JCL Roundtable: Gender differences in risk reduction with lifestyle changes

W. Virgil Brown, MD*, Harold E. Bays, MD, FNLA, Ralph La Forge, MSc, CLS, FNLA, Geeta Sikand, MA, RDN, FAND, CDE, CLS, FNLA

Emory University School of Medicine, Atlanta, GA, USA (Dr Brown); L–MARC Research Center, Louisville, KY, USA (Dr Bays); Department of Medicine, Duke University, Durham, NC (Mr La Forge); and University of California Irvine School of Medicine, Irvine, CA, USA (Ms Sikand)

KEYWORDS:
Gender; Cardiovascular disease; Lifestyle habits; Myocardial infarction; Risk reduction

Abstract: The first efforts to uncover the causes of cardiovascular disease focused on the behavioral, now called lifestyle habits of populations. Diet, exercise, and smoking were recognized as important issues with strong relationships in community-based observational studies such as the Seven Countries study, the Framingham Heart Study, and the Western Electric Study in Chicago. The first meaningful intervention in the United States was the dietary recommendations made by the American Heart Association in 1963 and the Surgeon General’s Report on Smoking and Health in 1964. The American public listened and a very large change occurred in food consumption data and cigarette smoking over the next decade. These changes were mainly focused on men because the incidence of myocardial infarction was much higher in middle aged and older men than women. As smoking prevalence has decreased in men and increased in women and the population has aged, the differences in major vascular events have virtually disappeared. Women still enjoy a longer period of low rates but eventually the incidence rates approach those of men. As we constantly attempt to demonstrate ways of reducing risk by improved lifestyle it behooves us to re-evaluate the potential differences in gender response and adjust our expectations accordingly as clinicians.

Dr Brown: In the United States from a population perspective, dietary and smoking changes have been made. It seems that most of those healthy changes had occurred by the 1990. They now seem somewhat stable in Western societies. The only negative change during the last quarter of the 20th century appears to be gain in weight and the associated rise in diabetes and the metabolic syndrome. What does the data show in regard to differences in risk factors and the incidence of clinical end points between men and women over this same period?
Mr La Forge: Using the latest Center for Disease Control (CDC) cardiovascular disease trends from 2015, which defer back to 2011 to 2012, the absolute number of annual cardiovascular disease (CVD) deaths in women exceeded that of the male sex since 1984. These data are often confused with CVD mortality rates, which, when adjusted for differences in age distribution, reveal that the CVD mortality rate is substantially higher in men than women. Still, more than 1 in 3 female adults has some form of cardiovascular disease.

Fewer women than men survive their first heart attack. The symptoms of a heart attack can be different from women than men. Women have higher lifetime risk of stroke than men, and each year about 55,000 more women than men have a stroke in the United States.

Dr Brown: As we examine the current state of the prevalence of the classical risk factors, is there a trend in lipoprotein values in women vs men?

Ms Sikand: Yes there are differences. A 20-year follow-up of a prospective population-based cohort study in Netherlands published in the British Medical Journal in November 2014 showed that out of 8419 subjects (60.9% women) age 55 years and older that were free from CVD at baseline, 2888 subjects developed CVD (826 coronary heart disease, 1198 cerebrovascular disease, 762 heart failure, and 102 other CV death). At baseline, lipids and body mass index were higher in women vs hypertension and smoking were higher in men. Considerable differences were noted in the first manifestation of CVD and type of CVD by gender. Men more likely developed CHD at their first event and women more likely developed cerebrovascular accident or heart failure at their first event. So their recommendation was that lifestyle modification and blood pressure control are the main targets for preventing CHD, cerebrovascular accident, and heart failure.

Dr Brown: One of the things that we have noticed for many years dating back to Lipid Research Clinic was that men showed a much earlier rise in cholesterol and triglycerides. You know, of course they have had low high-density lipoprotein (HDL) cholesterol often indicates the presence of many more small dense LDL particles. HDL cholesterol often indicates the presence of many more small dense LDL particles.

Mr La Forge: As we examine the current state of the prevalence of the classical risk factors, is there a trend in lipoprotein values in women vs men?

Dr Brown: That probably has meaning in the total metabolism of the lipoproteins. We now know that lower HDL cholesterol often indicates the presence of many more small dense LDL particles.

Mr La Forge: Absolutely. As does the higher TG levels in men and its relationship to higher LDL particle number.

Dr Brown: Of course cigarette smoking also lowers HDL cholesterol. Smoking was much heavier in men 30 years ago. So that was an aggravating factor, but men have reduced their smoking rates. Over 50% of adult men in America smoked after World War II. Women smoked much less. The changes in cigarette smoking over the decades between men and women are dramatic. Women have shown a rise and stable prevalence, close to the level that men have assumed, but men have shown a dramatic reduction in cigarette smoking over the last 50 years. Now it is almost equivalent but approximately 20% of women and men still smoke cigarettes. This may be one of the main reasons that men and women are closer together in terms of vascular disease event rate.

