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Incorporating Sex- and Gender-Based Medicine into Journal Club

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Reviewing current scientific literature and keeping up to date with emerging evidence and evolving guidelines is an expectation for Emergency Physicians (EP) to make informed clinical decisions. Often, there is also a reliance upon academic EPs to take part in state-of-the-art research to continue growing the knowledge base required to provide increasingly effective patient care.

Incorporating the concepts of biological sex and sociocultural gender-based medicine (SGBM) into the practice of emergency medicine (EM) is critical to achieving equitable and precise patient care. Additionally, prominent scientific journals, including those in EM, are increasingly encouraging authors to follow the Sex and Gender Equity in Research (SAGER) guidelines and to include sex and gender considerations where relevant, which makes an understanding of these guidelines imperative. The international SAGER guidelines were reached by a consensus building process that included representatives from nine different countries and included over 700 responses to a stakeholder survey.¹ They were developed to help authors, but also editors, in evaluating the sex and gender assessments contained in a particular study. The guidelines specifically address the correct and precise usage of the terms sex and gender, which should not be used interchangeably. They also recommend that sex and gender be considered during the study design phase, to ensure adequate representation. Furthermore, the guidelines recommend analyses of sex and gender differences where these data are available, regardless of the original intent of the study.

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Lastly, authors are expected to address the implications of sex and gender in their results. It is notable that these guidelines do not apply only to sex- and gender-specific research, but that the principles instead apply to *all* research.

As the evidence base continues to increase around SGBM, undergraduate and graduate medical education programs, along with practicing EPs, have struggled to keep up with this new knowledge and incorporate it into already crowded curricula.² Whether conducting clinical research or learning critical appraisal of the literature, bringing a sex and gender lens into existing journal club-style teaching remains an underutilized strategy. In this Viewpoint, the authors illustrate the utility of this concept by reviewing specific examples of cutting-edge revelations of sex and gender differences and the research methodologies that illuminated these discoveries.

Sex and gender-based differences in cardiovascular disease are among the most well-known in acute care medicine, given the substantial amount that is published on the impact of biological sex on disease progression, as well as the morbidity and mortality associated with gender disparities in cardiovascular care. High sensitivity (hsT) troponin assays are now FDA approved in the United States and in wide usage across Europe. In the High STEACS study,³ investigators found that the use of sex-specific hsT cut-off values increased the diagnosis of MI in women by 25%, however women remained less likely to receive evidence-based interventions. Use of this sex-specific threshold did not translate to a difference in clinical outcomes at one year and thus is deserving of further study to elucidate whether this is due to differences in sex, gender, or both. While this study had important implications for the care of women with ischemic heart disease (IHD), it also illustrates important core epidemiologic principles, such as the utilization of a receiver operating characteristic (ROC) curve. An ROC curve allows for visual representation of an "ideal" cut point for continuous data like hsT, designed to optimize sensitivity and specificity. Discussions of this statistical model encourage learners to think about the impacts of false negative and positive results, and the relative importance of sensitivity and specificity, as well as to consider any sex-specific implications (e.g. bleeding complications in women).⁴

In another example highlighting that SGBM not only affects the care of women but also men, a recent cardiovascular study from the Korean Heart Failure Registry⁵ found that pro-B type natriuretic peptide (BNP) is actually more predictive of major adverse cardiac event (MACE) in men than in women. This study also found that pro-BNP levels are higher in women due to the influence of estrogen. Sex specific strata were utilized in this study to derive a hazard ratio (HR) for MACE, which is another popular methodologic tool for structured analysis of sex differences.⁶

The VIRGO investigators found that women with myocardial infarction (MI) were more likely than men to present with greater than three symptoms and were more likely to perceive their own symptoms as stress/anxiety.⁷ This study allowed us to illustrate Bayesian reasoning, specifically the idea that likelihood ratios can be used to improve the probability estimation of a particular disease.⁸ Using studies of historical and exam findings such as JAMA's Rational Clinical exam,⁹ EPs can ask serial historical questions to work towards a diagnosis.

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Also of particular importance to the EP are sex differences in the care of neurovascular emergencies, particularly in stroke care. A recent meta-analysis found a persistent disparity in that women remain less likely to receive IV thrombolysis, even in controlled analysis; the magnitude of this disparity has, however, decreased in recent years.¹⁰ This study illustrated the concepts of pooling data for a meta-analysis, assessing heterogeneity (I²) across studies, and how to interpret a Forrest plot, all of which are critical appraisal skills for the EP. A related study found that women and Black patients are also more likely to decline thrombolytics,¹¹ leading one to question the role of patient/provider dyads in discussing this important treatment option. This study allows for a robust discussion of shared decision making,¹² including ways in which it may augment or mitigate existing health disparities related to sex and gender.

The DOUBT study group⁶ found that women are more likely to be diagnosed with stroke mimics, and less likely to have their diagnoses revised, even in light of imaging demonstrating ischemia. This study utilized adjusted and unadjusted odds ratios (OR)¹³ to compare outcomes in women and men and was utilized to discuss not only the interpretation of ORs but also to underscore the difference between clinical and statistical significance and the need for EPs to discern the difference.

