

Factors Associated to Obesity

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Review Article

Received: 02/02/2017
Accepted: 23/02/2017
Published: 28/02/2017

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Keywords: Leptin, Genetic obesity, Childhood obesity, Fats

ABSTRACT

Obesity is defined as the accumulation of the abnormal or excessive adipose tissue that may impair health. A fat cell is an endocrine cell and adipose tissue is an endocrine organ. Adipose tissue secretes a variety number of products along with metabolites, lipids, cytokines and coagulation factors among others. Being overweight means having additional weight than is taken as normal or healthy for one's age or build. On the opposite hand, [obesity](#) is that condition of being weighty, i.e., excess quantity of body fat with a BMI of over 30. Whereas association with overweight person can carry excess weight, he could or might not have excess accumulation of [fat](#). Obesity may be a multi-factorial disorder that is commonly related to several different important diseases like polygenic disease, cardiovascular disease and different vas diseases, degenerative joint disease and some [cancers](#). The management of obesity can thus need a comprehensive vary of methods engrossment on those with existing [weight](#) issues and conjointly on those at high risk of developing obesity. Hence, hindrance of obesity throughout [childhood](#) ought to be taken as a priority, as there's a risk of persistence to adulthood.

INTRODUCTION

Obesity may be allocated as the "New World Syndrome". Its prevalence is on continuous rise altogether age teams of the many of the developed countries within the world. Statistical data reveals that the staple of obesity has exaggerated from 12–20% in men and from 16–25% in girls over the last 10 years ^[1]. Recent studies counsel that just about 15–20% of the middle aged European population area unit weighty ^[2] which in USA alone it's liable for as many as 3,00,000 premature deaths annually ^[3]. [Obsessed patients](#) are related to exaggerated risk of morbidity and mortality relative to those with ideal weight ^[4]. Even modest weight reduction within the range of 5–10% of the initial weight is related to important enhancements during a wide selection of co-morbid conditions ^[5-9]. Obesity, that was once viewed because the results of lack of will power, or a life-style "choice" – the selection to scarf out and beneath [exercise](#), is currently being thought by the modern world as a chronic unwellness, which needs effective methods for its management.

Obesity, in straightforward terms, could also be outlined as a state of imbalance between calories taken versus calories gone which might cause excessive or abnormal fat accumulation. [Body Mass Index \(BMI\)](#) is a measurement tool of weight corrected for height and that reflects the overall body fat and has been the foremost accepted parameter for outlining over weight ^[10].

BMI= Weight of an Individual (in kgs)/Height²(m²)

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[British Dietetic Association](#) specialist mass represents dietitians operating in adult and childhood obesity hindrance and management, recognising obesity as being a specialist in that field of dietetic practice. The obesity specialists works to speak evidence-based standards, support post-registration coaching for obesity management, contribute to national tips, campaign for health improvement, and to develop and foster a network of overweight management

professionals. [Canadian Obesity Network](#) support to get rid of the stigma from fatness and convey positivism and give importance to the peoples who are suffering with obesity. Credible and evidence-based info and tools designed to alter however they tend to understand and discuss fatness reasons. Connecting to a community of researchers, health professionals and policy creators who wish to form a distinction for the lives of those are suffering with fatness. [American Society for Nutrition \(ASN\)](#) is a non-profit organization dedicated to accumulate the world's high researchers, clinical nutritionists and business to advance the knowledge and application of nutrition for the sake of humans and animals. Main focus ranges from the foremost important details of analysis and application to the broadest applications in society, in the U.S. and round the world.

[Journal of Obesity & Weight Loss Therapy](#) deals with the medical study of obesity and body mass index. Obesity and Weight Loss measure are well-known risk factors for several medical conditions. Therapeutic Weight Loss in people that measure overweight or obese will decrease the probability of developing these diseases. The [Journal of Childhood Obesity](#) deals with all fields of treating childhood obesity involving child nutrition, pediatrics obesity, skinfold thickness, insulin resistance, physical education, weight management, food choice, hypothyroidism, diabetes mellitus, fasting blood glucose, energy balance, etc.

