

# Promoting attention to the gender dimension in health research: experiences from three centers of excellence in the EU

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Specific Support Action GenderBasic: Report on Work Package 3,  
June 2007

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*Design: Océ Business Services / Universiteit Maastricht*

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# Promoting attention to the gender dimension in health research: experiences from three centers of excellence in the EU

## Summary

The GenderBasic project focuses on researchers in the field of biomedical and health related research in the EU. It has the aim to contribute to the EU gender equality policy by developing practical tools to help researchers integrate attention to the gender dimension into the content of basic and clinical research. 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 and ideas and experiences of those who are to implement these measures: the researchers themselves. For that reason one of the aims of GenderBasic is to explore how researchers view and manage the integration of the gender dimension in research (see also the Report on WP2).

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 concentrated on making an inventory of guidelines and / or institutional policies regarding integration of the gender dimension among a selected number of high profile 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. This 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.

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 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 for 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 opinion, 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.

## Introduction

In 2000, the European Parliament made a clear commitment to promote gender equality in EU-funded research. The aim was to achieve a balanced participation of male and female scientists in projects (40% women), while ensuring that studies also pay appropriate attention to the gender dimension. According to the definition of the European Commission, attention to the gender dimension in the content of research comprises the address of both sex and gender and requires a clear distinction between the two concepts. 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, behaviors and values that society ascribes to men and women on a differential basis. In EU publications, the gender equality policy is commonly represented by the following formula:

GE=GD + WP

GE: Gender Equality

GD: Gender Dimension of the Research Content

WP: Encouraging Women's Participation

To promote attention to the gender dimension in the content of studies, researchers participating in the Sixth Framework Programme for Research and Development (FP6), which runs from 2002 to 2007, were asked to describe and justify the composition of their study populations according to sex, and to indicate how they plan to integrate a focus on sex and gender issues, where appropriate, into the objectives and methodology of their research proposals. They were also asked to provide a gender action plan. The gender action plans are currently the subject of monitoring studies, the results of which will be made available following the completion of FP6 in 2007.

The GenderBasic project focuses on researchers in the field of biomedical and health related research in the EU. It has the aim to contribute to the EU gender equality policy by developing practical tools to help researchers integrate attention to the gender dimension into the content of basic and clinical research. GenderBasic acknowledges that the EU gender equality policy may meet with resistance in the research community. For example, some researchers may question the scientific relevance of a sex and/or gender sensitive research approach. Others may have questions regarding the ethical, conceptual, methodological issues or practical or financial consequences of this approach. The successful development of practical tools requires not just attention to policy measures but also to the attitudes and ideas and experiences of those who are to implement these measures: the researchers themselves. For that reason one of the aims of GenderBasic is to explore how researchers view and manage the integration of the gender dimension in research. In a prior work package (WP2) we explored how researchers of Integrated Projects (IP's) and Networks of Excellence (NoE's) financed by the Thematic Priority Food Quality and Safety (TP5) of FP6 experienced the process of integrating the gender dimension into their research activities. The participants of those projects were given specific instructions on how to integrate attention to the gender dimension in their studies when they applied for a grant.

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). In the FP7 part 'Cooperation', the themes "Health" and "Food, Agriculture, Biotechnology" seem to have continued the FP6 gender equality policy as is evidenced by the quotations from the work programme.<sup>1</sup> However, information about the concrete instruments by which this will be done was still lacking.

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<sup>1</sup> FP7 Work Programme

**Theme 1: Health**

Gender aspects in research

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.

**Theme 2: Food, Agriculture and Biotechnology**

Participation of women and gender aspects in research

The pursuit of scientific knowledge and its use in service to society requires the talent, perspectives and insight that can only be assured by increasing diversity in science and technological workforce. Therefore, an equal representation of women and men at all levels in research projects is encouraged. Gender aspects in research have a particular relevance to this theme as risk factors, biological mechanisms, behaviour, causes, consequences, management and communication of diet related disease and disorders may differ in men and women. Furthermore, roles and responsibilities, the relationship to the resource base (land management, agricultural and forest resources etc) and the perception of risk and benefits may have a gender dimension. Applicants should systematically address whether, and in what sense, sex and gender are relevant in the objectives and in the methodology of projects.

After consultation with the Commission it seemed of utmost relevance to investigate how the scientific community views the incorporation of attention to sex and gender issues in the content of basic and clinical research. Do they consider it, as does DG Research, a contribution to scientific excellence? For that reason it has been decided (December 2005) to add a new work package to the GenderBasic project namely to make an inventory of guidelines and / or institutional policies regarding integration of the gender dimension among a selected number of high profile 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. We selected three European Centers of Excellence in biomedical research with strong programmes in gender and health research. Our aim was to make an inventory of why and how these institutions had developed those programmes and of what the experiences are and the achievements have been so far.

# Material and Methods

## Informants

In consultation with the Women and Science Unit of the Directorate-General for Research we selected three institutions with an outstanding research programme focusing on sex and gender issues in basic and clinical biomedical research.

- The Institut National de la Santé et de la Recherche Médicale (INSERM) E 361 Pathologies of the Nervous System: Epidemiological and Clinical Research at the Hôpital La Colombière in Montpellier, France.
- The Karolinska Institute in Stockholm, Sweden.
- The Center for Cardiovascular Research/ Gender in Medicine & Cardiovascular Disease in Women. Charité-University Medicine in Berlin, Germany.

To solicit information for our inventory we selected six informants, all of whom had been closely involved in developing a gender sensitive research programme within the selected institutions.

*Dr Karen Ritchie (KR), Director of Research INSERM E 361, Montpellier.*

*Professor Dr. Karin Schenck-Gustafsson (KSG), Director of the Centre of Gender Related Medicine at the Karolinska Institute, Stockholm.*

*Professor Dr. Zsuzsanna Wiesenfeld-Hallin (ZWH), Chair of the Board of the Centre of Gender Related Medicine at the Karolinska Institute, Stockholm.*

*Professor Dr. Jan Ake Gustafsson (JAG), Director NOVUM, chairman of the strategy group for equality in science at the Karolinska Institute, Stockholm.*

*Professor Dr. Vera Regitz-Zagrosek (VRZ) Director of the Center for Gender in Medicine & Cardiovascular Disease at Charité-University Medicine, Berlin.*

*Prof. Dr. Patrizia Ruiz Noppinger (PRN) Professor at the Center for Gender in Medicine & Cardiovascular Disease at Charite-University Medicine and Max Planck Institute for Molecular Genetics, Berlin.*

## Interviews

To conduct our inventory, we used a semi-structured method of interviewing, guided by a topic list (Box 1). This method of “open” interviewing was chosen as it offers respondents the opportunity to express their own ideas and to raise relevant issues the researcher had not anticipated.

