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The Role of Sex and Gender in Precision Emergency Medicine: A Scoping Review and Proposed Hierarchy

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Abstract

Background—Precision medicine utilizes individual patient data to guide decision making. Sex and gender medicine is likewise focused on individual patients' biological sex or sociocultural

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Presentations: Portions of this work was presented at the 2023 Society for Academic Emergency Medicine Consensus Conference in Austin, TX, USA (May 16, 2023) and at the NIH Building Interdisciplinary Research in Women's Health (BIRCWH) annual meeting (Dec 5, 2023). A written abstract from the BIRCWH meeting will be published in the Journal of Women's Health.

gender as determinants of disease. How these two fields intersect with one another and with acute care medicine is unclear.

Methods—We conducted a scoping literature review utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews to evaluate the primary research in three related areas: sex & gender medicine, emergency medicine, and precision medicine. We searched six databases and screened eligible studies for inclusion. Included studies were reviewed in full, and study characteristics were compiled using a standardized data extraction form. Research questions were drafted by workgroup members and ranked by all participants of the consensus conference.

Results—A total of 401 studies were screened for inclusion. Of these, 70 met inclusion criteria and were evaluated in full text. The majority (84%, 59/70) reported evaluating sex, whereas only 16% (11/70) reported evaluating gender. The most common clinical topics were cardiovascular diseases and trauma/injury prevention, comprising 50% (35/70) of the included manuscripts. Cumulatively, 77% (54/70) of the manuscripts reviewed cited at least one funding source. The vast majority (66/70, 94%) of studies were included because their statistical analysis accounted for sex or gender, and very few studies (4/70, 6%) were included due to their use of biomarker or genomic data.

Conclusions—Sex and gender based medicine and research commonly employ precision medicine concepts to evaluate the effects of sex and gender in a variety of clinical topic areas, but much of this literature is not commonly described as precision medicine. We propose a hierarchy to categorize, label, and advance sex and gender precision medicine research. Fundamental to this advancement are implementation of guidelines regarding the correct use of sex and gender and continued research funding for sex and gender precision EM research.

Introduction

Sex and gender specific medicine is a field in which both one's biological sex (sex assigned at birth) and sociocultural gender identity are understood to be essential determinants of an individual's health. Once thought to be synonymous with "Women's Health," sex and gender specific medicine has now made clear that sex and gender differences transcend reproductive health and that, in fact, every cell in the body has a sex. Sex and gender-based research has shown that sex differences exist from the most microscopic level of DNA - with male and female cells having different transcriptomics and gene expression - to the macro level at which male and female bodies have different phenotypes. The field of sex and gender medicine seeks to understand further the roles of both sex and gender in clinical and basic science.

Precision medicine utilizes the concept that clinical decisions can be tailored to each individual patient based on genomic, biological, environmental, and public health data.^{1–3} Sex and gender research increasingly employs precision medicine concepts to tailor healthcare approaches based on individual characteristics rather than a one-size-fits-all model. Precision medicine considers biological differences between sexes, such as differential gene expression and hormone profiles. Research explores how these differences affect disease susceptibility, treatment responses, and outcomes and can

develop personalized treatment plans. Additionally, incorporating sex and gender into risk assessments allows for more accurate predictions of disease prevalence and outcomes. For instance, certain conditions may manifest different or have varying risk factors based on sex. Precision medicine promotes the collection and analysis of data disaggregated by sex and gender to ensure research findings are relevant to all populations. Finally, gender roles and social determinants of health play a significant role in health outcomes, recognizing that mental and emotional well-being can impact physical health.

While some specialties, such as oncology, have long utilized genomic testing to personalize treatment plans, incorporating this approach into the practice of Emergency Medicine (EM) has been challenging due to the very nature of acute care of undifferentiated patients. Precision Emergency Medicine has lacked a unifying definition but involves using information and technology to deliver acute care effectively, efficiently, and authentically to individual patients and their communities.^{4,5} As a new approach to acute care, there is limited understanding of precision emergency medicine as a concept and of the existing literature.

