Narrative Review

Weight, Shape, and Body Composition Changes at Menopause

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Abstract

Obesity and overweight are associated with increased risks of cardiovascular and metabolic disease and overall poor health outcomes. Menopause is associated with significant changes in body composition and the accumulation of peri-abdominal or visceral fat. Changes in energy expenditure and spontaneous activity have been noted. These mid-life changes can add further to the burden of obesity and its associated risks. An understanding of the role of estrogen, gonadotrophins, gut hormones, sleep deprivation and the microbiome is still rudimentary, but research will ultimately provide further targets for more effective management. This narrative review will explore the pathogenesis of body composition changes at menopause, the impact on health outcomes and therapeutic and management options.

Keywords: *Body composition, menopause, metabolic syndrome, obesity, visceral fat, weight gain*

Submitted: 10-Jul-2021
Revised: 03-Sep-2021
Accepted: 04-Sep-2021
Published: 16-Oct-2021

Introduction

Many women will experience changes in body shape and composition at menopause. These changes can be among the most frustrating symptoms experienced at that time. Although actual weight gain may be modest for many women, it can add significantly to the burden for those women who are already overweight or obese.

There has been controversy surrounding the exact contribution of aging and menopause to any increase in weight, but we do know that the majority of any weight gain is distributed around the periabdomen adding to the woman's long-term cardiovascular and metabolic risks. We are now beginning to understand the pathophysiology of body composition changes at menopause, and this will ultimately lead to more focused strategies for managing the problem.

The aim of this review is to summarize the current understanding of weight, body shape, and body composition changes at menopause to allow appropriate management and prevention of long-term health complications.

Methods

We searched the PubMed, Embase, Medline, Google Scholar, Web of Science, Scopus, World Health Organization, and local Ministry of Health and Family Welfare databases focusing on publications related to obesity, weight gain, and body composition changes at menopause. We included basic science studies, randomized controlled trials, reviews, original prospective studies, cross-sectional studies, retrospective studies, and best practice guidelines using different combinations of the keywords: menopause, weight gain, obesity, body composition, energy expenditure, metabolic syndrome, and weight management. Studies from 2000 onward were considered for inclusion.

Obesity

Worldwide, obesity has nearly tripled since 1975. In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these, over 650 million were obese. Thirty-nine percent of adults aged 18 years and over were overweight in 2016, and 13% were obese. Most of the world's population live in countries where overweight and obesity kills more people than underweight.[1]

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Access this article online

Quick Response Code:

Website: www.jmidlifehealth.org

DOI: 10.4103/jmh.jmh_123_21

How to cite this article: Fenton A. Weight, shape, and body composition changes at menopause. J Mid-life Health 2021;12:187-92.

India has more than 30 million obese people, and the number is increasing alarmingly.[2-4] In urban India, more than 23% of women are either overweight or obese, which is higher than the prevalence among men (20%).[5] In a study of 500 women in rural India, assessed on average 4.7 years postmenopause, 78% were overweight or obese, and 68% had truncal obesity.[6] A clear rural/urban split is obvious in the latest 2019–20 National Family Health Survey-5, which shows overall rates of overweight or obesity of 9.7%–36% among rural women across the 22 states and union territories examined. Among urban dwelling women in the same states the rates were consistently higher and ranged from 17% to 44.4%.[7] The women were not further categorized on the basis of age.

Research has studied many of the risk factors for weight gain, but is inconclusive as to the role of lifestyle differences in food intake and diet.[8] Increasing consumption of energy dense, processed foods has tracked along with the global rise in obesity. Known triggers for weight gain include medications, particularly antidepressant and psychotropic agents. Depression is associated with obesity, but it is unclear whether the obesity is a symptom of the mental health disorder and whether the depression/anxiety is a reaction to the distress associated with obesity or due to the medication. Hormonal disorders such as hyperandrogenism, Cushing's syndrome, and Prader–Willi syndrome are frequently associated with central weight gain. Genetic factors are likely to be important. Medical conditions associated with inactivity as well as social and economic factors also play a part. Increasingly a role for the gut microbiome is becoming apparent.[9]