In men, each pack of cigarettes produces about a 3 or 4 mg/dL drop in HDL cholesterol. If a man consistently smokes 2 packs a day, it goes down 7 or 8 mg/dL. Do women show the same response?

Dr Brown: The Jackson Heart Study has many volunteer participants with African ancestry and there are some interesting differences in African American women and men vs Caucasian or white women and men.

Ms Sikand: Overall, the prevalence of obesity among adults aged 20 years and over by gender and race in the United States from 2009/2010, statistics was similar in all racial groups except non-Hispanic blacks had the highest obesity 49.5% vs non-Hispanic white 34%, Hispanic 39%, and Mexican Americans 40%. When split by gender, in men the prevalence of obesity was similar in all racial groups. Prevalence of obesity was higher in women especially non-Hispanic black women.

The prevalence of obesity affects both genders though higher in women especially African American women. In 2009 to 2010, black women had the highest prevalence of obesity, which was 58.5% vs 32.2% in non-Hispanic white
and 41.4% in Hispanic and 45% in Mexican American women.

**Dr Brown:** What do we know about ethnic differences regarding obesity in women?

**Ms Sikand:** In 2011 to 2012, the abdominal obesity rates were 54% with 44% in men and 65% in women. Women aged 65 years and older had the highest rates of abdominal obesity at 74% vs younger women. The prevalence of diabetes was concordant in US adults with 14% in men and 11% in women. Diabetes rates also increased as age increased and was 26% for adults aged 60 years and older.

**Dr Brown:** In the 1980s, I had responsibility for a very large diabetic clinic at the Mount Sinai Hospital in New York. There were about 800 patients followed there. The ethnic census was about 45% Hispanic and about 40% to 45% African American and about 10% white. The one thing that stood out was that the men had the same weight distributions in both Hispanic and black. The African American women were heavier than Hispanic women. The mean fasting glucose and the triglyceride values were linked to body weight or BMI across the board. When the lipid values were adjusted for BMI, the differences disappeared.

We do not have enough data on people from South Asia. We know we have a problem there in terms of the response to obesity because it seems that they also develop central obesity very easily and have a relationship with regard to triglyceride elevations and blood sugar elevations as well. I would like to know if you have data on gender differences in populations from India, Pakistan, or the Malaysian peninsula.

**Dr Bays:** One thing very interesting with Asians, particularly South Asians, is that with positive caloric balance, Asians tend to have difficulty in proliferating more functional peripheral subcutaneous adipocytes and are especially prone to adiposopathy (dysfunctional adipose tissue). This results in hypertrophy of existing adipocytes, with energy overflow resulting in accumulation of adipose tissue within other body tissues, such as the visceral region. This causes adiposopathic endocrinopathies and immunopathies that are clinically manifested by increased glucose levels, maybe increase in blood pressure, and elevated C-reactive protein. Perhaps the metabolic abnormality most known by lipologists is the characteristic adiposopathic, mixed dyslipidemia, manifested by high triglyceride, low HDL cholesterol, and increased proportion of small dense LDL particles. These metabolic abnormalities may be exacerbated by increased carbohydrates. So I think Asian Indians certainly do represent a unique responder to caloric intake, particularly high carbohydrate diet.

**Dr Brown:** This intra-abdominal obesity seems to be particularly prevalent in men and earlier in life. Is this exaggerated in South Asian men? For years we have tried to explain gender differences on the postulated protective effects of estrogen. Do you think that the story has been fully investigated and is totally negative?

**Dr Bays:** As a background, I think it is reasonable to conclude estrogens have clinically meaningful vascular activity given the profound effects that a lack of estrogen can have was with regard with flushing and such, whether it be surgically induced menopause or natural menopause. If you consider that women have collectively, have the same risk of cardiovascular disease approximately 10 years later than that of men, then I think trying to attribute at least some of this to estrogen make a lot of sense.

Estrogens may increase nitric oxide synthase and the release of nitric oxide. From a lipid perspective, estrogens often decrease LDL cholesterol, increase HDL cholesterol, may decrease lipoprotein (a), but may also increase triglyceride levels. With regard to inflammation, some evidence exists of decreased vascular inflammation with estrogens, but here we go again. Estrogens may actually increase C-reactive protein. With regard to thrombosis, you may get some fibrinolysis, but particularly at higher doses, and especially in women who smoke, estrogens can increase the risk of thrombosis.

Regarding clinical trials, some may remember the Coronary Drug Project as a niacin trial. However, also in this trial was the use of estrogens. In this trial, not only did men administered estrogen have an increased risk of cardiovascular disease, but many years ago, I recall talking to participating investigators who stated they could tell which men were on estrogens because of the onset of gynecomastia. Given the negative effect of estrogens in men, and the negative effect of high dose estrogens in women (such as those administered some of the early oral contraceptives that increased the risk of thromboembolic events), and then, you add the results of the HERS study and the Women Health Initiative wherein overall, estrogens did not appear to reduce CVD risk, then I think the overall lessons are just like our National Lipid Association Annual Summary of Clinical Lipidology. Menopausal hormone therapy should not be administered solely to reduce atherosclerotic risk.

