

GenderBasic Final Report

**Promoting integration of the gender dimension
in biomedical and health-related research
Gendered and translational approaches in basic,
clinical and public health research**

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GenderBasic



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Promoting integration of the gender dimension in biomedical and health-related research
Gendered and translational approaches in basic, clinical and public health research
EU FP6 Women and Science Specific Support Action
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Attention to the gender dimension in research

Attention to the gender dimension in research requires a clear distinction between the concepts sex and gender. Sex refers to biological characteristics as chromosomes, physiology and anatomy that distinguish men and women. Gender refers to the array of socially constructed roles and relationships, personality traits, attitudes, behaviours, norms and values that society ascribes to men and women on a differential basis.

To this background, attention to the gender dimension in research in the life sciences and biomedicine, requires attention to both sex characteristics and gender characteristics (when relevant) and if possible also to the complex interactions between sex and gender. (Based on: Klinge and Bosch, 2001. Gender Impact Assessment Study of the Thematic Programme “Quality of Life and Management of Living Resources” of the Fifth Framework Programme, EUR 20017).

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Specific Support Action GenderBasic: Promoting integration of sex and gender in (basic) life sciences research

Introduction

The European Commission (EC) has adopted Framework Programmes for Research with the aim to finance research that is in line with their policy goals. A long standing policy goal has been to promote gender equality. This policy has become enshrined in consecutive treaties and was for the first time applied to *research* under Framework Programme 5 (FP5). (Klinge & Bosch, 2005). Mainstreaming gender equality in research embraces both the stimulation of the participation of women in research at all levels and the consideration of the gender dimension of the research content.

In 2000-2001 the EC commissioned a series of Gender Impact Assessment (GIA) studies of the specific programmes of FP5. The aim of these studies was the evaluation of the gender dimension in the development, management, and implementation of the Framework Programmes. These studies, which were executed by 7 research teams, investigated the participation of women in research and analyzed whether the research themes, methods, and issues prioritized in FP5 affect women and men differently. Conclusions and recommendations were intended for the preparation and implementation of the next Framework Programme, FP6.

We conducted the GIA study of the *Quality of Life and Management of Living Resources* Programme that addressed the broad range of life sciences research (Klinge & Bosch, 2001). An important conclusion was that the term 'gender dimension' for life sciences research should be understood as attention to both sex differences and to socio-cultural gender effects if relevant. The study has had a big impact. Its recommendations were firmly implemented in FP6 (2002-2006). New guidelines were introduced for applicants submitting proposals in thematic priority 1.1.1. *Life sciences, genomics and biotechnology for health* but were also relevant to thematic priority 1.1.5 *Food Quality and Safety*.¹ Applicants had to answer a set of specific questions as regards integration of the *gender dimension*.² Integrated Projects and Networks of Excellence also had to write a Gender Action Plan (Vademecum, 2003, European Commission, 2004).

GenderBasic Project

Biological and socio-cultural differences between women and men may result in different epidemiological patterns and effect modification of diagnostic, preventive and therapeutic interventions. For many researchers integrating a sex and gender dimension in their research presents a new challenge. They furthermore may encounter a variety of conceptual, methodological, practical, ethical and financial problems as they try to integrate sex and gender aspects in their research. Some progress has been made in clinical research in the USA. (Roth, 2000; Vidaver, 2000). However, recommendations by influential bodies such as the Institute of Medicine (IOM) (Wizemann & Pardue 2001, Editorial 2001) and others (Greenberger 2001, Greaves 1999, Health Canada 2000) to address potential sex differences in *basic* research have not been widely taken on board. Applying the FP6 guidelines to basic (European) research involving cells, tissues, other materials and animals seems to be confronted with many practical problems and a lack of expertise. Researchers are not unwilling to take sex and gender into account, but are facing difficulties. Consider for example a shortlist

1 The rationale was given in a footnote to the FP6 work programme: *"Risk factors, biological mechanisms, clinical manifestation, causes, consequences of disease and disorders may differ in men and women. In such cases, diagnosis, prevention, treatment, and management need to be adapted according to sex and gender. Consequences for not doing so impinge on the health of both women and men"*.

In the FP7 work programme for Theme I Health (p.8) it said:

"Gender aspects in research have a particular relevance to this Theme as risk factors, biological mechanisms, causes, clinical manifestation, consequences and treatment of disease and disorders often differ between men and women. The possibility of gender/sex differences must therefore be considered in all areas of health research where appropriate."

2 Application Form (B 10): questions to answer:

Gender/sex aspects in a proposal if YES to any of the questions:

- Does the project involve human subjects?
- Does the project use human cells / tissues/ other specimens?
- If human subjects are not involved or human materials not used, does the research involve animal subjects or animal tissues (as models of human biology/physiology) in such a way that it is expected that it may have implications for humans?
- Does the project use collection of data related to human subjects, human materials, animal subjects or animal materials?

Are gender/sex differences with respects to the research documented in the literature? YES/NO

- If yes please give details
- A negative answer to this question may imply some innovation in the proposal towards this issue that will be taken into account in the evaluation process

of problems put forward at the meeting of the Commission Network on Gender Aspects in Food Quality and Safety Research (GENDFOODSAFE) on Jan 13th , 2004:

'Why is integration of the gender dimension a good thing to do?'

'What is the theoretical basis?'

'We foresee methodological issues (confounding, effect modification)'

'We foresee practical issues (the raising of female rats)'

'How about financing larger studies?'

'What are the ethical problems? (more persons exposed to testing)'

'Jokes were launched ridiculing the gender issue: 'what is the sex of your cells today?'

Apparently, a translation of the guidelines to the level of actual research practices was needed. As we had been involved in drawing up the recommendations, we were now challenged to answer the FP6 call concerning the development of tools for integration of the gender dimension in life sciences research. Thus, the GenderBasic project was conceived that ran from October 2005 to January 2008. Its main objective was to provide scientists involved in health-related research (with a focus on basic and clinical research) funded by the EU Framework Programmes with practical tools, relevant examples, and best practices regarding sex and gender differences in the content of their research.

The project consisted of the following activities:

- An assessment of facilitating and inhibiting factors for the incorporation of attention to sex differences and/or gender effects in basic and clinical research among selected FP6 life sciences research projects (WP 2)
- An assessment of facilitating and inhibiting factors for the incorporation of attention to sex differences and/or gender effects in basic and clinical research among research coordinators of acclaimed European Research Institutes in the life sciences (e.g., Inserm, Charité, Karolinska) (WP 3)
- The production of topical papers by experts, describing best practices and possible solutions for identified methodological and conceptual issues: (e.g. equitable inclusion of men and women, sub group analyses data, sex-gender interactions)(WP 5)
- A meeting for researchers and experts to discuss proposed solutions on issues regarding the incorporation of attention to sex differences and/or gender effects in the content of basic and clinical research. (January 26-27, 2007)(WP 5)
- The development of tools to advise EU services, researchers and research evaluators on how to improve attention to the gender dimension in basic and clinical research (WP6)

In this way GenderBasic aimed to contribute to the development of standards and to improve the quality of research in order to meet the goals set by the EU concerning scientific excellence.

