

Quantifying Health Inequity: An Umbrella Review of Systematic Literature Reviews on Sex-based Differences in Health Outcomes

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Background

- Sex, defined as the “the biological characteristics that define humans as female or male,”¹ is a genetic modifier of biology and disease that influences susceptibility to diseases, treatment responses, and overall health trajectories.^{2,3}
- The lack of attention to sex differences in research and clinical practice further contributes to health disparities.
- Previous reviews have mainly focused on qualitatively presenting information on gender health inequalities or health equity in specific indications; but an overall look at systematic evidence across all disease areas is lacking.

Objective

- The aim of this study was to summarize disparities between women and men in health outcomes, access to healthcare, and healthcare resource use (HCRU) based on the most recent peer-reviewed, quantitative evidence.

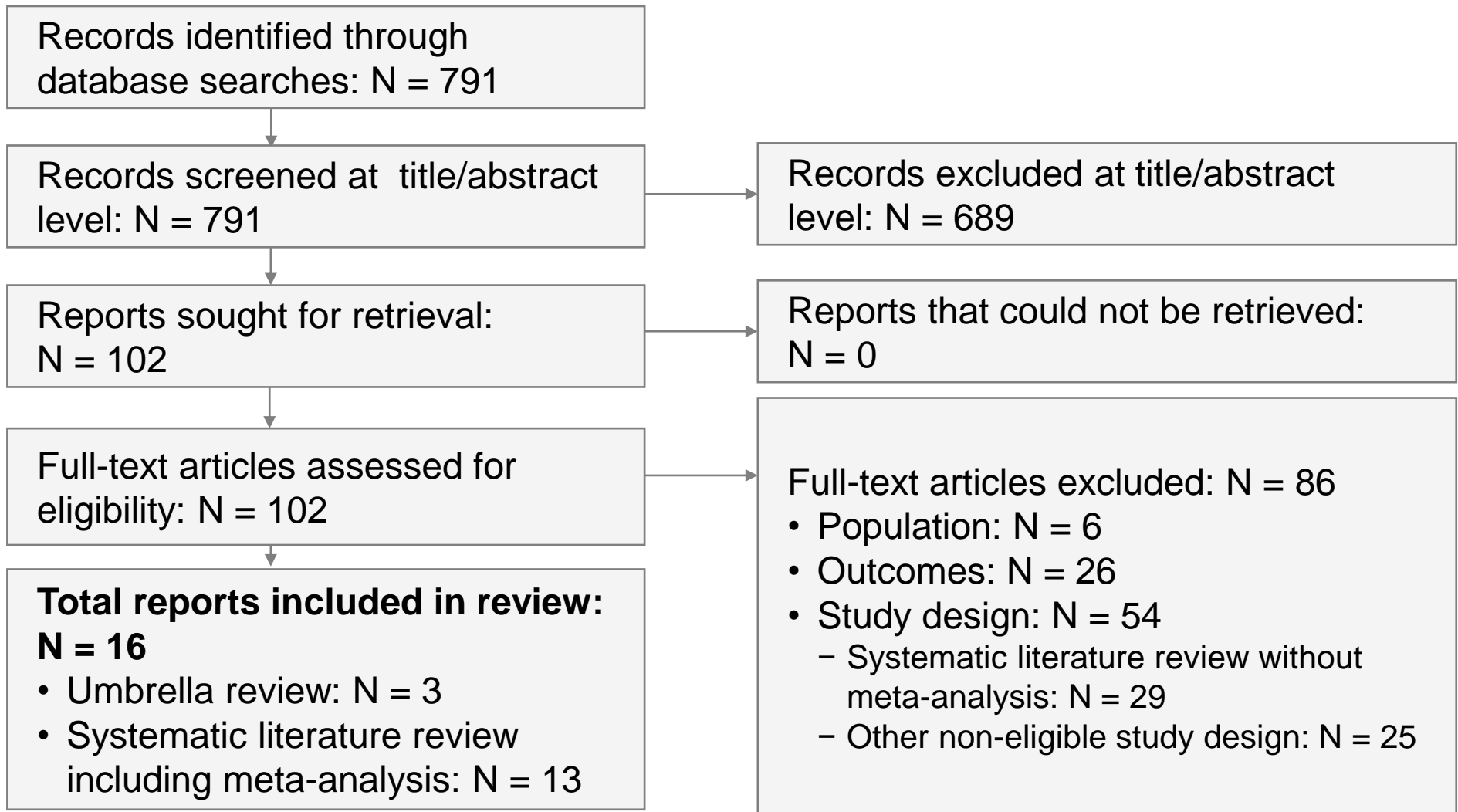
Methods

- This umbrella review was conducted according to the 2022 Preferred Reporting Items for Overviews of Reviews statement.⁴
- The MEDLINE and Embase databases were searched on April 17, 2024, to identify relevant English-language, peer-reviewed systematic literature reviews (SLR) and meta-analyses from the past five years. No geographic limits were placed.
- One reviewer manually screened studies at the title/abstract and full-text levels, with a blinded quality check of ≥25% of the excluded articles by a second reviewer.
- The population, intervention, comparators, outcomes, and study design – time criteria were tailored to select quantitative evidence on disparities between women and men of any age in terms of health outcomes, access to healthcare, or HCRU.
 - Only general, unrestricted study populations were eligible. Studies based exclusively on one sex, sex-specific diseases, or limited to specific professional (e.g., military personnel) or societal groups (e.g., migrants) were excluded.
- The methodological quality of included reviews was assessed by two reviewers using A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2.⁵
- Data were extracted by one researcher using a pre-designed template and independently validated by a second reviewer.