CHILDHOOD OBESITY

[Childhood obesity](#) has reached epidemic levels in developed countries. 25% of children's within the United States area are overweight. Regarding 70% of corpulent adolescents grow to become corpulent adults ^[11-14]. The prevalence of childhood obesity is increasing since 1971 in developed countries. In some European countries like the Scandinavian countries the prevalence of childhood obesity is lower as compared with Mediterranean countries; yet, the proportion of corpulent children is rising in each cases ^[15]. The very best prevalence rates of childhood obesity are determined in developed countries; however, similarly its prevalence is increasing in developing countries also. The prevalence of childhood obesity is high within the geographic region, Central and Eastern Europe ^[16-21]. For example, in 1998, the World Health Organization project watching of cardiovascular diseases (MONICA) according to that, Iran among the seven countries has large prevalence of childhood obesity. The prevalence of BMI (in percentage) between eighty fifth and ninety fifth mark in women was considerably over that in boys (10.7, SD=1.1 vs. 7.4, SD=0.9). Identical pattern was seen for the prevalence of BMI > 95th percentile (2.9, SD=0.1 vs. 1.9, SD=0.1) ^[22]. In Asian nation, one in each six kids aged 6 to 18 years recent is corpulent ^[23]. Moreover, in each developed and developing countries there are unit of proportionately additional women overweight than boys, notably among [adolescent](#) ^[24-27].

In omics's journal [Li Ming Wen](#) has published an article on topic "Obesity in Young Children: What Can We Do About?" where it has been described about the home-based early intervention to improve infant feeding practices, eating habits and active play, and reduce TV viewing time, as well as improve family behavioural risk factors for childhood obesity.

Causes of Obesity

The stability between calorie intake and energy expenditure determines a human weight. If someone grabs a lot of calories than he or she burns (metabolizes), the person gains weight (the body can store the surplus energy as fat). If someone grabs fewer calories than he or she metabolizes, than only fats will going to melt off. So, the foremost common causes of obesity are deadly sin and physical inactivity. Ultimately, weight is that the results of genetics, metabolism, environment, food habits, and culture.

Genetics

There is a lot of possible to develop obesity if one or both parents are fat. [Genetics](#) have an additional effect on hormones concerned in fat regulation. As an example, one genetic reason for obesity is leptin deficiency. Leptin could be an internal secretion synthesised in fat cells and additionally within the placenta ^[28-36]. Leptin controls weight by signalling the brain to eat less, once body fat stores are too high. If, for a few reason, the body cannot manufacture enough leptin or leptin cannot signal the brain to eat less, this management is lost, and obesity happens. The role of leptin replacement as a treatment for obesity is presently being explored.

[Muhammad Wasim](#) has an article on the topic "Obesity and Leanness Caused by Mutations in the Leptin Gene: Already 6 Pathogenic Mutations Reported in this Gene" where he has described about the leptin gene which is related to the obesity and weight control.

A Diet High in Easy Carbohydrates

The role of carbohydrates in weight gain isn't clear. [Carbohydrates](#) increase blood sugar levels, that successively stimulate insulin unleash by the pancreas, and insulin promotes the expansion of fat tissue and might cause weight gain [37]. Some scientists believe that simple carbohydrates (sugars, fructose, desserts, soft drinks, beer, wine, etc.) contribute to weight gain as they are quickly absorbed into the blood than complex carbohydrates (pasta, brown rice, grains, vegetables, raw fruits, etc.) and that causes an additional pronounced insulin unleash after meals than complex carbohydrates [38-43]. This extra insulin unleash, some scientists believe, contributes to weight gain.

Frequency of Eating

The association between frequency of [eating](#) (how usually you eat) and weight is somewhat debatable. There are several reports of overweight folks feeding less usually than folks with traditional weight. Scientists have ascertained that people who eat little meals 4 or 5 times daily, have lower cholesterol levels and lower and/or additional stable glucose levels than people that eat less often (two or 3 massive meals daily)[44-49]. One attainable validation is that tiny frequent meals manufacture stable insulin levels, whereas massive meals cause giant spikes of insulin after meals.

Physical Inactivity

Inactive individuals burn fewer calories than people who are active. The National Health and Nutrition Examination Survey (NHANES) showed that [physical](#) inactivity was powerfully correlative with weight gain in all sexes.

