Sex differences in health research and clinical guideline development
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Summary
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In current medical practice, research based evidence is an important foundation for clinical decision making. Clinical practice guidelines are a major instrument for keeping physicians up-to-date about this evidence. In order to provide optimal care to both men and women, it is important that sex differences are routinely considered in biomedical studies and that the results—positive or negative—are routinely reported in clinical guidelines. However, there is still limited attention given to sex differences in health research and in guideline development. Public organizations for the funding of health research and guideline development organizations can play a role in improving this situation.

This thesis presents a series of studies which evaluate the consideration of sex differences in health research and guideline development in the Netherlands by studying research proposals submitted to a Dutch financer of health research and the clinical guideline development process of two main Dutch guideline developing organizations.

Chapter 2

The second chapter describes a study on the effect of formal incentives to enhance the consideration of sex differences in health research proposals submitted to the Netherlands Organization for Health Research and Development (ZonMw). For this study we sampled 213 health research proposals submitted to ZonMw in 2003. Half of these proposals had been submitted to a ZonMw programme that provided specific instructions on how to consider diversity issues in health research proposals (Prevention), and the other half to a programme which provided a more general set of instructions regarding this issue (Innovation).

These proposals were analysed with regard to the expressed intention to take sex differences into consideration. Furthermore, those proposals in which such an expressed intention was absent were appraised by researchers to determine whether an intention of this kind would have been relevant. We found that 23% of proposals submitted to Prevention and 10% of those submitted to Innovation took sex differences into account (difference 13%; 95% CI: 3.1-22.9). Conversely, 66% of the research proposals in Prevention, and 20% in Innovation, failed to take sex differences into consideration, even though this might well have been relevant.

We conclude that the incentives provided by ZonMw are still insufficient to motivate researchers to describe if or how they plan to pay attention to sex differences in their research. Based on evaluations of similar initiatives in other countries we formulate recommendations on how ZonMw might amend its policy.
Chapter 3

In this chapter we examine the way in which two Dutch guideline organizations, the Dutch Institute for Healthcare Improvement (CBO) and the Dutch College of General Practitioners (NHG), addressed evidence on sex factors in their guideline development methodologies. We determined whether attention to these factors could be improved and, if so, how this could be done.

For this we selected seven recent guidelines on four conditions: hypertension, depression, osteoporosis, and rheumatoid arthritis. We studied information obtained from interviews with members of the guideline committees and analysed the content of the guideline documents. As part of our method, our findings were discussed at a meeting of experts.

We found that all the guideline committees concerned applied an internationally accepted framework for guideline development. The proportion of male members ranged from 67% to 100%. None of the guidelines we studied included a question (or subquestion) focusing on sex-related factors. In the literature searches no sex-specific search terms were used. Critical appraisals did not include any systematic focus on sex-related factors or effects. The number of sex-specific recommendations (relative to the total number of recommendations) ranged from 0 of 82 and 0 of 148 in the guidelines on depression to 16 of 84 in one of the guidelines on osteoporosis.

In this chapter we conclude that when developing guidelines, none of the committees systematically focus on sex-related factors that might be relevant to the way in which evidence is identified, appraised, or described. A number of recommendations are made with the aim of facilitating greater attention to sex-related factors in the current methods of guideline development.

Chapter 4

Based on the study reported in Chapter 3, in collaboration with CBO and NHG, we designed a tool kit and training course to encourage systematic attention to sex differences in guideline development procedures. Chapter 4 describes the development of this toolkit and training course. The course was targeted towards guideline developers. Its aims were to improve awareness of the relevance of considering sex differences in the guideline development process, as well as the competence and skills necessary for putting this into practice.

The design and teaching methods of the course were based on adult learning styles and principles of changing provider behaviour. It was adjusted to the working methods of guideline organizations. The course was taught to, and evaluated by, a group of staff members from CBO and NHG. We developed a course with five modules, each of which corresponds to a key step in the guideline development process.

The participants rated the training course positively in terms of content, programme, and trainers. Their written comments suggested that the course met its
objectives. In this chapter we conclude that the training course is the first to address sex differences in guideline development. Because the modules and teaching methods of the course are widely transferable, the course could be useful for many organizations that are involved in developing guidelines.

Chapter 5

Chapter 5 investigates the effect of the training course and a second intervention, expert feedback, to enhance the consideration of sex differences in clinical guideline development. The interventions were tested in six CBO and NHG guideline developing committees. The interventions were evaluated by means of a pre- and post-intervention questionnaire in intervention and control groups for measuring the attitudes of guideline developers concerning the importance of considering sex differences. A content analysis of intervention guidelines and former versions was performed to measure the number of sex-specific statements in the contents of guideline documents.

We found that the attitude of the intervention group did not change significantly relative to the control group. Consideration of sex-related factors in the guidelines increased relative to available previous versions.

We conclude that education and expert feedback may increase the consideration of sex differences in guidelines. However, further efforts are needed to implement and test these interventions.

Chapter 6

For the study presented in this chapter, staff members from guideline development committees (GDCs) were offered the training course and expert feedback to facilitate attention to evidence on sex differences. Characteristics of discussions on sex-specific issues in six GDCs supported by trained staff members were evaluated on subject matter, initiator, group approach towards the topic and themes, and whether or not conclusions were reflected in the final guideline text.

Evaluation was conducted by means of non-participant observation and transcriptions of audio recordings from 22 GDC meetings, and content analysis of meeting transcripts and guidelines. Of 87 identified discussion episodes, 68 dealt with sex-specific research issues potentially relevant to guidelines. Respectively 51%, 28% and 21% of these discussion episodes were initiated by committee members, staff members and chairpersons. Group approaches towards the subject matter were generally positive. Data from 60% of these discussion episodes were reflected in the final guideline text. Sex-specific data on reproductive issues were more often discussed and reflected in guideline texts than those on other health issues. Discussion episodes initiated by chairpersons were most often reflected in the guidelines.
In this chapter we conclude that the GDCs guided by staff members trained in using our framework regularly focussed on sex-specific issues. However, attention to sex-specific information on other than reproductive health issues was limited.

Chapter 7

In the final chapter, we provide a summary of the main findings and reflect on the research methods used. In addition, the findings of the studies are reflected upon, and recommendations for health financing organizations, guideline developing organizations and future research are made.

In short, the following main conclusions can be drawn from the studies: sex differences are not yet considered in health research proposals in which this might have been relevant. Therefore, efforts are still needed to enhance the consideration of sex differences in health research proposals. Two main guideline developing organizations in the Netherlands did not consider sex-related issues systematically during guideline development at the onset of this project (2002). During the past six years their consideration of sex-related issues in guideline development has been enhanced and both organizations are making efforts to further improve the attention given to these issues. Follow up research will be needed to enhance the consideration of sex differences in health research and guideline development.