Integrating attention to the gender dimension in the research activities of IP's and NoE's financed by the 1st and 2nd call of TP5 Food Quality and Safety of FP6. Summary of Work Package 2.

The full report is available from www.GenderBasic.nl

Objective

The aim of this work package was to explore how participants of Integrated Projects (IP's) and Networks of Excellence (NoE's) financed by the first and second calls of Thematic Priority Food Quality & Safety (TP5) of FP6 experience the process of integrating the gender dimension in their research activities³.

Background

In FP6 the European Commission introduced new measures to promote attention to the gender dimension in the content of EU funded research. In the view of the European Commission attention to the gender dimension in research requires a clear distinction between the concepts sex and gender. Sex refers to biological characteristics as chromosomes, physiology and anatomy that distinguish men and women. Gender refers to the array of socially constructed roles and relationships, personality traits, attitudes, behaviours, norms and values that society ascribes to men and women on a differential basis. To this background, attention to the gender dimension in research in the life sciences and biomedicine, requires attention to both sex characteristics and gender characteristics (when relevant) and if possible also to the complex interactions between sex and gender.

This work package focuses on researchers in the field of biomedical and health related research in the EU. GenderBasic acknowledges that the EU gender equality policy may meet with resistance in the research community. The successful development of practical tools requires not just attention to policy measures but also to the attitudes, ideas and experiences of those who are to implement these measures: the researchers themselves.

Material and methods

We conducted semi-structured interviews with researchers from 9 IP's and 4 NoE's that were financed in response to the first or second call of TP5. Twelve of them were gender contact persons for their project and one was a project director. To guide the interviews, we used a topic list that focused on the following issues: Are sex- and/or gender-related factors taken into account in the project? How are those factors addressed in the different components of research projects (the research questions, the research design, the methods for data collection, the methods for data analysis and the reporting of the data)? What has been achieved? What has proved difficult? In case the gender dimension was not addressed, we asked more specific questions about the underlying reasons. We also asked questions regarding the organizational aspects of the project and how those aspects facilitate or hinder a focus on the gender dimension in research.

The data were analyzed by means of content analysis and grouped under two overarching themes:

1. How is attention to the gender dimension integrated in the content of the main research activities in the project?
2. Which activities have been undertaken in the project consortia to mobilize attention to the gender dimension in research among the scientists?

Results

The thirteen projects had up to 40 partners and included many different research work packages or sub studies. Seven of the 13 projects included research on humans or human health. Six of the projects included only food-related research with no focus on human health. In all thirteen projects Gender Action Plans (GAP's) were written as an attachment to the main project proposal. With few exceptions these GAP's were not very explicit on how the project would pay attention to the gender dimension in research work packages. Through the interviews we were able to identify three different ways by which the gender dimension was addressed in research activities of the projects in question. Firstly, in five of the six projects which included only food-related studies that did not focus on human health, there was no attention to the gender dimension in the main research activities. The informants of these projects explained this phenomenon mainly by the fact that the topics in this area of research do not lend themselves for attention to sex and/or

3 Originally, projects funded by thematic priority *Life sciences, genomics and biotechnology for health* were also to be interviewed. However, in November 2005, on proposition of the Commission, it was decided to limit this Work Package to priority 5 projects.

gender factors⁴. Secondly, in four of the seven health-related projects occasional attention was given to sex and/or gender differences in the main research activities, as is in accordance with the common research practices in this field. Neither from the interviews nor in the documentation on these projects, however, it became clear where sex and gender differences were expected in the studies or how these differences would be identified. Thirdly, in one food-related and three health-related projects, paying attention to the sex- and gender-related factors was seen as a cross-cutting issue with potential relevance for all researchers. In these projects awareness-raising activities were organized for all researchers. Some researchers in this group were developing new approaches for integrating the gender dimension in research and were therefore also most likely to be aware of the problems that might be associated with the integration of the gender dimension in basic research. However, the informants observed that also in the latter projects many scientists were not interested in integrating attention to the gender dimension in their work. Nonetheless, several of the main research studies in these projects were clearly designed to answer questions regarding potential effect of sex or gender factors. In addition, in four of the five projects in which there was no attention to the gender dimension in the main research activities, small sub-projects were included with a focus on sex- or gender related topics.

In all 13 projects a gender contact person had been appointed who was in charge of the coordination and implementation of the GAP. This is probably an effect of the requirements of the EU gender equality policy. Most gender contact persons saw it as one of their main tasks to mobilize attention to a gender sensitive research approach among researchers in the project. But many of them were still grappling with the problem how this could be done. The data from the interviews suggested that, in order to facilitate this task, the following conditions are essential:

- a budget to implement the GAP,
- a central position of the gender contact person in the project organization,
- a gender contact person who is competent in gender studies,
- a gender contact person who is competent in communicating about gender issues with scientists.

These conditions were only present in a small number of projects, particularly those that had adopted a crosscutting or horizontal gender policy.

Conclusion

One aim of the Gender Equality Policy of the European Commission is to ensure that the consideration of the gender dimension becomes standard practice in research. To achieve this aim, this policy needs to be accepted in the research community. This sub-study has provided examples of three ways in which researchers may react when they are asked to take the gender dimension into consideration into research in the field of food quality and safety:

Some may argue that a gender sensitive approach has no relevance for the subject matter of their research (whether justified or not). Others may argue that such an approach is already incorporated in the existing models of science, and needs no further consideration. Finally, a third group may argue that the consideration of the gender dimension in research requires adaptation of existing ways of collecting and ordering scientific facts.

To gain acceptance for the Gender Equality Policy with respect to research, each of these reactions needs to be taken into account in discussions with the research community.

These findings will be taken into consideration in formulating the final recommendations of GenderBasic.

4 This explanation can be true. That is why a relevance check has been proposed when considering to address sex and gender. See also the question on the Bio form

Promoting attention to the gender dimension in health research: experiences from three centers of excellence in the EU. Summary of Work Package 3.

The full report is available from www.GenderBasic.nl

Background and objective

The GenderBasic project was conceived in Fall 2004, well before FP7 was born. Soon after the GenderBasic project had started in October 2005, new information on the outline of FP7 became available. A major change, as explained by the Commission at that time, was that there will be a new part called 'Ideas'. This new initiative is meant to stimulate creativity, excellence and innovation, and will support investigator and science driven research. There will be no requirements for projects to pay attention to horizontal issues (among which gender issues) and the programme will be steered by the scientific community (European Research Council, ERC). For that reason it seemed interesting to investigate how the research community outside the EU gender equality policy for research would view the integration of the gender dimension. Thus a new work package was added and concentrated on making an inventory of guidelines and / or institutional policies regarding integration of the gender dimension among a selected number of acclaimed European Institutes for life sciences research focusing on fundamental research. By doing so the EU research policy could be compared to non-EU research policies.

