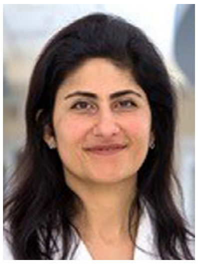
Editorial

Influence of Sex and Gender on Lifestyle Interventions for Cardiovascular Disease



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Lifestyle interventions have gained increasing popularity in recent years in addressing primary and secondary prevention of cardiovascular disease, the leading cause of death and disability.[1] Research on these interventions have primarily focused on the role of physical activity and nutrition but may extend to include other modalities, such as counseling, motivational interviewing, and stress reduction programs.[2,3] However, the sex and gender implications of these interventions, particularly across the life span, have not been teased out.

Promising data have been reported in an Australasian study on the differences in both sex and gender responsiveness to lifestyle interventions, with greater reductions seen lipid profiles and body mass index in men compared with women 30 days after intervention in 925 participants (34% men and 65% women).[4] Behavior factors, such as food preferences, commitments, and differential support methods, explained some of the gender differences.[4] Similar sex and gender differences were noted in rehabilitation after surgery and myocardial infarction—fewer women enter rehabilitation and complete it compared with men. Sex differences are seen in the degree of fitness achieved and the benefit women draw compared with men, with some pilot data indicating that women may derive greater benefit from the same level of rehabilitation than men. Similarly, a differential sex-specific association between physical activity and cardiometabolic health has been observed in population-based programs.[5,6] A differential effect of exercise on cognition has been found, with at least 1 study reporting a greater benefit of aerobic activity on cognition in women (because of increased levels of brain-derived natriuretic factor) than men, even though men achieved higher fitness than women.[7] Sex and gender have different associations in nutrition and diet programs in individuals with diabetes (eg, very low calorie diet in a randomized controlled trial found benefit on the 6-minute walk test in men but not in women).[8] Men do better with direction than choice compared with women for nutritional counseling.[9] Even for stress reduction interventions, women had greater reduction in symptoms than men after trauma.[10] The next 2 special issues focus on consolidating and reporting our current understanding of the evidence on the sex and gender implications of lifestyle interventions for cardiovascular disease.

Petek et al[11] effectively used a large database of young athletes to learn how female athletes had a greater change in systolic blood pressure with change in oxygen consumption compared with male athletes and how the response varies by type of exercise as well. The authors provide a nomogram for exercise-related changes in blood pressure for male and female athletes. Importantly, they report the importance of monitoring both change in blood pressures and peak blood pressures during athlete assessment. The study provides evidence of an alternate range of expected blood pressure changes in conjunction with exercise capacity and makes a good case of why such sex-specific nuanced measurements should be incorporated in standardized testing guidelines.

Rao et al[12])review the differential changes in electrical, structural, and functional adaptations that occur in the male versus female heart in response to vigorous exercise training. Structural adaptive changes in the cardiac chambers and electrocardiographic changes are observed to be more pronounced in male athletes. When these changes become maladaptive (for instance, hypertrophic cardiomyopathy), they possibly offer one explanation for the higher rates of sudden cardiac death seen in male athletes compared with female athletes. However, the exact causative association remains unknown.

Focusing on the differential effects of lifestyle interventions, Cheng et al[13] highlight the influence of age on modifying the biological effects of sex on muscle mass and functionality, glucose metabolism, and bone density. Sarcopenia, or age-related loss of skeletal mass and function, has been associated with increased risk of falls in elderly women compared with to men. Both the lower absolute and relative muscle mass and the higher rates of sarcopenic obesity observed in women have been linked with earlier loss of functional independence and disability in elderly women than in men. These differences in part could be explained by how interleukin 6 and insulin-like growth factor 1 behave differently in men versus women. The authors also highlighted gender differences in resistance training programs with group-based, mixed, higher-intensity but shorter sessions being more positively correlated with adherence in older women. Finally, they reviewed results of relevant studies to guide clinicians in providing strength-based exercise recommendations to elderly patients.