Effect of Menopause on Weight and Weight Distribution

Cross-sectional and longitudinal studies have suggested that the steady gain of weight of approximately 0.5 kg per year is largely related to age rather than menopause.[10] However, research continues to provide conflicting evidence. For instance, there is no apparent increase in weight among women with premature ovarian insufficiency, and although women with Turner syndrome have central obesity, they lack other metabolic features seen in women experiencing a natural menopause.[11,12] In contrast, women who develop ovarian failure because of chemotherapy gain substantially more weight than those who remain premenopausal, with proportionally more weight being distributed about the trunk.[13,14]

There are clearly some distinct changes that occur at menopause that appear to be directly related to hormonal changes and that do impact on body composition. Animal data have shown that estrogen deficiency is associated with transient hyperphagia and a reduction in spontaneous activity such as fidgeting.[15] These changes were reversed with Estrogen replacement. Data from human studies have confirmed a striking reduction in spontaneous activity but no change in energy intake.[15,16] Studies of mice who have undergone oophorectomy show this procedure results in obesity, adipocyte inflammation and hepatic steatosis. Supplemental estradiol protects the mice from insulin resistance, oxidative stress and fatty liver.[17] Mice lacking the aromatase gene show a similar and early tendency to central weight gain adding support to the concept that estrogen deficiency plays an important role in these changes.

Women in the menopause transition experience significant changes in metabolic and body composition indices with a reduction in fat free mass, and an increase in fat mass. It may be these opposing changes that result in weight changing very little in response to menopause itself. Waist circumference increases significantly over the transition and similar changes are seen across a variety of ethnic groups. Reducing Estrogen levels which seem to be an important trigger for these changes also alter total and resting energy expenditure. Research examining the effects of ovarian suppression using a GnRH antagonist has shown that the correction of the ensuing Estrogen deficiency preserves fat free mass and resting energy expenditure and prevents the increase in abdominal subcutaneous and visceral adipose tissue seen with unopposed use of the GnRH antagonist. The women receiving the Estrogen were also more physically active than those who were Estrogen deficient.[16]

Follicle-stimulating hormone (FSH) levels rise at menopause and elegant research from Wendy Kohrt and her colleagues has shown that this may have an independent effect on regulation of energy homeostasis.[18] It might also explain why the use of Estrogen replacement therapy, which does not completely suppress FSH levels, may fail to completely prevent the fat changes at menopause. In an intact animal model, antibodies to the β subunit of FSH, led to significant decreases in fat mass, increases in total energy expenditure and brown adipose tissue (BAT) activity. This all occurred in the absence of any alteration in estradiol levels suggesting FSH affects body composition and energy expenditure directly.

There are several lines of evidence that suggest BAT is regulated by gonadal steroids. Estrogen increases thermogenic activity whereas testosterone reduces it. BAT acts to produce heat and is stimulated by factors that increase sympathetic nervous system activity.[16]

Accumulation of fat around the heart is now considered to be a risk factor for heart disease. It is thought to be more detrimental than abdominal visceral fat as it causes local inflammation and significant increases in coronary artery disease risk. An analysis of data from the Study of Women Across the nation (SWAN) showed that volumes of cardiovascular fat increased as the Estrogen levels decline over menopause. This remained a significant finding even when adjusted for covariates.[19] Whether this perivascular fat can be decreased through lifestyle changes and weight loss is not clear, but this is clearly an area that warrants further attention.

Sleep is adversely affected by menopause for many women. This may be due to night flushing and sweating, random waking in the early hours of the morning or obstructive sleep apnea. Sleep deprivation is associated with fatigue and lower levels of physical activity. Studies have shown a clear association between low levels of sleep and greater weight gain.[20]

The impact of menopause on gut hormones, such as leptin, ghrelin and adiponectin, that regulate satiety, remains unclear.[21] The gut microbiome has been shown in animal studies to alter following ovariectomy and this is associated with significant changes in metabolic health. The microbiome has a role in regulating Estrogen metabolism and any interplay may be bi-directional. Exploring this relationship in menopausal women may provide further avenues for therapeutic intervention.[9]

Health Impacts of Body Composition Changes at Menopause

There is a well described association between visceral fat and cardiovascular disease risk. Women who are obese have a 4-fold increase in cardiovascular death rate. Normal weight women with central obesity may experience a similar mortality risk to those women with central obesity and higher overall body weights.[22] Despite being a major cause of death in women, recent studies have shown that women's awareness of the impact of cardiovascular disease (CVD) has diminished with time. Furthermore, the decrease in awareness is also seen in women with existing and significant risk factors for CVD.[23] This has important public health implications.