### Box 1. Topic list for interviews about institutional programmes focusing on the gender dimension in biomedical research

What is the gender policy of the institution the gender sensitive research programme belongs to, if any?  
How did the gender research programme come about?  
What have been barriers and/or facilitating factors in establishing the programme, if any?  
Who are involved in the programme?  
Who finances it?  
What is the scientific model the programme works from, if any?  
What are the scientific challenges of a sex and gender sensitive research approach, if any?  
What are the most important activities of the programme? (e.g., areas of research, specific projects/topics, training facilities for researchers, (inter)national cooperation)  
What are achievements?  
What are needs to sustain the programme in the future?  
What are experiences with DG Research or EU research funding, if any?  
Are there any ideas about topics that may be relevant for a future European gender sensitive health research agenda?



The interviews were held between July 2006 and September 2006 by JH. They lasted between 1-1.5 hours. One interview was conducted by telephone (KR) and six in person. All interviews were recorded with the consent of the informants. Unfortunately, the quality of two recordings was poor (VRZ, PRN). However, additional documents provided by VRZ make it possible to complete the report on Charité. All informants were asked to speak for themselves and not as official spokespersons for their institution. The researcher also attended the conference “Excellence in the Life Science Area –adding the gender dimension”, at the Karolinska Institute in Stockholm on October 5-6 2006. It was expected that this conference would provide additional information on programmes addressing the gender dimension in biomedical research. However, the main topic of the meeting was how to identify barriers and facilitating conditions for achieving excellence in science for women scientists, and not how to focus attention to the gender dimension in the content of research in the life sciences. Although relevant, the topic of the meeting is beyond the scope of this work package. For that reason the information acquired at the conference will not be reported here.

### **Analysis**

The transcriptions of the interviews and written materials provided by the informants were used as the basis for this report. The informants were given an opportunity to review and comment on the transcripts and other information used. The report is structured around the main topics mentioned in the topic list. Content analysis of the interviews and the written materials was used to identify relevant information for each topic. The report provides summaries or literal citations of the statements and the other information provided by the informants, as illustrations of the main findings.

## Results

Our inventory was held with informants from two different kinds of institutions. Our French informant, Dr Karen Ritchie (KR) works at the French National Institute for Health Research (INSERM). She is an epidemiologist and neuropsychologist and Director of Research of Laboratory E 361: Pathologies of the Nervous System: Epidemiological and Clinical Research. Our Swedish and German informants are working as professors at medical universities. In contrast to the two medical universities, INSERM does not have a specific 'gender medicine' programme, but rather a general way of work that facilitates attention to the gender dimension in the research it conducts, according to KR. This report starts with what we learned from KR about INSERM.

### INSERM

In France, the bulk of biomedical research is carried out by INSERM, the National Institute of Health Research. Research is also conducted in the universities and in hospitals, but INSERM is by far the most important medical research institution. In other areas of science autonomous research institutes have a central role. This is a result of developments of the French university system in the past decades, a situation one is currently trying to redress in order to reintegrate medical research back into the universities. INSERM is divided into nine Scientific Commissions. The Laboratory of which KR is the research director is attached to both the Commissions of Psychiatry and Epidemiology. The Headquarters of INSERM are in Paris and there are many different laboratories and networks (about 500) in the regions, one of which is KR's Laboratory in Montpellier that focuses on epidemiological and clinical research on pathologies of the nervous system. INSERM is financed by the Ministry of Health and the Ministry of Education. There is a central administration and regional administrations. The budget for each laboratory pays for the running of units, the salaries of the researchers, the technicians and the engineers and part of the research undertaken. At least half of the funding for research projects must be found externally by the research staff. All personnel members at INSERM have public service positions. There is a competition to get in. A limited number of people is recruited at each level each year by a Commission.

### Gender policy at INSERM

INSERM is an equal opportunities employer, but there is not an explicit policy relating to gender issues in research.

### Facilitating factors for studying sex and gender differences within INSERM

Nonetheless, there are a number of reasons why KR feels very comfortable working at INSERM, as a researcher interested in sex and gender differences:

"In INSERM there is no gender discrimination, both at the level of the institute and at the level of content. INSERM is a sex fair employer, although you may encounter some of the common issues. For instance there are very few women higher up in the hierarchy."

"INSERM is divided into nine commissions. There is no Commission to oversee whether gender related health issues are being dealt with adequately within each institution although the epidemiology commission is very attentive to the possibility of gender bias in population research. Otherwise I think the question of gender is probably adequately dealt with, within each commission."

"There are many women working at INSERM. Women usually bring women's issues with them and there is no trouble in having female health oriented projects."

"INSERM has a public health role. It is very sensitive to inequality such as, socio-economic inequalities in having access to health systems. If there is a new health alert or if a new pathology or disorder that appears, these problems are being dealt with fairly from a gender point of view. I think that when a gender issue is noticed, INSERM responds very quickly to it. There is no discrimination in the selection of areas for research as far as I know, although like elsewhere there is often more funding available for male predominant health problems such as cardiovascular disease and prostate cancer."

"My laboratory is attached to the Commission devoted to epidemiology, public health and social sciences. Since the 1970s, epidemiological research has been reasonably strong at INSERM. There is a lot of ongoing population research. There are many registers for diseases and big studies that focus on women. For example, there is a big national study focusing on osteoporosis, a big national study on female cancers. This creates an environment such that if there is a female issue, it is not difficult to establish a project."

"You may be limited in finding funding from outside but as an employee of the institute you do not constantly need to find money to fund your position. Therefore you have some independence from political and economic pressures. You don't have to worry about your salary and you also are quite free at INSERM to work on what you want. And we can change direction quite easily if new health issues arise."

## **Integrating the gender dimension in research: the scientific approach**

KR's Institute does not use a specific scientific model or specific guidelines for integrating the gender dimension in research. However, she points out that there is a common understanding among researchers in her groups that men and women may differ.

### *Common understandings*

"Many scientists have made the assumption that, apart from the sexual organs, men and women are essentially the same. But as neurobiologists we know that this is not the case. For, instance the male and female brains are different and that a lot of these differences are modulated by hormones."

KR adds that it is a golden rule for the researchers at the institute that "one shouldn't make assumptions that males and females are the same, unless we know. This goes right back from research in genetics to social research."

KR regards the consideration of sex and/or gender differences as a "normal" part of good science. "People often confuse a gender sensitive approach to research with feminist issues. What I am talking about, however, is an approach that must be aware of the fact that there may be differences between men and women for example in biology, disease expression and access to care, at every stage. I think the problem in the past has not just been one of discriminatory practice but rather that we did not realize to what extent gender-related factors might affect our research." According to KR, a gender sensitive approach does not require major adaptation of the existing research methodology.

### *Epidemiology*

"In epidemiology, population studies, sex differences are almost always reported. Even if you don't find this data in the publication, you can always write to the people who have the database and ask if you could have a particular variable by sex, and they usually tell you the result. Most population studies have data about sex, socioeconomic characteristics and education. So in the area we are in, this is not likely to be a problem. It might be a problem in that researchers claim they have looked at sex while this is not entirely true, that happens." Thus, according to KR recording sex (and gender?) differences has become "an intrinsic part" of the epidemiological methods used in population-based research.