Having said that, I do not think this means that you should with-hold estrogen from symptomatic women, especially young women who have undergone bilaterally oophorectomy and who may have profoundly troubling symptoms. Clinicians should consider the potential benefit of estrogen when administering for the purpose of treating perimenopausal symptoms.

**Dr Brown:** Women who do tolerate estrogen for a year or 2 without thrombotic events, seem to benefit from them. The question has been whether the use of estrogen replacement therapy after the menopause is just a marker of health conscious women who seek guidance from physicians. There are many studies that have found this reduced events in women already on estrogen when a community observational study is done. In the Rancho Bernardo study, what
we found was that women who were taking estrogen were 5 pounds lighter, they smoked less, and had other indicators of healthy behavior patterns. We did not have good dietary data but over time, they certainly had less heart disease.

With an opposite view, what do you think about the possibility that we have this sex hormone issue somewhat backward? Cold androgens be a more important problem in creating gender differences with regard to vascular disease?

Dr Bays: With an increase in body fat that leads to dysfunctional adipose tissue (“adiposopathy”), androgen levels in men tend to go down, while in women, androgen levels often go up. An increase in body weight associated with increased androgens is often found in women with the polycystic ovarian syndrome. This is a risk factor for type II diabetes mellitus, which once present, results in the woman having a CVD risk not unlike that of men of the same age. In essence, an increase in body weight accompanied by diabetes mellitus essentially negates much of the potential CVD risk advantage women may have over men.

Dr Brown: Well let us turn to that very important point. It is certainly tied to the issue of obesity as well.

Ms Sikand: In a 2015 systematic reviewed paper on the effectiveness of weight loss interventions focusing on if there was a difference between men and women by Williams et al in “Obesity Reviews” reported that out of 49 high-quality studies, 11 were direct comparison studies, 10 showed that men lost more weight although women also had significant weight loss. Effect size (Hedges’ g) analysis showed small differences in weight loss favoring men in both diet and diet plus exercise groups. The authors concluded that current evidence supports moderate energy restriction plus exercise. Little evidence supports that men and women should adopt different weight loss strategies.

Mr La Forge: Probably the most head-turning lifestyle trial up to that point was the Diabetes Prevention Program trial or Diabetes Prevention Program (NEJM 346:393–403, 2002). So here you had 3200 men and women, multiethnic groups, and major ethnicities in the country covered. The same lifestyle intervention for both men and women, and men again lost more weight from dietary and exercise strategies. Men after 3.5 years lost approximately 14 pounds. Women lost 10, but part of that differential is what we have seen in every exercise study in men and women that show men outperform women in losing weight. Well, they weighed more at the start. For any given level of effort or intensity of exercise, men are going to generate a greater net energy expenditure. So this difference in physical activity energy expenditure much of the weight loss differential. Although men in the Diabetes Prevention Program intensive lifestyle therapy group lost significantly more weight and reported more physical activity than women, their rate of progression to diabetes (or regression to normal glucose tolerance) was the same.

We just keep coming back to weight loss, which is important, but who knows what happened in real-time visceral and peripheral fatty acid changes.

Dr Brown: You are speaking about the intervention studies that are focused both on diet and exercise? The background for that is in the NHANES data where the study is in a representative population of adults in the United States by gender and ethnicity. What they saw during the 80s and 90s was an increase in calories that was greater in women. Compared to dietary data recorded in the initial NHANES observations recorded back in the 1960s and compare it to 30 years later, in the 90s, women were eating 200 calories more. This increase was attributable to an increase in carbohydrates, not fat or protein. Saturated fat intake was stable in both genders.

Perhaps, but men sustained their carbohydrate fat ratio, whereas women had a big increase in carbohydrates but maintained an intake of about 11% saturated fat. Cholesterol was less than 300 mg/day in women and somewhat greater in men, but it was related to total calorie intake. The death rates from coronary heart disease declined in a parallel fashion to cholesterol and saturated fat reduction. Cigarette smoking was delayed about 12 years. If you look at the Surgeon General’s report in 1964, people smoked more for the next 10 years. Vascular disease mortality peaked in 1968. Smoking rates did not fall until environmental smoke issues came in and states started significant taxation on cigarettes. The health issues that were raised by the surgeon general’s report seemed to have very little impact until several years after coronary and stroke rates had fallen markedly.

It appears that diet had the initial and major impact before better pharmacological control of blood pressure and LDL cholesterol. We must continue to do very high-quality research with dietary interventions or there will be great economic and industry pressure to liberalize our choice of foods. We also must remind our guideline and regulatory people of the excellent studies of the past 60 years.