Finally, an important study of pregnant women with stroke found that endovascular thrombectomy was successful with minimal complications and utilized propensity scoring.¹⁴ This method was discussed as a strategy to improve causal inference in observational studies by "pseudorandomizing" patients into groups with resultant pros and cons. This study also underscored the importance of enrolling vulnerable groups, such as pregnant patients, in clinical research studies to have information about efficacy and safety in this population, which has proven to be of particular importance throughout the Covid pandemic.

Critical appraisal of the biomedical literature is an invaluable skill for all EPs to have. The Accreditation Council for Graduate Medical Education (ACGME) EM residency requirements (USA) state that programs must train residents to be "responsive" to diverse patient populations, specifically noting both sex and gender, as part of the Professionalism Milestone.¹⁵ We can and should utilize creative ways to incorporate this ability into other core competencies; journal club is an ideal opportunity to evaluate and integrate novel sex and gender findings.

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References

- Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi:10.1186/ s41073-016-0007-6 [PubMed: 29451543]
- Madsen TE, McGregor AJ. Training emergency physicians in sex- and gender-based medicine: assessing attitudes of program directors and residency graduates. Biol Sex Differ. 2016;7(Suppl 1):48. doi:10.1186/s13293-016-0098-2 [PubMed: 27785350]

Eur J Emerg Med. Author manuscript; available in PMC 2023 March 11.

- Lee KK, Ferry AV, Anand A, et al. Sex-Specific Thresholds of High-Sensitivity Troponin in Patients With Suspected Acute Coronary Syndrome. J Am Coll Cardiol. Oct 22 2019;74(16):2032–2043. doi:10.1016/j.jacc.2019.07.082 [PubMed: 31623760]
- Zou KH, O'Malley AJ, Mauri L. Receiver-operating characteristic analysis for evaluating diagnostic tests and predictive models. Circulation. Feb 6 2007;115(5):654–7. doi:10.1161/ CIRCULATIONAHA.105.594929 [PubMed: 17283280]
- Kim HL, Kim MA, Choi DJ, et al. Gender Difference in the Prognostic Value of N-Terminal Pro-B Type Natriuretic Peptide in Patients With Heart Failure- A Report From the Korean Heart Failure Registry (KorHF). Circ J Aug 25 2017;81(9):1329–1336. doi:10.1253/circj.CJ-16-1345 [PubMed: 28442636]
- 6. Health IoGa. SEX AND GENDER IN THE ANALYSIS OF SECONDARY DATA FROM HUMAN PARTICIPANTS. Canadian Institutes of Health Research Accessed July 15, 2022. https://www.cihrirsc-igh-isfh.ca/?lang=en
- Lichtman JH, Leifheit EC, Safdar B, et al. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). Circulation. Feb 20 2018;137(8):781–790. doi:10.1161/CIRCULATIONAHA.117.031650 [PubMed: 29459463]
- Hayden SR, Brown MD. Likelihood ratio: A powerful tool for incorporating the results of a diagnostic test into clinical decisionmaking. Ann Emerg Med. May 1999;33(5):575–80. doi:10.1016/s0196-0644(99)70346-x [PubMed: 10216335]
- Fanaroff AC, Rymer JA, Goldstein SA, Simel DL, Newby LK. Does This Patient With Chest Pain Have Acute Coronary Syndrome?: The Rational Clinical Examination Systematic Review. JAMA. Nov 10 2015;314(18):1955–65. doi:10.1001/jama.2015.12735 [PubMed: 26547467]
- Strong B, Lisabeth LD, Reeves M. Sex differences in IV thrombolysis treatment for acute ischemic stroke: A systematic review and meta-analysis. Neurology. Jul 7 2020;95(1):e11–e22. doi:10.1212/ WNL.000000000009733 [PubMed: 32522796]
- Mendelson SJ, Zhang S, Matsouaka R, et al. Race-Ethnic Disparities in Rates of Declination of Thrombolysis for Stroke. Neurology. Apr 19 2022;98(16):e1596–e1604. doi:10.1212/ WNL.000000000200138 [PubMed: 35228335]
- Probst MA, Kanzaria HK, Schoenfeld EM, et al. Shared Decisionmaking in the Emergency Department: A Guiding Framework for Clinicians. Ann Emerg Med. Nov 2017;70(5):688–695. doi:10.1016/j.annemergmed.2017.03.063 [PubMed: 28559034]
- Singer AJ, Thode HC Jr., Hollander JE. Research fundamentals: selection and development of clinical outcome measures. Acad Emerg Med. Apr 2000;7(4):397–401. doi:10.1111/ j.1553-2712.2000.tb02249.x [PubMed: 10805631]
- Dicpinigaitis AJ, Sursal T, Morse CA, et al. Endovascular Thrombectomy for Treatment of Acute Ischemic Stroke During Pregnancy and the Early Postpartum Period. Stroke. Dec 2021;52(12):3796–3804. doi:10.1161/STROKEAHA.121.034303 [PubMed: 34538088]
- ACGME Program Requirements for Graduate Medical Education in Emergency Medicine. 2022. Accessed July 15, 2022. https://www.acgme.org/globalassets/pfassets/programrequirements/ 110_emergencymedicine_2022.pdf

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