Medications

Medications related to weight gain embrace bound antidepressants (medications employed in treating depression), anticonvulsants (medications employed in dominant seizures like carbamazepine [Tegretol, Tegretol XR , Equetro, Carbatrol] and valproate [Depacon, Depakene]), some [diabetes](#) medications (medications employed in lowering glucose like hypoglycaemic agent, sulfonylureas, and thiazolidinediones), bound hormones like oral contraceptives, and most corticosteroids like Liquid Prednisone [50]. Weight gain may moreover be seen with some high blood pressure medications and antihistamines. The description for the weight gain with the medications differs for every [medication](#).

PSYCHOLOGICAL FACTORS OF OBESITY

Food is usually used as a main mechanism for those with weight issues, mostly when they are unhappy, anxious, stressed, lonely, and pissed off. In several corpulent people there seems to be a perpetual cycle of mood disturbance, overeating, and [weight gain](#) [51]. When they feel distressed, they address food to assist cope, and although such comfort intake could end in temporary attenuation of their distressed mood, the load gain that results could cause an unhappy mood attributable to their inability to regulate their stress. The ensuing guilt could activate the cycle, resulting in an eternal pattern of victimization food to deal with emotions [52-56]. This pattern is especially applicable if there's a [genetic predisposition](#) for fatness or a "toxic" atmosphere during which calorically dense foods are accessible and physical activity is restricted. Sadly, these circumstances are common in America.

In addition to depression and anxiety, alternative risk factors express problematic intake behaviors like "mindless intake," frequent snacking on high calories foods, overeating, and night intake [57]. Binge eating disorder (BED) is presently enclosed in an appendix of the Diagnostic and statistical Manual of Mental Disorders (DSM-IV-TR)[58] and is characterised by: repeated episodes of intake throughout a distinct amount of your time (at least a pair of days every week over a 6 month period); eating quantities of food that are larger than the general people would eat throughout an identical quantity of time; a way of lack of management throughout the episodes; and guilt or distress following the episodes. BED is calculable to occur in just about a pair of the overall population and between 100 percent and twenty fifth of the bariatric population [59]. A vital differentiation between BED and bulimia/anorexia is that BED isn't related to any regular counteractive behaviour, like purging, fasting, or excessive exercise, [60] therefore the majority of people with BED square measure overweight. Night intake is another disorder which will cause important weight gain, although night intake syndrome (NES) isn't presently recognized as a definite designation within the DSM-IV-TR.

[Osama Hamdy](#) who is an editorial board member in Journal of Obesity & Weight Loss Therapy and his research of interest are metabolic and [cardiovascular](#) risk factors and body fat distribution and inflammation markers in obese individuals with diabetes.

Psychological Importance of Fat

Society views fat people terribly in a negative way. ^[61-64] People who are obese are “weak-willed” and “unmotivated” discriminated by the majority peoples. Some people are usually alert to these negative views. They have to face social and work-related discrimination, ^[65] as a result usually suffer from low shallowness, and feel uncomfortable with their bodies (i.e. body image dissatisfaction). ^[66] These feelings could cause strain on their intimate and romantic relationships. 20-70% of obese people opting for bariatric surgery suffer from a current and/or past medicine disorder, of that Major depression is that the most notable.

Obese people have usually created multiple tries to turn, with very little or no success. Their unsuccessful tries end in discouragement, frustration, despair, and learned helplessness regarding the prospect of losing weight within the future on their own. For this reason, several communicate bariatric surgery as a final resort. Not astonishingly, vital weight loss confers [psychological](#) further as medical edges, with improved mood, shallowness, motivation, and relationships. A meta-analysis of forty studies specializing in psychosocial outcomes of bariatric surgery projected that psychological health and psychosocial standing as well as social relationships and employment opportunities improved; and medicine symptoms and comorbidity, preponderantly emotional disorders, decreased. These changes lead to improve the quality of life for the bulk who had weight loss surgery.^[67]

DISEASES RELATED TO OBESITY

Being overweight or obesity is not a cosmetic disadvantage. These conditions greatly raise risk for different health issues.

High Blood Pressure and Stroke

Blood pressure is that the force of blood pushing against the walls of the arteries because the heart pumps blood ^[68]. If this pressure rises and stays high over time, it will injure the body in many ways. Extra weight leads to cause [high blood pressure](#) level and high cholesterol. Each of these conditions creates heart condition or stroke.