The visceral distribution of adipocytes is postulated to increase inflammation, an important trigger for cardiovascular and metabolic disease. Abdominal fat is considered to be an endocrine organ in its own right, able to produce many adipokines and substances that are associated with insulin resistance, type 2 diabetes, and metabolic syndrome. Hypertension and dyslipidemia are more common in women with central obesity.

In a prospective study of 200 women from Amritsar, metabolic syndrome was diagnosed in 16% of premenopausal women and in 42% of postmenopausal women. Waist circumference was elevated in 64% of postmenopausal women compared to 20% of the younger group. Both systolic and diastolic blood pressure were elevated in the postmenopausal women. Furthermore, high-density lipoprotein (HDL) levels were lower and triglyceride levels higher in that group.[24] A study in eastern India, revealed significant differences in lipid metabolism, plasma glucose and blood pressure between the subjects who differed primarily in their menopausal state independent of age and body mass index (BMI). In the study population, a significant rise in low-density lipoprotein (LDL), cholesterol, triglyceride and blood pressure was observed in postmenopausal women after adjusting for covariates age and BMI.[25]

A meta-analysis of menopause and its impact on components of the metabolic syndrome showed that all apart from HDL changed in an adverse direction. The incidence of metabolic syndrome was significantly higher in surgically menopausal women than in the naturally menopausal group. The effects of 17b estradiol and conjugated estrogens were also slightly different with greater benefits from 17b estradiol on triglyceride levels and diastolic blood pressure. HDL levels were higher and LDL levels lower in women taking conjugated Estrogens.[26]

The risk of all forms of dementia is positively associated with obesity and higher waist-hip ratios are correlated with a higher risk of late onset Alzheimer's disease. This may be mediated by the higher risk of insulin resistance and diabetes associated with obesity as seen in a variety of clinical and preclinical studies.[1] There is also research linking visceral fat to a reduction in physical functioning. The SWAN study has shown slower gait speed in those women with higher levels of perivascular adipose tissue.[27] Numerous other studies have linked obesity to poor health outcomes. This includes the global longitudinal study of osteoporosis in women which has shown higher rates of ankle and upper leg fractures in obese women but lower rates of wrist fracture. Death from all cancers combined is increased by over 60% in women with a BMI greater than 40 compared to normal weight women.[28]

Importantly when we are considering managing women at midlife, we see that obese and overweight women tend to experience more significant menopausal symptoms so weight loss in this group can improve quality of life, self-esteem, and psychological well-being. Studies examining the link between sexual function and weight/body shape are limited.

Some studies have suggested that obesity is strongly associated with sexual dysfunction and impacts on lubrication, orgasm, and satisfaction. Women with metabolic syndrome appear to have a higher prevalence of disorders affecting these same domains.[29] Associations between obesity/overweight and mental health, body image and self-esteem are likely to be important.[30]

Prevention and Treatment of Weight Gain

Management of overweight and obesity should be a holistic process and start with an understanding of the patient, their needs and goals and the barriers to achieving these.

Physical activity

It is well established that regular physical activity helps protect against age associated weight gain. Both cardio and resistance exercise appear important to target fat mass and muscle mass respectively. Recommendations state that adults should do at least 150–300 min a week of moderate-intensity, or 75–150 min a week of vigorous-intensity aerobic activity as well as resistance or muscle-strengthening activities on 2 or more days a week.[31] Higher levels of exercise are often advised in overweight and obese individuals to combat the loss of muscle mass.

Diet

The optimal weight loss program has been hotly debated. No one diet, whether it is low fat, low carbohydrate, or high protein is superior to any other. The mechanism behind the success of any dietary intervention is a reduction in total calories. The obesity guidelines from the American College of Cardiology/American Heart Association task force recommend a daily caloric reduction of 500–750 kcal, which will translate into an average weight loss of 0.5–0.75 kg/week for most women.[22,23]

The Women's Health Initiative (WHI) dietary modification trial has shown that women were able to lose and then maintain that lower weight over the menopause transition following group or individual sessions promoting a reduction in fat intake as well as an increase in fruit, vegetable, and grain consumption. Weight loss was greatest among women who decreased the percentage of energy gained from fat.[32] Interestingly, there is evidence that remote support and counselling is at least as effective as face-to-face consultations.