Methods

The inventory focused on three high profile medical research institutions in the EU where specific initiatives have been taken to facilitate attention to the gender dimension in biomedical research. Through interviews with key informants, who were well informed about these initiatives, we were able to obtain information on why and how those initiatives were taken, what the research activities are, how they are financed, what the achievements are, and what role the EU may play in supporting such initiatives.

Results

One of these institutions, an INSERM laboratory in Montpellier, introduced the golden rule in its research programme that "one shouldn't make assumptions that men and women are the same, unless we know." This means that researchers have to take account of the fact that there may be differences between men and women due to biologically determined sex factors or socially determined gender factors, at every step of the research process, and in all types of studies from basic research in genetics to social studies. The research programme of this laboratory looks at neurological, environmental and social aspects of pathologies of the nervous system.

The two other institutions, the KAROLINSKA INSTITUTE and CHARITÉ UNIVERSITÄTSMEDIZIN, had established Centers of Gender (in) Medicine, with their own specific programmes for promoting basic, clinical and other types of health research on differences between men and women in diseases and health care, with a focus on biological factors (sex) and gender (socially determined factors). Whereas the establishment of the Centers of Gender (in) Medicine, required good planning and lobbying, the implementation of the INSERM initiative/ golden rule does not seem to have taken much effort.

Despite these differences, the informants mentioned a number of similar conditions, which they perceived as facilitating factors for having been able to develop and sustain these initiatives:

1. Commitment of the management of the institution (and persons in high level position).
2. The presence of female researchers, who seem to be more likely than their male counterparts to identify sex or gender related aspects of health and of health research.
3. Someone in the programme with a tenured position, who has some freedom to develop the programme without institutional or funding pressures.
4. External funding.
5. The possibility to do interdisciplinary research.
6. The availability of scientific know how on how to formulate relevant sex and gender specific questions and on how to translate the concepts sex and gender into categories and variables that are relevant in specific areas of research.
7. Participation in institutional, national and international research networks and in gender and health research networks.
8. The production of published research papers.

While the informant from INSERM did not identify any major obstacles for pursuing the gender sensitive approach, other than that sometimes members of the research team needed to be reminded of it, the members of the Centers of Gender in Medicine identified several obstacles or challenges:

1. 'Gender Medicine' is a new and interdisciplinary approach, in medicine but also in gender studies.

2. How the concepts of sex and gender are defined and operationalized in different disciplines may vary, according to the subject matter of the discipline.
3. Attempts to create integrative approaches may cause territorial disputes between researchers in 'gender medicine' and those of the sub disciplines.
4. Because 'gender medicine' is "caught" between different disciplines, it does not have a recognized place in the programmes of the traditional funding organizations for scientific research. This makes it difficult to decide where to apply for research grants.

All the informants stated that their initiatives had given rise to studies on sex differences, gender differences or both. The way in which these terms were used in the interviews was however inconsistent and haphazard. This became all the more obvious in writing this report. Terms like sex, gender, men, women, gender medicine, gender related medicine, gender in medicine, gender sensitive, sex specific, women's health do not always refer to the same thing. This inconsistency may be partly due to the conversational nature of the interviews. However, a somewhat similar inconsistency is also reflected in the way in which these terms are used in the biomedical literature, or in other written documents. In our view, there is not yet a common conceptual framework for describing the relationship between sex, gender and health, although several authors and institutions have attempted to suggest such frameworks (this issue will be included in the GenderBasic expert meeting, WP 5).

The aim of the project GenderBasic is to provide tools to researchers, evaluators of research proposals and EU services that may facilitate the process of integrating attention to the gender dimension in the content of biomedical and health related research. In comparison to the EU gender policy for research, with the FP6 top down guidelines as regards sex and gender issues in research (the gender dimension in research), the three selected institutes did not have similar guidelines, rather attention to sex and gender was a bottom-up issue from the research community itself. On the basis of the interviews conducted for this work package, we may conclude that the creation of specific programmes or ways of work can be seen as a useful tool to stimulate attention to the gender dimension in research. Without exception, the three programmes that were the focus of our attention had produced a variety of reports on sex and/ or gender related factors in health and disease.

Salient quotes from interviewees on the relevance of sex and gender issues

“ KR: You know [...] we adjust to sex all the time and we constantly find differences. You find often differences in symptomatology, you find them in the number of symptoms that are important, you find them in access to care, and you find them in use and response to psychotropic medication. ”

“ KSG: First, we think that there are many biological differences between men and women. Some of these differences matter, that is, they are clinically relevant, and others don't. Secondly, we think that men and women experience health and diseases differently. This is related to both biology and society. Thirdly, we think that women are exposed to different risk factors. This is also related to biology and society. ”

“ KSG: I have created a rehabilitation programme for women with CVD. It consists of conventional rehabilitation combined with stress management. More than we expected, these women have stress related symptoms, depression or anxiety disorders. If we don't treat those problems we cannot rehabilitate them. ”

Gendered and
translational
approaches in
basic, clinical
and public
health research

“ ZWH:
For instance, sex and gender differences in the pharmacology of pain management and pain treatment in the clinic is a large area of interest. Not only in the clinic, but also in animal studies, sex differences in pain sensitivity and drug reactions have been identified. It's been clear to clinicians for a very long time that there are sex differences in the presence of pain conditions. ”

“ ZWH:
These are very exciting times. And, sex and gender related questions are now becoming mainstream. ”

“ JAG:
[..] For us in basic science, but also in applied science, studying sex differences has now really become an intrinsic part of our science. We don't study them because we have to, but because studying these differences happens to be our basic research interest. ”

“ JAG:
People who claim that promotion of gender related issues is a political issue and not in the interest of science are very short sighted. ”

“ VRZ:
The understanding of cardiovascular diseases in women requires a comprehensive, multidisciplinary research programme on sex- and gender specific-mechanisms leading to cardiovascular diseases, which should include basic, clinical, epidemiological, prevention and health care studies. ”

“ VRZ:
The understanding of the impact of sex and gender factors on the onset, diagnosis, treatment and prevention of diseases, requires an interdisciplinary approach, firstly among various sub disciplines in medicine and secondly among biomedicine and other relevant disciplines. Any multidisciplinary project requires at the outset a clear idea of what different (sub) disciplines may contribute to a given research problem, as well as on how data from different (sub) disciplines may be linked to each other. ”

“ VRZ:
Each of the (sub) disciplines needs to have a clear understanding of the “mechanisms” by which biological sex and social gender may have an impact on the topic of research in question and a clear idea of the different categories that are involved in those mechanisms and how they may be linked. This means that a constant reflection on the operationalization of concepts such as men, women, sex, gender and the German concept “Geschlecht” is needed in research work. ”

“ *VRZ: However, in biomedical literature, the key word gender is not (yet) commonly used as a concept for classifying research reports. Instead, other terms may be used that refer to sex- or gender mechanisms (for example “estrogen receptor”). So, many articles that are dealing with sex- or gender related mechanisms are classified under other terms or key words. ”*

“ *VRZ: Which concepts are used and combined to analyze sex- or gender related mechanisms in health, is also for a large part determined by how those concepts can be broken down within the different disciplines participating in a study. That is in basic research, other concepts are useful than in for instance psychology. Linking the outcomes of interdisciplinary research on sex and gender differences in diseases is therefore another challenge. ”*

The GenderBasic Reviews.