The good news is that losing a little quantity of weight will cut back your possibilities of developing heart condition or a stroke. Losing 5%-10% of your weight is evidenced to lower your likelihood of developing heart condition

Type 2 Diabetes

Diabetes could be an illness within which the body's blood sugar, or glucose, level is simply too high. Normally, the body breaks down food into glucose and so carries it to cells throughout the body ^[69-72]. The cells use secretion hormone insulin to convert glucose into energy.

In [type 2](#) diabetes, the body's cells do not use insulin properly. At first, the body reacts by secreting additional insulin ^[73]. Over time, however, the body cannot build enough insulin to regulate its glucose level.

Diabetes could be a leading reason for early death, CHD, stroke, nephrosis diseases, and vision defect. Most of the people who have type 2 diabetes are overweight.

Cancer

Cancers of the colon, breast (after menopause), mucosa (the lining of the uterus), kidney, and gullet area coupled with fatness ^[74]. Some studies have additionally reported links between fatness and cancers of the bladder, ovaries, and duct gland.

Gallstones

Gallstones are a [fatigue](#) stone like material. They are highly contrived from cholesterol. Gallstones mostly cause abdomen or back pain ^[75-79]. People who have overweight are at high-risk of getting gallstones. Also, being overweight might lead to enlargement of the gallbladder that does not work well.

Ironically, weight loss itself, notably fast weight loss or loss of an oversized quantity of weight, is an indication to urge gallstones ^[80]. Losing weight at a rate of about one pound every week is a smaller amount for causing gallstones.

Osteoarthritis

Osteoarthritis may be a common joint condition that usually affects the knee, hip, or back. The condition happens if the tissue that protects the [joints](#) wears away. Further weight will place additional pressure and decline joints, inflicting pain ^[81-89]. Weight loss will ease stress on the knees, hips, and lower back and will improve the symptoms of degenerative arthritis.

CONCLUSION

Obesity has reached epidemic proportions and is currently affecting to younger age ^[90-93]. The raised consumption of calorie-dense nourishment and sucrose-enriched drinks, along with progressively inactive [lifestyle](#), seem to be major factors for the obesity. Whereas the prevention of obesity ought to receive high priority, there's rising study about treating fat, notably those with metabolic syndrome or sort a pair of type2 diabetes, has short-run effects on the diabetes; improves glucose, lipid, and pressure parameters; and is probably going to possess helpful effects on semi-permanent health outcomes ^[94-100]. There's proof that anti-obesity agents are efficacious and have a favorable impact on parameters related to cardiovascular outcomes.

REFER ENCES

1. Shetty P. India faces growing breast cancer epidemic. *Lancet*. 2012;379:992-993.
2. WHO (World Health Organization). Global action plan for the prevention of non-communicable diseases 2013-2020.
3. WHO (World Health Organization). Obesity and overweight. 2014:311.
4. Paradis G. Have we lost the war on obesity? *Can J Public Health*. 2012;103:163.
5. Ginsburg OM, et al. The global cancer epidemic: opportunities for Canada in low- and middle-income countries. 2012;184:1699-1704.
6. Kones R. Primary prevention of coronary heart disease: integration of new data, evolving views, revised goals, and role of rosuvastatin in management. A comprehensive survey. *Drug Design, Development and Therapy*. 2011;5:325-380.
7. Kones R. Molecular sources of residual cardiovascular risk, clinical signals, and innovative solutions: relationship with subclinical disease, undertreatment, and poor adherence: implications of new evidence upon optimizing cardiovascular patient outcomes. *Vascular Health and Risk Management* 2013;9:617-670.
8. Westley RL and May FE. A twenty-first century cancer epidemic caused by obesity: the involvement of insulin, diabetes, and insulin-like growth factors. *Int J Endocrinol*. 2013:632-461.
9. Sechang OH, et al. New Approach for Obesity Treatment Incorporating Individual Self-Management Education. *J Obes Wt Loss Ther*. 2013;3:164.
10. Slobod D and Fuks A. Military metaphors and friendly fire. *CMAJ*. 2012;184:144.
11. Kaplan RM. Behavioral epidemiology, health promotion, and health services. *Med Care*. 1985;23:564-583.
12. Kinch SH, et al. Risk factors in ischemic heart disease. *A.J.P.H.* 1963;53:438-442.
13. Skrabanek P. The death of humane medicine and the rise of coercive healthism. Social Affairs Unit, Edmunds, Suffolk. 1994.
14. Starfield B, et al. The concept of prevention: a good idea gone astray? *J Epidemiol Community Health*. 2008;62:580-583.
15. Saposnik G, et al. Heart Outcomes Prevention Evaluation 2 Investigators: Homocysteine-lowering therapy and stroke risk, severity, and disability: additional findings from the HOPE 2 trial. *Stroke*. 2009;40:1365-1372.

