear growth; support of breast feeding, and promotion of healthy eating and physical activity; and limitation of television and video time to 2 h per day (37). The treatment of obesity in children is not dissimilar to that of adults and includes the use of low-calorie diets, increased physical activity, and pharmacotherapy and bariatric surgery when indicated (70).

Adult obesity

The NHLBI Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults recommends routine assessment of body mass index, waist circumference, and medical comorbid conditions in all adults (50). It is not necessary to measure waist circumference in individuals with a body mass index of ≥ 35 kg/m², because it adds little to the predictive value of the disease risk classification of body mass index. Diseases or conditions that convey high absolute risk, and thus would mandate more aggressive management of obesity, include established coronary heart disease, other atherosclerotic diseases, type 2 diabetes, and sleep apnea.

Weight loss therapy is recommended for patients with a body mass index of ≥ 30 and for patients with a body mass index of 25–29.9, or a high-risk waist circumference, and two or more risk factors. An initial weight loss of 10% of body weight achieved over a 6-month period is optimal.

The rate of weight loss should be no more than 0.5–1 kg each week. Weight loss can usually be achieved at this rate by reducing the caloric intake by 500–1000 kcal/day from the current level. Faster rates of weight loss are no more effective over the long term. Generally, diets containing 1000–1200 kcal/day for most women, and 1,200–1,600 kcal/day for men, are effective. Once weight goals have been achieved, patients should be encouraged to maintain weight through a combination of dietary changes and physical activity.

Behavioral therapy, serving as a useful adjunct to dietary therapy, includes self-monitoring [recording dietary intake (food choices, amounts, time or daily weighing)]; stress management; stimulus control (recognizing the social or environmental cues that seem to encourage undesired eating and then modifying those cues); problem-solving, contingency management (the use of rewards for specific actions), cognitive restructuring (unrealistic goals and inaccurate beliefs about weight loss and body image are modified to help change self-defeating thoughts and feelings), and social support.

If lifestyle changes do not lead to weight loss in 6 months, pharmacotherapy should be considered. Currently, pharmacotherapy is only recommended for those patients who have a body mass index of ≥ 30 , or for those who have a body mass index of ≥ 27 if concomitant obesity-related risk factors or diseases exist. The two medications currently available for the treatment of obesity are sibutramine, a selective

inhibitor of neuronal reuptake of norepinephrine and serotonin at the receptor sites that affect food intake, and orlistat, a gastrointestinal lipase inhibitor that reduces fat absorption in the intestine. Adverse effects of sibutramine may include increases in blood pressure and pulse and therefore it is contraindicated in individuals with high blood pressure, coronary heart disease, congestive heart failure, arrhythmias, or a history of stroke. Adverse effects associated with the use of orlistat include decreased absorption of fat-soluble vitamins, and oily and loose stools. For this reason, individuals taking orlistat should also take a multivitamin. A new drug on the horizon is rimonabant, a selective cannabinoid-1 receptor antagonist in the endocannabinoid system (53).

Weight loss surgery is recommended for well-informed and motivated patients who have clinically severe obesity (body mass index ≥ 40) or a body mass index of ≥ 35 and serious comorbid conditions. Weight loss surgery provides medically significant sustained weight loss for more than 5 years in most patients. Two types of operations are routinely performed: those that restrict gastric volume (banded gastroplasty) and those that, in addition to limiting food intake, also alter digestion (Roux-en-Y gastric bypass). From 1990 to 1997, the number of weight loss or bariatric surgeries has increased from 4,925 to 12,541 annually (57). With the advent and increasingly routine use of laparoscopic bariatric surgery since 1998, the number of bariatric operations has increased, by more than fourfold in 3 years, to 53,658 cases (51). Between 1996 and 2002, the population-adjusted rates of bariatric surgery have increased by more than sevenfold in the US population, from 3.5 per 100,000 in 1996 to 24.0 per 100,000 in 2002. During this period, among individuals <20 years of age, the rates of bariatric surgery increased from 0.23 per 100,000 to 0.73 per 100,000; and among older adults (> 65 years of age), the rates increased from 0.30 per 100,000 to 1.69 per 100,000 (13). The mean percentage of excess weight loss is 61.2% for all patients, 47.5% for patients undergoing gastric banding, 61.6% for gastric bypass, and 68.2% for gastroplasty, and 70.1% for biliopancreatic diversion (10).