### *Clinical research*

"In some of the clinical research I find it becomes more tricky. For example researchers working with specific genes or biological samples often don't think to ask whether they came from male or female subjects – because of the likelihood of pregnancy, male biological samples are often more common. This may have caused biases that we were unaware of, particularly now that we are also dealing with epigenetics. Environmental factors, inside or outside the body, can actually alter the expression of genes and this can be inherited. So, when you take a disease with a fixed DNA, maybe the way it is expressed during the lifetime may be determined by the environment. And of course men and women live in different environments."

### *Sloppy research*

"If clinical research is not taking sex differences into account it is just bad research. If people are doing that they are probably pretty sloppy also in other areas as well. It is as simple as that. I mean any clinician knows that men and women often do not present with the same biological changes, often complain about different symptoms for the same disorder and are not likely to have the same access to the health care system or comply in the same way to treatment. There are also treatments to which they might not respond in the same way, because their biology is different. Take body weight. Body weight alone can make a difference in how people metabolize drugs."

### *Bias*

"But to be fair there are some situations where you know that gender doesn't say very much. And there are others where it has a huge impact. I think what you have to be sure of, as in any good research project, is that there isn't any bias. Bias because you haven't taken into account that there might be biological or sociological differences between men and women."

### *The right questions*

KR states that she is not aware of any important methodological obstacles for looking at sex or gender difference in her area of research. Her main idea is: "You just have to look for differences. And, more importantly, you have to be imaginative in developing questions how sex and gender may determine things."

## **Training facilities**

Asked if there were any specific educational facilities at her institute to teach researchers the concepts and skills that are needed to conduct sex or gender sensitive research KR answered: "Obviously, they (the researchers) have the knowledge and the skills to investigate sex and gender related factors. Otherwise they wouldn't be doing this research." Interestingly, she emphasized that having an interdisciplinary team is very important in formulating the right questions.

"I think the main thing is that we have a multi disciplinary group. We have epidemiologists, we have mathematicians, we have pharmacologists, we have psychiatrists, we have immunologists, we have psychiatrists, and we have neurologists. We have every kind of specialty we want. So if we put a new project out we constitute a workgroup around it, according to the type of knowledge that we need and the expertise that is required. For example the hormonal group here consists of biostatisticians and mathematicians as well as biologists and neurologists, because it is not only a question of speculating where gender bias may arise, but in adequately investigating it at a statistical level too."

## **Attention to the gender dimension in the research programme of Laboratory E 361 at Montpellier**

### *Overview of the research*

KR's research programme is looking at pathologies of the nervous system both neurological and psychiatric. She summarizes the programme as follows: "We consider psychiatric disorders to be essentially complex neurological disorders in which there may be a significant environmental or social component. We are divided in a number of sections or groups. We have a group working on neurodegenerative diseases: all types of brain changes due the aging process including Alzheimer's and Parkinson's disease. We have a big epidemiological study following up 10.000 people regularly. We have another group, working in psychiatric epidemiology. They are doing population research looking at the life-time causes of psychiatric disorders. They are particularly interested in psychiatric disorders in the elderly, while looking at determinants that start from childhood. In this group we also do clinical research, for instance, by looking at depression. Then there is a group working on biology and neuropsychiatry that is particularly working on hormone replacement and hormonal fluctuations throughout the lifespan. They are interested in seeing what sort of cumulative patterns of hormonal exposure across the lifespan will have an effect on the way the brain develops and ages. The same team also looks at how people react to stress, how people's cortisol systems react. Another group looks at suicide, violent suicide, particularly at the genetics of it. The next group is the sleep disorder group. They are interested in the structure of sleep and changes in the structure of sleep at the time of brain aging and brain pathology. The last group is the biostatistical modelling group. The statisticians and mathematicians form a team together to develop new models for the analysis of these very complex data banks."

### *Examples of research questions focused on sex and/or gender differences*

KR gave a number of examples of how sex and gender differences are being addressed in these research groups

#### *Sex differences in Alzheimer's disease*

"No one has really looked at this very much. From the little bit of research that has been done we know that there are certainly differences in the symptomatology and in the way in which men and women lose verbal capacities. Women seem to hold up verbal capacities a little bit longer. The disease seems to declare itself slightly different in women than in men. It is considered a female disease, because it is more common in women. And we need to know why this is the case. There are also differences at the treatment level, for example, why is it mostly women who are going to care and not men? And, at what point do men go into care? At what point do women go into care? We know very little about sex differences in the response to drug treatment."

#### *Depression*

"This is a good example of a disorder that probably has slightly different causes and clinical expression in men and women. There may also be differences in the way in which people access care and have treatment. It also has quite different rates of mortality for men and women. Suicide risks differ between men and women. So like Alzheimer's disease this is typically a disorder that has to be looked at differently for men and women."

### *Hormone fluctuations throughout the lifespan/hormone replacement*

“This is very much an area where sex differences are involved. For example, we know that some women are born with (not everything is perfect in the body) an overproduction of estrogen and some have an underproduction of estrogen. Those with an underproduction for example are more likely to have the blues before they have periods, post partum depression, and probably also depression at menopause than their counterparts. And these are the women who may benefit from hormonal replacement therapy (HRT). And we want to look not just at women but at subgroups. So that you don’t just prescribe something like HRT across the board or not at all. For that reason we should be looking at the hormonal history of women to see if replacement may be useful.”

“One of the problems with epidemiology is that if you mix everybody together you may come up with a quite erroneous conclusions. For instance after the Women’s Health Initiative study, it was concluded that we shouldn’t touch HRT. I think this is probably going to change in the next few years. I think it is very important not to throw it (HRT) out. We have to look at subgroups of women. And we have to look at men obviously quite separately, as men also have hormonal changes which may affect their health and functioning, for example men lose testosterone but then produce estrogen later in life.” “At present we are looking at a database of women with hormonal dysregulation. We can certainly see that there is an overall effect that women who have cognitive difficulties and depressive symptomatology tend to be those with a long history of hormonal dysregulation. After that we would like to look at men separately. What are the different types of hormone exposure that men have in different conditions?”

### *Stress*

“One of our teams looks at how people’s cortisol systems react to stress, and here we also see significant sex differences. This may have important implications for men and women’s vulnerability to disorders such as anxiety, depression and post-traumatic stress.”

### *Suicide*

“The group that looks at suicide, violent suicide, is of course very interested in sex differences, because violent suicide tends to be more a male phenomenon while suicide attempts are more a female phenomenon. They are looking particularly at the genetics of it and they do look at male - female differences.”

### *Statisticians*

“The statisticians and mathematicians form a team that, along with the epidemiologists in the group, are responsible for looking at sources of bias in our research – this of course includes sex bias.”

### **Achievements**

As is evidenced in the previous paragraphs, one important achievement of the INSERM Laboratory at Montpellier is that researchers are focusing on sex and gender differences as a standard procedure of their research. When I asked if KR could mention any (clinically) important results, she answered: “You know for us this is really hard to say, because 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.”