Dr Bays: Virgil, I would like to echo what you said. Irrespective of all the controversy—and you are correct—there is a lot of controversy, I think we should all be able to agree to be very cautious about the suggestion that unlimited intake of saturated fats is now perfectly fine. I believe we should be cautious in suggesting no evidence exists to suggest adverse health consequences with saturated fats. I think that is the wrong message. Maybe we can argue about unique properties of medium-chain saturated fats. Or perhaps we can talk about the wisdom of cooking with polyunsaturated fats. But given that the United States encompasses a population in whom the majority are overweight or obese and whose greatest risk for death is heart disease (and cancer), it seems unreasonable to convey a message that folks can eat however much saturated fats they want. I think that that betrays clinical science and betrays the history you just cited.

Dr Brown: Yeah. This—it came about in part because the American Heart Association (AHA) placed great emphasis on reducing total fat for a long time. We felt that most of the fat being consumed was saturated and monounsaturated fat from meat and eggs. The thought
was that reducing fat would mandate a reduction in animal fat. The only concern about vegetable fat was the calories added to the diet and the potential for increasing obesity. However, we now know that fat (including vegetable fat) tends to suppress appetite much better than carbohydrate.

Dr Bays: Look, as an Endocrinologist, I am favorable to “low carb” nutritional interventions, especially in patients with diabetes mellitus and hypertriglyceridemia. I also believe a reduction in simple/refined sugars is helpful with weight reduction. Within my instructions to patients about a carbohydrate-restricted diet, just as I do not recommend increased consumption of processed carbohydrates, I also do not recommend an increased intake of long-chain saturated fats. Overall, I believe the evidence best supports a Mediterranean-type diet that might include plant-based foods (eg, fruits, vegetables, whole grains, legumes, and nuts), olive oil, herbs and spices (instead of salt), and fish/poultry. Red wine for those inclined might not be a bad idea for some patients.

Dr Brown: There seem to be gender differences in the population-wide dietary contributors to obesity? Do you think that women are more subject to the effects of carbohydrate in the diet in a manner that would explain the increased intake and greater rise in prevalence of obesity?

Ms Sikand: As we know, all carbohydrates are not created equal. There are good carbohydrates, for example, legumes, lentils, whole grains, fruits, and vegetables and there are the bad carbs, for example, refined flour and sugar-sweetened foods and beverages. Evidence shows that sugar-sweetened foods and beverages and refined grains are detrimental.

Dr Brown: The data on that issue seem clear cut, both from population and metabolic ward studies.

Ms Sikand: The 2013 AHA/American College of Cardiology (ACC) Guideline on Lifestyle Management to Reduce Cardiovascular Risk did not provide a recommendation for dietary cholesterol intake because of “insufficient evidence to determine whether lowering dietary cholesterol reduces LDL-C” (Eckel et al, 2013).

The National Lipid Association (NLA) recognizes that there are individuals who are hyper-responders to dietary cholesterol intake because of genetic or other variables, along with other dietary factors that influence serum total cholesterol and LDL cholesterol levels. Additionally, the NLA recognizes that elevated serum levels of atherogenic particles (ie, LDL cholesterol and non-HDL cholesterol) is associated with the development of ASCVD (8-Jacobson et al., 2014). The NLA Expert Panel Part II Recommendations expected to be published in 2015 support the cardioprotective eating pattern recommended by the 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk, with the addendum that dietary cholesterol intake is limited to <200 mg per day in individuals at high risk of CVD or in secondary prevention patients.

The 2015 Dietary Guidelines Advisory Committee (DGAC) Report did not recommend to continue the limit of dietary cholesterol to <300 mg per day because “available evidence shows no appreciable relationship between consumption of dietary cholesterol and serum cholesterol” (2015 DGAC, 2015).

The 2015 Dietary Guidelines for Americans (DGAC) Report recommends a cardioprotective dietary pattern, for example, healthy US style pattern, a healthy Mediterranean-style pattern, and a healthy vegetarian pattern. These eating patterns include the dietary components associated with health benefits. The overall body of evidence examined by the 2015 DGAC identifies that a healthy dietary pattern is higher in vegetables, fruits, whole grains, low-fat or nonfat dairy, seafood, legumes, and nuts; moderate in alcohol (among adults); lower in red and processed meat; and low in sugar-sweetened foods and drinks and refined grains. Vegetables and fruit were consistently identified in every conclusion statement across the health outcomes. Whole grains were identified slightly less consistently compared to vegetables and fruits, but were identified in every conclusion with moderate-to-strong evidence. For studies with limited evidence, grains were not as consistently defined and/or they were not identified as a key characteristic. Low-fat or nonfat dairy, seafood, legumes, nuts, and alcohol were identified as beneficial characteristics of the diet for some, but not all, outcomes. For conclusions with moderate-to-strong evidence, higher intake of red and processed meats was identified as detrimental compared to lower intake, as well as refined grains was identified as detrimental in almost all conclusion statements. There are 128 statements with moderate-to-strong evidence.