In patients without comorbidities and with a body mass index of <50 kg/m², surgical mortality rates are <1%. In massively obese patients with a body mass index of >60 kg/m² who are also diabetic, hypertensive, and in cardiopulmonary failure, may have mortality rates that range from 2–4%. Surgical complications, including anastomotic leak, subphrenic abscess, splenic injury, pulmonary embolism, wound infection, and stoma stenosis, occur in approximately

10% of all obese patients (41). Late complications include the development of incisional hernias, gallstones, and, less commonly, weight loss failure and dumping syndrome. Vitamin deficiencies are relatively common, especially for vitamin B12 and iron, and require close monitoring.

Obesity and dental practice

Knowledge about obesity by dental professionals

Very little information exists regarding the experience of dental professionals with obesity management. In a study of 464 dental and dental hygiene students, the majority reported 5 h or less of obesity education, with over one-third of students reporting less than 1 h (44). Given the potentially negative effect of obesity on oral health-related outcomes, dental professionals would benefit from the inclusion of obesity education in the curricula and continuing medical education.

Screening

Health screening by oral health providers could have a significant impact on obesity prevention and management, as many individuals seek dental care who do not routinely seek medical care. In Glick's evaluation of National Health and Nutrition Examination Survey data, he identified 332,262 men who had a moderate risk of experiencing a cardiovascular event within 10 years, had not seen a physician in the previous 12 months, but had seen a dentist (26). These individuals would greatly benefit from obesity screening.

The Centers for Disease Control currently recommends that children of 2 years of age and older should be screened for overweight. Growth charts to track body mass index can be obtained from <http://www.cdc.gov/growthcharts/>. All adults should have their height and weight recorded and a body mass index calculated at each visit.

Assessment

Beyond calculating body mass index, oral health care providers could consider obtaining waist circumferences in patients with a body mass index of ≥ 25 , but <35 , as these individuals may carry more risk than their body mass index alone may suggest. In addition, the medical history should take note of comorbid conditions, including hypertension, dyslipidemia,

coronary heart disease, type 2 diabetes, and sleep apnea.

Counseling

The NHLBI Guidelines recommend that all patients with a body mass index of ≥ 30 should attempt to lose weight. However, it is important to ask the patient whether or not they want to lose weight. Those with a body mass index of 25–29.9 kg/m², and who have one or no risk factors, should work on maintaining their current weight rather than embark on a weight-reduction program. The decision to lose weight must be made in the context of other risk factors (e.g. quitting smoking is more important than losing weight) and patient preferences.

The decision to lose weight must be a collaborative one made jointly between the clinician and patient. Patient motivation and confidence in making a change is crucial to success. Although the guidelines recommend the loss of 10% of baseline weight at a rate of 0.5–1 kg per week, and the establishment of an energy deficit of 500–1000 kcal/day, smaller, more incremental goals may be preferable in order to instill confidence on the part of the patient. For individuals who are overweight, a deficit of 300–500 kcal/day may be more appropriate, providing a weight loss of about 250 g per week. If, after 6 months, dietary therapy, increased physical activity, and behavior therapy are ineffective, patients should be referred to a medical provider for consideration of pharmacotherapy.

Conclusion

Obesity has taken on epidemic proportions, both in the U.S.A. and internationally. Many comorbidities are associated with obesity and have consequences for oral health professionals. Because many patients see their dentist more often than their primary care provider, the oral health provider can serve to screen and identify patients with obesity. They can be engaged in collaborative decision making with the patient about their care and refer to medical professionals if the patient's risk profile dictates more aggressive measures.