To address this gap, the 2023 Society for Academic Emergency Medicine's (SAEM) Consensus Conference (CC) was focused on precision emergency medicine as broadly defined as "The use of information and technology to deliver acute care effectively, efficiently, and authentically to individual patients and their communities."⁵ The authors led a working group of the consensus conference focused specifically on the roles of sex and gender in delivering precision emergency medicine. As part of that work, we conducted a scoping literature review to assess the existing research utilizing precision medicine concepts within the intersecting fields of emergency medicine and sex and gender specific medicine. Specifically, we sought to characterize the contemporary literature with regard to clinical topics, funding sources, and usage of precision medicine strategies. In addition, as part of the consensus conference, our goal was to identify gaps in the literature, recommend consensus-based definitions, and identify research priorities for the future of sex and gender related precision EM research.

Methods

The methodology for this scoping review was guided by the JBI Manual for Evidence Synthesis and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).^{6,7} The PRISMA-ScR Checklist is included in the supplementary material for reference. The protocol was registered with Open Science Framework and is available online at (https://osf.io/fty8s).

Eligibility Criteria and Search Strategy

In concert with other topic-specific workgroups of the consensus conference, we conducted a literature review in which articles were eligible for inclusion if they addressed **each of three main concepts simultaneously in the research publication:** 1) precision medicine, 2) emergency medicine, and 3) sex and gender. Here the search term for "precision medicine" included synonyms like personalized and individualized and was limited to title, abstract, and keyword. The search strategy was developed as a combination of controlled

vocabulary and free-text terms to describe the three main concepts. The precision medicine and emergency medicine search terms were developed with the larger consensus conference workgroup for consistency, which included several health sciences librarians. For the sex and gender terms, we consulted a validated search tool designed specifically to filter for sex- and gender-specific research.⁸ The search strategy was tailored to the formatting and syntax requirements for six databases (Ovid Medline, Embase, Web of Science, Cochrane CENTRAL, ClinicalTrials.gov, and Google Scholar), and a systematic search was performed in each of these databases on February 22, 2023 by a health sciences librarian. Search results were limited to English-language, full-length articles, and primary literature; abstracts and review papers were specifically excluded. We also restricted the search to articles published in the last ten years (2013–2023) to focus on contemporary literature. The complete search strategy can be found in the supplemental material.

Study Selection

Following the search, results from all six databases were uploaded into EndNote V20 (Clarivate Analytics, PA, USA), and all duplicates were removed. The remaining citations were imported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), where two reviewers independently screened the titles and abstracts against the eligibility criteria. Any disagreements about eligibility were resolved by discussion and consultation with a third reviewer.

Data Extraction

Studies that met the inclusion criteria were retrieved in full text for further review by one author. Authors completed a standardized data extraction form to document: publication year, journal, clinical topic of primary outcome, type of precision medicine, and usage of either sex or gender (as stated by the original authors of the research manuscript). Many contemporary studies strive to explicitly define and differentiate sex and gender, recognizing their unique influence on health outcomes and this was consistent with our search results. Please see supplemental material for the full data extraction tool. Following data extraction, studies were grouped by clinical topic areas and were reviewed qualitatively by one author with expertise in that area.

Data Synthesis

Quantitative data on study characteristics were summarized and analyzed descriptively. Major themes were summarized in narrative form and discussed in the results section. Themes addressed in few studies (three or fewer) were only included in the narrative results if reviewers perceived them to be significant or innovative.

