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Let's Talk About Sex...and Gender: The Varying Ways in Which Sex and Gender are Operationally Defined in Current Medical Research

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Abstract

Sex-based differences are a common area of study in health research, specifically in relation to disease manifestation and treatment. Hormonal makeup, genetic factors, and reproductive organs are a few factors lumped under the definition of sex while broad and varying social paradigms are examined as a framework for gender or excluded altogether. Operational definitions of sex and/or gender were compared within varying sectors of healthcare in western medicine, elucidating the differences in medical research practices overall. This content analysis shows limitations in how current studies define what sex characteristics are being examined, how sex/gender are defined, and if these distinctions are relevant. Studies often conflate sex and gender while failing to address the unique and often independent factors that contribute to their influences on the conditions being examined. These discrepancies create murky findings that often leave out intersex and transgender people from receiving adequate medical care and do not allow for differences within cisgender dyadic individuals. This preliminary study aims to review how sex and gender were operationally defined in previous healthcare studies, determine how sex and gender data were collected and reported from participants, and suggest a protocol to standardize data collection for these characteristics in future studies.

Background

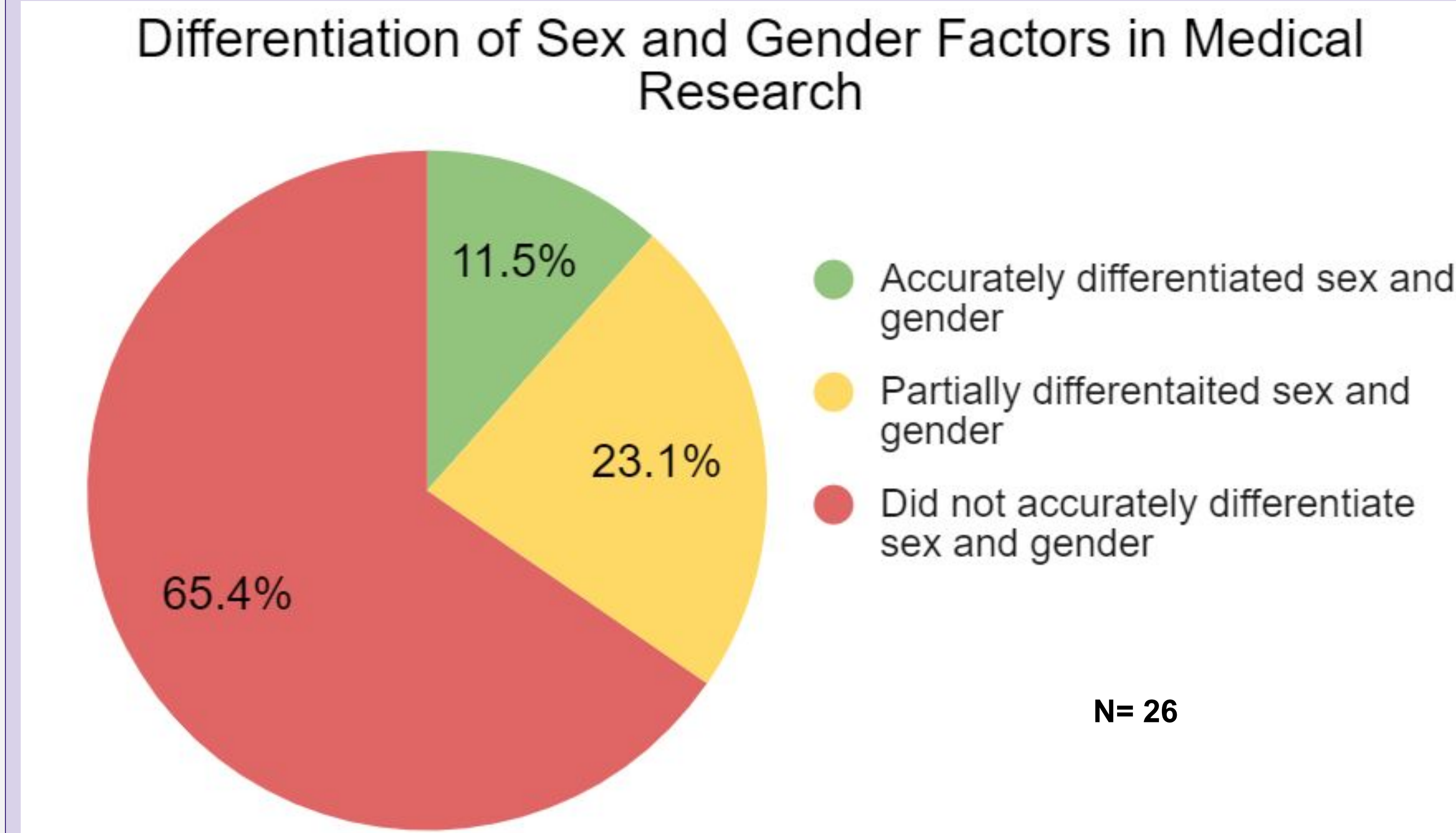
The medical field has a long history of using predominantly [assumed cisgender] males within medical research (Kalliainen et al, 2018; Vidaver et al, 2004). In 1993, the NIH passed the Revitalization Act in the aim of including more women in clinical research applications along with other minority groups. While this act aimed to include more women in research, it did not require that sex and/or gender differences be explicitly studied within the research framework. Research looking at the study of sex and/or gender differences in health research has shown that there is no consistency in how sex and/or gender are conceptualized in research. Additionally, there is a general failure to recognize the complexity of sex and gender within the context of other health factors and conditions (Hankivsky et al, 2018). There have been attempts made at creating a framework that evaluates the integration