16. Clinical Policy Bulletin: Cardiovascular Disease Risk tests.
17. Schwartz MW, et al. Central nervous system control of food intake. 2000;404:661-671.
18. Rodriguz-Artalejo F. Strengthening primordial and primary prevention of cardiovascular disease to increase life expectancy. Rev Esp Cardiol. 2013;66:837-838.
19. Garlapati S. A Highly Suggested Surgical Method for a Most Unwanted Problem -Bariatric Vs Obesity.J Obes Wt Loss Ther. 2012;2:104
20. Ozawa S and Sripad P. How do you measure trust in the health system? A systematic review of the literature. 2013;91:10-14.
21. Hafizuallah AM. Leptin: fights against obesity. Pak J Physiol. 2006;2:1-7.
22. Pasco JA, et al. Serum leptin levels are associated with bone mass in non-obese women. J Clin Endocrinol Metab. 2001; 86:1884-1887.
23. Fatima W, et al. Leptin deficiency and leptin gene mutations in obese children from Pakistan. Int J Pediatr Obes. 2011;6:419-427.
24. Kenney RT, et al. 2nd meeting on novel adjuvants currently in/close to human clinical testing. World Health Organization-Organization Mondiale de la Santé FondationMérieux, Annecy, France. Vaccine. 2002;20: 2155-2163.
25. Frühbeck G. Intracellular signalling pathways activated by leptin. Biochem J. 2006;393:7-20.
26. Hakansson-Ovesjo ML, et al. Downregulated STAT3 messenger ribonucleic acid and STAT3 protein in the hypothalamic arcuate nucleus of the obese leptin-deficient (ob/ob) mouse. Endocrinology. 2000;141:3946-3955.
27. Shimada M, et al. Mice lacking melanin-concentrating hormone are hypophagic and lean. 1998;396:670-674.
28. Montague CT, et al. Congenital leptin deficiency is associated with severe early onset obesity in humans. 1997;387:903-907.
29. Strobel A, et al. A leptin missense mutation associated with hypogonadism and morbid obesity. Nat Genet. 1998;18:213-215.
30. Mazen I, et al. A novel homozygous missense mutation of the leptin gene (N103K) in an obese Egyptian patient. Mol Genet Metab. 2009;97:305-308.
31. Fischer-Posovszky P, et al. A new missense mutation in the leptin gene causes mild obesity and hypogonadism without affecting T cellresponsiveness. J ClinEndocrinolMetab. 2010;95:2836-2840.
32. Wasim M and Fakhar N. Carrier Frequency of Congenital Leptin Deficiency in Central Punjab Region of Pakistan. J Obes Weight Loss Ther. 2015;5:260.
33. Farooqi IS, et al. Leptin regulates striatal regions and human eating behavior. Science. 2007;317:1355.
34. Heymsfield SB, et al. Recombinant leptin for weight loss in obese and lean adults: a randomized, controlled, dose-escalation trial. JAMA. 1999;282:1568-1575.
35. Ahima RS. Revisiting leptin's role in obesity and weight loss. J Clin Invest. 2008;118:2380-2383.
36. Wasim M. Role of Leptin in Obesity. J Obes Weight Loss Ther. 2015;5:258.
37. Pediatric Anorexia Nervosa.
38. Fairfield WP, et al. Effects of testosterone and exercise on muscle leanness in eugonadal men with AIDS wasting. J ApplPhysiol. 2001;90:2166-2171.
39. Tourkantonis I, et al. The Role of Leptin in Cancer Pathogenesis. J Cancer Ther. 2013;4:640-650.