Dr Brown: Exactly. We need to very carefully and objectively examine all data on the relationship between dietary intake and risk factors for cardiovascular disease. A mistake in guidelines in that area could be very costly in morbidity and mortality.

Dr Brown: When people review the literature in the modern era, they go back to the electronic files. If the work was done before the 1970s it may not be in an electronic format. That is where much of the carefully done studies are published. If cholesterol intake is not important, why does a drug that blocks cholesterol absorption from the intestine work so well? I am speaking of ezetimibe, which recently was shown to prevent vascular disease in proportion to the LDL cholesterol reduction in the IMPROVE-IT study.

Ms Sikand: Absolutely.

Dr Brown: Are there gender differences in weight loss and weight loss maintenance?

Ms Sikand: A 2013 systematic review of 37 studies by Stroeble-Beschop et al published in J Obes Weight Loss Therapy on gender differences in obesity outcomes showed that out of 32 studies that examined weight loss outcomes, 16 studies reported higher absolute weight loss in men; 16 reported no gender difference. However, out of 12 studies that examined weight loss maintenance 8 showed no gender difference, 3 reported men maintained their weight better, and 2 reported that women did better.
In another 2015 study by Tsai et al NHANES 2009 to 2010, data on gender differences were analyzed to examine the weight-related attitudes and behaviors in 5225 males and 5312 females that were overweight or obese published in Amer J Men's Health, men were more likely to lose and maintain >10 lbs over 1 year. Men exercised more and ate less fat. Women joined structured weight loss program, took prescription diet pills, and attempted special diets. Overall, men had less accurate weight perception, less weight dissatisfaction, and lesser attempts at weight loss than women.

**Dr Brown:** That’s interesting. Men became somewhat self-satisfied and comfortable with their increased body weight. Weight loss is very difficult so there may be a degree of rationalization involved with us men.

**Ms Sikand:** But they also went on to mention that men were more likely to lose and maintain 10 or more pounds over 1 year. This was significantly different from women. They also said men exercise more and ate less fats. Women joined more weight loss programs, prescription diet pills, and special diets. So they concluded that a need exists for male-specific intervention to improve overweight and obese men’s weight perception, attempted weight loss, and ultimately successful weight loss.

**Dr Brown:** So if I understand this study, men were less likely to start a weight loss program but if they did, they accomplished more weight loss. Perhaps those who do are aware of the health consequences and are motivated by that rather than cosmetics?

**Mr La Forge:** Joe Donnelly at University of Kansas, who is one of the key authorities investigating gender differences and exercise generated weight loss, conducted the Midwest Exercise Trial and the Midwest Exercise Trial-II. Donnelly et al came to the conclusion that there is virtually no difference when both genders are exercising at the same absolute energy expenditure. That said, Hagopian at Cal Tech among others have shown that it may be more challenging for women to achieve the same target exercise expenditure as men given that they have a lower weight and lower total daily energy expenditure. To achieve the same target exercise expenditure as men, women may need to exercise for a longer duration and/or at a higher intensity. This makes the most sense to me.

**Dr Bays:** One of the things that I would like to add is weight perception. We did a survey study wherein we used Stunkard figures that display a range of thinner to larger individuals. The data support what I think a lot of us already knew. Most men and women respondents chose an ideal body image that was thinner than their self-selected, self-image. However, compared to men, women picked lower numbers (thinner figures) on the Stunkard rating scale as their perception of an ideal body image. So this objectively supports the notion that magazines, culture, and such tend to promote or imprint ideal body images in a way that differs between women and men.

**Ms Sikand:** Based on my 30 plus years of experience with helping both men and women in the arena of weight management, I have observed that it is harder for women to lose weight. Women have a greater need for comfort foods, which are high in sugar. It is likely that women are the nurturers and caregivers in most relationships and allow comfort foods to serve as a metaphor to replenish their emotional needs. This food reward addiction arena is a new area of research. It is very complex of course.

**Dr Brown:** I agree that it must go beyond just the chemical stimulus, the nutrient supply to the brain beyond the various satiety factors.

**Ms Sikand:** In a 2012 review paper published in Obesity Review, Fitzgibbon et al examined 25 studies that reported weight loss in black women from 1990 to 2010. Findings showed that more intense behavioral trials yielded more weight loss. Overall, black women lost less weight than other racial groups. The authors recommended that it was critical to integrate biological, social, and environmental factors that influence obesity treatment in black women.

**Dr Brown:** Thank you for sharing that data with us. Let us turn now another type of intervention, which is growing in the frequency of its use, namely bariatric surgery. What about gender differences there? Is there more bariatric surgery in men vs women?

