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Advancing Emergency Medicine by Incorporating Sex and Gender: It Benefits Women, It Benefits Men

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Biological sex and gender identity are challenging the way we deliver acute medical care.

It is another busy day in the emergency department (ED). As you look around, the ways in which men and women differ in risk, presentation, diagnosis, treatment effects, and outcomes are evident in each shift. The man with the hip fracture has a 10% greater mortality than if he were a woman.¹ The young female patient next door with the myocardial infarction is more likely to die before being discharged from the hospital than a similarly aged man.² Down the hall, a woman undergoing conscious sedation for her shoulder reduction requires higher and more frequent dosing of propofol than if she were a man because of her greater body fat percentage.³ The man in the hallway needs additional morphine for his abdominal pain because of the more rapid onset and offset of the drug in men compared with women.⁴

The medical and scientific understanding of the significant effect that sex and gender has in health and disease has evolved, and we must evolve along with it. We now know that sex, the biological and physiologic characteristics, affects a wide range of conditions observed in emergency medicine, including cardiovascular, autoimmune, and neurologic disease, as well as pain responses, substance use, and mental health disorders. In addition, other factors such as gender identity, the socially constructed behaviors and attributes, also influence important outcomes such as incidence, prevalence, morbidity, and mortality of disease states in one person versus another. The historical lack of consistency in including sex in analyses limits the generalizability of many past research findings and their applicability to clinical practice for both men and women.

Clinical research equity in regard to women and minorities was first highlighted by the National Institutes of Health (NIH) Revitalization Act of 1993 (Public Law 103-43) and was amended in 1994,⁵ 2000,⁶ and 2001⁷ to

provide further guidance on inclusion of women in clinical trials and support reporting analysis of sex and gender on intervention effects for NIH-defined phase 3 clinical trials.⁷ The guidelines were meant to ensure that all NIH-funded clinical research is carried out in a manner sufficient to gain information on important differences between men and women. Since then, it has been clear that better oversight is needed to ensure continued progress. For instance, a Government Accountability Office report⁸ indicated that analyses of research outcomes by sex are not required in compliance reporting. To address these developments, the NIH implemented the most recent policy this year to encourage scientists to account for the possible role of sex as a biological variable in vertebrate and human studies.⁹ Applicants for NIH-funded research will be required to factor consideration of sex as a biological variable into their research design, analysis, generalizability, and reporting. For the first time, strong justification will be required for proposing single-sex studies. Ideally, this new requirement will have an effect on biomedical research by creating an abundance of new evidence that will improve our understanding of the influence of patient sex and gender on emergency conditions. The subsequent challenge will be translating this new knowledge to routine clinical practice in the near future.

To align clinical practice with current evidence, the American Medical Association (AMA), in conjunction with the Institute of Medicine, the US Preventive Services Task Force, and the NIH Office of Research on Women's Health and Health Research and Services Administration, recently passed the Council on Science and Public Health resolution 604-A-15, "An Expanded Definition of Women's Health."¹⁰ The council recommended 2 important policies that will affect clinicians:

- The AMA now recognizes the term "women's health" as inclusive of "all health conditions for which there is evidence that women's risks, presentations and/or

responses to treatments are different from those of men, and encourage that evidence-based information regarding the impact of sex and gender incorporated into medical practice, research, and training.”

- The AMA encourages “the inclusion of women, including pregnant women when appropriate in all research on human subjects, except in those cases for which it would be scientifically irrational.”

This represents a shift in how the term “women’s health” has evolved from a primitive understanding of reproductive health, or “bikini medicine,” to encompass all aspects of clinical medicine. It is now better aligned with the study of sex and gender health. As major organizations such as the AMA begin to create policy to acknowledge the role that sex and gender play in health, how has the field of emergency medicine responded? Although some specialties (cardiology, for example) have had a more long-standing pattern of initiating sex-specific research, emergency medicine has also evolved in this regard. In 2011, Safdar et al¹¹ identified how few emergency medicine research studies even reported gender as a variable when presenting health outcomes. In 2014, by means of the Academic Emergency Medicine Consensus Conference “Gender-Specific Research in

Emergency Care,” the field of emergency medicine acknowledged the importance of a sex- and gender-informed medical practice and established current and future research priorities for the profession in this domain.^{12,13} See the Table for resources about sex and gender in emergency medicine that have been developed since then.

