Journal of Women's Sports Medicine

Evolution and Future Directions of Sports Medicine Research Focused on Women

Julie Agel, MA, ATC[1], Elizabeth A. Arendt, MD[1]

[1] *Department of Orthopedic Surgery, University of Minnesota, Minneapolis, Minnesota, USA*

It is now recognized that males and females may present differently with similar diagnoses and /or respond differently to various treatments. This article outlines the history of research focused on women's health issues, with a specific focus on key research in sports medicine concerns in the active and athletic female. Recommendations for future strategies in research, including stratification of subgroups for all clinical results, will enable researchers and clinicians to translate research into clinical practice resulting in best patient care and improved outcomes for all.

Research focused on women is part of a storied journey. To understand research in women's sports medicine, one must understand the history of research as it relates to women's health.

Women make up 50% of the American population and are physiologically different from men. Assumptions that disease occurrence, treatment responses, and presenting symptoms will be similar between men and women has led to poor outcomes for women over time.[1, 2] There are also female-specific diseases that have been ignored in favor of male dominated diseases. As the rate of women participating in sports has grown over years the potential for sports related injury has also grown; injury profiles that focus on women's sports as well as treatments specific to women have become critical. It is anticipated that 45% of the athletes participating in the Beijing 2022 Olympics will be women compared to 23% in 1984.[2]

In 1991, the Women's Health Initiative (WHI),[3] a part of National Institute of Health (NIH), was established to better understand how diseases affected women, particularly after menopause. The most common diseases are cardiovascular disease, breast cancer, colorectal cancer, and osteoporosis. The first three are the leading causes of death among women in United States. Osteoporosis is the leading cause of bone fractures in women.

The NIH Revitalization Act of 1993 directed the NIH to establish guidelines for inclusion of women and minorities in clinical research. The statute included specific provisions pertaining to clinical research and in particular clinical trials.[4] One reason for the historical exclusion of females was concern for negative ramifications on women's reproductive systems, in particular the potential for causing negative present or future effects to a developing fetus.

The Women's Health Equity Act was passed in 1993 having failed in 2 previous attempts (1991/1992).[5] It allocated money to fund health research in particular areas of concern to women: contraception, fertility, breast cancer, ovarian cancer, HIV and AIDS. Through improved access to health care services and expanded research on women's health issues, it was hoped to provide greater equity in the delivery of health care services to American women.

In 1997, the US Food and Drug Administration banned drug studies involving women of childbearing age because they felt they need to protect the most vulnerable population, i.e,

DOI: 10.53646/jwsm.v2i1.20
Published online: April 5, 2022

the fetus. This applied to all Phase 1 and early Phase 2 drug trials. The policy excluded women even if they were using contraception, were single, or whose husbands had vasectomies. This was a cautious approach mainly motivated by the tragedies that resulted from the use of the thalidomide drug. Thalidomide was a widely used drug in the late 1950s and early 1960s for the treatment of nausea in pregnant women. It became apparent in the 1960s that thalidomide resulted in severe birth defects in thousands of children.

In 2002, WHI released findings that post-menopausal women taking a combination of estrogen and progesterone hormone therapy for menopause symptoms had an increased risk for breast cancer, heart disease, stroke, blood clots, and urinary incontinence.[6] One of the most important outcomes of the WHI work was a sharp decline of breast cancer in 2003 after these results were released.

In 2011, a report from the Institute of Medicine stated that sex must be considered in all aspects and at all levels of medical research.[7]

In addition to the exclusions of female participants in drug trials and in many NIH funded clinical trials, the NIH had done little to encourage researchers to analyze study results by sex.

The decision to exclude all women, not just pregnant ones, spoke to a long-standing opinion in science that males represent the normal or the default biologic situation and the females are more complex. Certainly, there was an under appreciation of how much information was missed when studies focused solely on men.

Basic research to understand the symptoms and underlying pathology of common illnesses also suffered from lack of female representation in cardiovascular disease, the number one cause of death in both men and women in United States. Women may experience different symptoms in a heart attack than men, which may explain why, in part, the survival rate for women is lower than for men. A seminal research trial showed a reduced risk of a heart attack with a daily low-dose aspirin: this 20,000-person seminal study did not include a single woman.[8] Follow up studies conducted years later showed that aspirin did not have a protective effect in women similar to men. This disparity in female versus male recruitment can be seen in illnesses that disproportionately impact women such as Alzheimer's disease, lung cancer, psychiatric illness, etc.

Turning to the musculoskeletal domain, a study published in 2012 critically assessed peer-reviewed scientific articles for the presence of sex-specific analyses from five high impact orthopedic journals from 2000 to 2010.[9] The inclusion of the sex specific analysis and reporting in the orthopedic literature did improve during this decade but were present in less than 1/3 of the studies. In a similar study reviewing 2016 orthopedic journals, only 34% (241 of 712) of the studies published in six orthopaedic journals included gender as a variable in a multifactorial statistical model. Of these studies, 39% demonstrated a difference in the outcomes between men and women patients.[10] Though subgroup analysis and reporting is required by NIH guidelines, this is not a consistently reported in non-NIH funded studies.[11]

In the field of sports medicine, there have been many significant advances in research on female injuries and conditions. Two of the more impactful investigations in the treatment of the female athlete is acknowledgment of the female athlete triad, and differences in the rate of anterior cruciate ligament (ACL) injuries.