Consensus Building Process

The Sex and Gender workgroup was formed as one of nine key domains by consensus conference leadership. Members were recruited by workgroup co-chairs (AJ and AM) given their expertise in the areas of sex and gender and precision medicine. Four workgroup members are former or current NIH-funded investigators (three current), who specifically study sex and gender precision medicine topics. This ten-member group met monthly to

design and conduct this literature search and to draft research priorities and questions, informed by the literature search. On the day of the conference, working group members met with attendees in a series of break-out sessions, as previously described.⁵ In the first session, we presented results from the literature review and a preliminary collection of proposed research questions. In the second session, our group combined with the population health and data science groups for a "cross-pollination" of ideas, in which we discussed areas of common interest. In a third session, our group consolidated the research questions and proposed their ranking by priority. In a closing session, all conference attendees were able to see our proposed research questions, which were informed by the literature search but not a direct product of it, and also to vote on their priority. We have presented the top three research questions, ranked by the entire conference attendance (115 attendees) in the results section Table 2.

Results

The initial search strategy yielded 401 abstracts across all databases that were screened for inclusion, of which 70 met inclusion criteria and were reviewed in full text (see Figure 1 for PRISMA Flow Diagram; see Supplemental Material for all included studies). The majority of included studies (84%, 59/70) reported evaluating sex, whereas only 16% (11/70) reported evaluating gender. Of note for consistency, the authors chose to use the terms female/male throughout the results discussion, given that most studies utilized sex.⁹ Nearly half (47%, 33/70) of the manuscripts focused primarily on comparing outcomes by sex or gender. The number of papers that met inclusion criteria increased over time, with the largest portion published in the last three years (See Figure 2).

The most common clinical topics were cardiovascular diseases and trauma/injury prevention, comprising 50% (35/70) of the included manuscripts. Other clinical topics are shown in Table 1. Cumulatively, 77% (54/70) of the manuscripts reviewed cited at least one funding source. Other funding sources are shown in Table 1, both overall and by clinical topic. The vast majority of studies were included due to their statistical analysis, which accounted for sex or gender; examples include sex-stratified analyses, sex-matching, or controlling for sex as a predictor variable in the statistical model (often a regression analysis). Very few studies were included due to their use of biomarkers (2 studies), genetics/genomics (1 study), or precision technology (machine learning) (1 study). Final research questions and priorities, as ranked by all 115 consensus conference participants, are shown in Table 2.

Leading Clinical Topics in Sex and Gender and Precision Medicine in Emergency Medicine

Cardiovascular—Twenty eligible studies focused primarily on cardiovascular diseases, 15 of which were observational studies (please see Supplemental material for full list of studies). Seventeen of the studies reported patient sex, and three reported patient gender. While one study found no difference by patient sex on the utility and prognosis of chest pain choice aid,¹⁰ all other studies highlighted the differential effects of patient sex in cardiovascular care and the need to incorporate it into precision emergency medicine.

Five studies leveraged large multicenter data to debunk the longstanding belief that females with acute myocardial infarction (AMI) present more often with atypical symptoms and emphasized that chest pain is the most common presentation for both males and females with AMI.^{11–15} Nuanced presentations, including differences in the frequency and type of symptoms that may accompany chest pain, were observed more commonly in females than in males.¹¹

Females with ST-segment elevation myocardial infarction (STEMI) experience prehospital care delays of 10 minutes compared to males.¹⁶ After AMI, females reported worse health-related patient reported outcomes as compared to males in adjusted analysis.¹⁷ The higher psychosocial burden and worse health state explained the higher rates of rehospitalization seen in females in several studies.^{18,19}

Two studies assessed the prognostic implication of using sex-specific upper reference limit (URL) thresholds for high sensitivity troponin assays. Both advocated for using a universal threshold for clinical testing, with slightly different reasoning. Gimenez suggested continuing the use of a universal threshold given the concern for decreased sensitivity in males using sex-specific thresholds.²⁰ Sandoval supported the prognostic implication of using universal thresholds for hs-TnT and again expressed concern for underdiagnosis of MI in males using sex-specific thresholds.²¹ Similarly, a study using the HEART score in 831 females and 1084 males presenting to the ED found markedly higher 6-week MACE risk in males across all HEART risk categories,²² implying that early discharge with a low-risk HEART score appeared to be less safe for males than for females with acute chest pain.