Results

- Thirteen SLRs^{7-11,14-21} and three umbrella reviews^{5,12,13} were included (**Figure 1**).
- Most studies were considered of high or moderate quality.

Figure 1. Literature flow diagram



- The study characteristics of included articles are summarized in **Table 1**.
- None of the studies covered multiple diseases. The reviews mainly reported on health outcomes and only three SLRs mentioned access and HCRU.^{10,15,21}
- Identified evidence on health disparities is presented in **Figure 2**.

Limitations

- This review did not consider the relationship between sociodemographic variables and health disparities.
- Sex-based disparities were summarized based on findings from the included SLRs without further considering the methodological flaws of primary studies.

Conclusions

- This is the first umbrella review aiming to holistically present the quantifiable evidence on sex differences across health outcomes.
- Most evidence was centered on outcomes for mental health and type 2 diabetes mellitus patients.
 - Compared to men:** women from the general population had a significantly higher risk of mental health disorders, including depression and suicide behavior, and those with type 2 diabetes mellitus had a disproportionally higher risk of adverse cardiac events, including mortality.
 - Compared to women:** men were significantly more likely to have adverse events after specific types of surgeries (except for abdominal aortic aneurysm repair) and higher mortality after COVID-19.
- Limited evidence was identified on access barriers or HRCU.
- More research is warranted to understand the biological and contextual links between sex and differences in health outcomes and in specific subgroups (pediatric, elderly), including prioritization of investment in addressing well-documented women’s health disparities.

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Results

Figure 2. Differences in health outcomes between women and men



Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; EVAR, endovascular aneurysm repair; IBD, inflammatory bowel disease; OR, odds ratio; PR, prevalence ratio; RR, pooled risk ratio; RRR, relative risk ratio; STEMI, ST-segment elevation myocardial infarction; SMD, standardized mean difference; T2DM, type 2 diabetes mellitus

Table 1. Characteristics of included systematic and umbrella reviews

Study	Publication type, search end date	Databases (studies)	Age group	Geography	Disease area of measured outcome (indication of subpopulation in focus)	Total sample size
General populations						
Richardson et al., 2024 ¹²	Umbrella, December 2022	5 (33)	Youth	Worldwide	Mental health (NA)	-
Witteveen et al., 2023 ¹³	Umbrella, August 2022	6 (43)	All ages	Worldwide	Mental health (NA)	-
Platt et al., 2021 ¹⁴	SLR, October 2019	5 (41)	All ages	US	Mental health (NA)	813,189
van't Hek et al., 2023 ¹⁸	SLR, December 2022	4 (15)	All ages	Central/ South America	Oncology (NA)	6,815
Tarricone et al., 2023 ²⁰	SLR, March 2022	4 (8)	Adults	North America	Surgery (NA)	1,164,630
High-prevalence populations						
Yaow et al., 2023 ⁶	Umbrella, August 2022	2 (27)	All ages	Worldwide	Cardiovascular (T2DM)	-
Jeffery et al., 2021 ¹⁵	SLR, May 2021	8 (9)	Adults	US	Mental health (depression and T2DM)	13,674
Armoon et al., 2023 ¹⁷	SLR, February 2021	4 (67)	All ages	Worldwide	Addiction (users of illicit opioids)	4,207,068
Other populations						
Shah et al., 2021 ⁷	SLR, December 2019	1 (56)	Adults	Worldwide	Cardiovascular (STEMI)	705,098
Pouncey et al., 2021 ⁹	SLR, January 2021	3 (24)	Older adults	Worldwide	Cardiovascular (after aneurysm repair)	436,680
Chiang et al., 2021 ⁸	SLR, February 2021	2 (11)	Older adults	Worldwide	Geriatrics (after hip fracture surgery)	2,314
Bianchi et al., 2023 ¹⁰	SLR, July 2023	3 (13)	Adults	Worldwide	Immunology (IBD)	113,191
Galbadage et al., 2020 ¹¹	SLR, April 2020	3 (31)	Adults	Worldwide	Immunology (lab-confirmed COVID-19)	7,556
Dong et al., 2023 ¹⁶	SLR, December 2022	3 (16)	Adults	Worldwide	Neurology (after HNC cancer surgery)	3,289
Liu et al., 2021 ¹⁹	SLR, July 2020	3 (17)	Adults	Worldwide	Oncology (cancer and COVID-19)	3,268
Fialka et al., 2022 ²¹	SLR, May 2021	3 (16)	All ages	Worldwide	Surgery (after acute type A aortic dissection surgical repair)	15,567

Abbreviations: COVID-19, coronavirus disease 2019; CV, cardiovascular; HNC, head and neck cancer; IBD, inflammatory bowel disease; lab, laboratory; NA, not available; SLR, systematic literature review; STEMI, ST-segment elevation myocardial infarction; T2DM, type 2 diabetes mellitus