Adherence to the Mediterranean diet appears to reduce the risk of weight gain at menopause as well as improving cardiometabolic risk factors and reducing menopausal symptoms.[33] There is good evidence that this style of eating reduces cardiovascular risk.

Intermittent fasting has been popularized in recent years with research in rats and humans showing it is an effective way to lose weight and reduce the incidence of metabolic and cardiovascular risk factors. However, it is probably no more effective than other methods of restricting calories. It is a technique that is sustainable by many and that may offer an approach that suits some of our patients.[22]

With modern technology, apps available online and downloaded on to smart phones provide tracking of calories and activity. These can be encouraged to reinforce adherence to any program. Advice about the appropriate weight loss program ultimately needs to be tailored to each woman's needs and her likely compliance.

Alternative approaches

Several studies have shown that yoga improves metabolic indices and aids in weight loss. Small studies have also suggested benefit from Chinese herbal medicine and acupuncture.[34,35]

Medication

Estrogen

BMI and waist circumference decreased in women taking estrogen and progestin therapy compared to those taking placebo in the WHI study. Fasting insulin levels and glucose were reduced in women on active treatment and the incidence of new diabetes was reduced in this group. The reductions in insulin resistance were independent of changes in body size. To prevent one case of diabetes over 5.6 years, 143 women would need to be treated with estrogen and progestin therapy.[36] This is consistent with data from the Heart and Estrogen/progestin replacement study and the Nurses' health study.[37,38]

Weight loss medication

A wide variety of medication is available world-wide to suppress appetite, promote satiety and to target insulin resistance and therefore assist with weight loss. The currently approved or off-label medications and their mode of action is summarized in Table 1.

Bariatric surgery

For our patients with a BMI over 40 and weight-related health complications, bariatric surgery can be a useful option. This will improve health outcomes and lead to significant weight loss. However, there are significant side effects and long-term issues associated with surgery so careful selection of candidates is vital.[44]

Table 1: Weight loss medications

Drug	Mode of action	Efficacy
Phentermine	Appetite suppressant	Mean weight loss of 12-13 kg versus 4.8 kg with placebo over 36 weeks[39]
Liraglutide	GLP-1 receptor agonist delays gastric emptying and reduces appetite	4-6 kg weight loss with 25% losing >10% body weight over 56 weeks[40]
Semaglutide 2.4	GLP-1 receptor agonist delays gastric emptying and reduces appetite	Average 15% weight loss over 68 weeks compared to 2.4% loss on placebo[41]
Lorcaserin	Selective serotonin 2C agonist that promotes satiety	3.2 kg compared to placebo over 1 year[39]
Topiramate	Suppresses appetite and increases satiety	6.58 kg in studies of >28 weeks[42]
Orlistat	Reduces fat absorption	3.4 kg compared to placebo over 1 year[39]
Metformin	Targets insulin resistance and may be useful for those women at risk of diabetes	1-2 kg over 12 months[43]
Bupropion	Unclear mechanism. Norepinephrine and dopamine uptake inhibitor	2.8 kg compared to placebo over 6-12 months[39]
Phentermine/ topiramate		9.3 kg compared to placebo over 1 year. On 15/92 mg 67% lost >5% of initial weight and 47% lost ≥10%[39]

GLP-1: Glucagon-like peptide-1

Maintenance of weight loss must remain a life-long effort as the weight loss itself triggers a number of changes in hormones that fuel hunger as well as a reduction in energy expenditure that are long lasting. The National Weight Control Registry has identified practices for achieving and maintaining weight loss among a group of registrants who have lost at least 13.6 kg and sustained that for over a year. These include eating breakfast each day, high levels of volitional physical activity (1 h per day), reduced fat intake, self-monitoring of dietary intake and activity, consumption of low or no calorie sweeteners, regular monitoring of weight and limiting TV viewing.[45]