In three large population-based studies of out of hospital cardiac arrest (OHCA) patients, males were consistently found to have higher survival than females.^{23–25} Females also received fewer life-saving procedures in hospital than males.²⁴ In one of the three studies, the higher survival was explained by favorable prognostic factors in males (younger age, initial shockable rhythm, MI as the underlying cause, witnessed arrest).²⁵

Trauma & Injury Prevention

Fifteen publications focusing on sex and gender in trauma and injury prevention were identified. While several were small, single-center cohort studies whose data may not be generalizable to other populations,^{26–28} four used large, nationwide databases including the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project,²⁹ the Trauma Quality Improvement Program,³⁰ and the Canadian Institute of Health Information National Ambulatory Care Reporting System and Discharge Abstract Database^{31,32} to study traumatic injuries. Overall, the distribution of presentations for traumatic injuries differs across the lifespan between females and males, with males comprising the majority of traumatic injuries in younger adults and females comprising the majority of traumatic injuries in older adults. Exceptions include a) sexual trauma that tends to be more frequent in females, but of greater severity in male victims³³ and b) sports and recreation injuries that are more commonly seen in males, while females are more likely to have knee and lower extremity injuries, specifically.³⁴ Available data suggest that females differ from males in their mechanisms of injury, injury patterns, and symptoms during follow-up.^{28,35,36} While one study showed no difference between females and males in symptom duration

following mild traumatic brain injury,²⁷ two others suggested that females were more likely to experience health dissatisfaction at one year following a motor vehicle collision²⁶ and had more severe somatic symptoms within 21 days following a concussion.³⁷ Females were more likely to be admitted to the inpatient setting,²⁹ to receive operative treatment for their injuries,²⁹ and to be discharged to long-term care facilities³⁰ than their male counterparts. They also experienced longer delays in care, including time to triage and time to operative fixation of femur and pelvis fractures.³⁰

Infectious Diseases

Seven studies were identified that focused on infectious diseases, most of which were related to SARS-CoV-2.³⁸ One study found that females were slightly less likely to get tested for SARS-CoV-2, while males had slightly higher case prevalence and a higher risk of mortality.³⁹ Another study developed a predictive model to assess the need for hospitalization of patients testing positive for SARS-CoV-2 and indicated that more males were admitted than females.⁴⁰ Several papers studied scoring systems to help identify SARS Cov2 infected patients at higher risk for poor outcomes. Vizcaychipi found that males scored higher on models predicting greater risk for acute respiratory distress syndrome, cytokine storm, and thromboembolism.⁴¹ Several studies found males to be at increased risk of severe disease and death⁴²⁴⁰⁴³ There were sex specific differences in comorbidities, with females having greater rates of chronic lung disease and asthma and having higher body mass indexes, while males were more likely to have hypertension and chronic kidney disease. Laboratory markers of inflammation also showed sex-specific patterns, with males showing lower absolute lymphocyte counts, higher neutrophil-lymphocyte ratios, and higher ferritin, interleukin-6 and C reactive protein levels than females.⁴³

The one study unrelated to SARS-CoV-2 noted that although 90% of diagnoses of a urinary tract infection were made in females but the percentage of males with a positive culture was significantly greater than that of females⁴⁴.

Neurologic Emergencies

Seven manuscripts met criteria for inclusion in the neurologic emergencies category. Six studies focused on stroke, and all of them were observational; four used data from multiple centers or large national registries, and two were single-center studies. Investigating sex differences was a primary objective in five of the six studies. For example, in a paper based on data from a large U.S. stroke registry,⁴⁵ major findings were that white females were the group most likely to use EMS for stroke, compared with other race/sex demographic groups.

