Applicability of Retrospective and Prospective Gender Scores for Clinical and Health Data: Protocol for a Scoping Review

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Abstract

Gender is known to have a strong influence on health and illness in humans. Despite its relevance for treatment and outcome, gender is insufficiently considered in current health research. One hindering factor is the poor representation of gender information in clinical and health (meta) data. The protocol for a scoping literature review will further explore the state of the literature by identifying existing gender scores and understanding how these scores are currently being used in clinical and health settings. The protocol describes how gender scores will be evaluated along the dimensions of applicability and usage in scientific investigations. By identifying scores that can be applied on existing large-scale datasets it will suggests steps towards a retrospective gender assessment. Secondly, we will establish the basis for a recommendation of standardized gender scores for future investigations.

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Protocol

Applicability of Retrospective and Prospective Gender Scores for Clinical and Health Data: Protocol for a Scoping Review

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Abstract. Gender is known to have a strong influence on health and illness in humans. Despite its relevance for treatment and outcome, gender is insufficiently considered in current health research. One hindering factor is the poor representation of gender information in clinical and health (meta) data. The protocol for a scoping literature review will further explore the state of the literature by identifying existing gender scores and understanding how these scores are currently being used in clinical and health settings. The protocol describes how gender scores will be evaluated along the dimensions of applicability and usage in scientific investigations. By identifying scores that can be applied on existing large-scale datasets it will suggests steps towards a retrospective gender assessment. Secondly, we will establish the basis for a recommendation of standardized gender scores for future investigations.
Keywords: gender score, gender medicine, medical informatics, data integration, core data set

1. Introduction

The interaction of sex and gender plays an important role in symptoms, diagnostic, therapy, outcome, life expectancy, and generally in health and disease of men and women [1, 2, 3]. Gender also includes awareness of diverse sexual orientations and identities and their relevance to daily life, including queer, trans, and non-binary individuals (LGBTQI+; lesbian, gay, bisexual, trans, queer, inter). Neglecting or inadequately considering gender aspects in medical research and practice can have serious consequences for diagnosis, treatment, or risk prediction.

The German Ethics Council defines biological sex assigned at birth by genetic, hormonal, and anatomical conditions or markers, more precisely, by chromosomes, hormones, internal, and external sex organs. Gender, on the other hand, is defined by social attributes, an interaction of biological and psychosocial factors, an individual's social biography, and is shaped by someone's role in society. The psychological attributes determine the individual self-perception and the sexual identity of a person. The sexual identity may be different to someone's physical appearance or biological sex [4].

Despite the known importance of gender on health, gender is currently not sufficiently represented in health science and for most diseases it is not possible to differentiate between sex and gender effects yet [5].The work of Vader et al. [6], for instance, highlights the importance of gender and showed that gender can be seen as a mediator of sex differences. Specifically, a model considering gender showed that sex differences in chronic health problems narrowed or almost disappeared. This particularly concerns chronic diseases with a higher prevalence in women (arthritis, chronic pain, migraine). The authors even claim, in theses diseases, sex differences would not exits if there was no gender.

To improve the validity and reliability of medical research, it is necessary to encode gender information, in addition to information about the biological sex, in health datasets. A systematic gender assessment should be mandatory in future scientific investigations based on clinical and health data. Adding gender scores to existing data requires a retrospectively applicable score, ideally, suited for a wide range of databases. Integrating gender in future studies requires a reliable and valid score, able to predict gender with a high accuracy. The goals of this review are:

- to identify and characterize existing gender measures reported in the literature in health sciences
- to systematically assess the applicability on clinical and health studies (restricted to selected use cases).

2. Methods

Design.

The scoping review method, as defined by Grant and Booth [7], was selected to gain an overview of the topic and map existing literature on the problem. It is well suited since our study deals with heterogeneous methods across different research domains, and will inform future investigations on the topic [8]. In general, we followed the stepwise approach for scoping reviews described by Mak and Thomas [9] and adapted as many characteristics of the systematic review method as possible [10]. Particularly, the review follows the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines for scoping reviews [8] and the following steps were carried out: (1) identification of research questions; (2) identification of relevant studies; (3) study selection; (4) data extraction and charting; (5) collating, summarizing, and reporting the results.
Due to limited resources, the coding of the articles was conducted by a single reviewer and based on the database PubMed. PubMed was selected, since it is widely used as a standard database for biomedical systematic literature research and recommended as one of the most important databases for comprehensive systematic reviews [11], while the authors further recommend to include Embase, Web of Science, and Google Scholar. Moreover, the search was restricted to publications in the English language.