**Dr Bays:** The first thing is, Virgil, you may remember when we did our NLA consensus statement on adiposity. One of the things you wanted to ensure we included was the global effects in both men and women regarding bariatric surgery and cardiometabolic risk factors. We therefore included the data wherein bariatric surgery most consistently improves triglyceride and HDL cholesterol levels. It is with substantial weight loss through bariatric surgery, especially with the more “malabsorptive” procedures, where we most consistently observe reductions in LDL cholesterol.
The other thing is that a nonlipid metabolic disease that improves substantially with either bariatric surgery or weight management pharmacotherapy is glucose levels among patients with type II diabetes mellitus.

Regarding differences between men and women, women seek bariatric surgery about 5 times more often than men. This is consistent with our antiobesity, weight management pharmacologic clinical trials wherein it is not uncommon that 80% to 90% of those who volunteer to participate in weight management clinical trials are women.

Dr Brown: So that is really interesting. This indicates that women are more concerned about obesity than men. They are willing to go through surgical treatment and to take medication for long periods of time. In the more recent trials of weight loss drugs women dominate the numbers in those studies?

Dr Bays: That is what I am saying. Even with weight management pharmacotherapy trials, it is common to have 80% to 90% of women participants. Sometimes we have to close the study entry to women because we do not have enough men. It is curious the degree by which there is a disproportionate amount of women who participate in antiobesity pharmacotherapy trials—which may relate to the gender body image differences we previously discussed.

Dr Brown: Is the response to bariatric surgery equivalent? Do we find the same degree of weight loss for males and females?

Dr Bays: The literature is mixed regarding potential differences in weight loss between men and women. Some men may lose weight quicker because men typically have greater muscle mass, and the loss of glycogen postoperatively may also result in a loss of glycogen accompanying water (which is similar to why rapid weight loss can sometimes be found with carbohydrate-restricted diets). However, it is unclear that fat weight loss substantially differs between women and men, given the same degree of postweight loss nutritional intervention and physical activity.

Mr La Forge: The buzzword in clinical exercise science research over the last 2 to 3 years is inactivity. I do not care how fit you are. The number of hours you sit is as or maybe even more important. Two major studies, one just published recently in the British Journal of Sports Medicine reflects so much of what has been demonstrated over the last 3 years in this country about all-cause mortality in women who sit for 7 or more hours per day. All-cause mortality, for which about 65% is related to cardiovascular disease, increased approximately 55% in women who were sedentary or sitting for 7 or more hours a day.

There is evidence that for either gender if you get up and walk or move twice on the hour for 5 minutes each time you can significantly reduce CVD risk and all-cause mortality. That outcome has been repeated several times.

Finally, the 1.1 million woman UK Women’s Health Study recently published by Miranda Armstrong from Oxford showed that women who walked, who do housework, who garden on a daily basis but not to extreme ends, just the moderate level of activity, can reduce their all-cause mortality about 25%. Armstrong found a U-shaped trend, however. That is if they overindulged in exercise (both intensity and duration) their risk increased dramatically, but moderate levels of activity—meaning anywhere from 120 to 150 minutes per week of moderate physical activity, especially household chores and utilitarian tasks was the best to reduce risk.

Dr Bays: It is interesting how that turns the concept of “taking a break,” on its head. People engaged in strenuous sports often take breaks for rehydration and other health reasons. But routine strenuous activity in the US population is not near as common as the hours upon hours of relative inactivity. So maybe what we really should be focused upon is ensuring people take a break from inactivity. Maybe that ought to be one of the major messages. If you are sitting at a computer all day—and I will include myself—then we need to periodically get up and go up and down the steps and talk to people or whatever. Periodically taking a break from inactivity should be just as common a practice as taking a periodic break from strenuous activity.

Dr Brown: If additional studies confirm these findings, it very encouraging because so many of us are sitting in front of a computer screen all day and then go home and sit in front of a television screen for another 3 or 4 hours. So if getting up and taking a break now and then will make such a large difference that is very, very good news.

Ms Sikand: Current research provides evidence of moderate-to-strong links between healthy dietary patterns, lower risks of obesity, and chronic diseases, particularly cardiovascular disease, hypertension, type II diabetes, and certain cancers. Emerging evidence also suggests that relationships may exist between dietary patterns and some neurocognitive disorders and congenital anomalies. The overall body of evidence examined by the 2015 DGAC report identifies that a healthy dietary pattern is higher in vegetables, fruits, whole grains, low-fat or nonfat dairy products, seafood, legumes, and nuts; moderate in alcohol (among adults); lower in red and processed meats; and low in sugar-sweetened foods and drinks and refined grains. Additional strong evidence shows that it is not necessary to eliminate food groups or conform to a single dietary pattern to achieve healthy dietary patterns. Rather, individuals can combine foods in a variety of flexible ways to achieve healthy dietary patterns, and these strategies should be tailored to meet the individual’s health needs, dietary preferences, and cultural traditions. Current research also strongly demonstrates that regular physical activity promotes health and reduces chronic disease risk.