Yet subsequently she mentioned some examples of new insights. The first example is concerned with the impact of anesthesia on the brain and particularly on the aging brain. “We know anesthetics seem to have an effect on diminishing cognitive performance. And in some people this leads to permanent dysfunction. We have found that men, who have had slightly diminished cognitive performance before they were operated, tended to have more serious symptoms following anesthesia. This wasn’t the same for women. We are not quite sure what that is. Maybe it has something to do with the dosage given to women. So we are in the process of looking at this particular vulnerability in men and women. The second example is concerned with education as an indicator for gender. “In a lot of our work we find sex differences, but in fact these differences are determined by differences in education. In brain development and aging, quite often education has a bigger impact than sex. But they are tied together, particularly because older generation women have often received less education. So the impact of gender is reflected in a sort of indirect way.” The third example concerns the outcomes of a study on differential reactions of men and women to stress: “In another study we are looking at the way in which the cortisol system functions in elderly men and women in reaction to stress. We monitor cortisol on an ordinary day and on a day they are given a quite dreadful examination. And we find that while men and women have fairly similar resting cortisol patterns, they change quite differently under stress. It is quite complex but we find that when confronted with stress, the cortisol systems of men and women don’t react in quite the same way. This might explain some of the differential symptomatology that you see in men and women under stress.”

## **Funding**

The INSERM Laboratories receive much of their funding from INSERM itself. As KR put it “the INSERM contribution is not more than half of our total budget – we have to find at least half of our research funds externally. Salaries are paid, and there is usually also enough funding after overheads, to at least get some new projects started while they are looking for outside funds.”

KR did not mention any particular problems in finding funding for research projects that focus on sex or gender differences. “We can apply where we want, we can get EU funding, funding from the ministries, from foundations and from the private sector.” In contrast to the EU many other health research funding organizations do not have a gender policy. Asked if the EU gender policy regarding the integration of the gender dimension in research had made a difference in the way in which research groups she belongs to, draw up EU proposals, she stated: “Well, now it is written into the grant conditions, that it has to be gender fair. This is what we noticed in a proposal we wrote a few years ago. So I think people are aware of that.” In reaction to the remark that in an earlier inventory GenderBasic has found that scientists do not always recognize the relevance of including attention to the gender dimension in research proposals, for instance those working on basic or animal research she reacted: “Yes that may be a danger. But we are not a group that is particularly in danger because we are an epidemiology unit. We are also linked to clinical research. In clinical research, we often have to remind the clinicians that they have to look at their data from a male and female and a social class point of view and that the findings have to be generalized to everybody. But I think the epidemiologists are already incredibly aware of that.”

## **European cooperation**

From other remarks it became clear that INSERM is increasingly involved in international cooperation. “INSERM increasingly sees itself as a European research institute.” For example, the Director General (DG) has recently created laboratories in two other European countries: one in Prague and one in Glasgow. So if there is a certain expertise in another part of Europe, instead of bringing the experts here, we put our laboratory there. And the DG is also in the process of creating what he calls “European laboratories”, where we link up with another group and share resources. My laboratory has a link, for example, with the Institute of Psychiatry in London (Kings College). Both parties contribute to collaborative research projects. We follow also very much what the European policy is. And if there is a call to develop any particular area, then INSERM would probably also put money in to develop that area.”

## **Relevant topics for a future European gender sensitive health research agenda**

Asked if she had any suggestions for research areas that should receive attention in a future European gender sensitive health research programme, KR gave the following ideas:

“What we now know on hormonal changes and hormonal influences is rather poor. I think this is a central area that might have implications for other research. We need to know more about that. On the basis of an inconclusive study in the USA, the Women’s Health Initiative (WHI), today HRT has practically been withdrawn. But in fact we don’t know enough about what hormones do. We always assume that they regulate the sexual part, but they also have an enormous influence throughout the brain, and we just don’t know enough about it. That should be a priority area of research in Europe. Especially as the population is aging and chronic health problems are increasing. Old age problems are also related to hormonal changes. Women are doing great until they get into menopause. And then it is a real problem, for instance the problem of mental health. How many women become very unhappy and depressed, develop osteoporosis or multiple joint disorders? And for men we don’t even know yet what happens as they age.”

Asked if she thought if a similar initiative as the Women’s Health Initiative would also be relevant for Europe, KR answered: “Yes, because the living conditions in Europe are quite different than in the USA. The WHI study was conducted among women who were more often overweight, had started HRT long after menopause when there may be insufficient neuroreceptors left for estrogens. In the USA study women were also taking estrogens from horses (equine estrogens) and for the most part unbalanced by progesterone. In Europe we use much smaller dosages of natural estrogen and it tends to be prescribed for the individual case and not across the board. And if HRT is going to have an effect you probably have to start much earlier in life, certainly before menopause. After menopause it has much less effect. You might modulate the menopause effect. And the other thing is that we have reduced HRT simply as a technique to reduce a few menopausal symptoms. But it is really more fundamental than this. Estrogen receptors are in the hippocampus and the forebrain, the parts of the brain that deal with memory and cognition. And you should ask yourself, why is it that women don’t have certain problems until their fifties, such as Alzheimer’s disease, and certain mood disorders, and then suddenly the incidence of these problems explodes?”

“I think there are many countries that would be willing to pull together and start a new study on these questions. And I think it would be an interesting thing to do at an EU level. Starting with epidemiological data throughout Europe, all the countries can contribute to it.”

## In sum

Our informant, Dr. Karen Ritchie directs a research programme at INSERM that pays a great deal of attention to sex and gender factors, both in epidemiological and clinical studies. INSERM does not have a policy or guidelines for enhancing attention to the gender dimension in health research. However, there are several conditions that have made it possible to develop the research programme in question:

1. In INSERM there is no gender discrimination, both at the level of the institute and at the level of content.
2. The financing and management structure of INSERM allows researchers a relatively large degree of freedom to focus on their own research interests. (investigator driven research) For Dr. Ritchie this structure has provided an opportunity to continue and develop her earlier research interests in the field of sex and gender differences in mental health.
3. Within the institute's scientific area of interest itself, the relevance of looking at sex and gender differences has become obvious, and not disputed as may be the case in other areas of biomedical research. This means that the researchers at the institute have the knowledge and the skills to look at these differences.
4. The rule that one shouldn't make assumptions that males and females are the same, unless we know, is seen as a basic quality standard of all research conducted at the institute, from basic and clinical studies to sociological studies.
5. In epidemiology, it is more and more common to collect data about sex, age, socioeconomic characteristics and education. For that reason, at INSERM and elsewhere datasets that allow for an analysis of sex and gender differences in specific populations are now widely available.
6. The interdisciplinary composition of the research team. This makes it possible to develop a comprehensive approach of which sex and gender related factors may have a potential impact on health and disease and also of how those factors may be interrelated.
7. The very fact that the studies at the institute have proven that sex or gender differences are relevant, are an important trigger for continued interest in this area and new research questions.

