Fair inclusion of men and women in Australian clinical research: views from ethics committee chairs

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ABSTRACT

Objective: To explore the role played by human research ethics committees (HRECs) with regard to the fair inclusion of men and women in Australian clinical research.

Design and participants: Semi-structured face-to-face and telephone interviews with 25 chairs (or their nominees) of Australian HRECs between 9 June 2006 and 24 January 2007.

Main outcome measures: Chairs' views about the role of HRECs in identifying sex discrimination, monitoring the inclusion of men and women in clinical research, and interpreting and applying National Health and Medical Research Council (NHMRC) guidelines relating to fair inclusion in research.

Results: In general, HRECs do not take an active role in monitoring the sex of research participants. They do not ask for or often receive information about the sex of participants. Most HREC chairs did not believe that sex discrimination in research is currently a significant or widespread problem, and were confident that their committees would be able to identify arbitrary exclusion of either men or women from research. However, many chairs expressed a lack of familiarity with debates about sex equity in research. Most chairs were unaware that anti-sex-discrimination legislation could apply to research. "Fair inclusion" was interpreted in a number of ways by chairs, but most frequently that the sex balance among research participants should reflect the sex distribution in the community of the condition under investigation. Chairs said their committees would be reluctant to reject a research protocol on the grounds that the sex balance among participants was perceived to be unfair.

Conclusion: Views about, and expertise on, sex equity in research vary among chairs of HRECs. Many HRECs require further guidance about the appropriate standards for fair inclusion of men and women in Australian clinical research.

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There is clear historical evidence that women have been excluded from landmark research studies.[1] Recent research shows that women over the age of 65 years continue to be under-represented in research, and that men are over-represented in studies of heart disease, and colorectal and lung cancer trials.[2-4] Yet, there are recognised sex (biological) and gender (sociobehavioural) differences in the incidence, treatment responses and prognosis of a range of diseases, including arthritis, depression, heart disease and infectious diseases.[5-10] Conducting research on unrepresentative research populations limits the applicability of research findings. Lack of evidence about the effectiveness of medical interventions in women may result in both withholding treatments from women that may be beneficial and exposing them to treatments that may be harmful.[11]

Research guidelines now argue that sex and gender should be considered when designing and analysing the results of studies in all areas of biomedical and health-related research.[12,13] For example, in 1993, the United States introduced the NIH Revitalization Act (Public Law 103-43), which mandated the inclusion and monitoring of women and minorities in all health research funded by the National Institutes of Health (NIH).[14] Research on humans in Australia is governed by the *National statement on ethical conduct of research involving humans* (hereafter the National Statement),[15] issued by the National Health and Medical Research Council (NHMRC), supported by the *Human research ethics handbook*.[16] The 2007 National Statement contains a revised section about the inclusion of men and women in research; see Box 1 for a comparison with the 1999 version.

In this study, we explored how human research ethics committees (HRECs) understand their role in interpreting and monitoring sex equity among Australian research participants. Our focus was on the inclusion of men and women in Australian research; some research participants referred to this as sex equity and others as gender equity.

METHODS

We interviewed chairs of HRECs to determine how they interpret and apply the principle of "fair inclusion of participants" prescribed by the National Statement. Interviews were structured around six topics: enquiries about the sex of participants; monitoring of recruitment by sex; legal requirements; the role of HRECs in ensuring appropriate inclusion of women in Austra-

1 Requirements relevant to the inclusion of men and women in research in the *National statement on ethical conduct of research involving humans* in 1999[16] and 2007[15]

Title	1999 National Statement	2007 National Statement
Section	1. Principles of ethical conduct	1. Values and principles of ethical conduct
Sub-section	Integrity, respect for persons, beneficence and justice	Justice
Requirements	Para 1.5b . . . design research so that the selection, recruitment, exclusion and inclusion of research participants is fair	Para 1.4a . . . taking into account the scope and objectives of the proposed research, the selection, exclusion and inclusion of categories of research participants is fair
	Para 1.5c . . . not discriminate on the grounds of sex	Para 1.4b . . . the process of recruiting participants is fair
		Para 1.4d . . . there is fair distribution of the benefits of participation in research

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lian research; use of guidelines regulating sex of participants in research; and defining "fair inclusion" of men and women. The interviews were semi-structured, and conducted either face to face or by telephone, between 9 June 2006 and 24 January 2007. Participants' responses were taped, transcribed and deidentified.[17,18] Pseudonyms are used throughout this article. Participants gave written permission for the use of selected quotes in publications.[19] To maintain consistency in data collection, one researcher (A J B) conducted all of the interviews.