References

1. Al-Zahrani MS, Bissada NF, Borawskit EA. Obesity and periodontal disease in young, middle-aged, and older adults. *J Periodontol* 2003; **74**: 610–615.

2. Appel LJ, Moore TJ, Obarzanek R, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997; **336**: 1117–1124.
3. Aronne LJ, Segal KR. Adiposity and fat distribution outcome measures: assessment and clinical implications. *Obes Res* 2002; **10**: 14S–21S.
4. Asia Pacific Cohort Studies Collaboration. Body mass index and cardiovascular disease in the Asia-Pacific Region: an overview of 33 cohorts involving 310,000 participants. *Int J Epidemiol* 2004; **33**: 751–758.
5. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, Smith WC, Jung RT, Campbell MK, Grant AM. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess* 2004; **8**: 1–182.
6. Barlow SE, Dietz WH. Obesity evaluation and treatment: expert committee recommendations. *Pediatrics* 1998; **102**: E29.
7. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. *Circ Res* 2005; **96**: 939–949.
8. Bouchard C, Tremblay A. Genetic effects in human energy expenditure components. *Int J Obes* 1990; **14**(Suppl. 1): 49–58.
9. Boustany CM, Bharadwaj K, Daugherty A, Brown DR, Randall DC, Cassis LA. Activation of the systemic and adipose renin-angiotensin system in rats with diet-induced obesity and hypertension. *Am J Physiol Regul Integr Comp Physiol* 2004; **287**: R943–R949.
10. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrenbach K, Schoelles K. Bariatric surgery: a systematic review and meta-analysis. *JAMA* 2004; **292**: 1724–1737.
11. Busetto L, Sergi G, Visceral fat and respiratory complications. *Diabetes Obes Metab* 2005; **7**: 301–306.
12. Correia ML, Haynes WG. Obesity-related hypertension: is there a role for selective leptin resistance? *Curr Hypertens Rep* 2004; **6**: 230–235.
13. Davis MM, Slish K, Chao C, Cabana MD. National trends in bariatric surgery, 1996–2002. *Arch Surg* 2006; **141**: 71–74.
14. DeTaeve B, Smith LH, Vaughan DE. Plasminogen activator inhibitor-1: a common denominator in obesity, diabetes and cardiovascular disease. *Curr Opin Pharmacol* 2005; **5**: 149–154.
15. Dollman J, Norton K, Norton L. Evidence for secular trends in children's physical activity behaviour. *Br J Sports Med* 2005; **00**: 892–897.
16. Dulak J, Jozkowicz A, Frick M, Alber HF, Dichtl W, Schwarzwacher SP, Pachinger O, Weidinger F. Vascular endothelial growth factor: angiogenesis, atherogenesis or both? *J Am Coll Cardiol* 2001; **38**: 2137–2138.
17. Dyer AR, Elliott P, Shipley M. Body mass index versus height and weight in relation to blood pressure. Finding for the 10,079 persons in the INTERSALT Study. *Am J Epidemiol* 1990; **131**: 589–596.
18. Engeli S, Schling P, Gorzelniak K, Boschmann M, Janke J, Ailhaud G, Teboul M, Massiera F, Sharma AM. The adipose-tissue renin-angiotensin-aldosterone system: role in the metabolic syndrome? *Int J Biochem Cell Biol* 2003; **35**: 807–825.
19. Fabsitz RR, Sholinsky P, Carmelli D. Genetic influences on adult weight gain and maximum body mass index in male twins. *Am J Epidemiol* 1994; **140**: 711–720.
20. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. *Ann Intern Med* 1992; **116**: 535–539.
21. Field AE, Coakley EH, Must A. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Arch Int Med* 2001; **161**: 1581–1586.
22. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. *JAMA* 2005; **293**: 1861–1867.
23. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of life lost due to obesity. *JAMA* 2003; **289**: 187–193.
24. Freedman DM, Ron E, Ballard-Barbash R, Doody MM, Linet MS. Body mass index and all-cause mortality in a nationwide US cohort. *Int J Obes* 2006; **30**: 822–829.
25. French SA, Linn BH, Guthrie JF. National trends in soft drink consumption among children and adolescents age 6 to 17 years: prevalence, amounts, and sources, 1977/1978 to 1994/1998. *J Am Diet Assoc* 2003; **103**: 1326–1331.
26. Glick M, Greenberg BL. The potential role of dentists in identifying patients' risk of experiencing coronary heart disease events. *J Am Dent Assoc* 2005; **136**: 1541–1546.
27. Greenburg AS, Obin MS. Obesity and the role of adipose tissue in inflammation and metabolism. *Am J Clin Nutr* 2006; **83**: 461S–465S.
28. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, Narayan KM, Williamson DF. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA* 2005; **293**: 1868–1874.
29. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F. Diagnosis and management of the metabolic syndrome. An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005; **112**: 2735.
30. Harnack LJ, Jeffery RW, Boutelle KN. Temporal trends in energy intake in the United States: an ecologic perspective. *Am J Clin Nutr* 2000; **71**: 1478–1484.
31. Haslam DW, James PT. Obesity. *Lancet* 2005; **366**: 1198–1209.
32. Huang, Z, Willett WE, Manson JE, Rosner B, Stampfer MJ, Speizer FE. Body weight, weight change, and risk for hypertension in women. *Ann Intern Med* 1998; **128**: 81–88.
33. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26 year follow-up of participants in the Framingham Heart Study. *Circulation* 1983; **67**: 968–977.
34. James WPT, Rigby N, Leach R. The obesity epidemic, metabolic syndrome and future strategies. *Eur J Cardiovasc Prev Rehabil* 2004; **11**: 3–8.
35. Karlson EW, Mandl LA, Aweh GN, Sangha O, Liang MH, Grodstein F. Total hip replacement due to osteoarthritis: the importance of age, obesity, and other modifiable risk factors. *Am J Med* 2003; **114**: 93–98.
36. Kenchaiah S, Gaziano JM, Vasani RS. Impact of obesity on the risk of heart failure and survival after the onset of heart failure. *Med Clin North Am* 2004; **88**: 1272–1294.
37. Krebs NF, Jacobson MS. American Academy of Pediatrics Committee on Nutrition. Prevention of pediatric overweight and obesity. *Pediatrics* 2003; **112**: 424–430.
38. Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults. The

