Exploring physician gender bias in the initiation of prescribing cascades for older men and women: a qualitative clinical vignette study protocol

ABSTRACT
Introduction A prescribing cascade occurs when a drug is prescribed to manage the often unrecognised side effect of another drug; these cascades are of particular concern for older adults who are at heightened risk for drug-related harm. It is unknown whether, and to what extent, gender bias influences physician decision-making in the context of prescribing cascades. The aim of this transnational study is to explore the potential impact of physician implicit gender biases on prescribing decisions that may lead to the initiation of prescribing cascades in older men and women in two countries, namely: Canada and Italy.

Methods and analysis Male and female primary care physicians at each site will be randomised 1:1 to a case vignette that features either a male or female older patient who presents with concerns consistent with the side effect of a medication they are taking. During individual interviews, while masked to the true purpose of the study, participants will read the vignette and use the think-aloud method to describe their ongoing thought processes as they consider the patient’s concerns and determine a course of action. Interviews will be recorded, transcribed verbatim and thematic analysis will be conducted to highlight differences in decisions in the interviews/transcripts, using a common analytical framework across the sites.

Ethics and dissemination This study has received ethics approval at each study site. Verbal informed consent will be received from participants prior to data collection and all data will be deidentified and stored on password-protected servers. Results of this study will be disseminated through peer-reviewed journal articles and presented at relevant national and international conferences.

INTRODUCTION
A prescribing cascade is defined as the process whereby a drug is prescribed to manage the side effect of another drug, often occurring when the side effect is misinterpreted and treated as a new medical condition. Prescribing cascades can result in unnecessary and costly prescribing, contribute to problematic polypharmacy, and increase the risk for adverse drug events (ADEs). Older adults are at greater risk for prescribing cascades due to the increased prevalence of multimorbidity with age consequent polypharmacy. As women tend to live longer than men, with more chronic conditions and gender-related differences in prescribing cascades is particularly important.

Prior studies have revealed the influence of patient sex on physician referrals and recommendations for surgery, and the provision of more aggressive end-of-life care.

STRENGTHS AND LIMITATIONS OF THIS STUDY
⇒ This will be the first study to explore the influence of physician gender bias on the risk of initiating prescribing cascades among older men and women.
⇒ The rigorous and iterative process of the vignette development, including choosing the prescribing cascade among the international study team, will help to ensure its clinical accuracy, relevance and suitability for examining gender bias.
⇒ The transnational design of the study, including primary care physicians from two different countries, will improve the transferability and generalisability of findings.
⇒ This study only reflects the decision-making of primary care physicians (ie, not physicians in other settings or non-medical prescribers).
⇒ Evaluation of hypothetical behaviour of physicians cannot definitively determine whether actual behaviour would be consistent with real-life clinical scenarios.
patients have been shown to be at higher risk of receiving potentially inappropriate prescriptions compared with male patients. Women are prescribed more medications and are less likely to receive the medication treatment and monitoring recommended by clinical guidelines. A patient’s sex can influence the type of care they may or may not receive in ways that are not well understood, but may be due to gender-related sociocultural factors. Physician sex may also play an important role in prescribing decisions; previous work has shown that female physicians appear to be more careful and conservative in their prescribing for older patients.

Gender (sociocultural), distinct from sex (biological), refers to socially constructed roles, behaviours and expressions (eg, how they act and interact, roles they take on) associated with being a man, woman or gender-diverse person. Social context plays an important role in shaping gender norms, attitudes and interpersonal relations—including those in clinical settings. Importantly, the understanding and experiences of gender can vary greatly across borders and thus between health systems based on factors related to institutions, laws and policies, cultural norms and beliefs, gender roles, responsibilities and engagement, and access to assets.