Stage 1: Identification of Research Questions.

As outlined in Section 1, gender is currently inadequately reflected in a majority of scientific studies. The research questions, therefore, arose from an initiative to standardize gender encoding in large scale data collections maintained by the Medical Informatics Initiative Germany (MII; Medizininformatik-Initiative) [12] and Study of Health in Pomerania (SHIP) [13], and to establish recommendations for standardized gender encodings in routine data provided by the Data Integration Center (DIZ; Datenintegrationszentrum) at the University Medicine Greifswald, Germany [14].
The research questions themselves were formulated by five domain experts, three people with a primary background in medicine, one person with a background in medical informatics, and one person with a background in medical documentation.
The identified and agreed-upon research questions for the scoping review are the following:

(1) What gender scores exist in medicine?
(2) Which gender scores are applicable on the data of SHIP and MII?
(3) How are gender scores currently applied or are they purely theoretical constructions?

Stage 2: Identification of Relevant Studies.

For the first assessment of the topic, a small number of relevant papers [15, 16, 17], identified by an initial manual search, were examined to identify keywords and important phrases. Furthermore, literature regarding gender awareness in the medical context [18, 19, 20] was examined to identify

commonly used scientific terminology regarding gender.

Based on the extracted keywords a query was designed to capture the key elements identifying these studies. The query was optimized for recall regarding the initial literature, while considering the amount of results. Specifically, the query was designed using Boolean operators, proximity search and a timeline. The time limit was introduced to identify more recent literature and exclude obsolete research, such as the well known Bem Sex-Role Inventory (BSRI) [21] shown to be outdated by the research of Donnelly and Twenge [22]. The limit was determined based on the distribution of articles which showed that the majority of research on the topic has been published in the last five years. Throughout the entire review process, secondary literature matching our topic was collected. This particularly concerns older scores, which allows an identification of earlier published literature that is still applied or cited in more recent publications. Even though excluded through our initial time limit, we decided to consider them as secondary literature to evaluate if they are still reasonable to apply or obsolete.

The final query is illustrated in Listing 1. It was executed on August 16th, 2023 and resulted in a total of 724 publications.

Listing 1. Developed PubMed query.

```
("gender* score*"[tiab:~1] OR "gender* measure*"[tiab:~1] OR
"gender* analys*"[tiab:~1] OR "gender* index*"[tiab:~1] OR
"gender* indices"[tiab:~1] OR "gender* model*"[tiab:~1] OR
"gender* classifier*"[tiab:~1])
AND
(create*[tiab] OR establish*[tiab] OR develop*[tiab] OR
implement*[tiab] OR use*[tiab])
AND
("2018"[Date - Create] : "3000"[Date - Create])
```

Stage 3: Study Selection.