40. Morgen CS and Sørensen TI. Obesity: global trends in the prevalence of overweight and obesity. *Nat Rev Endocrinol.* 2014;10:513-514.
41. World Health Organization. Fact Sheet #31, Obesity and Overweight, updated January, 2015.
42. Prentice AM. The emerging epidemic of obesity in developing countries. *Int J Epidemiol.* 2006;35:93-99.
43. Mendez MA, et al. Overweight exceeds underweight among women in most developing countries. *Am J Clin Nutr.* 2005;81:714-721.
44. Global status report on non-communicable diseases 2010. Geneva, World Health Organization, 2012.
45. Rolls BJ, et al. What can intervention studies tell us about the relationship between fruit and vegetable consumption and weight management? *Nutr Rev.* 2004;62:1-17.
46. Luke A and Cooper RS. Physical activity does not influence obesity risk: time to clarify the public health message. *Int J Epidemiol.* 2013;42:1831-1836.
47. Dugas LR, et al. Energy expenditure in adults living in developing compared with industrialized countries: a meta-analysis of doubly labeled water studies. *Am J Clin Nutr.* 2011;93:427-441.
48. Drewnowski A and Specter SE. Poverty and obesity: the role of energy density and energy costs. *Am J Clin Nutr.* 2004;79:6-16.
49. Walker TB and Parker MJ. Lessons from the war on dietary fat. *J Am Coll Nutr.* 2014;33:347-351.
50. Kris-Etherton PM and Innis S. Position of the American Dietetic Association and Dietitians of Canada: dietary fatty acids *J Am Diet Assoc.* 2007;107:1599-1611.
51. Kushi LH, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin.* 2012;62: 30-37.
52. Gudzone KA, et al. Efficacy of commercial weight-loss programs: an updated systematic review. *Ann Intern Med.* 2015;162:501-512.
53. Atallah R, et al. Long-term effects of 4 popular diets on weight loss and cardiovascular risk factors: a systematic review of randomized controlled trials. *Circ Cardiovasc Qual Outcomes.* 2014;7:815-27.
54. Arora SK and McFarlane SI. The case for low carbohydrate diets in diabetes management. *Nutr Metab.* 2005;2:16.
55. Llanos AAM, et al. Favorable effects of low-fat and low-carbohydrate dietary patterns on serum leptin, but not adiponectin, among overweight and obese premenopausal women: a randomized trial. *SpringerPlus.* 2014;3:175-185.
56. Liu X, Zhang G, et al. Effects of a low-carbohydrate diet on weight loss and cardiometabolic profile in Chinese women: a randomised controlled feeding trial. *Br J Nutr.* 2013;110:1444-1453.
57. Kitabachi AE, et al. Effects of high-protein versus high carbohydrate diets on markers of B-cell function, oxidative stress, lipid peroxidation, proinflammatory cytokines, and adipokines in obese, premenopausal women without diabetes. A randomized controlled trial. *Diabetes Care.* 36:1919-1925.
58. Foster GD, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med.* 2010;153:147-157.
59. De Luis DA, et al. Evaluation of weight loss and adipocytokine levels after two hypocaloric diets with different macronutrient distribution in obese subjects with rs6923761 gene variant of glucagon-like peptide 1 receptor. *Ann Nutr Metab.* 2013;63:277-82.

