


BMJ Open Consideration of sex and gender in European clinical practice guidelines in internal medicine: a systematic review protocol

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ABSTRACT

Introduction Clinical practice guidelines (CPGs) are a powerful instrument to ensure evidence-based practice in clinical diagnostics and disease management. As knowledge about the impact of sex and gender on health and disease is emerging, the need for its transfer into clinical practice is becoming more urgent. However, a systematic evaluation of the incorporation of sex-related and gender-related knowledge into CPGs in Europe is currently not available. This systematic review will fill this gap. We will analyse the operationalisation of sex and gender in internal medicine CPGs in Europe and the translation of this information into tailored recommendations. The results will offer a baseline assessment to inform prospective sex-sensitive and gender-sensitive guideline development.

Methods and analysis CPGs published by European internal medicine guidelines will be analysed according to a pre-established analysis framework. CPGs will be identified by a two-step approach, that is, through direct contact with the organisations and by a PubMed search, to ensure capture of all relevant guidelines. Prespecified keywords will be employed to identify the representation of sex-related and gender-related content throughout the CPGs. Structured data will be collected through machine-assisted text mining. Identified texts will then be manually reviewed by two independent coders using a specifically developed checklist.

Ethics and dissemination This study does not require approval by an ethics board. It will provide an overview of sex and gender considerations in European CPGs in the field of internal medicine regarding the time frame 2012–2022.

INTRODUCTION

The inclusion of sex-related and gender-related evidence into clinical practice guidelines (CPGs) is essential to overcome the widely established ‘one-size-fits-all approach’ in medical research and clinical practice.¹ As knowledge about sex and gender differences and their relevance towards clinical practice is emerging,² transfer into CPGs should follow.

Ideally, CPGs should be systematically developed, methodologically robust documents,

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Clinical practice guidelines (CPGs) in internal medicine and its subspecialties produced in the last decade in Europe will be analysed to provide the first systematic overview of the inclusion of sex-related and gender-related knowledge into CPGs.
- ⇒ The European perspective captures a concerted input rather than individual national approaches.
- ⇒ To ensure due diligence, a two-step methodological approach will be applied: European medical societies will be individually contacted and their websites used to identify CPGs and a systematic search in PubMed will be conducted to ensure capture of all relevant guidelines.
- ⇒ Collection of guidelines according to our inclusion criteria can be challenged by insufficient standardisation and synchronisation of the European guideline development and dissemination procedures.

which formulate evidence-based recommendations for sound clinical decision-making based on the most recent knowledge in the field.³ CPG development and implementation is a multiprofessional and interdisciplinary process.

In the context of the European context three aspects have to be considered. Most of the countries in the European Union develop individual national guidelines for clinical management,¹ but only a fraction of them have standardised procedures in place to ensure the quality of the guidelines² and there are insufficient data to systematically evaluate the implementation of the guidelines across member states.^{3,4} Hence, mapping the practices of individual member states is complex and suffers from inherent methodological inconsistencies. At a pan-European level, the guideline development process is, instead, decentralised and carried out by specialised European medical societies’ guideline committees with representatives from individual member states.⁵ To assess and ensure quality the GRADE system^{6,7} and the AGREE

instrument⁸ are widely employed tools, providing a degree of standardisation.

Information about the consideration of sex and gender in CPGs is limited overall, but trends in Canada and the USA have been investigated. Tannenbaum *et al* reported an inconsistent implementation of sex and gender into CPGs in Canada. In their analysis, 35% of the examined Canadian guidelines included sex-specific and gender-specific considerations and only 25% ‘used the terms ‘sex’ and ‘gender’ correctly’.⁹ In the US context, the US Preventive Services Task Force concluded that ‘limited evidence to inform the preventive care of populations based on gender identity’ was available. It also emphasised how (insufficiently inclusive) primary studies limited the evidence base for sound CPG development.¹⁰ Comparable information about European CPGs is still lacking to date.

To fill this gap, we will conduct a systematic review of the inclusion of sex-related and gender-related knowledge in European CPGs in the field of internal medicine in the years 2012–2022. We will map the operationalisation of sex and gender in these guidelines and the transfer of this knowledge into tailored recommendations. The results will offer a baseline assessment to inform prospective sex-sensitive and gender-sensitive guideline development in the field of internal medicine.

STUDY DESIGN AND METHODS

Amendments

No amendments. In case of important protocol amendments the updated Open Science Framework (OSF) protocol will be uploaded distinct from the original one with clear visualisation of changes.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols-Checklist 2015

This report was written under thorough consideration of the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols-Checklist 2015.