## THE KAROLINSKA INSTITUTE

In Sweden, universities play a major role in the production of scientific research. The Karolinska Institute (Karolinska) is the top ranked medical university in Sweden. It has also an excellent reputation worldwide. Forty percent of the medical research in Sweden is carried out at the Karolinska Institute. Karolinska itself finances part of the ongoing research, but scientists also need to find a substantial part of their research funding externally.

### Gender Policy

The Karolinska Institute has an equal opportunities policy for male and female employees. It is thought that this policy not only adds to gender fairness in employment opportunities, but also to the quality of science production. The Institute has also created the Centre of Gender Related Medicine to help stimulate research and education on sex and gender factors in biomedicine. Karolinska does not have an institutional research code that includes specific requirements for researchers to address sex and gender differences in their work. Nonetheless, besides the Centre of Gender Related Medicine, also a number of other research programmes are paying systematic attention to the potential impact of sex and gender differences on health and disease.

### Equal opportunities policy

At Karolinska about 20% of the full professors are women. This male/female ratio among the full professors has remained stable for about two decades. Nonetheless, the number of female students, PhD's, post doc's and assistant professors has significantly increased during that same period. A similar phenomenon has also been observed in other countries. In Sweden, the persistent under-representation of women in higher academic positions has led to much discussion and considerable concern in recent years. This was also reflected in an article published in Nature in 1997. The Swedish government has recently set the goal that universities should increase the ratio of female professors to at least 25% in the next few years. The rector of Karolinska, Professor Dr. Harriet Walberg-Henriksson, has made it one of her policy goals to increase the ratio of female professors at the Karolinska Institute. To this end, she has appointed a "strategy group for equality in science." This group is chaired by Professor Dr Jan Ake Gustafsson (JAG). He is our key informant regarding the activities of this group.

#### *Strategy group for equality in science*

Since its foundation in 2004, the strategy group has made two major contributions according to JAG. The first contribution is that the group has laid the groundwork for the introduction of a new and efficient mechanism to bring more women to the professorial level at the Karolinska. "This has been tried before without success, because according to EU regulations you must have an unbiased way to deal with the selection of personnel", according to JAG. But "the strategy group has found a way around this." "We have asked all the departments to give the names of their best female scientists and their CV's. This has been distributed to several experts. Subsequently, they have selected the best scientists on the basis of their CV's. This process is

still ongoing. The idea is that we will then create a certain number of professorships, tailor-made around the area of interest of the selected women. We cannot avoid, of course, that a certain number of those professorships will go to males, but the chances that the females will get them are good. We have checked this procedure and it is completely legal." JAG also emphasizes that "it has taken some time to introduce this measure. "There were many people who were against it." "For that reason, ultimately it had to be a decision of the Board of Karolinska."

The second contribution of the "strategy group" is that it has laid the groundwork for the introduction of a new series of courses for women who are working in senior positions just below the level of professor. This programme was created because the strategy group acknowledged that there may be specific factors that make it more difficult for women than for men working in the sub-top, to reach more senior levels. Such factors may be related to personal or psychological issues, coping with stress, discouraging influences from the environment or to a lack of experience in administration. The new series of courses is meant to provide (personal) coaching and support to women scientists so that they are better equipped to seek, perform and cope with high-level positions in science. In 2006 a first series of courses with 20 participants has started. Also the introduction of this measure has been "a bit sensitive" according to JAG "because the women also have to accept that they are perhaps in need for more support than males."

#### *Equal opportunities and science*

JAG stressed that, in the view of the strategy group, promoting an equitable representation of men and women in science may also contribute to the quality of science itself. "The reason that we believe in a 50/50 representation of male/female scientists is not only because of the fairness principle per se, although this is a good reason in and of itself. We also believe that women scientists can contribute to science in a special way. Perhaps, they can add new aspects to science. Women have perhaps another way to look at things than men do. So we think an equitable representation of women in science will also increase the intellectual potential or the creative potential of science itself."

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#### *Future*

At the time of the interview the strategy group had worked for two years. This work hasn't always been easy, according to JAG. "Some people had problems with our work." "It is very 'unswedish' to favor one side over the other." But, if we were confronted with such arguments we would say "women have been treated in an unfair way for decades or centuries even." "If you take this into account, it is morally acceptable to say that, in order to balance this in a reasonable amount of time, you have to accept some unfairness towards males." The strategy group has received a new mandate to continue its work for another two years. "We are quite happy with what we have achieved. And the rector has given us another two years. So we are in the middle of formulating new ideas."

#### **The Centre of Gender Related Medicine**

In 2001, the Karolinska took the initiative to start a Centre of Gender Related Medicine. The Centre started its work in 2002 and it was officially inaugurated by the queen of Sweden in 2003. The information on the Centre presented here is based on interviews with the Director, Karin Schenk-Gustafsson (KSG) and the Chair of the Board, Zsuzsanna Wiesenfeld-Hallin (ZWH).

#### **The development of the Centre**

Karin Schenk-Gustafsson has taken the initiative to create a Centre of Gender Related Medicine at Karolinska. Her experiences, working as a cardiologist in the 1980s and 1990s, were an important incentive for starting such a Centre, as is reflected in the following account: "I am a cardiologist and I worked with patients for my whole career. For ten years, I was the only woman cardiologist. There were only men around me. In the late 1980s, early 1990s I began to realize that women were absent in research and in the research methods. Cardiology didn't seem to be created for women. At that time I had just moved from Huddinge Hospital, which is now part of Karolinska, to the Thoracic Clinics at Karolinska. When you do such a thing, when you change something in your life like that, you all of sudden begin to see things with other eyes. And I saw, when I sat at the X ray rounds, where it is decided whether patients should be operated upon or not, that many of the discussions among my (male) colleagues about female patients were not backed up by research findings. For example, when we saw a normal angio in a female patient they would say "Oh, it is a woman, typically a woman. This is a simulant, psychological reasons, send her home and stop all the medication." At the time it was neglected that it might have been syndrome X or spasm. It was also commonly thought that women don't have myocardial infarctions. But when I went to the coronary care unit I saw that half of the patients with myocardial infarctions were women. So what I read in the textbooks didn't match what I saw in the clinic. In the early 1990's a lot of us got angry about this approach. In the US, NIH, Bernadine Healy and some research centers had started a movement to change this." "I visited some of these centers in the US in the early 1990s. It was very inspiring to talk about their experiences. I was particularly inspired by the ideas of Marianne Legato at Columbia University. When I came back in Stockholm I started to plan for a center at Karolinska. I got a little money from the Karolinska hospital to work on this for about three years half time.



I had a project group at Karolinska. I had made a plan and a programme. By that time I had also realized that there were not only problems in cardiology but also in a lot of other medical specialisms. However, many people did not really understand what I wanted. Then I met with Harriet Walberg-Henriksson, at that time the dean of research at the Karolinska Institute. She understood immediately what I said. She is a clinical physiologist by training, so she understands a little bit about cardiology. Therefore, it may have been easier for her to realize what the problem was. She felt it was a very good thing to begin a Centre for Gender Related Medicine. We started to work on this. I rewrote my programme, got it even better and with that in our hands we went out fundraising. We got some money from Karolinska and the Wallenberg family and in 2001 the Centre started. It started out with a Board, with Zsuzsanna Wiesenfeld as the chair in 2001. Later on the position of Director was advertised. There were eight applicants and I was selected. I started on 1-4-2002. We had an inauguration with the queen. It was fantastic.”