Conclusion

Although changes in weight at menopause may be modest for many women, there are significant shifts in body composition. These can increase the risk of adverse health outcomes. Managing these issues is an important part of caring for women at mid-life, so it is incumbent on practitioners to have a clear understanding of the treatment options and how they may be adapted to an individual woman's needs. An in-depth understanding of the pathogenesis of menopausal weight and body composition changes is still in its infancy, but further research will provide additional targets for effective management.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organisation. Available from: https://www.who.int/health-topics/obesity. [Last accessed on 03 May 2021].
2. International Institute for Population Sciences. National Family Health Survey (NFHS-2), 1998-99: India. Mumbai: International Institute for Population Sciences; 2000. p. 438.
3. International Institute for Population Sciences. National Family Health Survey (NFHS-3), 2005-06: India. Vol. II. Mumbai: International Institute for Population Sciences; 2007. p. 168.
4. International Institute for Population Sciences. National Family Health Survey (NFHS-3), 2005-06: India. Vol. I. Mumbai: International Institute for Population Sciences; 2007. p. 540.
5. Gouda J, Prusty RK. Overweight and obesity among women by economic stratum in urban India. J Health Popul Nutr 2014;32:79-88.
6. Tandon VR, Mahajan A, Sharma S, Sharma A. Prevalence of cardiovascular risk factors in postmenopausal women: A rural study. J Midlife Health 2010;1:26-9.
7. National Family Health Survey 2019-20. Ministry of Family Health and Welfare and International Institute for Population Sciences. Available from: http://www.rchiips.org/nfhs/index.shtml. [Last accessed on 03 May 2021].
8. Davis SR, Castelo-Branco C, Chedraui P, Lumsden MA, Nappi RE, Shah D, *et al.* Understanding weight gain at menopause. Climacteric 2012;15:419-29.
9. Becker SL, Manson JE. Menopause, the gut microbiome, and weight gain: Correlation or causation? Menopause 2020;28:327-31.
10. Guthrie JR, Dennerstein L, Dudley EC. Weight gain and the menopause: A 5-year prospective study. Climacteric 1999;2:205-11.
11. Michalakis K, Coppack SW. Primary ovarian insufficiency: Relation to changes in body composition and adiposity. Maturitas 2012;71:320-5.
12. Ostberg JE, Thomas EL, Hamilton G, Attar MJ, Bell JD, Conway GS. Excess visceral and hepatic adipose tissue in Turner syndrome determined by magnetic resonance imaging: Estrogen deficiency associated with hepatic adipose content. J Clin Endocrinol Metab 2005;90:2631-5.
13. Goodwin PJ, Ennis M, Pritchard KI, McCready D, Koo J, Sidlofsky S, *et al.* Adjuvant treatment and onset of menopause predict weight gain after breast cancer diagnosis. J Clin Oncol 1999;17:120-9.