Objectives

Primary objectives

The primary objectives are to investigate the incorporation of sex-related and gender-related knowledge into European Clinical Guidelines using specific sex-related and gender-related keywords and define two subcategories of analysis according to implementation depth: (1) terminology and (2) recommendations.

Terminology

1. Terminology—Quantitative: Is sex-related and gender-related terminology used?
 1. Is the terminology used? (text-positivity).
 2. Is the terminology not being used? (text-negativity).
2. Terminology—Qualitative: How is the sex-related and gender-related terminology applied?
 1. Is the terminology defined?
 2. Is the terminology used correctly? (‘appropriate use’ as stated in SAGER¹¹)

Recommendations

Do recommendations explicitly include sex-related and gender-related aspects?

1. Are sex-related and gender-related aspects explicitly mentioned in the text-positive clinical recommendation?
2. If so, in what way do the recommendations consider sex-related and gender-related aspects?

Eligibility criteria

Inclusion criteria

1. Guideline in internal medicine and its subspecialties: Cardiology, nephrology, (microbiology and) infectious diseases, oncology, rheumatology, pneumology, endocrinology, vascular medicine, intensive care and gastroenterology.
2. Guideline developed by a European Medical Society: Societies with >1000 members were selected or the society with the largest member base for small fields.
3. Selected documents: Published (clinical practice) guideline by the respective medical society; one exception: European Alliance of Associations for Rheumatology (EULAR) (since EULAR does not publish CPGs, their published recommendations will be considered).
4. Language: English language.
5. Years considered: 2012–2022.

Exclusion criteria

1. Clinical guidelines exclusively developed for the paediatric population.
2. Publication date before 2012.
3. Language other than English.
4. Discipline other than Internal Medicine and subspecialties.
5. Publications by the societies other than (clinical practice) guidelines such as original research, opinion pieces, recommendations (with the sole exception EULAR), position papers, statements, consensus and reviews.

Choice of internal medicine specialties and organisations

After contacting the European Union of Medical Specialists and the umbrella organisation for internal medicine, the European Federation of Internal Medicine (EFIM), we were informed that there is no systematic archive or database including all internal medicine-related CPGs in Europe. CPGs are published individually by each organisation. We then contacted all relevant organisations individually and they all confirmed this practice. Therefore, we selected the most relevant subspecialty organisations in the field of internal medicine in the European Union and will proceed to collect and analyse their published guidelines. We selected the following ten subspecialties, which are an inherent and integral part of the specialist training worldwide: cardiology, nephrology, (microbiology and) infectious diseases, oncology, rheumatology, pneumology, endocrinology, vascular medicine, intensive care and gastroenterology. We conducted a thorough web search to identify matching organisations for each

subspecialty and included the largest (>1000 members) for each discipline or the single most prominent organisation (potentially <1000 members) for smaller fields. The EFIM was selected as the sole overarching organisation for internal medicine in Europe. The EFIM does produce own guidelines but the majority of CPGs is developed and published by subspecialty organisations. The application of our selection criteria (see additionally inclusion criteria) led to the selection of 22 organisations stated as follows:

- ▶ Cardiology—European Society of Cardiology (ESC).
- ▶ Nephrology—European Renal Association (ERA).
- ▶ Infectiology—The European Society of Clinical Microbiology and Infectious Diseases (ESCMID).
- ▶ Oncology—The European Society for Medical Oncology (ESMO).
- ▶ Rheumatology—The European Alliance of Associations for Rheumatology (EULAR).
- ▶ Pneumology—The European Renal Association (ERA).
- ▶ Endocrinology—The European Society of Endocrinology (ESE).
- ▶ Angiology—The European Society of Vascular Medicine (ESVM).
- ▶ Intensive care—European Society of Intensive Care Medicine (ESICM).
- ▶ Gastroenterology—No single society could be identified. United European Gastroenterology (UEG) is an umbrella organisation that mostly publishes CPGs in cooperation with other associations subspecialising within gastroenterology. We organised and scanned all CPGs provided in cooperation with the UEG and included all organisations that the UEG partnered with. This yielded the following:
 - ▶ European Society for the Study of Diabetes (EASD).
 - ▶ European Society for Clinical Nutrition and Metabolism (ESPEN).
 - ▶ European Association for Gastroenterology, Endoscopy and Nutrition (EAGEN).
 - ▶ European Society of Gastrointestinal Endoscopy (ESGE).
 - ▶ European Society of Neurogastroenterology and Motility (ESNM).
 - ▶ European Association for the Study of the Liver (EASL).
 - ▶ European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB).
 - ▶ European Society of Coloproctology (ESCP).
 - ▶ European Microscopic Colitis Group (EMCG).
 - ▶ European Society for the Study of Coeliac Disease (ESsCD).
 - ▶ European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN).