Three of the seven other studies evaluated disparities in diagnosis or treatment. In an analysis of a stroke registry from Florida and Puerto Rico,⁴⁶ females with ischemic stroke were less likely to receive defect-free care, less likely to receive intravenous thrombolytics, and less likely to have intravenous thrombolytics administered within 60 minutes of arrival compared with males. Data from a Danish stroke registry also confirmed lower rates of intravenous thrombolysis compared with males, with major contributors including age, stroke severity, and living alone.⁴⁷

Yu *et al.* found that females were more likely to receive a diagnosis of stroke mimic but had similar rates of recurrent events (both 90-day stroke as well as a composite outcome of stroke, MI, or death).⁴⁸ Interestingly, in contrast with other literature on presenting stroke symptoms,^{49,50} symptoms as defined by focal vs. focal and non-focal were similar by sex. One single-center stroke study found that male sex was significantly associated with infarct volume in a multivariable model, but in other models evaluating NIHSS at discharge and functional status at discharge, sex was not significant.⁵¹

In the one study on a topic other than stroke, the study of sex differences in seizure treatment with IV phenytoin,⁵² males had slightly lower serum concentrations, but levels for both male and female patients were in the therapeutic range.

Mental Health/Substance Use Disorders

The six mental health studies included in the review spanned a wide breadth of topics from the objective detection of serum biomarkers associated with pain in subjects with psychiatric disorders to the prediction of post-traumatic stress disorder amongst trauma patients to the influence of developmental (childhood) factors on the psychosocial profile of psychiatric emergency patients.

Sex or gender were not the primary focus of any of the included studies, however, they were most often included as comparative variables or in stratified analysis. Sex was found to impact results, to a variable degree, in four of the studies. As an example, in the study by Karasouli et al., male sex was found to be predictive of subsequent suicide in the setting of prior nonfatal self-harm.⁵³ A study by Myran,⁵⁴ found that males were likewise at increased risk of death in the one year following an ED visit for an alcohol-related complaint than females. In the study by Niculescu et al.,⁵⁵ sex differences were noted in several biomarkers, with implications for the predictability of future emergency department visits for pain.

Health Economics

We identified four eligible articles in health economics and health services research. In a retrospective study of population-based care management programs, Hewner et al. found that male sex was associated with slightly shorter times to readmissions but not associated with differences in overall survival.⁵⁶ A case-control study on healthcare utilization by Mosen et al. concluded that male sex was associated with a significantly higher risk of hospitalization after adjustment for age, chronic disease, and socioeconomic needs.⁵⁷

Discussion: Defining precision SGEM

The authors set out to characterize the existing research in Sex and Gender Precision Emergency Medicine by performing a scoping review, which revealed a number of important conclusions. First, nearly all studies included in our review found sex or gender differences across a wide breadth of clinical topics. While these differences may be due in part to the specific conditions being studied or to publication bias, they more likely reflect real and widespread sex and gender differences in EM. The findings from these studies as well as others not captured by our search highlight the importance of expanding research

We also found that three of every four articles (54/70, 77%) in our review had some type of funding, though this did vary by clinical topic. This is in stark contrast to a prior evaluation of funding for sex and gender scholarship in EM from 2008–2011 and 2014–2017, at which time over 60% of published studies had *no* funding source.⁵⁸ A government agency (26/70, 37%) was the most common funding source in our review, which is nearly twice the proportion reported (16–20%) previously.⁵⁸ This may reflect progress, given that the National Institutes of Health began requiring that investigators address sex as a biological variable in all grant applications starting in 2016.⁵⁹ Industry sponsorship does not seem to be robust in this arena currently and suggests an opportunity for future growth. Studies funded by federal support are clearly necessary for the progression of this topic, and the prioritization of funding from multiple sources will continue to be vital to the success of the mission to provide sex/gender specific precision in emergency medicine.