Gender bias has yet to be explored in the context of prescribing cascades; specifically, how implicit gender bias and/or the prescriber’s sex may affect prescribing practices leading to different treatments for older men and women. Given the harms associated with prescribing cascades, it is important to understand if and why one sex may be at greater risk for these cascades in order to prevent their occurrence. As such, the overarching goal of this study is to use a case vignette, presenting a realistic clinical scenario, to examine whether a patient’s gender affects their risk of experiencing a prescribing cascade due to an implicit gender bias among primary care physicians. As primary care physicians are largely responsible for prescribing medications for older adults, understanding the conscious and unconscious factors contributing to their clinical decisions is key to preventing potentially inappropriate and harmful prescribing. We will also explore whether and in what ways the prescriber’s gender affects prescribing decisions and if these differences are consistent for both female and male patients.

This study is planned as part of the iKASCADE project—a transnational project funded by the international GENDER-NET Plus ERA-Net Co-fund, which aims to investigate the development, experience and management of prescribing cascades in older adults through a sex and gender lens. To better understand how decision-making may be influenced by varying geographic and sociocultural contexts, results will be compared between two sites across North America and Europe: Canada and Italy.

METHODS AND ANALYSIS

Study design

This qualitative study aims to explore the decision-making processes of primary care physicians and the potential role of gender bias in their prescribing decisions for older men and women. This will be done through the use of clinical vignettes and the think-aloud method of cognitive interviewing. At each site, we will employ a two-by-two factorial design. Randomisation of a case vignette varying 1:1 by patient gender (man vs woman) will be stratified by participating country and physician gender. This design will allow us to explore if and how physician gender, patient gender and their intersection leads to a differential risk of experiencing prescribing cascades between older men and women. It will also afford us an understanding of whether varying geographical, and thus sociocultural contexts, may influence this process.

Patient and public involvement

Patients and the public have not been involved in the research process thus far.

Vignette

Clinical vignettes have high internal and external validity and are among the most commonly used tools for examining implicit biases among healthcare professionals. To select an appropriate prescribing cascade for the vignette, we began by reviewing a list of clinically important cascades highly rated by a panel of clinicians through a modified Delphi process—a study completed as part of a separate objective of the iKASCADE project. Through brainstorming and collaboration within the international study team, the aim was to choose a prescribing cascade that met the following requirements:

1. The cascade is not strongly associated with any major physiological sex differences (ie, a prescribing cascade that has been shown not to have a significantly higher prevalence in one sex over the other). This is to help ensure that our examination of gender bias in decision-making was not influenced by a provider’s knowledge and understanding of a condition and its association with certain male or female physiological traits. Other prescribing cascades were considered and ruled out for this reason, such as the diuretic ->incontinence ->overactive bladder medication cascade, due to the higher prevalence of urinary incontinence in women compared with men.

2. The cascade includes drug classes that are commonly prescribed and well known to physicians in each of the participating countries (Canada and Italy). Other cascades were ruled out for varying reasons, such as being too easily recognisable (eg, antipsychotic ->extrapyramidal symptoms ->antiparkinsonian agent), or because they may be too difficult to directly attribute (eg, non-steroidal anti-inflammatory drug ->hypertension ->antihypertensive medication). Ultimately, the following prescribing cascade was chosen as best suited based on the above criteria: calcium channel blocker ->peripheral oedema ->diuretic cascade (figure 1).

The final vignette (online supplemental file 1) was developed through an iterative and collaborative process among international research team members, particularly...
among the iKASCADE Sex and Gender Working Group, and was designed to present a case where a patient, recently prescribed amlodipine (calcium channel blocker) for hypertension, reports concerns of swelling in the lower legs and feet. Clinician members of our team, including physicians and pharmacists, added clinical details that reflect a realistic patient encounter with an older adult. Two versions of the vignette were developed, identical in all details except for patient gender.