Dr Brown: There have been several studies that have shown if you replace some of your calories with walnuts or other types of nuts as well the LDL cholesterol is reduced a bit. Although they do not make up a huge number of calories for most of us, have never been impugned as being a cause for vascular disease. Do you think the data are strong enough to recommend replacing some carbohydrate calories with nuts? Are these studies to small and short to be adequate for a dietary recommendation?
Ms Sikand: A recent meta-analysis by Afshin et al in 2014 Am J Clin Nutr reported that nut consumption was associated with a decreased risk of incident ischemic heart disease and diabetes. Nuts are a source of plant proteins, bioactive peptides, unsaturated fatty acids, fiber, phytosterols, polyphenols, and antioxidant vitamins.

Dr Brown: I would like to close our Roundtable on Gender differences in Response to the Lifestyle interventions by asking you to give your opinion on the following question: What are our greatest opportunities to intervene at the population level to improve risk factor prevalence?

Dr Bays: So that is something I have been really passionate about lately. To me, I believe one of the greatest opportunities to intervene at the population level can be found within the context of epigenetics. Virgil, you might remember in our NLA Annual Summary of Clinical Lipidology, we included a discussion about how the dysfunctional transport of nutrients from the mother to the fetus may contribute to epigenetic effects, adversely affect stem cell fate, and thus, contribute to abnormalities in postnatal biological processes. This speaks to an inadequate attention to appropriate prenatal, perinatal, and postnatal nutritional and general medical care. I believe reasons exist to believe that while nutritional and physical activity factors apply, the generational effects of epigenetic imprinting may also be operative, especially with regard to the increased risk of metabolic diseases such as dyslipidemia, diabetes mellitus, and obesity.

Consider if US leadership would make it a national priority to ensure the worldwide very best in nutritional, physical activity, medical, and lifestyle care (ie, no smoking) before conception, for both the father and the mother. What if we prioritized perinatal and postnatal care? What if we were to fully commit to doing what was required to ensure the next generation had the best potential for future metabolic health, through avoiding what could be lifelong (and perhaps generational) epigenetic adverse consequences? If we did so, I believe a good chance exists that we could make some real inroads to reversing not only the obesity epidemic, but also the diabetes epidemic, lipid epidemic, CVD epidemic, and so forth.

Dr Brown: The genome-wide association studies show scores on strength of relationships between polymorphisms in specific genes and vascular disease or risk factors for vascular events.

A recent paper examining very large populations identified 181 different genes that are linked to composites of risk factors we use to define the metabolic syndrome. Some of these are linked to 2 or 3 or even 4 of those particular characteristics; high triglycerides, glucose, blood pressure, and obesity. You know, the metabolic syndrome is obviously a complex polygenic disorder that is caused by multiple low-impact genes occurring in the same individual but different from person to person. Obesity has genetic factors but is often the driver of the causative risk factors in a given genetic setting.

This brings me back to another question, which I have puzzled over. It looks as though most of the rapid weight gain in America, occurred beginning in the late 80s and through the 90s. The prevalence of obesity has shown much less change after 2000. It looks as though we have reached a plateau. Do you think we are seeing an effect of the effort to educate the public on the risk related to obesity and diabetes?

Dr Bays: I think we may simply be reaching the limit of our population bell shaped curve. I do not necessarily think it is because we have been especially effective in public health policies. I think we are approaching our biological limit.

Dr Brown: Don’t you think we could get fatter than we are? There is social pressure now. The First Lady of this country has made a big effort to inform both children and adults about this matter. There is social pressure that we did not have 20 years ago.

Mr La Forge: That is true. Let me just add 2 most helpful physical activity resources out there for patients and providers: There is wisewoman.com. Wise Woman is probably the most diverse and practical source of useful information on physical activity for women. The other resource is Exercise is Medicine (EIM) http://www.exerciseismedicine.org/ . The EIM resource is ranked at the top of the list for practical physical activity advice with resources for health care professionals, exercise specialists, and patients and community.

Dr Brown: Are there online programs that the doctor might recommend for support in achieving weight loss in both women and men?

Ms Sikand: I would like to encourage primary care physicians to do 3 things:

1. Partner with a registered dietitian nutritionist for providing weight management counseling including intense behavior therapy, which is now a covered benefit by Medicare. A minimum of 14 visits over 6 months with the registered dietitian are recommended by the 2013 ACC/AHA/TOS obesity management guidelines.
2. Ask their patients about their weight history including past failures and successes.
3. Be viewed by their patients’ as their partner in their weight management journey along with their registered dietitian nutritionist.

Dr Brown: I believe that the physician should express a genuine interest in food intake. It has been my habit to have a few specific questions about food intake on a form as I take a history. I enter my notes as the patient answers the questions. The purpose is to impress the patient with the importance of dietary habits. They need ongoing support that is not possible at short visits in the office.