Work Package 5.

Ten reviews were commissioned which together cover various aspects of sex and gender in research as well as six health areas in which attention to sex and gender issues is urgently needed. The methodological reviews address basic, translational, clinical, and public health research. The identified health areas are anxiety disorders, asthma, metabolic syndrome, nutrigenomics, osteoporosis, and work-related health. Experts identified in WP4 and through further networking contacts were invited to write the reviews.

The reviews are meant to provide state-of-the-art information about specific problems and opportunities (challenges) and to propose widely supported solutions for integrating sex and gender. We asked the authors to address the following questions: (1) What is the state of the art in integrating sex and gender issues in the methodologies of basic, translational, clinical, and public health research? (2) What do we know? Which gaps in knowledge can be identified that deserve further research? (3) What is the state of the art in integrating sex and gender aspects in selected health areas identified as being in urgent need of addressing sex and gender factors (anxiety disorders, asthma, the metabolic syndrome, nutrigenomics, osteoporosis, and work-related health)? (4) What do we know? Which gaps in knowledge can be identified that deserve further research? and (5) Which tools are needed to promote better integration of sex and gender aspects among researchers?

The reviews were prepared in the second half of 2006, and high-level experts were invited to write critical comments about each review. In January 2007, at an Expert Meeting in Maastricht, the review papers were refereed by the invited experts and discussed by the audience. A report on the discussions and the full text of the comments can be found in the Proceedings, which are available at www.genderbasic.nl/expert_meeting

Expert Meeting GenderBasic

Promoting attention to sex and gender in biomedical and health related research Maastricht, January 26-27, 2007.

Work Package 5.

Objective

To provide scientists involved in health related research (with a focus on basic and clinical research) funded by the EU Framework programmes, with practical tools, relevant examples and best practices as regards paying attention to sex and gender differences in the content of their research.

The Expert Meeting hosted scientists from a wide range of backgrounds because we intended to cover reviews ranging from molecular research on gene polymorphisms to the effects of health promotion in public health. Basic researchers, clinical researchers, epidemiologists, social scientists, and gender researchers all have different historical positions regarding sex and gender issues. It was necessary to make a clear conceptual distinction between biological sex and socio-cultural gender to avoid misunderstandings. What connected us was a passion to innovate health and biomedical research so that the needs of men and women are met in an equitable way.

Expected Results

- Tools to be used by EU services, researchers and research evaluators for the improvement of attention to the gender dimension in biomedical and health related research
- Recommendations on how to further the implementation of the gender equality policy for research in the EU 7th Framework Programme (2007-2013)

Results from the reviews and discussions at the expert meeting.

How the challenges of integrating sex and gender were addressed by GenderBasic

Conceptual and methodological issues

Levels in research

As stated, we promoted a conceptual distinction between sex and gender. However the focus in the GenderBasic project is on *interaction* of sex and gender at all *levels*, from the subcellular (molecular/genetic) to the societal (population). Depending on the level studied, sex and/or gender aspects might be involved. At the *basic/molecular, cellular and organ* level we are dealing with a biological environment that concerns sex related interactions. Examples are gene-gene interactions, sex specific gene expression/polymorphisms, cellular processes, organ (specific) processes, sex hormone dependent receptors, systemic processes. At the level of an *organism* we are dealing with a biological and social environment that concerns sex related and social interactions. For example: environmental influences (physical), between animal influences (physiological, cycle synchronization), influences between animal and person handling the animal. At the *human* level we speak about biological and socio-cultural influences that concern sex differences and gender effects. Research involving humans concerns the interaction between possible sex differences and gender *and* other dimensions of difference (age, ethnic origin, socio-economic status, sexual orientation, (dis)ability) as well.

On methodologies

Research into health and disease benefits from different methodological approaches and researchers working in a variety of epistemological traditions. It will result in a highly pluralistic evidence base. This applies to the contents of the GenderBasic reviews as well. Where randomized controlled trials are the standard in *clinical* research (Prins et al 2007), in the context of *public health*, research methods with a gender perspective include but are not limited to: case studies, large scale data sets, historical reports, qualitative data drawn from interviews, focus groups or observation, social surveys, economic and econometric reports, epidemiological data, evidence synthesis, other forms of literature reviews, meta analysis, accounts of lay or tacit knowledge (comments made by Piroška Östlin on Lawrence and Rieder review, see also Sen et al 2002). Because gender is a social-cultural-political concept that addresses socio-cultural aspects, the socio-cultural sciences are needed for health related research. The message could be: stick to your field, but work in multidisciplinary teams.

On measuring gender

It appeared that the concept of gender still is a difficult one for life sciences researchers. As such that is not surprising as the concept was launched by the social sciences in the second half of the 20th century. Although a lot of 'missionary work' (see letter to the editor by Judith Lorber in BMJ Sept 2003) has been done to define the concept and to distinguish it from sex, a lot of confusion still prevails. Medical discourse tends to address differences between women and men as 'gender differences', sometimes denoting sex differences only. Perhaps it has to do with a resistance felt towards using the term sex differences for humans. On the other hand gender studies research in the non-biomedical disciplines has emphasized the dynamic aspects of the interaction between sex and gender and sometimes is resistant to make a distinction. As we have argued in other places (Klinge & Bosch 2001, FP5 Gender Impact Assessment study) for the implementation of attention to sex differences and gender effects in biomedical and health related research, we adhere to the distinction for strategic reasons while acknowledging the interaction. For various experts in the GenderBasic expert meeting, the concept of gender and the distinction from sex, served as an eye-opener and triggered new research questions.

Resulting views from the Expert Meeting were:

- Gender cannot be treated as a variable (Hammarström, 2007). It is always in the making.
- At present there is no means to measure gender.
- The importance of gender in epidemiology highlights the need to interpret findings through a gender lens, that is, to be aware of gender as an explanatory factor for findings (comments made by Phillips of Prins review).
- The idea of creating a gender index (suggested by Susan Phillips) was discussed. Its feasibility was questioned: which elements to include?
- More insight into the workings of gender at the individual level (gender role behaviour) was called for (research on asthma, osteoporosis, food allergy, anxiety disorders, and work-related health).