### Challenges

The creation of the Centre has, however, also raised considerable debate among potentially relevant stakeholders in Sweden. As ZWH puts it “In Sweden we have a double problem: mainstream scientists may not consider our approach very important and we also have a problem with more politically oriented gender scientists.” Overcoming this problem is one of the challenges the Centre is faced with. As ZWH said, “In our view there are social and power differences between men and women and biological differences. These differences interact, and we are interested in the question what are the mechanisms: how can this happen? So it is a complicated approach, which needs different kinds of research and it is difficult to explain this.” Explaining the cornerstones of the Centre KSG reports: “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. From a clinical point of view, we are aiming to have a healthy patient. Considering all these different factors is very important if we want to handle the patient in the right way. And, an additional contribution of our approach to science may be that, if you compare men and women and the mechanisms that explain differences between them, perhaps you can learn something new about diseases themselves or about risk factors. So we are not only biologists but also interested in gender. Both elements are always there. As a clinician you know this the moment you see patients: every patient is either male or female.”

But making people understand this approach has not always been easy. Recalling the first reactions of her colleagues in cardiology, KSG says: “When I started here they thought I was an idiot. They didn’t understand what I was talking about. This was in the early 90s when I had just started a study on Stockholm women. We did coronary angiographies on them to study risk factors. My colleagues would always make jokes about this. So it was difficult. But when they saw I was able to get money for more research, they looked a little bit more seriously. And now they are my good friends.”

“Also, when I was talking about ‘gender medicine’, medical doctors would often think that I was a communist, a die hard feminist, member of the anti men movement, and they would stop listening. So it took a lot to make them listen.”

Interestingly, also the ‘gender researchers’ in Sweden questioned the approach of the Centre according to the informants. KSG recalls: “They said we were not allowed to use the name gender.” ZWH provided the following explanation for this: “The ‘gender researchers’ don’t like our biological approach. In their view gender research mainly involves the study of social and power relationships.” Indeed, according to ZWH, Karolinska’s view is sometimes considered ‘odd’ in Sweden. She adds, “ But worldwide, there is more and more attention to this approach. We participated in the organization of the first World Conference on Gender Medicine in Berlin in February 2006. There were participants from many countries and it was quite a success.” The Centre has also been criticized by journalists in the popular press in Sweden, according to KSG. One of their main concerns was that the Centre was “not paying enough attention to men.” In the eyes of KSG and ZWH, these public debates and the (mis)interpretations of what the research at the Centre is aiming for, may be seen as one of the back drops of the fact that, so far, the Centre has not received funding for its activities from any of the national research funding agencies in Sweden, neither from those funding gender research nor from those funding biomedical research. Nonetheless, the Centre has been able to carry on, aided by Karolinska, and other funding agencies (see below section funding).

### Training facilities

The Centre has started with a focus on research. However, KSG reported that it is now also focusing on medical education. “A new development is that last year, after a lot of lobbying, we got extra money from the Stockholm City Council. They want us to raise awareness of ‘gender medicine’ in all the clinical specialties at Karolinska. Therefore, we are now looking for someone who is going to work on the integration of attention to gender issues in the educational curriculum of the Institute. This is still lacking here. Today, there is only structural attention to gender issues in a few programmes (general medicine and neurology).”

## **Integrating the gender dimension in research: the scientific approach**

The Centre has started out with a research programme. “We thought if we can identify and initiate new research groups on ‘gender medicine’, this would be a good start” , says KSG.

### *Scientific model*

When asked if the Centre had developed a theoretical or a conceptual model on how sex, gender and health are related, KSG responded: “This would be very good. We are working with biological determinants of health and also social and psychological determinants, but we have not elaborated these relationships properly in a model. We use these variables in our research projects. However, we are now planning to write a book about this.”

Another aspect of the Centre’s scientific approach is that most research is conducted by multidisciplinary teams. Members of the research teams can include people from all clinical specialties and nursing, social scientists, psychologists and epidemiologists. However, “unlike our colleagues in Berlin, at Karolinska we don’t have a philosopher on board yet”, says KSG, “and we might have to change this.”

### *Example: Borrelia*

To illustrate the research approach in ‘gender medicine’ KSG gave the following example. It describes the way in which recent discoveries were made concerning *Borrelia burgdoferi* or Lyme disease. This is a bacterial infection transmitted by tick bites. “The symptoms are a red ring, and if it is not treated it can cause encephalitis and other central nervous system conditions. In Southern Sweden Lyme disease is quite prevalent.” “Quite recently a GP from this part of Sweden reported that she had observed in her practice that in elderly female patients Lyme disease didn’t manifest itself by the typical ring. They just had erythema: an irritation or reddening of the skin. She began to investigate this phenomenon further, by keeping a patient register. Now she has the largest existing patient registry on *Borrelia*. And on the basis of this registry she has been able to confirm her hypothesis that women over 45 do not get the typical ring, but only irritation. She also found that those women without the typical ring have more CNS manifestations. Probably, they had been under-diagnosed and thereby under-treated. As the next step in her investigation, she contacted the immunology department at Karolinska. She wanted to know if the observed differences were due to sex differences in the immunological response to this bacterial infection. They did some immunological tests, and it became clear that the absence of a ring has to do with the decreasing hormone (estrogen) levels as women enter the climacterium. Estrogen is part of your immune defense system, and as estrogens are decreasing the immune responses may also change. That is the theory. So while men keep a ring as they age, women do not.” “This is part of gender related medicine, or at least one example of it”, according to KSG.

## **Achievements**

The creation of a Centre of Gender Related Medicine within an institution with an outstanding record of excellent biomedical research, such as the Karolinska Institute is an important achievement in and of itself. But there are more achievements worth mentioning.

The Centre of Gender Related Medicine, offers scientists working at Karolinska and throughout Stockholm the opportunity to apply for grants. “We have external examiners, so the procedures are absolutely transparent”, says ZWH. So far, the Centre has spent 20 million Swedish crowns on grants for research activities. This money came from Karolinska, an insurance company and a private foundation. It has been used to support salaries for excellent ‘gender medicine’ scientists and research grants. Since 2002, thirty-two research groups were supported. “But we had over a hundred applicants”, says KSG. “We supported 9 PhD theses, which are now finished. The researchers were already doing their PhD research, and we financed part of it.”

A second achievement to which the Centre has been able to pay a contribution, according to KSG is that “cardiology is now one of the medical specialisms that is very well penetrated and analyzed from a gender perspective.”

The Centre also organized and participated in many national and international symposia and meetings, such as the previously mentioned First International Conference on Gender Medicine in 2006. “We organize at least one national and one international meeting every year” says KSG, “and then also seminars.”

