

Sex and gender in intensive care research: practical limitations and methodological challenges

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Summary

Gathering nuanced sex and gender data in biomedical research is mandated by Swiss law and ethical recommendations but not supported by current practices in clinical medicine. Exploring this issue in the intensive care context, we highlight the urgent need for differentiated data collection to support inclusive and equitable clinical research.

Introduction

There is an increasing demand to consider and distinguish sex and gender in research. The Swiss law on research involving human beings (Art 6 Human Research Act [HRA]) requires that *Nobody is to be subjected to discrimination in connection with research*. In June 2024, the Federal Council adopted the clinical trial ordinance (Art 4a KlinV) which explicitly demands to consider the distribution of sex and age. In 2024, the Swissethics National Board revised the European Association of Science Editors' Sex and Gender Equity in Research (SAGER) guidelines to be more inclusive [1]. For sex, the essential information needed is *sex assigned at birth*; however, in certain instances, measuring sex hormones can provide additional insight, allowing for a view of sex as a continuous rather than binary variable [1].

This change was motivated by the underrepresentation of women's research, leading to insufficient healthcare [1, 2]. The insufficient declaration of sex and gender diversity leads to subtle discrimination and underrepresentation of specific groups [1]. Approximately 1.7% of the global population is born with variations of sex characteristics [3]. A Swiss survey indicates that 0.4% of citizens do not identify as binary and a further 5% subjectively see themselves as closer to the another gender identity deviating from their own biological sex [4].

In addition, when differences between women and men are reduced to biological mechanisms, this biological reductionism ignores social or behavioural dimensions, such as risk exposure, health-related behaviours, or access to care [1].

In response to the Swiss National Science Foundation's (SNSF) call *Gender Medicine and Health* (National Research Programme [NRP] 83) [5], we developed a study design to investigate sex- and gender-related factors in intensive care unit (ICU) care. However, our interdisciplinary research team of experts in different fields encountered major difficulties in operationalising gender-related factors. This viewpoint illustrates the challenges and limitations in gender-related clinical research within the example of Swiss ICUs. While many of these challenges apply to healthcare in general, they are especially vexing in intensive care as patients are typically limited in their ability to communicate. A comatose patient, for example, cannot personally communicate their gender identity.

Practical limitations in operationalising sex and gender

Before delving into ICU research, it is essential to consider the Swiss bureaucratic framework as a starting point to understand the challenges in accurately collecting sex- and gender-related data. Since 2022, it has been possible to change one's legal sex without major bureaucratic obstacles [7]. The civil registry record change can be made without personal statements and without a medical certificate [8]. Although the change can benefit individuals with a trans identity [7], official passport terminology still refers to *sex* (*Geschlecht, Sexe, Sesso, Schlattaina, Sex*). In 2022, the Swiss Federal Council reported in response to a parliamentary postulate that conditions for introducing a third sex were not met and that the binary sex model remains deeply rooted in Swiss society [8]. Thus, it is unclear whether the data recorded in the civil registry reflects sex assigned at birth or gender identification. Also, the civil registry record does not refer to information on further sex and gender dimensions, such as hormone levels, genetics, gender norms and roles [9]. This lack of clarity and granularity in the registry system directly affects the downstream process in clinical settings. During the admission process, personal data such as name and date of birth are requested. Then, the patient administration uses the AHV number, which is found on health insurance cards, to request a unique patient identification from the central registry [10]. Thus, hospital electronic information systems,

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such as KISIM (KISIM-TM; Cistec® Zurich, Switzerland), remain limited to binary categories within the demographic data (*Stammdaten*). ICU-specific information systems, such as the Patient Data Management System (MetaVision Suite; iMDsoft®, Tel Aviv, Israel), label the sex and gender category as *sex assigned at birth* – still, these systems display data from the central information system.

As a result, retrospective studies conducting chart reviews rely on medical records or official statistics offering only vague or incomplete information on sex and gender. Prospective studies could theoretically collect more nuanced data, but data collection on ICUs is challenging: Many patients are unconscious or unable to provide information. Loved ones are often distressed and overwhelmed. In addition, the often life-threatening situations in the ICU make it inappropriate to take a detailed sex- and gender-related history.

Consequently, hypotheses about gender-specific differences cannot be adequately tested, promoting biological reductionism. This results in influential studies on gender differences often lacking precise terminology and definitions, where the terms sex and gender are used interchangeably [11]. For example, the challenge became evident when the Swiss Federal Office of Statistics (*Schweizer Bundesamt für Statistik*) provided a dataset on ICU patients without detailing how the sex/gender category was collected [9].

Towards inclusive data collection

The SAGER guidelines were developed to aid researchers in considering sex and gender dimensions in study design, analysis and reporting [1]. The role of research ethics committees is crucial in reviewing research protocols and ensuring the integration of sex and gender issues [1]. This review must consider the structural limitations in the availability of sex and gender data that researchers face within their institutional and national contexts. We also support the request for sex- and gender-sensitive education of medical health professionals such as clinicians and nurses to raise awareness of possible discrimination [12].

To make meaningful progress, we must establish a robust framework for systematically gathering data related to sex and gender. This structured approach will empower us to understand better and address all individuals' unique needs and experiences. To achieve this, healthcare institutions, such as hospitals, should actively gather demographic data in addition to the information stored on the health insurance card. As a minimum requirement, the patient record should report sex assigned at birth, self-reported gender identity and – where relevant – variations of sex characteristics. We are aware that adjustments in existing IT systems such as SAP, KISIM or Polypoint are elaborate and expensive. However, IT updates should incorporate those standardised characteristics. As a practical first step, sex- and gender-related topics could be incorporated into the patient history and next-of-kin questionnaire (*Angehörigenfragebogen/Fremdanamnese*). Further research about the collection and operationalisation of sex- and gender-related data is necessary to avoid discrimination and follow legal requirements.

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