- National Health and Nutrition Examination Surveys, 1960–1991. *JAMA* 1994; **272**: 205–211.
39. Kumada M, Kihara S, Sumitsuji S, Kawamoto T, Matsumoto S, Ouchi N, Arita Y, Okamoto Y, Shimomura I, Hiraoka H, Nakamura T, Funahashi T, Matsuzawa Y, for the Osaka CAD Study Group. Association of hypoadiponectinemia with coronary artery disease in men. *Arterioscl Thromb Vasc Biol* 2003; **23**: 85–89.
 40. Lievense AM, Bierma-Zeinstra SM, Verhagen AP, van Baar ME, Verhaar JA, Koes BW. Influence of obesity on the development of osteoarthritis of the hip: a systematic review. *Rheumatology* 2002; **41**: 1155–1162.
 41. Livingston EH. Procedure, incidence and complication rates of bariatric surgery in the United States. *Am J Surg* 2004; **188**: 105–110.
 42. Lundin M, Yucel-Lindberg T, Dahllof G, Marcus C, Modeer T. Correlation between TNF- α in gingival fluid and body mass index in obese subjects. *Acta Odontol Scand* 2004; **62**: 273–277.
 43. Magliocca KR, Helman JI. Obstructive sleep apnea: diagnosis, medical management and dental implications. *J Am Dent Assoc* 2005; **136**: 1121–1129.
 44. Magliocca KR, Jabero MF, Alto DL, Magliocca JF. Knowledge, beliefs, and attitudes of dental and dental hygiene students toward obesity. *J Dent Educ* 2005; **69**: 1332–1339.
 45. Matsuzawa Y. White adipose tissue and cardiovascular disease. *Best Pract Res Clin Endocrinol Metab* 2005; **19**: 637–647.
 46. Mavri A, Alessi MC, Bastelica D, Geel-Georgelin O, Fina F, Sentocnik JT, Stegnar M, Juhan-Vague I. Subcutaneous abdominal, but not femoral fat expression of plasminogen activator inhibitor-1 (PAI-1) is related to plasma PAI-1 levels and insulin resistance and decreases after weight loss. *Diabetologia* 2001; **44**: 2025–2031.
 47. McCollough AJ. The clinical features, diagnosis and natural history of nonalcoholic fatty liver disease. *Clin Liver Dis* 2004; **8**: 521–533.
 48. Miyazawa-Hoshimoto S, Takahashi K, Bujo H, Hashimoto N, Saito Y. Elevated serum vascular endothelial growth factor is associated with visceral fat accumulation in human obese subjects. *Diabetologia* 2003; **46**: 1483–1488.
 49. National Center for Health Statistics. *Health, United States, 2005 with chart book on trends in the health of Americans*. Hyattsville, MD: National Center for Health Statistics, 2004.
 50. National Heart, Lung and Blood Institute. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults – the evidence report. *Obes Res* 1998; **6**: 1–78.
 51. Nguyen NT, Root J, Zainabadi K, Sabio A, Chalifoux S, Stevens CM, Mayandadi S, Longoria M, Wilson SE. Accelerated growth of bariatric surgery with the introduction of minimally invasive surgery. *Arch Surg* 2005; **140**: 1198–1202.
 52. Niemann-Jonsson A, Dimayuga P, Jovinge S, Calara F, Ares MPS, Fredrikson GN, Nilsson J. Accumulation of LDL in rat arteries is associated with activation of tumor necrosis factor- α expression. *Arterioscler Thromb Vasc Biol* 2000; **20**: 2205–2211.
 53. Nisoli E, Carruba MO. Emerging aspects of pharmacotherapy for obesity and metabolic syndrome. *Pharmacol Res* 2004; **50**: 453–469.