14. Gordon AM, Hurwitz S, Shapiro CL, LeBoff MS. Premature ovarian failure and body composition changes with adjuvant chemotherapy for breast cancer. Menopause 2011;18:1244-8.
15. Proietto J. Obesity and weight management at menopause. Aust Fam Physician 2017;46:368-70.
16. Gavin KM, Kohrt WM, Klemm DJ, Melanson EL. Modulation of energy expenditure by estrogens and exercise in women. Exerc Sport Sci Rev 2018;46:232-9.
17. Stubbins RE, Najjar K, Holcomb VB, Hong J, Núñez NP. Oestrogen alters adipocyte biology and protects female mice from adipocyte inflammation and insulin resistance. Diabetes Obes Metab 2012;14:58-66.
18. Kohrt WM, Wierman ME. Preventing fat gain by blocking follicle-stimulating hormone. N Engl J Med 2017;377:293-5.
19. El Khoudary SR, Shields KJ, Janssen I, Hanley C, Budoff MJ, Barinas-Mitchell E, *et al.* Cardiovascular fat, menopause, and sex hormones in women: The swan cardiovascular fat ancillary study. J Clin Endocrinol Metab 2015;100:3304-12.
20. Patel SR, Malhotra A, White DP, Gottlieb DJ, Hu FB. Association between reduced sleep and weight gain in women. Am J Epidemiol 2006;164:947-54.
21. Rettberg JR, Yao J, Brinton RD. Estrogen: A master regulator of bioenergetic systems in the brain and body. Front Neuroendocrinol 2014;35:8-30.
22. Kapoor E, Collazo-Clavell ML, Faubion SS. Weight gain in women at midlife: A concise review of the pathophysiology and strategies for management. Mayo Clin Proc 2017;92:1552-8.
23. Cushman M, Shay CM, Howard VJ, Jiménez MC, Lewey J, McSweeney JC, *et al.* Ten-year differences in women's awareness related to coronary heart disease: Results of the 2019 American Heart Association National Survey: A special report from the American Heart Association. Circulation 2021;143:e239-48.
24. Mehndiratta N, Sharma S, Sharma RK, Grover S. A prospective study on the incidence of metabolic syndrome in premenopausal and postmenopausal women. J Midlife Health 2020;11:17-21.
25. Dasgupta S, Salman M, Lokesh S, Xaviour D, Saheb SY, Prasad BV, *et al.* Menopause versus aging: The predictor of obesity and metabolic aberrations among menopausal women of Karnataka, South India. J Midlife Health 2012;3:24-30.
26. Pu D, Tan R, Yu Q, Wu J. Metabolic syndrome in menopause and associated factors: A meta-analysis. Climacteric 2017;20:583-91.
27. El Khoudary SR, Chen X, Nasr A, Shields K, Barinas-Mitchell E, Janssen I, *et al.* Greater periaortic fat volume at midlife is associated with slower gait speed later in life in women: The SWAN cardiovascular fat ancillary study. J Gerontol A Biol Sci Med Sci 2019;74:1959-64.
28. Compston JE, Watts NB, Chapurlat R, Cooper C, Boonen S, Greenspan S, *et al.* Obesity is not protective against fracture in postmenopausal women: GLOW. Am J Med 2011;124:1043-50.
29. Esposito K, Giugliano F, Ciotola M, De Sio M, D'Armiento M, Giugliano D. Obesity and sexual dysfunction, male and female. Int J Impot Res 2008;20:358-65.
30. Esfahani SB, Pal S. Obesity, mental health, and sexual dysfunction: A critical review. Health Psychol Open 2018;5:2055102918786867. doi: 10.1177/2055102918786867.
31. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK, *et al.* American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc 2009;41:459-71.
32. Howard BV, Manson JE, Stefanick ML, Beresford SA, Frank G, Jones B, *et al.* Low-fat dietary pattern and weight change over 7 years: The Women's Health Initiative Dietary Modification Trial. JAMA 2006;295:39-49.
33. Pugliese G, Barrea L, Laudisio D, Aprano S, Castelluci B, Framondo L, *et al*. Mediterranean diet as tool to manage obesity in menopause: A narrative review. Nutrition 2020;79-80:110991.
34. Moliver N, Mika E, Chartrand M, Burrus S, Haussmann R, Khalsa S. Increased Hatha yoga experience predicts lower body mass index and reduced medication use in women over 45 years. Int J Yoga 2011;4:77-86.
35. Sui Y, Zhao HL, Wong VC, Brown N, Li XL, Kwan AK, *et al*. A systematic review on use of Chinese medicine and acupuncture for treatment of obesity. Obes Rev 2012;13:409-30.
36. Margolis KL, Bonds DE, Rodabough RJ, Tinker L, Phillips LS, Allen C, *et al.* Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: Results from the Women's Health Initiative Hormone Trial. Diabetologia 2004;47:1175-87.
37. Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, *et al.* Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. JAMA 1998;280:605-13.
38. Manson JE, Rimm EB, Colditz GA, Willett WC, Nathan DM, Arky RA, *et al*. A prospective study of postmenopausal estrogen therapy and subsequent incidence of non-insulin-dependent diabetes mellitus. Ann Epidemiol 1992;2:665-73.
39. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: A systematic and clinical review. JAMA 2014;311:74-86.
40. Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, *et al*. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med 2015;373:11-22.
41. Wilding J, Batterham R, Calanna S, Davies M, Van Gaal L, Lingvay I, *et al*. STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021;384:989.
42. Kramer CK, Leitão CB, Pinto LC, Canani LH, Azevedo MJ, Gross JL. Efficacy and safety of topiramate on weight loss: A meta-analysis of randomized controlled trials. Obes Rev 2011;12:e338-47.
43. Yerevanian A, Soukas AA. Metformin: Mechanisms in human obesity and weight loss. Curr Obes Rep 2019;8:156-64.
44. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, *et al.* The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: A systematic review and economic evaluation. Health Technol Assess 2009;13:1-190, 215-357, iii-iv.
45. National Weight Control Registry Website. Available from: http://www.nwcr.ws/Research/default.htm. [Last accessed on 03 May 2021].