of sex and gender factors in healthcare research; however, these frameworks often conflate sex with gender or fail to address the complexity within each of these categories (Day et al, 2017; 2018). When sex and gender are clearly delineated in research, they are often narrowly defined by one factor such as sex being defined by a genotype test (Clayton et al, 2016). Sex and gender are distinct concepts, each of which can be broadly defined. Sex consists of several biological factors including hormones, gonads, genitalia, chromosomes, and secondary sex characteristics. These factors can all be non-dichotomously categorized and can change throughout an individual's lifetime (Ayala et al, 2015). Gender also consists of a wide range of cultural and social factors that vary across individuals and cultures. By deconstructing the concepts of sex and gender into their individual components, studies can gain a higher level of specificity in analyzing which specific factors lead to sex and/or gender differences seen across a variety of medical conditions. This can ultimately lead to elucidating the underlying mechanisms of diseases and aid in the development of specifically targeted therapies and pharmaceuticals for varying conditions (McCarthy et al, 2012).

Hypothesis

- H1: Sex and gender will not be clearly differentiated from each other in most studies.
- H2: In studies where sex and gender are delineated, sex and gender data will each only be collected via a single factor.

Results

The following chart includes preliminary results that illustrate the degree to which sex and gender factors are operationally defined in medical research.



Each article was classified using the following criteria:

Positive Factors	Negative Factors
Independent definitions of sex and gender provided	Sex/gender definitions missing or combined
Sex and/or gender defined as consisting of multiple factors	Sex and/or gender defined monolithically
Correct attribution of characteristics to gender or sex	Incorrect attribution of characteristics to gender/sex
Methods stated on how individual sex/gender factor data was acquired	No methods given for how sex/gender data was collected
Finding reported with precise terminology	Findings reported with imprecise terminology

Articles with 4 out of 5 or more positive factors were considered accurately differentiated, articles containing 2-3 positive and 2-3 negative factors were considered a partially differentiated, and studies containing 4 or more negative factors were classified as not accurately differentiating sex and gender.