60. Bazzano LA, et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med.* 2014;161:309-318.
61. Ruth MR, et al. Consuming a hypocaloric high fat low carbohydrate diet for 12 weeks lowers C-reactive protein, and raises serum adiponectin and high density lipoprotein-cholesterol in obese subjects. *Metabolism.* 2013;62:1779-1787.
62. Dalle Grave R, et al. A randomized trial of energy-restricted high-protein versus high-carbohydrate, low-fat diet in morbid obesity. *Obesity.* 2013;21:1774-1781.
63. Juanola-Falgarona M, et al. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: a randomized controlled trial. *Am J Clin Nutr.* 2014;100: 27-35.
64. Walker E, et al. Meta-analysis: Its strengths and limitations. *Cleve Clin J Med.* 2008;75:431-439.
65. Weigle DS, et al. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *Am J Clin Nutr.* 2005;82:41-48.
66. Santesso N, et al. Effects of higher- versus lower-protein diets on health outcomes: a systematic review and meta-analysis. *Eur J Clin Nutr.* 2012;66:780-788.
67. Bosse JD and Dixon BM. Dietary protein in weight management: a review proposing protein spread and change theories. *NutrMetab.* 2012;9:81.
68. Clifton PM, et al. Long term weight maintenance after advice to consume low carbohydrate, higher protein diets—a systematic review and metaanalysis. *NutrMetabCardiovasc Dis.* 2014;24:224-235.
69. Hu T, et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 176 Suppl. 2012;7:44-54.
70. Hardt J, et al. Prevalence of Chronic Pain in a Representative Sample in the United States. *Pain Med.* 2008;9:803-812.
71. Jakobsson U, et al. Old people in pain: A comparative study. *J Pain Symptom Manage.* 2003;26:625-636.
72. Elliott AM, et al. The epidemiology of chronic pain in the community. *Lancet.* 1999;354:1248-1252.
73. Català E, et al. Prevalence of pain in the Spanish population: Telephone survey in 5,000 homes. *Eur J Pain.* 2002;6:133-140.
74. Rustøen T, et al. Prevalence and characteristics of chronic pain in the general Norwegian population. *Eur J Pain.* 2004;8:555-565.
75. Yu HY, et al. Prevalence, interference, and risk factors for chronic pain among Taiwanese community older people. *Pain Manag Nurs.* 2006;7:2-11.
76. Miró J, et al. Pain in older adults: A prevalence study in the Mediterranean region of Catalonia. *Eur J Pain.* 2007;11:83-92.
77. Loeser JD and Treede RD. The Kyoto Protocol of IASP Basic Pain Terminology. *Pain.* 2008;137:473-477.
78. Flegal KM, et al. Prevalence and Trends in Obesity Among US Adults, 1999-2008. *JAMA.* 2010;303:235-241.
79. Hitt HC, et al. Comorbidity of obesity and pain in a general population: Results from the Southern Pain Prevalence Study. *J Pain.* 2007;8:430-436.
80. Andersen RE, et al. Relationship between body weight gain and significant knee, hip, and back pain in older Americans. *Obes Res.* 2003;11:1159-1162.

81. Tietjen GE, et al. Depression and anxiety: effect on the migraine-obesity relationship. *Headache*. 2007;47: 866-875.
82. Bigal ME, et al. Obesity and migraine: A population study. *Neurology*. 2006;66:545-550.
83. Scher AI, et al. Factors associated with the onset and remission of chronic daily headache in a population based study. *Pain*. 2003;106:81-89.
84. Marcus DA. Obesity and the impact of chronic pain. *Clin J Pain*. 2004;20:186-191.
85. Hurley RW and Adams MC. Sex, Gender, and Pain: An Overview of a Complex Field. *Anesth Analg*. 2008;107:309-317.
86. Riley JL III, et al. Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain*. 1998;74:181-187.
87. Unruh AM. Gender variations in clinical pain experience. *Pain*. 1996;65:123-167.
88. Smith YR, et al. Pronociceptive and antinociceptive effects of estradiol through endogenous opioid neurotransmission in women. *J Neurosci*. 2006;26:5777-5785.
89. Ohayon MM and Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. *Arch Gen Psychiatry*. 2003;60:39-47.
90. Hardt J, et al. Prevalence of Chronic Pain in a Representative Sample in the United States. *Pain Med*. 2008;9:803-812.
91. Jakobsson U, et al. Old people in pain: A comparative study. *J Pain Symptom Manage*. 2003;26:625-636.
92. Elliott AM, et al. The epidemiology of chronic pain in the community. *Lancet*. 1999;354:1248-1252.
93. Català E, et al. Prevalence of pain in the Spanish population: Telephone survey in 5,000 homes. *Eur J Pain*. 2002;6:133-140.
94. Rustøen T, et al. Prevalence and characteristics of chronic pain in the general Norwegian population. *Eur J Pain*. 2004;8:555-565.
95. Yu HY, et al. Prevalence, interference, and risk factors for chronic pain among Taiwanese community older people. *Pain Manag Nurs*. 2006;7:2-11.
96. Miró J, et al. Pain in older adults: A prevalence study in the Mediterranean region of Catalonia. *Eur J Pain*. 2007;11:83-92.
97. Loeser JD and Treede RD. The Kyoto Protocol of IASP Basic Pain Terminology. *Pain*. 2008;137:473-477.
98. Dabrowska J, et al. The role of physical activity in preventing obesity in midlife women. *Prz Menopauzalny*. 2015;14:13-19.
99. Flegal KM, et al. Prevalence and Trends in Obesity Among US Adults. 2010;303:235-241.
100. Hitt HC, et al. Comorbidity of obesity and pain in a general population: Results from the Southern Pain Prevalence Study. *J Pain*. 2007;8:430-436.