This project was approved by the Flinders University Social and Behavioural Research Ethics Committee and the University of Sydney HREC.

Data analysis

Data were managed within NVivo qualitative data analysis software (version 7; QSR International, Melbourne, Vic). Data analysis combined deductive and inductive methods: original coding categories were based on the interview questions and further categories were added as themes emerged from the data in an iterative process.[17-22] Both authors read all transcripts and contributed to the analysis.

RESULTS

From a possible 225 HRECs in Australia,[23] we interviewed 24 chairs and one nominee. Thirty-two per cent of our sample was female, reflecting the national average (in 2006, 31% of the chairs of Australian HRECs were women [Catherine Chippendale, Project Officer, Health Ethics, NHMRC, personal communication]). Our sample included chairs of committees serving institutions ranging from large public hospitals and universities to specialist or community committees. Their workloads varied from a low of 15 to a high of over 700 protocols reviewed per year.

Enquiries

HRECs do not specifically enquire about the sex balance of participants in research. No HREC had a set question about the sex of participants or the sex and gender dimensions of the research in their application forms. When studies are open to both sexes, researchers rarely provide a description of the intended balance of males and females or their recruitment strategies for achieving this. About a third of the chairs could recall a case where they had questioned researchers about possible sex discrimination. Specific examples of research which raised ethical concerns for chairs because of the exclusion or under-representation of men or women are presented in Box 2. However, no chair could recall a case where they had rejected a research protocol on the grounds of sex discrimination or unfair sex balance among participants.

2 Examples given by human research ethics committee chairs of potentially discriminatory research

Direct exclusion

Physiology studies: Women were excluded from studies on tissue samples because of the effect of female hormones on the physiological process being investigated. Researchers argued that it is easier, quicker and cheaper to conduct the study on a homogeneous male population.

Obstructive sleep apnoea: Researchers frequently include only men in these studies because oestrogen affects breathing patterns and can therefore complicate research results. Although the population affected by obstructive sleep apnoea is predominantly male, women are also affected by this condition.

Indirect exclusion

Alzheimer's disease: Patients with Alzheimer's disease in clinical trials require a full-time carer to provide objective assessment of their progress. Most eligible participants are men who are living at home, cared for by a female spouse. This results in most patients in trials on Alzheimer's disease being male, despite the fact that most of the population affected by Alzheimer's disease is female.

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Monitoring

No HRECs request any reporting of participants' sex. Some chairs noted that this information might be provided incidentally if the final report included a publication, or if the researchers received funding from the NIH or from a pharmaceutical company.

Legal requirements

Most chairs were unaware of any Australian legal requirements concerning sex equity in research; however, four mentioned antidiscrimination legislation. No chair recalled discussion of antidiscrimination legislation in relation to sex balance among research participants. When prompted, most thought that this legislation would be relevant if it could be shown that a researcher was actively discriminating against one sex. Many chairs were sceptical of the utility of legislation in helping researchers and HRECs to think through the complexities of "fair" and "non-discriminatory" sex balance in research.

HREC roles

Chairs commonly noted that women had historically been excluded from research, but thought that researchers are now aware of the problems associated with unrepresentative research populations and that a cultural shift had taken place over the past 10–15 years. Most chairs thought the HREC system is adequately equipped to detect and respond to overt sex discrimination in research protocols:

> I'm sure if there was a [bias] in some way, someone would have picked it up in our committee. — *Frank*
>
> I don't think it's ever come up, but I certainly think the committee would deal with it if it did. A researcher that was aiming at studying males or females only, for no good reason, would probably be rejected. — *Victor*

Most chairs acknowledged that sex balance in research was not a high priority. During the course of the interviews, about half of the chairs questioned whether their committee did not see sex discrimination as a problem because they lacked familiarity with these issues, or because the research protocols they reviewed genuinely did not raise issues of under-representation. Committees that were concerned about how men and women were included in a research protocol often felt that they did not have the authority to enforce a particular normative standard. Some chairs maintained that, aside from arbitrary exclusion of males or females, sex balance in a study is a question of scientific merit, to be determined by the researchers.