On measuring sex

- We cannot randomize based on sex (Prins). Therefore the best solution is to test the two populations (men and women) separately (Prins,2007; Postma, 2007). This suggestion goes well beyond a recommendation to provide sex disaggregated data.
- Practical issues concern power issues, number of respondents involved and recruitment: usually only 30% women become enrolled in clinical trials, where the design would need 50%.
- It was suggested to re-analyze data on sex differences with a gender perspective. This represents an enormous potential of new data.

On social and ethical issues

- There is a need for establishing good practices regarding integration of sex and gender at laboratory level including normative issues ('good sex and gender practice': GS&GP)
- GS&GP is more expensive (see formula in Prins, 2007). Involved is a political decision on how to spend public money.
- Political considerations should not stop us doing genomics.
- More animals are needed if we want to take the female cycle into account (stratified research) (Holdcroft, 2007) This could create tensions with the EU rules on animal welfare (3R's: reduction, replacement, refinement)
- Obviously GS&GP involves ethical issues (point raised by the Commission represented by Mary Fitzgerald during the meeting: to include gender issues in the Ethical Review) (See also review by Lawrence & Rieder, 2007)

Research & funding by pharmaceutical firms

Pharmaceutical firms go for maximal profits. The pharmaceutical industry seems reluctant to fund sex based research. Experts at the meeting phrased it as follows: "Firm Z turned down all data directed at sex differences for their metabolic syndrome drugs" and "Pharmaceutical companies do not set out to study differences between males and females because it might affect incomes". They are not interested in paying for stratified research. A strategic approach, mentioned by another expert was: "to fiddle sex and gender into design", i.e. not naming stratification on application for funding but in the end stratify anyway. Could the food industry be considered an ally in nutrigenomics?

Summary of disease related reviews and expert's discussion

(for a full account see: GenderBasic: Promoting integration of Sex and Gender Aspects in Biomedical and Health-Related Research. Gender Medicine, Volume 4, Supplement 2 pp. S59-S193 (2007).

Summary on asthma

Dirkje S.Postma (2007) Gender Differences in Asthma Development and Progression. Gender Medicine, Volume 4, Supplement 2, pp. S133-S146

Asthma prevalence is higher in boys before puberty and in women in adulthood.

There exists a possible under diagnosis in girls (Yentl effect), especially in low-income groups. The Yentl syndrome refers to the fact that a woman has to masquerade as a man in order to receive the same treatment.

The role of gender is visible in parental reporting about symptoms of their sons and daughters (more reporting in boys); more boys receive treatment. Consequences of this bias affect recruitment and clinical data.

Severe asthma is more predominant in women; it has to be established whether this is a social, cultural, hormonal and /or genetic issue.

There is bias in diagnosis by physicians: adult women are diagnosed with asthma, men with COPD.

Sex differences in the development of the pulmonary system are visible in utero. Girls have relatively larger airways in proportion to lung volume than boys.

Hormonal changes and genetic susceptibility are likely to contribute to the change in prevalence around puberty.

The relative contribution of genetic disposition, hormonal influences and social environment (gender role behaviour) is under researched (breastfeeding boys/ vs girls, smoking behaviour mother / father, type of cooking, house mite reduction).

Gender role behaviour: Peer pressure on boys to hide their asthma (and allergy) from peers and not using inhalants when in company has been documented. Girls incorporate their asthma in their social circle.

Gender identity and socialization are thus important in therapy compliance.

Men and women may respond differently to treatments due to biological, environmental and social influences

Summary on osteoporosis

Piet Geusens and GeertJan Dinant (2007) Integrating a Gender Dimension into Osteoporosis and Fracture Risk Research. *Gender Medicine*, Volume 4, Supplement 2, pp. S147-S161

The incidence of fractures is higher in boys than in girls

The burden of fractures increases with age and is higher in women

With increasing life expectancy we will be confronted with increased mortality (more in men), increased morbidity (same in men and women) and high costs (more in women)

The difference in incidence is related to factors that determine fracture risk: factors related to bone and related to falls.

Risk factors are different for men and women.

Causes of falls should be explained by both different levels of activity (related to gender role) as well as differences in muscle control (biological difference; oestrogen effect on muscle tissue)

Women are the focus in research on osteoporosis and serve as standard for men.

Drugs are tested on women and prescribed to men (comment made by White)

Over exercise and dietary restrictions are detrimental for women and men. Running marathons is unhealthy especially for men.

Next to the biological factors there is a need to take into account co-morbidity, life style factors and social support from a gender perspective.

Osteoporosis is a clear example of candidacy (comments made by White). Candidacy refers to the neglect of the other sex if a condition is labeled as 'female' or 'male' disease.

Summary on metabolic syndrome

Vera Regitz-Zagrosek, Elke Lehmkühl and Shokufeh Mahmoodzadeh (2007) Gender Aspects of the Role of the Metabolic Syndrome as a Risk Factor for Cardiovascular Disease. *Gender Medicine*, Volume 4, Supplement 2, pp. S162-177

The prevalence of metabolic syndrome that used to be higher in men has increased considerably in young women driven by obesity.

Women check their weight regularly, men don't, and their overweight is not picked up.

Men are under diagnosed, despite the same symptoms; the prognosis on the long run is worse in men.

Diagnostic criteria for the metabolic syndrome vary for the cut-off points and definition of its components in sex specific ways (resulting in epidemiological differences).

Glucose and lipid metabolism are directly modulated by oestrogen and testosterone with induction of insulin resistance and a proatherogenic lipid profile by a lack of oestrogen or a relative increase in testosterone.

The risk factor hypertension rises steeper in aging women than in men.

Hypertension and diabetes (as components of the metabolic syndrome) carry a greater risk for cardiovascular disease in women.

Visceral 'male' fat seems to be a source of inflammatory mediators; subcutaneous 'female' fat seems to be protective.

Criteria for risk management in metabolic syndrome patients should take account of sex and gender.

The importance of changes in life style was emphasized such as a Mediterranean diet and exercise for women.

Salient quote "We know so much but do so little" (comment made by Swahn).

Summary on nutrigenomics

Jose M. Ordovas (2007) Gender, a Significant Factor in Cross Talk Between Genes, Environment, and Health. *Gender Medicine*, Volume 4, Supplement 2, S111-S122.

Nutrigenomics is a research field aimed at the health of the entire population.

The focus is on interplay between genes (genetic polymorphisms in the context of sex) and disease susceptibility. Additional complexity is brought up by dietary habits, environment (gender roles), alcohol drinking, in the modulation of the balance between health and disease.

This complexity underlies the poor replication obtained for most candidate gene association studies examining common diseases and their predisposing factors.

Research data from two important research areas in nutrigenomics i.e. cardiovascular disease and obesity, illustrated the interplay between genes, disease susceptibility, dietary habits and the relevance of sex differences.

Research data on polymorphisms of APOE (involved in lipid metabolism and risk for CVD) and PLIN (involved in obesity risk) support the role of sex specific polymorphisms in the differential response to the environment; differences between men and women and differences within women were demonstrated.