The time has come for emergency physicians to incorporate sex and gender research into routine clinical practice. As organizations such as the AMA begin to create policy to acknowledge the role that sex and gender play in health, what does it mean for emergency medicine practitioners? Does sex and gender research affect everyday clinical practice? Should a cardiac stress test be interpreted differently for a man versus a woman? Should the dose of postintubation sedation be adjusted for a man versus a woman? Should the ED intervention to address opioid abuse differ by gender? The answer is a resounding yes, and for clinicians, this means that the art of emergency practice will change. It is imperative for practicing clinicians to stay well informed of the evolving science as new evidence indicates differences in clinical assessment, diagnostic interpretation, treatment, and resource use according to the disease *and* sex or gender of the patient.

Table. Resources for sex and gender in emergency medicine.

Focus Area	Available Resources
Knowledge	See a list of open-access emergency medicine–relevant video didactics linked in data supplement S1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4340245/
Education	Sex and Gender Women’s Health Collaborative. A centralized online resource for educational and research resources on sex and gender medicine topics. http://sgwhc.org/#sthash.170jic5y.dpbs Texas Tech Sex and Gender-Based Medicine Curriculum. Patient case learning modules and didactic lecture materials that can be incorporated into preclinical and clinical education. https://www.ttuhschool.edu/som/curriculum/sex-gender-specific-health/ <i>Sex and Gender in Acute Care Medicine</i> . ¹⁶ Textbook focused on the relevance of sex and gender differences to emergency clinical care.
Research	Sex and Gender Equity in Research (SAGER) guidelines: Expert consensus guidelines on reporting of sex and gender information in study design, data analyses, results, and interpretation of findings. https://researchintegrityjournal.biomedcentral.com/articles/10.1186/s41073-016-0007-6 <i>Academic Emergency Medicine</i> sex and gender guidelines for submissions: http://onlinelibrary.wiley.com/doi/10.1111/j.1553-2712.2012.01303.x/full , under “Original Research Contributions, 6. Results” <i>Annals in Emergency Medicine</i> sex and gender guidelines for submissions: http://www.annemergmed.com/content/style , under “Annals’ General Style.” “How to Study the Impact of Sex and Gender in Medical Research: A Review of Resources.” Compendium of resources for researchers interested in sex and gender investigations. https://bsd.biomedcentral.com/articles/10.1186/s13293-016-0099-1 PubMed Search Tool: A free online tool that helps researchers and clinicians focus their literature search for studies that incorporate sex and gender. https://www.sexandgenderhealth.org/resources.html Research Integration Tool: a Webinar that describes the use of sex and gender in data analysis for human subjects. http://www.cihr-irsc-igh-isfh.ca Proceedings from Emergency Medicine Consensus Conference on sex and gender research: an open-access issue summarizing the topics of SGEM research in topics relevant to emergency medicine. http://onlinelibrary.wiley.com/doi/10.1111/acem.2014.21.issue-12/issuetoc
Training	Sex and Gender in Emergency Medicine fellowship, Alpert Medical School of Brown University Department of Emergency Medicine. This 2-year research- or education-focused fellowship provides emergency physicians with the background to build a career advancing knowledge around sex and gender difference in emergency care. https://www.lifespan.org/centers-services/sex-and-gender-emergency-medicine-sgem/our-team
Innovations	Based out of Stanford, this program provides resources to incorporate sex and gender in new innovations. http://genderinnovations.stanford.edu

SGEM, Sex and gender in emergency medicine.

Editors of major journals can be considered “gatekeepers of science” and play a crucial role in shaping the future of medicine. Journal editors, publishers, and professional associations need to implement detailed guidelines and procedures to ensure that sex and gender are considered and addressed to improve research design and reporting. For instance, *Annals of Emergency Medicine* and *Academic Emergency Medicine*, along with many high-profile nonemergency medicine journals such as *The Lancet* and *Stroke*, have recently updated their instructions for authors to include reporting of the effect of sex and gender on study outcomes. Reviewers need to be educated on the importance of this requirement through updated peer review templates that reflect this new standard of results reporting and guide the reinforcement of NIH and AMA policies by mentioning deficiencies in consideration of sex and gender in their recommendations for authors.

A committee of the Institute of Medicine in 2010 recommended that the International Committee of Medical Journal Editors institute a guideline that all scientific articles reporting the results of clinical trials analyze data separately for men and women. The European Association of Science Editors established a Gender Policy Committee in 2012 and developed a set of guidelines for reporting of sex and gender equity in research.¹⁴ Additionally, a review of resources was recently published that includes an annotated bibliography of currently available resource tools to assist researchers and clinical investigators in considering sex and gender in research design and methodology.¹⁵ These established guidelines and resources can help guide authors and represent an opportunity for emergency medicine journals to use and make formal recommendations that are in line with NIH current policies.

Because emergency medicine is an influential and ever-growing specialty, these actions may allow emergency medicine practitioners to become leaders in personalized patient-centered research by taking the first step toward incorporating the modern practice of sex and gender research into clinical care.

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