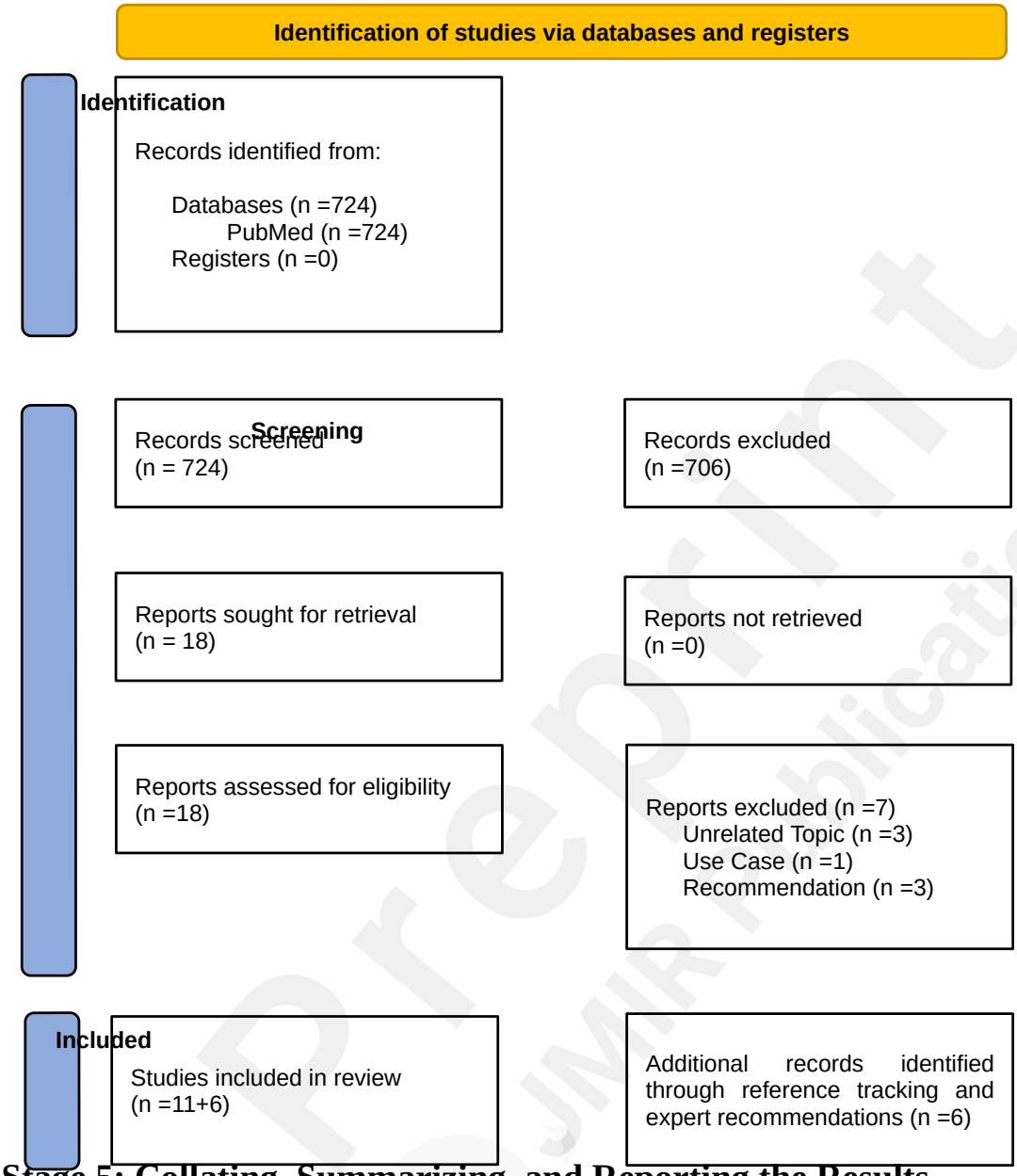
The obtained results were screened by title and abstract reducing the set to 40 and 18 potentially relevant publications, respectively, to exclude studies that do not relate to gender measurements. The title and abstract screening reduced the set of considered papers more than expected. We think this is the case, because the query is quite comprehensive and matches a broad scope of gender related topics, e.g. articles dealing with gender in mice. However, we deliberately wanted to achieve a broad coverage in order to identify all relevant papers.

Articles that could not be clearly excluded based on title or abstract only, were retained for further examination. The final relevance decision for the remaining articles was based on an examination of the full-text document. This led to a final set of 11 papers identified through the scoping review. Further, 13 articles were identified as secondary literature. They were also examined reducing the set to 6 secondary articles. In total, there are 17 studies included in the review. The described process is further illustrated by a PRISMA flow diagram [8] given in Figure 1

Stage 4: Data Extraction and Charting.

We developed a data-charting form, which will be used to determine eligible data extraction-points. The chart was initially based on Gierend et al. [23] and adjusted following discussions among the domain experts involved in this study (see Section 2). Furthermore, it was optimized during the process in an iterative manner and continuously updated. The chart will be organized by four main sections corresponding to an overview and the three research questions. The final data charting form is illustrated and explained in Table 1. When the data extraction points were completed, one author examined the papers critically and extracted the relevant data. To ensure high extraction quality, random double-checks were implemented covering more than 40% of publications by a second domain expert (see above). Disagreements were resolved through discussions. Irrelevant papers were removed from the chart.

Figure 1: PRISMA flow diagram illustrating the applied steps for the selection of relevant publications.



Stage 5: Collating, Summarizing, and Reporting the Results.