KSG has also been able to continue and expand her own research programme on women and coronary heart disease (CVD). “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. It is also very, very tough to make them stop smoking. They may even smoke immediately after a myocardial infarction. What is new about this rehabilitation programme is that it lasts five years. You cannot change behaviors in one year. Relationships between the group members are very important. By talking to each other they can cure themselves and help each other. And also the self-experienced health questionnaire is very important. It is a good prognostic marker. And we have reduced hospital stay and relapse with this programme. We can see this because we also have a control group. We are now analyzing all the data.”

In another study supervised by KSG, three PhD’s are doing a 10 year follow up study on Schenck’s earlier Stockholm female coronary risk factor study in a cohort of 600 patients. “There are already interesting

preliminary results.” A third project deals with arrhythmias in pregnancy. Finally, the previously mentioned project which has the aim to integrate attention to gender issues in the educational curriculum of the Karolinska Institute can also be seen as one of the achievements of the Centre.

### **Diffusion of a sex and gender sensitive research approach within the Karolinska Institute**

Working in collaboration with the Centre has also influenced scientists who had not been involved in ‘gender medicine’ before, as is evidenced by the account of ZWH: “My background is not in ‘gender medicine’, but I got interested in it through my engagement in the Centre for over 6 years. In my own field, which is in pain mechanisms, actually gender is now becoming one of the important issues. And my own research is also beginning to focus in that direction. In the area of pain until fairly recently few people have been interested in gender issues as a scientific issue. But it is actually starting to explode now. 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. For example migraine is much more prevalent in women. In general, various types of chronic pain are more prevalent in women than men. But now tools are becoming available to study this at a more basic level, including molecular biology, pharmacology, physiology and behavior in animals. Hopefully these studies will result in better pain treatments for men and women. “These are very exciting times. And, sex and gender related questions are now becoming mainstream.”

With KSG and some others, ZWH has recently started a basic and clinical study, looking at differences in pain in male and female cardiac patients and transgenic mice. “We have hypotheses about some of the mechanisms and we are testing these.” Indeed, as ZWH puts it, “one has to say this approach is becoming very clearly established in all areas of biomedicine.”

This was also illustrated by the account of JAG. Many of the projects that are conducted at his institute, NOVUM, are basic science studies involving sex steroids. “So it goes without saying that sex differences are very important to us. We see them as of one the bases of the mechanisms we study.” Ten years ago, his research group discovered a new estrogen receptor. Now much of the research efforts and the collaborations of the institute are devoted to studying the impacts of this discovery. According to JAG, “this is great fun. For instance, I have started to look at sex differences in metabolism in rodents, because in rodents the liver metabolism is extremely different in males and females. In humans this difference may also occur but maybe less pronounced. I just mention these examples to show, that 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.” He adds, “so I really hope that FP7 will still pay as much attention to the study of sex and gender differences as FP6 did or that it will maybe even expands the attention to these issues. But then it comes to the political level.”

### **Funding**

So far, the Centre of Gender Related Medicine has not received any external funding by national research agencies. ZWH explains that the situation with respect to national research funding is very complicated in Sweden. One aspect is “that in Sweden ‘gender research’ is associated with a feminist view. At Karolinska, we are also looking at biological differences, and this has had a lot of resistance. So far, the Centre of Gender Related Medicine has had no support from the Swedish State. In contrast, through a number of national financing agencies, the ‘feminist gender research’ has been generously supported, based on the number of academic positions in the field and the number of undergraduate and graduate students. Thus, although we are looking at biological differences as well as social differences, I mean to everything from molecules to society, in a scientific way, all the support we have had was from the Karolinska Institute, and some private foundations. Very recently we have also received funding from Stockholm County Council. Now we are actually trying to apply for a grant from the state-financed Swedish Research Council in competition with all the traditional gender researchers. And it will be very interesting to see whether or not we succeed.

A second complication in acquiring state funding for biomedical research, which involves all researchers in biomedicine, is related to the recent policy decisions in Sweden to concentrate the bulk of research funding to only a few areas.” ZWH explains this situation as follows: “You know Sweden is a small country and it has an outstanding scientific record. And that scientific record needs to be maintained. One of the problems in the past has been that the money was spread too thinly. And now there is a move to concentrate. I think this is correct. But what I am a little concerned about is that this is concentration at the exclusion of many other areas which are relevant. So the pendulum has swung from one extreme to the other. Funding organizations in Sweden have gone from flat funding to a funding system based on large networks of excellence. So now only relatively few areas have been selected as fundable on a large scale. Within medicine, for example, brain imaging and stem cell research is getting a tremendous amount of money. Now of course this produces very interesting science. But for research in ‘gender medicine’ concentration and the strictly excellence driven funding system implies that relevant research may be excluded only because they do not belong to the selected areas.”

Together with other centers of Gender Medicine in Europe, the Centre at Karolinska has also applied for a grant in FP6, on recommendation of civil servants in Brussels, who had explained the EU gender policy. KSG explains: “The idea was to create a network of experts and to write a book about key issues in ‘gender specific medicine’. Our thought was we should start with little money. We wanted to locate top scientists from many countries and make them write about their research and the gender issues in this. We had already engaged several interesting scientists. For example, the president of the European Cardiological Association had accepted to write about heart failure and gender. I worked a lot on this application. It got excellent grades 24 out of 25, but no money.” This has been a discouraging experience with the EU research funding system, especially because the group felt they had not received clear feedback about the reasons for rejecting the proposal.

### **European cooperation**

At the Karolinska Institute, much of the ongoing research is conducted in collaboration with research teams from other countries, inside or outside the EU. The Centre of Gender Related Medicine has a number of collaborative projects with Centers of Gender Medicine in Europe as well as in the United States and Australia. Two of our informants (JAG and ZWH) have (ample) experience with the recent European Framework Programmes (FP5 and FP6). Both have been part of projects that were financed through those programmes and were aware of the FP6 gender equality policy as regards to research. Both of them are involved in basic research. And, as was exemplified above, in their own research both are interested in studying sex differences for scientific reasons. They feel that studying sex and gender differences adds to the quality of their science. To this background, in their view the presence of attention to sex and gender differences should remain a quality criterion for evaluating research proposals in FP7. They also expressed concern, however, that there may be less of a focus on this issue, in this programme.

ZWH remarked: “The fact that much of the research funded by the EU in FP7 will be curiosity driven and not centrally determined seems to me an excellent development and a big change from FP5 and FP6. This is becoming similar to the established practice at the NIH in the US. But if this change means that attention to gender issues, which is now very well established, at least in America, would be unselected or negatively selected this would be a very serious mistake. So hopefully the panels judging the applications in relevant areas will be instructed to look for the presence of attention to gender issues.”

With a reference to the funding situation in Sweden she also stated: “If this new European Research Council is going to be as strictly excellence driven (as the Swedish Council), it may restrict the areas of research that are fundable. Then we are back to where we were in the previous Frameworks. In the previous frameworks it was a political decision what areas were going to be funded, which also meant that a lot of areas were being excluded. Now in FP7, hopefully more interest-driven projects will be funded and applications will be approved only on the basis of scientific excellence. But if this means that studies that focus on gender issues are going to be excluded because they are smaller and not scientifically interesting then we are back where we were. So hopefully a balance between “big science” and smaller, curiosity driven science will be possible.”