Thomas et al[14] elaborate on the role of gender differences that may contribute to obesity epidemic and cardiovascular disease and how obesity poses different risk for men and women. The authors explore the association of estrogen with satiety and the different cravings between men and women. The authors highlighted gaps in our current understanding of lifestyle interventions through a gender lens and make some useful recommendations for future researchers working in this area. In our own paper (ref), we reported the outcomes with standard real world cardiac rehabilitation program that primarily focuses on aerobics with variable element of resistance training. We found no difference in one-year cardiac outcomes between patients who entered cardiac rehabilitation program versus those who did not. While the sample size and single institution status of the data might influence the interpretability of the outcomes data, this study provided additional important sex based differences in exercise time, body composition and quality of life in patients undergoing cardiac rehabilitation.Mangi et al (ref) highlight the significance of strength training in CVD recovery and the sex gender differences in training to achieve this goal. The authors provide guidance to the clinicians as well as trainers with recommendations to start a resistance training program for patients with CVD that may serve complementary to a cardiac rehabilitation program.Finally Madsen et al (ref) provided a nice systematic review of the benefits of physical activity for primary prevention is clear in patients with cerebrovascular disease. While the overall benefits are clear, data is mixed when looking at sex and gender related effects and warrant further research.

Cardiovascular disease remains the leading cause of death worldwide and requires an expansion of our armamentarium to curtail its burden. In this special issue, our expert contributors have looked at this evidence through an age, sex, and gender lens to suggest lifestyle recommendations that can be personalized. To use the full potential of such interventions, we must explore the full range of diverse nutrition and exercise programs and couple observational science with molecular, translational, and genetic markers of these differences to advance mechanism-based precision medicine for our patients.

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REFERENCES

1. Maruthur NM, Wang NY, Appel LJ . Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER Trial. *Circulation*. Apr 21 2009;119:2026–2031.
2. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE . Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med*. Mar 14 2002;346:793–801.
3. Wister A, Loewen N, Kennedy-Symonds H, McGowan B, McCoy B, Singer J . One-year follow-up of a therapeutic lifestyle intervention targeting cardiovascular disease risk. *CMAJ*. Oct 9 2007;177:859–865.
4. Kent LM, Morton DP, Rankin PM, Mitchell BG, Chang E, Diehl H . Gender differences in effectiveness of the Complete Health Improvement Program (CHIP) lifestyle intervention: an Australasian study. *Health Promot J Austr*. Dec 2014;25:222–229.
5. Boule NG, Bouchard C, Tremblay A . Physical fitness and the metabolic syndrome in adults from the Quebec Family Study. *Can J Appl Physiol*. Apr 2005;30:140–156.
6. Ma J, Kim H, Kim J . Isotemporal Substitution Analysis of Accelerometer-Derived Sedentary Behavior and Physical Activity on

Cardiometabolic Health in Korean Adults: A Population-Based Cross-Sectional Study. *Int J Environ Res Public Health*. Oct 22 2021;18:11102.
7. Barha CK, Hsiung GR, Best JR, et al. Sex Difference in Aerobic Exercise Efficacy to Improve Cognition in Older Adults with Vascular Cognitive Impairment: Secondary Analysis of a Randomized Controlled Trial. *J Alzheimers Dis*. 2017;60:1397–1410.
8. Haywood CJ, Prendergast LA, Purcell K, et al. Very Low Calorie Diets for Weight Loss in Obese Older Adults-A Randomized Trial. *J Gerontol A Biol Sci Med Sci*. Dec 12 2017;73:59–65.
9. Coles LT, Fletcher EA, Galbraith CE, Clifton PM . Patient freedom to choose a weight loss diet in the treatment of overweight and obesity: a randomized dietary intervention in type 2 diabetes and pre-diabetes. *Int J Behav Nutr Phys Act*. May 16 2014;11:64.
10. Wade D, Varker T, Kartal D, Hetrick S, O'Donnell M, Forbes D . Gender difference in outcomes following trauma-focused interventions for posttraumatic stress disorder: Systematic review and meta-analysis. *Psychol Trauma*. May 2016;8:356–364.
11. Petek Bradley J, Gustus Sarah K, Churchill Timothy W, Sawalla Guseh J, Loomer Garrett, VanAtta Carolyn, Baggish Aaron L, Wasfy Meagan M. Sex-Based Differences in Peak Exercise Blood Pressure Indexed to Oxygen Consumption. *Clin Ther*. January 2022;44:41–49.
12. Rao Shiavax J, Shah Ankit B. Exercise and the Female Heart. *Clin Ther*. January 2022;44:41–49.
13. Cheng Ryan, Maloney Aidan, Moran Jay, Newman Thomas H, Gardner Elizabeth C. Resistance Training as Treatment for Sarcopenia: Examining Sex-Related Differences in Physiology and Response. *Clin Ther*. January 2022;44:33–40.
14. Thomas MD Ynhi T, Newman Connie B, Faynshtayn Nina G, McGregor Alyson J. Exploring obesity as a gendered contagion: Impact on lifestyle interventions to improve cardiovascular health. *Clin Ther*. January 2022;44:23–32.