"Genes have a sex: they respond differently; the effect of certain polymorphisms is apparent only in women".

Especially in lifestyle diseases there should be a focus on biomedical and socio-cultural aspects i.e. the interaction of genes, sex, gender, lifestyle and environment should be studied.

Important aspects that need to be studied are: Risk from accumulating life time exposure to certain determinants, menstrual cycle nutrition interaction, pregnancy related diets, menopause. These aspect are absent from mouse models.

Could the food industry be considered an ally in nutrigenomics?

Summary on anxiety disorders

Marrie H.J.Bekker and Janneke van Mens-Verhulst (2007) Anxiety Disorders: Sex Differences in Prevalence, Degree, and Background, But Gender-Neutral Treatment. Gender Medicine, Volume 4, Supplement 2, pp. S178-S193

Anxiety disorders are more prevalent among women than men: overall, for subtypes, across lifetime and various countries, and independent of specific health care settings.

Women are 'allowed' by society to show fear and anxiety; masculinity is not compatible with showing emotions; men internalize fear which then may erupt in (domestic) violence and suicide.

There are differences (m/f) in co-morbidity.

Symptoms are more severe in women.

Mental health research is conducted using instruments that are susceptible to gender effects (self report questionnaires and surveys).

Aetiological models underlying anxiety disorders in the literature are: genetic differences (neurotransmitters), biological differences (hormones and cortisol secretions), classical and operant conditioning paradigms, social role expectations, sex differences in environmental exposures to stimuli, learned helplessness: women are encouraged to be more fearful.

Three theories to explain prevalence data (on gender role perspective, learning perspective and attachment and schema theory) were examined on degree of attention paid to gender.

Gender role socialization was demonstrated to be of influence in:

- self-reporting and lower willingness to report in men; lower help seeking behaviour in men
- higher use of anxiety-reducing drugs in women and alcohol in men (relevant to agoraphobia)
- the division (m/f) of socio-economic roles hampers avoidance tendencies in men (agoraphobia)

When it comes to treatment, there is a lack of attention to m/f differences in prevalence of anxiety disorders.

A synoptic model was proposed that reviewed determinants in 5 groups: body, gender, differential diagnostics, m/f differences in exposure, person-related vulnerability factors.

What remained was the problem of conceptual complexity: Differential reporting is embedded in a cultural context of gendered notions and gender 'mandates' for women and men.

The discussion raised the question if high anxiety levels perhaps have a positive role in women? (fight/flight theory).

Under exposed in the review were biological differences between men and women.

Summary on work related health

Anne Hammarström (2007) A Tool for Developing Gender Research in Medicine: Examples from the Medical Literature on Work Life. Gender Medicine, Volume 4, Supplement 2, pp. S123-S132

There is a higher prevalence of work related disorders in specific occupations, but research on differences between men and women is scarce.

Workplaces are usually designed according to the anatomy of the "normal" male.

The health of women in waged labor is poorer.

Participating in labour market programmes is related to ill-health among women.

Influence of marriage, housing, socio-economic barriers on the consequences of unemployment are different for men and women.

The workforce is segregated according to gender.

A classification was proposed to give insight into characteristics of sex difference research as opposed to research from a gender perspective.

Gender is not a variable but should be used as an analytical category.

Sex difference research is still needed and could be a starting point for gender analysis.

Gender roles are influential: masculinity with values of self-reliance, control and strength is associated with less help-seeking behaviour and more risk-taking.

Conclusions

The Expert Meeting created great enthusiasm among the participants and a real exchange took place between researchers from various backgrounds. The sincere commitment of the male experts was particularly striking. Most life sciences researchers were familiar with the concept of sex differences but confessed that the effects of socially constructed gender had received, until recently, too little attention. This may partly explain why a literature search using the search term gender mainly retrieved articles on sex differences (see for example the review by Geusens & Dinant, in contrast to the review by Bekker and Mens-Verhulst). Peer review of the GenderBasic reviews yielded three major achievements.

- I. It stimulated and promoted research into sex differences
 - The relevance of studying sex differences was exemplified in many reviews, although to a different extent
 - Sex-specific gene expression at the transcriptional level in somatic tissue until now is mostly descriptive (Isensee/Ruiz, 2007) (“sex is in the kidney more than in the brain”, comments made by Wold)
 - The implementation of basic science results was questioned. How to go from sex differences in basic research to clinical importance / relevance (comments made by Mariman & Wold)
 - Suggestions were given on prerequisites for the study of small differences in animal research, because they may have additive or synergistic effects (Holdcroft, 2007; comments made by Franconi). Reference was made to the review by Jill Becker (2005) on methodology of study of sex differences in animals.
 - Sex differences are closely related to sex hormones and especially estrogens. Androgens seem to be studied less frequently.
 - Attention was drawn to the differences within the sexes (Ordovas, 2007)
- II. It stimulated research into workings/ mechanisms/effects of gender as visible in particular in:
 - Understanding masculinity, male gender role and the effects on individual health behaviour (White, in osteoporosis; Postma, in asthma, Hammarström for work-related health, DunnGalvin, for food allergy)
 - ‘Candidacy’ and Yentl syndrome. The unnoticed higher risk of cardiovascular disease in women with the metabolic syndrome (Regitz-Zagrosek, 2007), lack of screening for osteoporosis in men and osteoporosis drugs only tested in women (Geusens, 2007, comments made by White) can be explained by the notions of ‘candidacy’ and Yentl syndrome. Candidacy refers to the neglect of the other sex if a condition is labelled as ‘female’ or ‘male’ disease. Yentl syndrome refers to the fact that a woman has to masquerade as a man in order to receive the same treatment.
- III. It highlighted interaction and granted gender a prominent place in future research.
 - GenderBasic focused on the interaction of sex and gender at all levels, from the sub-cellular (molecular/genetic) to the societal (population level).
 - All reviews acknowledged the interaction between sex and gender and other dimensions of difference (age, ethnic origin, socio-economic status) as well. Future research is expected to yield more information regarding gender roles and health behaviour. At present such data are rare in the reviewed literature on the six conditions

Wider ideas

The Expert Meeting has brought together high profile researchers from a variety of disciplines (basic researchers, clinical researchers, epidemiologists, social scientists, gender researchers) with an interest in addressing sex and / or gender issues in research. The following wider ideas were discussed:

- Publication of reviews: as individual papers or together as a special volume?
- To develop a European Research Agenda for sex and gender sensitive biomedical and health related research. The reviews and identified gaps in knowledge constitute a first input. That agenda should be anchored in research institutes and supported by European and member state health councils and (governmental) health research policy
- Dissemination / translation of review papers to education: to health and medical curricula

Policy implications

- How can DG Research contribute to guarantee continuing attention to sex and gender aspects in research in FP7 and following work programmes?