Ms Sikand: Ideally have them write down what they eat and drink in the past 24 hours for breakfast, lunch, dinner, and snacks.
Dr Brown: With regard to support in the community, are there programs equally accessible and attractive to men and women? Are there programs that are more gender specific that we can recommend?

Dr Bays: I would say that for individuals, many commercial weight management organizations can be quite effective. New media and technologies can also be extraordinarily helpful, whether it be Facebook, YouTube, Twitter, or various Web sites and apps. Wearable technologies are also available that helps put patients in control, which is necessary for effective behavior modification.

Many are familiar with pedometers, which is a classic example of a technology or tool, which can help patients track their activity. Other more novel technologies are weight scales that transmit signals to a base location. In response to the weight metric, the individual who used the scale is sent feedback via email or text message regarding the value recorded on the scale. The bottom-line is that behavior modification is critical to any weight management program, and the success of behavior modification is dependent upon being doable, efficacious (ie, evidenced based), measurable, and allow for self-ownership.

Mr La Forge: I agree. I think clinical pedometry (the systematic clinical use of well-engineered step-counters), which should be used as an outcomes metric in every primary care office in the United States. In fact, in the Indian Health Service Diabetes Treatment and Prevention Division, we use well-engineered pedometers to practically and economically track activity—I am at 2400 steps right now. That translates to being sedentary but fortunately there is time left today. By midnight tonight if I am under 5000 that is the CDC’s metric for the sedentary lifestyle index category. So it is a motivator for me, like you say, Harold. It is a real-time motivator.

Let me just say, again, resources. Exercise is Medicine for both men and women has the longest spanning focus just on exercise for both providers and patients. It is excellent. Great downloads, and so forth. Finally, Wise Woman, which is all for women both diet and exercise is the longest standing resource for support, I think, for women, especially underprivileged and poor women.

Ms Sikand: I agree with Harold and Ralph there are some great technology programs including the Supertracker by USDA and some phone apps including “My Fitness Pal” and “Lose it.” I have seen great successes in our patients at the University of California Irvine Preventive Cardiology Program with excellent weight reduction outcomes. Also, there are great weight management programs in the community such as Weight Watchers was ranked in the top 10 by US News and World Report.

Finally, according to a recent National Institutes of Health Report, weight loss maintenance is a substantial problem in obesity treatment due to genetic and behavioral differences in individuals. We need to individualize weight management interventions and target specific populations with evidence-based strategies.

Dr Brown: So it seems to me there are 2 key features. One is building personal awareness and motivation. But there is also this important issue of social structure and accountability to your colleagues—woman or man. Some of the programs really take advantage of the latter.

Dr Bays: Education remains important. We now have apps on mobile phones, which allow real-time assessments of the caloric content of foods. That can be a real education. Many apps also help track daily physical activity, which is also an important lesson as well. The bottom-line is that with regard to weight management, we need a multidisciplinary approach. We need all the help we can get to promote appropriate nutrition, physical activity, behavior modification, and if needed, the appropriate use of weight management pharmacotherapy or bariatric surgery. For most folks with overweight or obesity, one approach is not going to be enough. We need an “all of the above” approach.

Dr Brown: The very important task of helping patients change a series of issues that we combine into the term “lifestyle” is daunting for most health professionals. I know the readership of this Journal will appreciate your sharing information that has come from many years of experience. You have made the important points that every clinician, dietitian, or exercise physiologist must maintain a strong interest in both acquiring information from our patients that can guide good planning for lifestyle change and the importance of personal and continuing education regarding the techniques for improving daily behavior patterns. This is crucial for both men and women. Tailoring this to the special needs of both genders requires a thoughtful plan and specific guidance if we are to be most successful in our preventive efforts as health professional.

Financial disclosures

Dr Bays’ research site received research grants from Amarin, Amgen, Ardea, Arisaph, California Raisin Marketing Board, Catabasis, Cymabay, Eisai, Elcelyx, Eli Lilly, Esperion, Gilead, Hanni, Hisun, Hoffman LaRoche, Home Access, Janssen, Johnson and Johnson, Merck, Necktar, Novartis, NovoNordisk, Omthera, Orexigen, Pfizer, Pronova, Regeneron, Sanofi, Takeda, TIMI, VIVUS, and WPU Pharmaceuticals. Dr Bays served as a consultant and/or speaker to Amarin, Amgen, AstraZeneca, Bristol Meyers Squibb, Catabasis, Daiichi Sankyo, Eisai, Eli Lilly, Isis, Merck, Novartis, NovoNordisk, Omthera, Regeneron, Sanofi, VIVUS, and WPU. Mr La Forge has received Speakers Bureau honoraria from AstraZeneca. Ms Sikand has no disclosures to report.

Gender differences in risk reduction with lifestyle changes: Recommended reading