**Study population, recruitment and sampling**

Eligible participants will include primary care physicians licensed in one of two participating countries (ie, Canada or Italy), with a minimum of 3 years of experience prescribing or managing pharmacotherapy for older adults. Study recruitment will vary by site given the need to adapt to the local institutions, health system structures and professional networks for the most efficient recruitment, as well as to adhere to research ethics board requirements for the respective institutions. In Canada, two approaches will be used: active recruitment of primary care physicians using publicly accessible contact information, and self-referral based on a study flyer distributed via a host of primary care networks and listservs (eg, Ontario College of Family Physicians). In Italy, primary care physicians will be recruited by direct contact or from small healthcare organisations. Teams will conduct purposive sampling of men and women in efforts to achieve balance of gender among participants as much as possible. We will have regular working group meetings to help sites stay on track and discuss status updates on recruitment. On recruitment, participants will be blinded to the main study objective to avoid interference with implicit processes and the introduction of social desirability bias (ie, tendency to respond in ways that are more appropriate or socially acceptable). Instead, they will be informed that the objective of the study is to examine clinical prescribing decisions for older adults. Additionally, participants will not be informed that this is a project of the iKASCADE Study Team until the conclusion of the interview, given the possibility that participants will know, or discover, that the purpose of the iKASCADE project is to examine prescribing cascades through a sex and gender lens.

A minimum of 10 and a maximum of 20 interviews will be conducted at each site, for a total of 20–40 participants; the high end of this sample size aligning with similar work examining racial and gender bias in clinical decision-making using qualitative vignettes. We will aim to recruit an equal number of men and women physicians to allow for even randomisation to man and woman patient vignettes. This will also allow for exploration of the intersection of physician and patient gender and the potential effect of gender concordance or discordance in clinical decision-making. To ensure that perspectives across all levels of experience are included, we will aim to recruit physicians at a variety of career stages (eg, <10 years of experience, 10–19 years and ≥20 years).

**Data collection**

Data will be collected through individual interviews to understand the decision-making processes of physicians and to determine if and how a patient’s or prescriber’s gender influences a physician’s likelihood to initiate a prescribing cascade.

**Interviews**

Interviews have been designed to take between 30 and 45 min and will be conducted through videoconference. Interviews will be audio recorded and transcribed using built-in transcription software, the accuracy of which will be confirmed against audio recordings. Interviews will be conducted in English in Canada and in Italian in Italy. Italian data will be translated into English prior to analysis using Google Translate. A study team member fluent in Italian and English will then review each translated transcript and verify against the original to make any necessary corrections, ensuring the quality and reliability of the translation.

Interviews will be conducted by experienced qualitative researchers who are familiar with prescribing cascades. All interviews will be provided with medical background information on the vignette in preparation for the interviews. In addition, interviewers will be trained on using the think-aloud approach to ensure they probe and elicit detailed descriptions from respondents about their approach to, and rationale for, their clinical decisions. The interviewer and/or assistant will be encouraged to write field notes following each interview, recording features of the setting (ie, mood, noises or distractions), the rapport between the participant and interviewer (ie, focused, excited, defensive), and overall impressions of the interview (ie, issues, new insights).

The interview will begin with a brief questionnaire to collect information on the participants’ demographics including age, sex, gender identity, year of medical graduation and area of specialisation. Information related to their clinical practice such as the location of their practice, composition of their team (ie, solo practice vs group practice), whether they work directly with a clinical pharmacist, and the percentage of older adults in their patient population, will also be collected.
Think-aloud
In this study, participants will be asked to use the think-aloud approach to share their unfiltered thoughts as they read through the clinical vignette. The think-aloud method of interviewing is designed to draw out participants’ conscious and unconscious thoughts by asking them probing questions throughout task completion. This method of cognitive interviewing is particularly valuable for better understanding of thinking and decision-making processes. This method has been used in similar studies in the past, including a recent qualitative clinical vignette study of gender and racial bias among clinicians treating heart failure patients. The interview guide was developed in collaboration with iKASCADE team members from each country (online supplemental file 1). The guide includes probes used to elicit the verbalisation of thoughts, including questions such as ‘what are you thinking about right now?’ as prescribing decisions are considered. The vignette and think-aloud method was pilot tested in a convenience sample of two physicians (one man, one woman) in Canada and two physicians in Italy (one man, one woman) for quality improvement of the interview guide in terms of clarity and flow of questions, and the timing of the interview. After an initial set of revisions prompted by the pilot testing, the study was replicated with an additional two physicians. Specifically, the clinical vignette was divided into two parts (as described below) as we found during the pilot phase that sharing all the clinical information at the beginning of the interview limited our ability to understand any additional information and tests the physician might wish to order when examining the patient.