Dissemination. Publication of review articles: Bringing gender expertise to biomedical and health-related research

All 10 review papers are published in the Journal Gender Medicine, (the official peer-reviewed journal of the Partnership for Gender-Specific Medicine at Columbia University.) *GenderBasic: Promoting integration of Sex and Gender Aspects in Biomedical and Health-Related Research. Gender Medicine, Volume 4, Supplement 2 pp. S59-S193 (2007).*

This journal states as its mission: to focus on the impact of sex and gender on normal human physiology, and the pathophysiology and clinical features of disease. The journal serves an international multidisciplinary audience in a mixture of academic and clinical practice settings.

“*Gender Medicine* welcomes original reports from the entire spectrum of academic disciplines devoted to the study of the human condition as it relates to both biological sex and the broader concept of gender. One of the most difficult tasks in gender medicine is to determine which phenomena are the results of biology and which are consequences of the environment. Therefore, the journal encourages scholars in disciplines such as anthropology, sociology, psychology, and other allied sciences to consider contributions to the journal”.

Reflection and connections

The driving force behind the GenderBasic project is the EU gender equality policy for research. This policy has brought together the elements of women's participation and the gender dimension of the research content in the formula GE= WP and GD.

GenderBasic focused on the gender dimension of the research content by stimulating attention to sex differences and gender effects in biomedical and health related research. Its mission can be viewed as striving for innovation of biomedical and health related research practices. The commissioned reviews and invited comments are promising examples of intended innovations. We can also perceive how this project is linked to existing scientific debates. Biologists who are also gender experts such as Lynda Birke and Anne Fausto-Sterling have expressed their concerns about many gender theories in general as well as social science studies of the body, questioning the lack of attention to processes inside the body. In the biologists' view, social science gender theorists engage exclusively with the sociocultural environment and constructivist epistemologies, leaving sex differences unaddressed.

Lynda Birke formulated her concerns as follows (Birke, 1999; see also Kuhlmann & Babitsch, 2002):
In general, social studies of the body tend to ignore the material inside or to relegate it to the world of biomedicine. Feminist theory is only skin deep. The omission is the inside of the body as organs and physiological processes. I acknowledge the deep cultural assumptions pervading scientific representations of the body. I want to reject biological determinism and to seek what I see as more contextual ways of describing / explaining biological processes. We need interactive models of causality

Anne Fausto-Sterling suggests an alternative point of view (Fausto-Sterling 2003 a&b):

The problem with sex/gender is not nature against nurture....but to look for a more complex analysis in which an individual's capacities emerge from a web of mutual interactions between the biological being and the social environment.

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She finds the developmental systems approach (DST) to be particularly helpful, for example in determining how a different experience leads to a divergence of brain development.

Can DST help to form a new research agenda, which depends on the mutual construction of sex and gender? Beginning to understand that the world works via systems will enable us to specify more clearly the links between culture and the body and to understand how nature and nurture, sex and gender are indivisible concepts.

The GenderBasic project promoted balanced, justified attention to both sex differences and gender effects, and proposed an agenda for future research. Differences of both kinds are interesting and relevant, and are best studied in multidisciplinary teams. The most interesting areas of study are not the differences per se, but the studies on how differences develop. The new perspectives and models developed through the GenderBasic project support this view and are helpful in realizing and executing the resulting research agenda.

Research Agenda: New perspectives and paradigms

Animal models

The review by Anita Holdcroft (2007) addressed the following issues:

Very small differences between the sexes produce clinical treatment effects because small differences may have additive/ synergistic effects and therefore have to be investigated. Current obstacles to discover small differences:

- Sex hormones, level of estrogens and the menstrual cycle are complex to consider, yet may be active in multiple ways.
- Oestrogen effects are leveled out due to variability (in cycle) among females (statistical mean). Effects are lost.
- Research hardly considers the importance of progesterone, or other neurosteroids that vary during the oestrus cycle. Levels of testosterone are not measured.

Holdcroft stated that animal models are needed that are adequate for studying human disease; current ones cannot consider comorbidity, age related changes, cycle changes, use of contraceptives. Her recommendations:

- For male and female animals, their age and weight should be recorded and for females, their reproductive status and ovarian cycle phase should be determined as accurately as possible.
- The sex of origin of biological research materials should be determined and disclosed on publication.
- In study design, reporting and peer review, the possible variations and impact of sex differences on all aspects of the experiment should be considered and be based on evidence relevant to the strain, species and environmental conditions.

In her comments Flavia Franconi pointed to sex dependent programming. She further emphasized the following issues:

- Social interactions and environment are relevant for laboratory animals and thus may have important consequences in preclinical research.
- Early life social interactions and environment should be emphasized; diet, mother-pup interaction and neonatal handling affect males and females differently.
- Attention is needed to non hormonal events, such as expression of sex chromosome genes.
- Life experiences (pregnancy, lactation) should be studied in pharmacological research.
- The scenario of activity of sex hormones is very complex depending on receptor subtypes, tissue co-activators and repressors.
- An animal model is needed that is similar to humans and includes oral contraceptive use.
- Understudied is whether males and females respond differently to placebo administration. This is also relevant to animal research and concerns vehicle use and sham operations.

Life style diseases

Life style diseases are paradigmatic for the interaction between sex and gender (and other dimensions of difference). To address life style diseases a focus on both biomedical and socio-cultural aspects is necessary. Research questions are best studied in multidisciplinary teams. Two reviews explicitly addressed life style diseases i.e. obesitas and metabolic syndrome. The Ordovas review (Ordovas 2007) pointed to differences between countries, candidacy and sex differences. Regitz-Zagrosek (2007) stated that metabolic syndrome is a difficult syndrome to assess: biological, genetic dispositions interact with life style factors; this is a plea for analysis from a life time perspective.

To adequately study not only the interaction between sex and gender but also between other dimensions of difference an *intersectional* approach was advocated: keep the panoramic view, combine the genome-proteome-environment in studying sex & gender (and other dimensions of difference) (Ordovas, 2007; Schulz & Mullings, 2006; Wieringa et al, 2005; Wely et al 2005)

Research Agenda: Priorities/suggestions for further research on specific conditions

Explicit assignment for the authors and peer reviewers was to propose new research questions based on their reviewing of the state of the art. Their ideas in fact constitute the buildings blocks for a future research agenda.

(for a full account see the Gender Medicine Supplement, December 2007).

Asthma:

Study of fetal lung development in interaction with hormonal factors.

Stratification of genetic studies on asthma by sex since some polymorphisms are in particular related to asthma in women.

Further studies on hormone-gene interactions and e.g. X-chromosome genes in relation to asthma and atopy. Study cellular hormonal influences in asthma and atopy in relation with innate and acquired immunity

in both sexes. This would benefit many other diseases where sex differences in prevalence, severity and treatment response exist.

Animal models to study the observed differences between men and women.

Study differences in treatment response to asthma in females and males separately.

Osteoporosis

Aetiology: More detailed studies are needed to define the material and structural basis of bone growth and bone loss, the pathogenesis of bone loss, and the association with deficits in estrogen and testosterone, the role of the sex hormone receptors and the relation with other endocrine functions, such as growth factors, even more so in men.