 54. Ouchi N, Kihara S, Funahashi T, Funahashi T, Nakamura T, Nishida M, Kumada M, Okamoto Y, Ohashi K, Nagaretani H, Kishida K, Nishizawa H, Maeda N, Kobayashi H, Hiraoka H, Matsuzawa Y. Reciprocal association of C-reactive protein with adiponectin in blood stream and adipose tissue. *Circulation* 2003; **107**: 671–674.
 55. Owen CG, Martin RM, Whincup PH, Davey Smith G, Gillman MW, Cook DG. The effect of breast feeding on mean body mass index throughout the lifecourse; a quantitative review of published and unpublished observational evidence. *Am J Clin Nutr* 2005; **82**: 1298–1307.
 56. Perlstein MI, Bissada NF. Influence of obesity and hypertension on the severity of periodontitis in rats. *Oral Surg Oral Med Oral Pathol* 1977; **43**: 707–719.
 57. Pope GD, Birkmeyer JD, Finlayson SR. National trends in utilization and in-hospital outcomes of bariatric surgery. *J Gastrointest Surg* 2002; **6**: 855–861.
 58. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 2001; **286**: 327–334.
 59. Raben A, Vasilaras TH, Moller AC, Astrup A. Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am J Clin Nutr* 2002; **76**: 721–729.
 60. Rajala R, Partinen M, Sane T, Pelkonen R, Huikuri K, Seppalainen AM. Obstructive sleep apnoea syndrome in morbidly obese patients. *J Intern Med* 1991; **230**: 125–129.
 61. Reaven GM. The metabolic syndrome: requiescat in pace. *Clin Chem* 2005; **51**: 931–938.
 62. Reilly MP, Iqbal N, Schutta M, Wolfr ML, Scally M, Localio AR, Rader DJ, Kimmel SE. Plasma leptin levels are associated with coronary atherosclerosis in type 2 diabetes. *J Clin Endocrinol Metab* 2004; **89**: 3872–3878.
 63. Ridker PM, Rifai N, Pfeffer M, Sacks F, Lepage S, Braunwald W. Elevation of tumor necrosis factor- α and increased risk of recurrent coronary events after myocardial infarction. *Circulation* 2000; **101**: 2149–2153.
 64. Ridker PM, Rifai N, Stampfer MJ, Hennekens CH. Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation* 2000; **101**: 1767–1772.
 65. Ridker PM, Willerson JT. Inflammation as a cardiovascular risk factor. *Circulation* 2004; **109**(Suppl. 2): II2–II10.
 66. Rissanen AM, Heliovaara M, Knekt P, Reunanen A, Aromaa A. Determinants of weight gain and overweight in adult Finns. *Eur J Clin Nutr* 1991; **45**: 419–430.
 67. Ruhl CE, Everhart JE. Relationship of serum leptin concentration and other measures of adiposity with gallbladder disease. *Hepatology* 2001; **34**: 877–883.
 68. Seidell JC, Muller DC, Sorkin JD, Andres R. Fasting respiratory exchange ratio and resting metabolic rate as predictors of weight gain: the Baltimore Longitudinal Study on Aging. *Int J Obes* 1992; **16**: 667–674.
 69. Simons PJ, van den Pangaart PS, van Roomen CP, Aerts JM, Boon L. Cytokine-mediated modulation of leptin and adiponectin secretion during in vitro adipogenesis: evidence that tumor necrosis factor- α and interleukin-1 β -treated human preadipocytes are potent leptin producers. *Cytokine* 2005; **32**: 94–103.
 70. Speiser PW, Rudolf MCJ, Anhalt H, Camacho-Hubner C, Chiarelli F, Eliakim A. Childhood obesity. *J Clin Endocrinol Metab* 2004; **90**: 1871–1887.