Another notable finding was that "sex" and "gender" were often not explicitly defined in the study methods. They also appeared to be used incorrectly, with "gender" used to describe biological sex, in an unfortunately common⁶⁰ form of misclassification bias that does depart from widely accepted current guidelines. Using "sex" and "gender" interchangeably leads to inaccurate reporting and limits the generalizability of research findings. While guidelines on accurate usage of the terms sex and gender exist,^{9,61,62} misunderstanding and misuse remains common.⁶³ We encourage journals to include these standards in their guidelines for authors, include them in training for all editors, and encourage continued engagement with partners in this process, including universities, professional societies, ethics committees, funders, industry and policy-makers.⁶⁴

Lastly, our literature search made clear that there is no consistent definition of sex and gender precision medicine. While the 2023 SAEM Consensus Conference sought to create a definition and shared mental model of Precision Emergency Medicine, the same must be done for Sex and Gender Precision Medicine, which transcends clinical specialties. Precision medicine is arguably the future of healthcare, and we must prioritize the integration of it into acute care delivery. Although EM physicians are unlikely to have the detailed genomic profiles often associated with precision medicine available to guide initial clinical decision-making, we can and should embrace many concepts from precision medicine. Thus, we propose a hierarchy of precision sex and gender medicine research, as shown in Figure 3.

At the bottom of the hierarchy, Tier 1 comprises simple research design and analytical methods to account for sex and gender, including but not limited to stratifying results by sex, matching by sex, and adjusting for sex in regression models. These methodologic approaches represent research best practices and are recommended by both the National Institutes of Health (Office for Research in Women's Health)⁶⁵ and the Canadian Institutes of Health.⁶⁶ However, these alone are insufficient to advance sex and gender precision EM.

Tier 2 of the hierarchy includes data regarding hormone profiles and biomarkers. Hormone profiles may be determined by endogenous and exogenous hormone alterations, as each is known to influence physiology and gene expression. Other examples at this tier include utilization of an individual's hormone profile for transgender or gender expansive patients. Tier 3 includes-omics data, which may include genomic, transcriptomic, proteomic, or metabolomic data, which represents the most precise genetic data currently available with the potential to directly inform mechanisms of sex differences in disease. An example of this type of data if pharmacogenomics, which may predict patients' response to pain and ED utilization. The hierarchical design reflects the degree of precision offered by each tier to assist researchers in designing studies that utilize the highest tier that is possible or reasonable for their research questions.

As noted in the results section, the vast majority (66/70, 94%) of studies included in this review were limited to Tier 1 in our proposed hierarchy of sex and gender precision EM. While these studies lay the foundation for future work, studies that address hormone and biomarker profiles (Tier 2) and -omics questions (Tier 3) are essential for advancing sex and gender precision EM, as is a consideration of the roles of technology, "big data", and artificial intelligence.

Limitations

We encountered several challenges in performing the literature search, specifically in defining an appropriate search strategy for sex and gender precision EM within the confines of the larger consensus conference. First, a great deal of literature published outside of EM is *relevant* to our practice. It was not feasible, however, to review the available literature in all other specialties, and it also proved challenging to operationalize a definition of "relevant" to EM. Second, articles may not have included specific terms pertaining to "precision medicine," even when they utilized precision medicine tools. The literature review thus had a narrow scope, and as a result excluded a number of articles that may have been relevant based on the conceptual criteria. For instance, a large body of literature of sex disparities in cardiovascular disease does exist, however, it may not have the three necessary search terms within the same research paper. This is contributed by the fact that universal language in this area has continued to evolve. Lastly, given the lack of a clear operational definition of "precision emergency medicine," which was one of the goals of the consensus conference, we did not screen out studies based on this search term.