> The researchers have got to work out the science of their study and . . . I don't think it's up to ethics committees to go around saying you can't do that because you've got the gender balance wrong. — *Nathan*

Guidelines

No chair could recall their HREC actively consulting guidelines about fair inclusion of men and women in research. Most were aware that the National Statement requires "just" selection of the research population, and assumed that this required researchers to avoid sex discrimination in recruitment. Most chairs had not considered the question of fair inclusion of men and women in clinical research before this interview. Some chairs took a normative stance and argued that the sex of research participants was not an important ethical issue for either researchers or HRECs.

> I'm not sure that, you know, being a human guinea pig is just such an honour that, you know, women are queuing up to not be discriminated against or males are queuing up to not be discriminated against. — *Wendy*

Definitions of "fair inclusion"

The 2007 National Statement does not explicitly mention sex discrimination, but relies on the concept of "fair participation/inclusion" of research participants (Box 1). It is therefore important to understand how HRECs interpret this standard. Four different definitions of fairness were discussed: (i) no arbitrary exclusion on the grounds of sex; (ii) equal numbers of men and women (for conditions that affect both sexes); (iii) proportional numbers of men and women according to the sex distribution in the patient population; and (iv) sufficient numbers of men and women to support valid analysis of sex differences in the research results. Definitions (i) and (iv) were most frequently endorsed, with most chairs arguing that research should reflect the patient population. No chairs supported a requirement for equal numbers of men and women in trials. Some chairs would like to require analysis of sex and gender differences in well funded studies, but thought this would impede smaller studies.

Having considered the four potential definitions of fairness, many chairs concluded that HRECs do not have sufficient guidance about the standards of fair inclusion they should be applying to research.

> The problem with gender issues is that it's not really clearly articulated in the National Statement and it is open to interpretation. — *Quentin*

> So while [HRECs] recognise it's an issue, and some more legitimately than others, it's sort of the too hard basket . . . unless you've got some fairly clear tools to be able to handle those sorts of complex issues. — *Grant*

Chairs' opinions were divided as to whether cost and convenience were justifiable grounds for excluding men or women from research. Some said that they accepted studies that excluded one sex on the grounds of cost in cases where, in their view: (i) participation conferred no direct benefit to participants; (ii) it was better that the studies were undertaken on one population than on no one; (iii) the results from one sex would be applicable to all populations; and (iv) the studies would be replicated in other populations in the future. The combination of these arguments demonstrates the historical assumption that female biological processes are, paradoxically, thought to interfere with research to a sufficient degree to justify the exclusion of women, and yet men and women are thought to be homogeneous enough that research results from male studies can be generalised to women.

Many chairs were concerned that stricter regulations regarding sex equity in research would impede research.

> It is more unethical to have no research than to have gender [in]equality research. — *Sam*

> Because, you know, at the end of the day, it's probably better someone was studied rather than no [one]. — *Jason*

DISCUSSION

Our findings indicate that Australian HRECs do not play an active role in monitoring the inclusion of men and women in Australian clinical research, for three key reasons. First, HRECs in general do not consider this to be an important issue, possibly because they lack familiarity with complex international debates about sex and gender equity in research. Second, when HRECs do identify apparent sex discrimination or unfair recruitment strategies, they do not believe they have a clear mandate to reject research protocols on these grounds alone. Third, some HRECs do not believe that research should be impeded on the grounds of sex inequity among the research participants.

It remains unclear whether HRECs are missing important gender and sex dimensions of studies because these issues are not considered to be priorities during ethics review, or whether Australian researchers are not submitting protocols that discriminate on the grounds of sex.

HRECs require further instruction from the NHMRC about how to interpret and apply the generic principle of fair inclusion. Other jurisdictions have provided explicit instruction on appropriate standards for the inclusion of men and women in research. For example, section 492B of the 1993 US NIH Revitalization Act prohibits the use of "cost" as a reason for excluding or under-representing women in NIH-sponsored research.

Australian HRECs apply varying standards of fair inclusion of men and women in research, lack a unified view about appropriate exclusions, and are reluctant to impede clinical research. As one chair pointed out, including questions about sex and gender in the National Ethics Application Form would both raise awareness of sex equity issues and systematically lead researchers and HRECs through relevant questions about when and in what proportion to include men and women in research, and when to include planned statistical analyses of sex differences.

COMPETING INTERESTS

None identified.

AUTHOR DETAILS

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