71. Stunkard AJ, Foch TT, Hrubec Z. A twin study of human obesity. *JAMA* 1986; **256**: 51–54.
72. Summerbell C, Waters E, Edmunds L, Kelly S, Brown T, Campbell K. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2005: Issue 3. Artt.No.:CD001871.pub2.DOI:10.1002/14651858.CD001871.pub2(3).
73. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004; **92**: 347–355.
74. Troiano RP, Flegal KM, Kuczmarski RJ, Campbell SM, Johnson CL. Overweight prevalence and trends for children and adolescents. The National Health and Nutrition Examination Surveys, 1963 to 1991. *Arch Pediatr Adolesc Med* 1995; **149**: 1085–1091.
75. Tsigos C, Kyrou I, Chala E, Tsapogas P, Stavridis JC, Raptis SA, Katsilambros N. Circulating tumor necrosis factor alpha concentrations are higher in abdominal versus peripheral obesity. *Metabolism* 1999; **48**: 1332–1335.
76. Vgontzas AN, Papanicolaou DA, Bixler EO Hopper K, Lotsikas A, Lin HM, Kales A, Chrousos GP. Sleep apnoea and daytime sleepiness and fatigue: relation to visceral obesity, insulin resistance, and hypercytokinemia. *J Clin Endocrinol Metab* 2000; **85**: 1151–1158.
77. Wannamethee SG, Shaper AG. Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. *Diabetes Care* 1999; **22**: 1266–1272.
78. Whitaker RC, Dietz WH. Role of the prenatal environment in the development of obesity. *J Pediatr* 1998; **132**: 768–776.
79. Wood N, Johnson RB, Streckfus CF. Comparison of body composition and periodontal disease using nutritional assessment techniques: Third National Health and Nutrition Examination Survey (NHANES III). *J Clin Periodontol* 2003; **30**: 321–327.
80. World Health Organization. *Obesity: preventing and managing the global epidemic. Report of WHO Consultation on Obesity, 3–5 June, 1997*. Geneva: WHO, 1998.