In total, this resulted in 22 European Organisations publishing CPGs to be included in our review, with the addition of EULAR as they publish ‘Recommendations’ instead of formal CPGs.

Information retrieval

We developed a two-step process to ensure thorough review.

1. We identified the most relevant internal medicine societies as described above (Inclusion criteria). The primary sources of information for the CPGs are the official websites of the selected medical organisations. To verify the accuracy of the gathered information and sources, direct personal contact will be established with each target organisation via email and telephone.
2. We will then proceed with a second step using the PubMed database as source. We will use the search string “*guideline*” OR “*guidelines*” AND “*European organization’s abbreviation*”, for example, ESC for European Society of Cardiology” OR “*European organization e.g. European Society of Cardiology*” to identify published CPGs. The search is limited to title and abstract, time-span 1 January 2012–31 December 2022, English language and category guidelines. This step will minimise the risk of missing relevant CPGs.

Measures of sex and gender considerations

Definition of sex and gender

Sex is currently operationalised by three factors known as the 3G-sex-definition or the genetics-gonad-genitalia-triad and defined as female, male and intersex.¹² Gender is a psychosociocultural process that affects ‘attributes, behaviours, stereotypes, technologies and knowledge’. It is commonly captured in the form of different dimensions, such as gender norms, gender relations, gender identity and gender relations.¹

Selection of keywords

The selection of keywords consists of “sex” and “gender”, terms for adult sex: “male”, “female” and “intersex” and further includes gender dimensions with the terms “man”, “men”, “woman”, “women”, “trans”, “non-binary”, “gender-fluid”, “genderdiverse” and “agender”. To ensure a complete detection of keywords, we will also include the plural and hyphenated keywords in the search string, for example, “gen-“, “wom-“, “non-bi-“ etc. Since in CPGs sex-specific or gender-specific recommendations are often found (only) in relation to pregnancy or fertility, the terms “pregnan*”, “*fertil*” and “*menopaus*” will also be considered for completeness.¹³

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

STUDY RECORDS

Data management: data items, data collection, data selection, data processing and storage

An ad hoc machine-assisted process will be developed to analyse the guideline texts using sex-specific and gender-specific keywords. The Python library Textract and Regular Expressions will be used to identify specified sex and gender

keywords in the individual PDF documents. This search process will be divided into three steps as follows: keyword search and keyword evaluation (frequency distribution of individual keywords), extraction of the sentence containing the keyword and extraction of the sentence preceding and following it as well as storage as CSV (Comma-separated values) file and development of a relational database.

Outcomes and approach

Depending on the outcome of the text mining process with the applied keywords, the collected CPGs will be divided in 'text-positive' and 'text-negative'. Output will be analysed independently by two reviewers using a specific checklist. Outcomes will be compared and potential disagreements resolved in discussion. Text-positive results will be examined for incorporation of sex-specific and gender-specific knowledge in the context of: (A) terminology and (B) recommendations. Terminology will be assessed quantitatively (Is sex and gender related terminology used?) and qualitatively (How is the sex and gender related terminology applied?). In the second step, the incorporation of sex-specific and gender-specific information into recommendation development will be analysed.

RISK OF BIAS IN INDIVIDUAL STUDIES

Minimising the risk of bias

We will implement a two-step search process to minimise the risk of bias. Data gathering and review is performed by two reviewers.

Data synthesis

The extracted keywords will be quantitatively mapped and analysed by descriptive statistics. Further analysis regarding the contextualisation of the keywords and their evaluation will be qualitatively assessed and interpreted as stated in the objectives.

Meta-biases

We are aware that the choice of the organisations holds an inherent unavoidable selection bias. In addition, the publications inherently contain a publication bias, since CPGs are developed by Clinical Guideline Committees which decide on relevance of included studies in the development process.

Confidence in cumulative evidence

The strength of the body of evidence is upheld by choosing the highest available standards of evidence (guidelines) provided, facilitating confidence in the cumulative evidence.

Ethics and dissemination

No ethical approval was required for this study as it is literature based.

Contributors SO-P initiated the project. MG and EB advised on study methods. AN wrote the first drafts of the paper. All authors reviewed and approved the final version of the paper.

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Competing interests None declared.

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