The female athlete triad was first widely acknowledged in a 1997 American College of Sports Medicine position statement, as the inter-relationship of amenorrhea, osteoporosis, and disordered eating.[12] Since that time, the triad has evolved to include each item as a spectrum of disease states, including menstrual function, bone mineral density, and energy availability.[13] This more accurately represents the disease spectrum of each component from optimal health to disease; athletes can present with 1 or more of the components. Recognition of the female athlete triad and its components, along with advances in treatment, has allowed more females to more safely participate in sports at all levels.

A landmark paper in 1995 identified a significantly higher rates of ACL injuries occurring in women compared to men in the similar sports of basketball and soccer.[14] This paper launched the focus of sex specific comparisons of injury rates in sports particularly at the collegiate level.[15-17] While the question of why women injury their ACL at higher rates than men remains unresolved, there

DOI: 10.53646/jwsm.v2i1.20
Published online: April 5, 2022

have been numerous focused biomechanical and physiologic studies focused on this question.

While NIH requires demographic reporting by sex, race, and ethnicity, it does not require this level of subgroup analysis in result reporting. When evaluating injuries and disease that impact males and females, study designs should be adequately powered for subgroup analysis by sex. It is imperative for educators and researchers to improve and support data stratification that bisects clinical and basic research science and for journal reviewers/editors to mandate this. Journal editors should adopt a consistent style of data reporting to allow the accumulation and comprehension of comparative outcome data.

CONCLUSION

It is now recognized that males and females may present differently with similar diagnoses and/or respond differently to various treatments. Only with stratification of subgroups can researchers and clinicians translate this knowledge into clinical practice for best patient care and improved outcomes for everyone.

Conflict of Interest Statement

The authors report no conflict of interest with the contents of this manuscript.

Corresponding Author

Elizabeth A. Arendt, MD
Department of Orthopedic Surgery
University of Minnesota
2450 Riverside Avenue South
Suite R 200
Minneapolis, MN 55454
612-273-1177
arend001@umn.edu

REFERENCES

1. Harvey, R.E., K.E. Coffman, and V.M. Miller, *Women-specific factors to consider in risk, diagnosis and treatment of cardiovascular disease.* Womens Health (Lond), 2015. **11**(2): p. 239-257.
2. International Olympic Committee. *Women in the Olympic Movement*. Factsheet 2021 December 9, 2021 [cited 2022 January 24]; 1-6]. Available from: https://stillmed.olympics.com/media/Documents/Olympic-Movement/Factsheets/Women-in-the-Olympic-Movement.pdf.
3. *WHI (woman's Heatlh Initiative), Changing the furture of women's health: A landmark study since 1992.* [cited 2022 January 24]; Available from: https://www.whi.org/.
4. (NIH). *National Institutes of Health. NIH guidelines on the inclusion of women and minorities as subjects in clinical research.* [cited 2022 January 24]; Available from: https://grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm.
5. *"S. 2961 — 101st Congress: Women's Health Equity Act of 1990."* [cited 2022 January 24]; Available from: www.GovTrack.us. 1990. January 25, 2022 <https://www.govtrack.us/congress/bills/101/s2961>.
6. Bieber, E.J. and R.B. Barnes, *Breast cancer and HRT--what are the data?* Int J Fertil Womens Med, 2001. **46**(2): p. 73-8.
7. IOM (Institute of Medicine), *Sex-specific reporting of scientific research: A workshop summary*. 2012, Washington DC: The National Academies Press.
8. Peto, R., et al., *Randomised trial of prophylactic daily aspirin in British male doctors.* Br Med J (Clin Res Ed), 1988. **296**(6618): p. 313-6.
9. Hettrich, C.M., et al., *Sex-specific analysis of data in high-impact orthopaedic journals: how are we doing?* Clin Orthop Relat Res, 2015. **473**(12): p. 3700-4.
10. Gianakos, A.L., et al., *Sex- and Gender-specific Analysis in Orthopaedic Studies.* Clin Orthop Relat Res, 2020. **478**(7): p. 1482-1488.
11. *National Institutes of Health Office of Extramural Research. What Are the Requirements for Reporting on Human Study Participant Age, Sex/Gender, and Race/Ethnicity?* extramural NEXUS 2021 [cited 2021 January 25]; Available from: https://nexus.od.nih.gov/all/2021/04/29/what-are-the-requirements-for-reporting-on-human-study-participant-age-sex-gender-and-race-ethnicity/.
12. Otis, C.L., et al., *American College of Sports Medicine position stand. The Female Athlete Triad.* Med Sci Sports Exerc, 1997. **29**(5): p. i-ix.
13. Nattiv, A., et al., *American College of Sports Medicine position stand. The female athlete triad.* Med Sci Sports Exerc, 2007. **39**(10): p. 1867-82.
14. Arendt, E. and R. Dick, *Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature.* Am J Sports Med, 1995. **23**(6): p. 694-701.
15. Agel, J. and E.J. Harvey, *A 7-year review of men's and women's ice hockey injuries in the NCAA.* Can J Surg, 2010. **53**(5): p. 319-23.
16. Chandran, A., et al., *Multifactorial examination of sex-differences in head injuries and concussions among collegiate soccer players: NCAA ISS, 2004-2009.* Inj Epidemiol, 2017. **4**(1): p. 28.

DOI: 10.53646/jwsm.v2i1.20
Published online: April 5, 2022

17. Stanley, L.E., et al., *Sex Differences in the Incidence of Anterior Cruciate Ligament, Medial Collateral Ligament, and Meniscal Injuries in Collegiate and High School Sports: 2009-2010 Through 2013-2014.* Am J Sports Med, 2016. **44**(6): p. 1565-72.

DOI: 10.53646/jwsm.v2i1.20
Published online: April 5, 2022
2769-4895 © Journal of Women's Sports Medicine