Conclusion

Sex and Gender based medicine and research commonly employ precision medicine concepts to evaluate the effects of sex and gender in a variety of clinical topic areas, but much of this literature is not commonly described as precision medicine. We propose a hierarchy to categorize, label, and advance sex and gender precision medicine research. Fundamental to this advancement are implementation of guidelines regarding the correct use of sex and gender and continued research funding for sex and gender precision EM research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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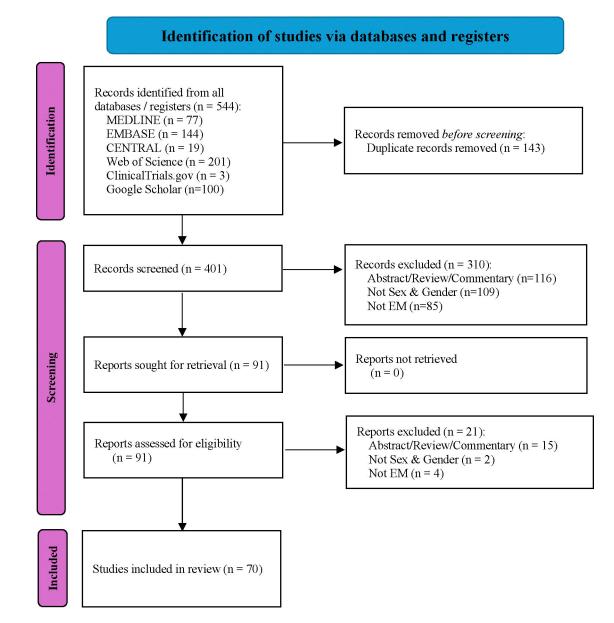


Figure 1: Prisma Flow Diagram

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Jarman et al.

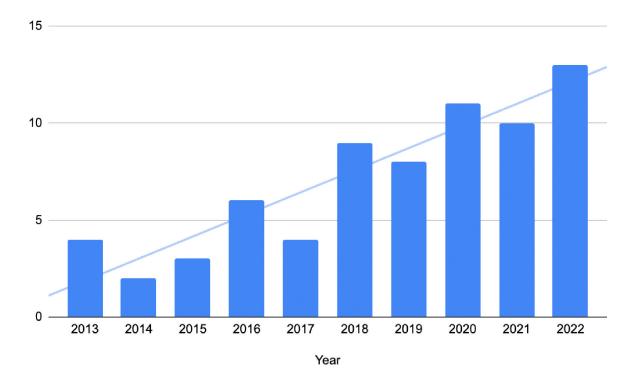


Figure 2: Included Manuscripts by Year

Jarman et al.

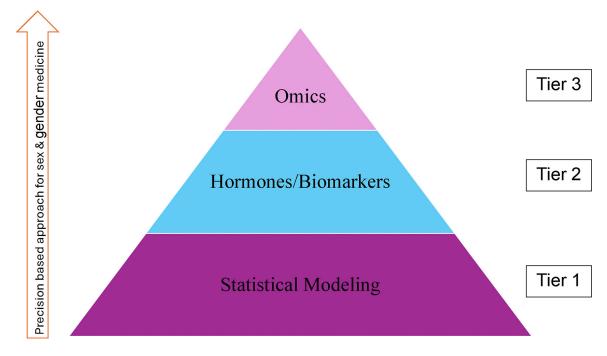


Figure 3: Precision Based Approach for Sex & Gender Medicine

Table 1:

Study Characteristics

Clinical Topic	n = 70 (%)	Funding, n (%)
Cardiovascular Diseases	20 (29%)	19 (95%)
Trauma/Injury Prevention	15 (21%)	10 (67%)
Infectious Diseases	7 (10%)	4 (57%)
Neurologic Emergencies	7 (10%)	7 (100%)
Mental Health/Substance Use	6 (9%)	3 (50%)
Health Economics	4 (6%)	4 (100%)
Geriatrics	3 (4%)	1 (33%)
Health Communication	2 (3%)	1 (50%)
Other (Heme, GI, Pulm, Reproductive Health, Tox, Critical Care)	6 (9%)	5 (83%)
Primary Funding Mechanism	n = 70 (%)	
Federal/Government Agency	26 (37%)	
None/Unknown	16 (23%)	
Foundation	14 (20%)	
University	7 (10%)	
Other	5 (7%)	
Industry	2 (3%)	

Table 2:

Leading Research Questions

Ranking	Question
1	How can we translate relevant scientific research regarding sex and gender-specific care from other fields into EM in a timely manner?
2	How do changing sex hormone profiles (including endogenous & exogenous) across the lifespan affect the presentation, diagnosis, treatment, and prognosis for emergency department patients?
3	How do patient and provider sex and/or gender identity and the associated dyads affect clinical decision making and implementation in the EM?