Case finding: Much more epidemiological data are needed that could be the base for case finding for men at increased risk for fractures.

Treatment: Randomised controlled studies are necessary to expand the possibilities for treatment of osteoporosis in men.

There is a need to explore the role of bone forming agents, such as based on the Wnt signalling, sclerostin and other mediators that influence the osteoblast.

Furthermore, the understanding of the role of the osteocyte is increasing and should be further explored for its diagnostic and therapeutic potentials.

Studies are necessary that focus on the total patient, including targeting and integrating bone-directed drug therapy and fall prevention

Metabolic syndrome

Focused mechanistic studies on sex specific endpoints.

Sex specific studies in animal models for diabetes and aging.

Focus on individual risk factors; no fight about definition of the syndrome.

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Anxiety disorders

To study to gender-relevant individual differences leading to anxiety disorders via learning processes focusing on attachment experiences and styles and on autonomy-connectedness.

Attention to sex-differences in prevalence studies (and background of these sex differences), potential sources of gender bias.

Increase treatment effect studies are.

Studies on masculinity theories and gender relations could give more information

Work related health

The distinction between 'sex difference research' and gender research in itself can be productive. It made men visible in an important way. It highlighted notions of masculinity and femininity, which until now are scarcely addressed in life sciences research.

Focus in further research should be on the role of masculinity and femininity in risk behaviour and/or health seeking behaviour.

Nutrigenomics

Gene-diet interactions could be of great interest for a more individualised and effective dietary therapy.

Differences in response to therapeutic modifications associated with specific genetic mutations may affect men and women differently.

Much of nutrient information used for nutrigenomic studies in large populations is obtained from dietary questionnaires. It remains to be determined whether the validity of these data is similar for men and women. Developing reliable biomarkers of dietary intake might represent more sensitive and objective measures than the current instruments.

Differences between men and women regarding dietary compliance and in adherence to dietary recommendations remain to be studied.

Consensus is emerging about the need for messages specifically tailored to women or men in order to increase dietary modification programmes.

Despite the potential confounder due to differences in reporting and/or adherence to tests, intrinsic sex differences in dietary response need to be studied.

Women have different dietary needs at different life stages; final goal is to maintain health at all phases.

Therefore recommendations to decrease the risk of a specific age-related disorder (i.e. cardiovascular disease) should take into consideration the effects over others (i.e. cancer, osteoporosis and neurological disorders).

Resolving these challenges is only possible through close interaction and collaboration of researchers and professionals representing a wide range of expertise and knowledge.

Recommendations

Recommendations on research content

- Extend the GenderBasic approach to a new project addressing upcoming dynamic areas in the life sciences that are of deemed interest for the near future and where attention to sex, gender and diversity until now is completely absent. These areas are:
 - o Neurosciences: with novel issues as cognitive enhancement and mood enhancement. Aim of this research is not only to mend disabilities but to enhance human capacities
 - o Biology of human performance and health; physical activity and health: research issues such as fitness and life span extension
- Development of joint research projects based on the GB Research Agenda.

Recommendations on research processes and methodologies

- For male and female animals, their age and weight should be recorded and for females, their reproductive status and ovarian cycle phase should be determined as accurately as possible.
- The sex of origin of biological research materials should be determined and disclosed on publication.
- In study design, reporting and peer review, the possible variations and impact of sex differences on all aspects of the experiment should be considered and be based on evidence relevant to the strain, species and environmental conditions.
- Research should include both men and women as subjects. If this is not the case, researchers need to explain the reasons for the exclusion of men or women.
- Results should be reported disaggregated by sex; the influence of sex on participation, continuation and drop-out rates must also be reported.
- Gender factors should be assessed a priori on the basis of their hypothesized role in the causation, course, treatment-seeking patterns, attitudes, treatment effectiveness, impact and outcome of health problems.
- The impact of other exposures, such as socioeconomic variables, on health problems should be examined differentially for men and women, and should be critically analysed from a gender perspective.
- Women should be included in clinical trials and other health studies in appropriate numbers and the data generated from such research should be analysed using gender-sensitive tools and methods.
- Ensure collection of data disaggregated by sex, socioeconomic status, and other social stratifiers by individual research projects as well as through larger data systems at regional and national levels, and the classification and analysis of such data towards meaningful results and expansion of knowledge for policy.
- Research into lifestyle diseases in which biological genetic dispositions interact with life style factors are best studied in multidisciplinary teams from a life time perspective.

Recommendations on how integration of sex and gender in research contents and processes / methods could be promoted , facilitated and ensured by different tools, guidelines and institutional arrangements

- International conference on GenderBasic Results
- Maintenance and extension of GenderBasic Network
- Development of a training module based on the GenderBasic results, in sex and gender aspects of biomedical and public health research targeted at the research community. Supported by website and help desk. Ideal format would be an e-learning course.
- Training of evaluators (EU staff, member state research councils)
- Call upon **disease related professional societies and organisations** (f.e. European Society of Cardiology, Osteoporosis Foundation, ESF 10-year program Systems biology to combat metabolic syndrome; and many others) to adopt our proposal for guidelines for Good Sex and Gender Practice(GSGP); to endorse the GenderBasic Research Agenda and to support proposed research projects.
- Call on Member State **Research Councils** to stimulate dissemination and promotion of adoption of GenderBasic Results.
- **Editorial boards** of journals: innovation of guidelines for authors. Medical and related journals should request that papers present data disaggregated by sex and explain sex and gender differences adequately.
- **Research funding agencies** should promote research that broadens the scope of health research and links biomedical and social dimensions, including gender considerations.
- **Pharmaceutical companies** should see stratified research as an opportunity to express their corporate social responsibility and to demonstrate good governance.
- Strengthen women's role in health research. Redress the gender imbalances in research committees, funding, publication and advisory bodies.
- Chairs in sex and gender medicine at **European Universities**; translation of new insights to biomedical and health sciences education.

- Harmonisation of clinical guidelines: to secure attention to relatively new groups in pharmacological research (women, children, the elderly, different ethnic backgrounds). Call to integrate guidelines for Good Sex and Gender Practice(GSGP) into:
 - o ICH-GCP-International Conference on Harmonisation (ICH) for clinical studies/ WHO Good Clinical Practice standards
 - o EMEA (The European Agency for the evaluation of medicinal products)
 - o EU Directives on clinical trials
- **Governments** should take action to improve the evidence base for health policies by changing gender and other imbalances in both the content and the processes of health research.
- Role of Governments: to mainstream gender equality in all policy areas including health research. In this way governments can influence research councils in a very strong way (best practice: Sweden since 1994) Research councils are requested to integrate gender perspectives into their research strategies and monitor this regularly.
- Good governance in the production of health and medical knowledge should incorporate the gender dimension (sex and gender issues) and the role of women.

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