After receiving consent and collecting relevant demographic information, details regarding their clinical experience and the nature and setting of their practice, participants will be introduced to the think-aloud method and given a chance to practice with a short exercise adapted from Leighton. Once attuned to the process, the vignette will be displayed on a computer screen in two parts. Part 1 will describe the patient (ie, age, sex, race), their medical history, the medications they take and their current concern, described as swelling in the lower legs and feet. Interviewers will probe participants to verbalise their thoughts, as well as ask whether there is any additional information they might wish to have. Part 2 will present clinical details that would be gathered through physical examination (eg, heart rate, blood pressure, lung or abdominal abnormalities).

At the end of the interview, participants will be asked to share their final recommendations or suggested course of action for the patient, including how they arrived at their decision and which components of the vignette influenced their recommendation. Participants will also be asked to consider their course of action should the sex of the described patient been different. To further investigate the influence of patient gender, additional explicit questions will probe the extent to which the physician’s decision would hypothetically be affected by a variety of sociocultural correlates of gender such as caregiver status, living situation (alone or with a partner), and occupation/income level.

Participants will be verbally debriefed as to the true purpose of the study immediately after completion of the interview and consent to permit use of the data will be sought again at this time.

Should data from a participant require further clarification, study coordinators may request a brief (15–20 min) follow-up interview. These follow-ups will not be recorded, though deidentified notes will be taken and included in the analysis.

Analysis
We will undertake a qualitative thematic analysis of all transcripts, field notes and notes from any potential follow-up interviews; data will be coded using MAXQDA software. The process has been adapted from Jenkins et al, in efforts to account for the contextual factors of each site.

The study’s trustworthiness (ie, credibility, transferability, dependability and confirmability) will be ensured by tracking internal analysis processes, for instance, through frequent debriefing and reflective commentary sessions within the research team, as described below.

The analysis will proceed in four stages, as follows:

Stage 1: within-site analysis
As a first step, a within-site analysis will be conducted at each site. This will allow each research team to become familiar with the data generated at their site, and to reflect on their own data. Initial observations from each site will be written in an analytical memo using a standard template for discussion within their team (online supplemental file 1). This template includes guiding questions for reflection after each interview (eg, reflexivity, surprising responses, noted contradictions, poignant quotations, unanswered questions), as well as for reflection on the interviews collectively (eg, common elements or patterns noted across interviews), and observations related to gender (eg, do female and male physicians reach similar recommendations? Do they provide a similar recommendation for female and male patients?).

Stage 2: between-site analysis
Next, we will collectively discuss the analytic memos generated by each site, first considering each site individually to deepen our understanding of site-specific observations. We will then collaboratively identify patterns across sites, exploring similarities and differences to develop overarching themes. This work may require several meetings. Each meeting will be conducted via Zoom and audorecorded to create an audit trail of discussions and decisions.

We will use our meetings and discussion to develop a standardised codebook (ie, master codebook with definitions and representative quotations), to improve reliability and consistency of coding across sites. The codes in the codebook will focus on issues related to the research
questions and patterns generated from our discussions, rather than exhaustive line-by-line coding of the entire dataset.

Stage 3: second within-site analysis
Each site will then proceed with a second within-site analysis to apply the master codebook to their data. This will ensure that all relevant data from the interviews will be identified and included in the analysis. Site-specific data will also be maintained separately at each site and will be used to inform ongoing discussions of findings.

After coding two transcripts per site, a multisite meeting will be held to discuss how this second analysis is progressing. Coders will have the opportunity to discuss any gaps in the codebook, or challenges and inconsistencies in the coding process. If needed, the codebook will be modified and applied at each site to the site-specific data.