This scoping review aims at summarizing recently developed gender scores in health research. The extent of the review is limited to PubMed, the most relevant database for medical research outcomes. Nevertheless, we assume that the majority of relevant publications related to health sciences will be contained in the resulting data set. The commonly applied tools for analytical interpretation of literature such as summary statistics, charts and figures will be applied to discuss the collected relevant data [24]. Additionally, we will follow the PRISMA guidelines [8] and discuss the general interpretation of the results compared to other evidence, the overall aim of the study, effects for practice and future research, limitations, and recommendations.

Table 1: Summary of data charting

Section	Description
Section 1: Overview	Summary of the basic publication information
Article Metadata	Title, DOI, Year of publication (YYYY), Keywords
Corresponding author information	Name, research discipline, institute, ROR (registry of open persistent identifiers for research organizations)
Publication type	Peer reviewed or grey literature
Study type	Gender Score development, use case or recommendation
Continent	continent(s) where the study took place or focused on
Funding source	Public, industry, none or missing
Citation count	Citation count as reported by PubMed and Google Scholar
Objective	Aim or objective of the publication
Methods	The procedures or techniques used to identify, select, process and analyze information
Summary results	Short description of results
Conclusion	Short description of conclusion
Section 2: Research questions	Includes the research questions and the required data
What gender scores exist in medicine?	• Necessary variables for the developed gender score • Retrospective or prospective application • Clinical or epidemiological study • Size of cohort • Target variables (feminine, masculine, binary, continuously) • Model type (statistical model, questionnaire)
Which gender scores are applicable on the data from SHIP and MII?	• Existence of tool support or executable model • Availability of raw data or code • Reproducibility • Validation • Limitations (e.g. restricted scope) • Variable coverage
How are gender scores currently applied?	• Applicability in other research domains • Practical example of usage • Name and number of used records or databases • Expert evaluation

3. Results

In preparation of the scoping review a search of the database PubMed in August 2023 resulted in 724 matches. In the next step, these papers will be examined for relevance through a title-abstract screening, followed by a full-text screening.The relevant papers will be included into data charting.We plan to finalize the data extraction process during the first quarter of 2024 and the review will subsequently be concluded by summarizing and analyzing the results in the second quarter of 2024. The scoping review will provide an overview of recently developed gender scores in the literature. The research questions will allow to select suited gender scores based on the quality criteria and underlying research fields. The charting process will further provide information about their quality and retrospective applicability. This will serve as a basis to select eligible gender scores for retrospective application on existing data. Furthermore, the identified prospective scores allow to

formulate recommendations on inclusion of gender-dependent variables in future investigations. Particularly, to incorporate standardized gender scores in investigations performed in the scope of the Medical Informatics Initiative Germany. The review will also reveal potential gaps and limitations of current gender scores, e.g., regarding restrictions in underlying cohorts or research fields.

4. Discussion

Our review will investigate the current development and usage of gender scores in health research. Appropriate consideration of gender aspects in clinical and health studies remains a fundamental issue and we believe further work is required to establish the standardized use of gender scores in the recording of medical data. On the one hand, it is of high relevance to model gender information in existing data, since a high amount of collected patient data should be evaluated in this manner. On the other hand, future studies should target the design and development of a standardized prospective approach of gender assessment, which should be general and efficient to implement. Our study will provide an overview of existing gender scores. However, a general, broader awareness of the topic remains of high importance and solutions need to be found to systematically apply gender scores to clinical and health studies in future. Therefore, further efforts should be made to make this topic more present in the scientific community.

4.1. Ethics. Ethical approval is not required, since literature will be analyzed without sensitive patient data.

4.2. Acknowledgments. This work was funded by the German Federal Ministry of Education and Research as part of the projects InkE (01FP23G10A) – Excellence through Inclusiveness in Medicine – and Medical Informatics Initiative MIRACUM (01ZZ2301E) – Medical Informatics in Research and Care in University Medicine.

4.3 Conflicts of Interest. None declared.

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Abbrevations:

BSRI: Bem Sex-Role Inventory
DIZ: Datenintegrationszentrum (Data Integration Center at the University Medicine Greifswald, Germany)
MII: Medizininformatik-Initiative (Medical Informatics Initiative Germany)
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses
SHIP: Study of Health in Pomerania