Conclusion

Overall, in studies looking at sex and/or gender differences, specific sex and gender factors were inconsistently defined, the methodology for collection of sex and/or gender data was not often explicitly stated, and results were not often reported with precise terminology. These findings are in support of H1. Among the papers where sex and gender were clearly differentiated, it was rarely specified what characteristics that make up sex and gender were being studied. Due to the lack of data where sex and gender were accurately delineated, H2 can neither be supported nor opposed. These results are preliminary and include only a small sample of medical literature concerning sex and gender factors. Future expansions of this study should aim to comprehensively sample current research practices in order to produce statistically significant results. Additionally, the use of a single or multiple factor approach to the study of sex and gender characteristics in medical research can be further explored in future works. *All references are available upon request*

Method

The purpose of this content analysis was to begin to discover how sex and gender discrepancies, as well as measurements of sex characteristics, are used in contemporary biomedical and psychological articles published in peer reviewed journals. The databases PubMed, PsycINFO, and Google Scholar were used in the search with the following search terms: "sex and gender discrepancies", "sex and gender characteristics", "sex and gender differences", "measurements of sex", "sex variation", "sex vs gender", "sex disparities in health", and "gender disparities in health". The types of articles analyzed included experimental studies on rats where findings were extrapolated to humans along with experimental and quasi-experimental studies on human subjects. Articles from earlier than 2009 were excluded. Previous content and meta analyses concerning how sex and gender have been studied were also reviewed to ensure our suggested protocol is novel.

Discussion

The following table includes a protocol proposed on how to undertake and report findings from research on sex/gender factors. This protocol aims to increase the precision with which sex and gender characteristics are studied within human subjects and provide clarity in how data concerning specific characteristics are reported and discussed.

Sex/Gender Factor	Types of Data that can be Collected	Testing Methodology	Example Description of Findings
Chromosomes	XX, XY, X0, XXY, XYY, etc	Karyotype test	Differences in [X] rates between XX, X0 and XY individuals.
Sex Hormones	Concentrations of Estrogens, Testosterone, Progesterone, etc in the body	Hormonal Assays	The impact of testosterone concentration on [condition X].
Gonads	Presence/absence of Ovaries, testes, ovotestes, etc	For internal: Ultrasound For external: visual inspection/ self report	How rates of [X] vary between people with ovaries vs testes.
External Genitalia	Presence/absence of a penis, scrotum, prostate, labia, clitoris, uterus, vagina, etc	Visual Inspection/ self report	The variation in [X] between people with a penis vs people with a clitoris.
Secondary Sex Characteristics	Development of facial hair, breasts, pubic hair, etc.	Visual Inspection/ self report	The effects of differing secondary sex characteristics on [X].
Gender Identity	Man, Woman, Nonbinary, Gender Fluid, Two-Spirit, etc	Self Report	The disparity in [X] between men, women, and nonbinary people
Gender Roles	Femininity, masculinity, androgyny, social expectations including conformity to stereotypes, etc	A testing metric such as those found in "Gender Roles: A Handbook of Tests and Measures" (Beere, 1990)	Impact of social expectations and performance/adherence to these roles on [X].

While this framework includes several common sex and gender factors, there are many additional factors that can also be systematically studied using this protocol. It is important that many sex and gender characteristics be assessed, especially for studying populations who do not fit into traditional sex and/or gender frameworks such as transgender and intersex patients. These factors should be studied independently when possible to ensure proper data is collected on which sex and/or gender characteristics are being measured, how this data is being collected from participants, and care is taken in the language used to report back findings related to sex and/or gender differences. Future studies should aim to avoid assuming these characteristics based on an individual's sex recorded at birth, gender presentation, or other conjecture. Increasing the specificity with which sex and gender are studied will greatly aid in the ability for future research to arrive at mechanisms that drive sex and gender differences within certain conditions. This will allow for more specific and reliable treatments to be developed, and for these treatments to be used safely for outliers of the traditional sex and gender binary.