The two coded transcripts from Italy will then be securely transferred to the Canadian site where coded transcripts will be compared with assess consistency in coding between coders and across sites. This comparison will be used to gauge agreement and understanding of the definitions of the codes among team members and to facilitate discussions and reflections on the data at a subsequent meeting to improve any required coding consistency.

Stage 4: final manuscript
To write the final manuscript, all coded transcripts from the two sites will be analysed. The Canadian analysis team will follow the last three steps of thematic analysis from Braun and Clarke—review themes for coherence and consistency, define and name themes, and weave themes into a narrative.28

The manuscript will include focused consideration of how observed nuances or differences may be explained by how gender is conceptualised and enacted in each participating country. To facilitate this exploration, we created country-level gender portraits that consolidate existing gender equality information on a country (from sources like the World Economic Forum’s Global Gender Gap Report and the Organisation for Economic Co-operation and Development’s Social Institutions and Gender Index Reports)33 34 and organised information into four domains from an adapted Jhpiego gender analysis framework.15 These domains include: (1) institutions, laws and policy, (2) access to assets, (3) practices and participation and (4) beliefs and attitudes. We will contextualise findings with these portraits to explore how socially constructed power relations and gender norms in each country may explain patterns we observe across sites.

Each site team will critically review the manuscript and ensure its analysis and presentation of data is consistent with the data and discussions throughout the analysis stage.

Data storage and protection
All audio recordings will be downloaded from the Zoom Cloud and securely stored on the password-protected server at each study site. Transcripts will be deidentified to protect the confidentiality of each participant. The coded Italian transcripts will be securely transferred to the Canadian site. These files will be transferred according to European Standards of Data Transfer. Once in Canada, these documents will be stored on the Women’s College Hospital password-protected network server.

DISCUSSION
With a rapidly ageing global population, promoting healthy ageing and the well-being of older adults is a chief public health priority. More recently, reducing polypharmacy and inappropriate prescribing have been recognised as primary components of this priority. For example, the WHO’s third Global Patient Safety Challenge, the Medication without Harm initiative, acknowledges the increased risks of drug-related harms among older adults.33 While there exists evidence of unequal risk of drug-related harm between men and women, efforts to address these harms have not adequately integrated sex and gender considerations. In fact, a recent review of the existing tools and frameworks for reducing inappropriate prescribing reported that none of the products addressed sex or gender differences in prescribing.3 The aim of the iKASCADE project is to help fill this knowledge gap by advancing research on prescribing cascades among older men and women to ultimately improve drug safety for older people globally.

In recent decades, various mandates and guidelines have required the inclusion of sex and gender considerations in all health research to improve rigour, inclusivity and impact.36–39 This study, as the first to explore the potential role of gender bias in the context of prescribing cascades, can help to provide further insight into the ways in which physicians’ implicit attitudes surrounding gender may influence prescribing decisions and potentially introduce harm through inappropriate prescribing. By applying a multinational perspective to the project, we can further dissect how varying geographical and health system contexts and sociocultural constructions of gender may lead to differential patterns of prescribing for men and women between countries. The results of this study can thus contribute to improving and tailoring medical education to encourage awareness and challenge personal biases.

ETHICS AND DISSEMINATION
The study protocol has been reviewed and approved by the Women’s College Research Institute’s Research Ethics Board (2022-0036-E), and the Italian National Institute of Health and Science on Ageing (IRCCS INRCA) Ethics Committee. Verbal informed consent will be received from participants at the beginning of the interview and...
again at the end once they have been debriefed on the true objective of the study. All data will be deidentified and stored on a password-protected network server at the Women’s College Hospital. We plan to disseminate results in a peer-reviewed manuscript, in addition to presentations at relevant national and international conferences.

Current status of the study
Data collection will begin in September 2022. Results are expected by March 2023.

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Correction notice This article has been corrected since it was published. Affiliation 5 and 10 has been corrected.

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