JAG also was hoping that FP7 will continue to pay attention to the integration of the gender dimension in EU funded research or maybe even expands its attention to this issue. One reason is that ‘gender medicine’, the study of sex and gender differences, has already proven to have “scientific value in its own right.” For instance in endocrinology, one of JAG’s own areas of interest, the study of sex differences has opened many up new possibilities and insights, and will thereby remain an important focus. The new FP7 Programme reflects the philosophy that the EU wants to get away from politically defined cross cutting issues or policy driven science in order to focus on real science. It is thought that this may increase the competitive edge of the science produced in the EU. In the view of JAG, however, this approach raises questions if we look at promoting the integration of attention to the gender dimension in science. For instance, promoting equitable representation of men and women in science may be seen as a political issue. But, as was mentioned before, in the view of the strategy group at the Karolinska, letting more women in may also contribute to a new approach in science and thereby to a more competitive edge of science. “There are books written about this that women have different ways of looking at problems. Women may also be better collaborators because sometimes they are less aggressive than men. This means they can more easily interact in networks and be more productive. And it is also possible that women are more creative because, as some people say, they have a more intuitive tendency.” Indeed, according to 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.”

### **Relevant topics for a future European gender sensitive research agenda**

The informants from Karolinska also had several suggestions for projects or research areas that may be relevant in view of the integration of attention to the gender dimension in future European funded research. JAG stated that the experiences of the strategy group for equality in science at Karolinska, had led to the idea that it would be relevant to create a network of European biomedical universities, This network could have two major tasks. The first is concerned with research. The network could make an inventory of sex and gender

related questions that are relevant in 'gender medicine' in Europe, make a programme of how these questions may be addressed, and it could also conduct some preliminary research. The second task would be to make an inventory of which policy measures are effective in enhancing attention to the gender dimension in science at a country and EU level. Members of such a network could be representatives from institutions with experience in paying attention to these issues, and representatives from institutions that have very little or no experience in these matters. At Karolinska there is a keen interest to participate, contribute and even to coordinate such a network. With respect to FP7, this means that the possibility to create such a network should be opened up.

There were also some ideas about specific topic areas. As Dr. Karen Ritchie from France, KSG and JAG felt that what we now know on HRT is based on the results of an inconclusive study in the USA, the Women's Health Initiative (WHI). They both think that our current knowledge of hormonal changes and hormonal influences on health is still rather poor, and this could be one area of interest for research in 'gender medicine' in Europe. ZWH believes that neuroscience is also such an area. "There is overwhelming evidence on sex differences in the brain. So I believe neuroscience should be an important focus. And I don't just mean pain. For instance autism is seven times more common in men than in women whereas depression is more common in women than men. So there is overwhelming evidence for biological differences in the brain, which leads to differences in behavior, diseases and society."

### **In Sum**

Our interviews indicate that the study of sex and gender differences is becoming an increasingly important part of the scientific research that is carried out at the Karolinska Institute. The Karolinska Institute does not have a formal research code that requires researchers to include attention to the gender dimension in health research. However, several factors have facilitated the current focus on sex and gender differences in health research at Karolinska. 1. The rector of the Karolinska Institute and several full professors with outstanding scientific records have made clear commitments to enhancing attention to the gender dimension in biomedicine. 2. The Institute has an equal opportunity policy for employees and has installed a committee that has the task to design and oversee the implementation of clear plans for interventions to address barriers that enhance the participation of women at high level positions. 3. A woman scientist who had come to the conclusion that the gaps in knowledge regarding women's health which she had identified in her own field were also common in other areas in biomedicine. 4. In order to enhance greater attention to sex and gender differences in health research and clinical practice, she drew up clear plan for the establishment of a Centre of Gender Related Medicine, based on an analysis of barriers and facilitating factors. 5. The Board of Karolinska supported the plan for the foundation of the Centre in 2002. 6. The Centre has been able to acquire funds for its own funding programme to stimulate research on a variety of sex and gender related questions. This has resulted in many applications and 32 funded studies. 7. The Centre has organized many informational outreach activities for the research community. 8. Also outside the Centre, in many areas of biomedical research, the awareness of the relevance of studying sex and gender differences is growing. 9. With its multi-disciplinary approach focusing on biomedical determinants of health (sex) and social determinants of health (gender), the Centre of Gender Related Medicine moves into the territory of other (sub)disciplines that have traditionally studied those determinants (biomedicine and gender studies) in Sweden. On the one hand the Centre has been successful in developing interdisciplinary research projects that link data concerning biological (sex) determinants of health to those concerning social or psychological determinants of health (gender). On the other hand, however, overcoming territorial disputes with sub disciplines that have traditionally studied gender and health issues still remains a challenge.

### **CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN**

The Center for Gender in Medicine (GiM) is part of Charité Universitätsmedizin in Berlin. Since the unification of the medical schools and hospitals of the Freie Universität and Humboldt-Universität in Berlin in 2003, Charité is the largest medical school and university hospital system in Europe. It has nearly 15,000 employees. From the 128 former medical departments, 17 centers have been formed according to patient care, research and education needs. Information about general Charité policies with respect to equitable participation of men and women in the work force or the integration of attention to the gender dimension in research is not available, because our enquiry has only focused on GiM.

### **The Center for Gender in Medicine (GiM)**

The initiative to start a Center for Gender in Medicine was taken by Prof. Dr Vera Regitz-Zagrosek (VRZ). VRZ is a cardiologist. She worked since 1985 at the German Heart Institute in Berlin in different functions, as a clinician and a researcher. Through her clinical work and her research, during the 1990s VRZ became increasingly aware and concerned about the existing gaps in knowledge with respect to cardiovascular diseases in women. She also felt that the understanding of cardiovascular diseases in women required 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. To develop such a programme in 2002 VRZ was appointed as a professor of cardiovascular disease in women at the Ger-

man Heart Institute in Berlin. At the same time VRZ had drawn up a plan to develop a Center of Gender in Medicine, linked to her chair in cardiovascular disease in women. She has been careful to acquire support for this plan from a wide range of relevant professors within the Charité system and the Berlin Universities. In 2003 she became the deputy director of the Cardiovascular Research Center of Charité. In the same year the Center for Gender in Medicine started, of which VRZ is the Speaker. The Center has the following aims:

- Studying sex- and genderspecific differences in the biological basis of clinical syndromes, in the manifestation and course of diseases, in prevention, diagnostics and therapy as well as in health care structures.
- Promotion of specific research in the above areas.
- Implementation of the research findings in medical practice.
- Mediation of the research findings to the public, policy makers, authorities, and institutions of the health care system.
- Adoption of the findings into medical education at the Charité.
- Creation of a curriculum and its integration into medical education.

In designing the organizational structure of the Center, a key consideration has been that there must be sufficient “critical mass” within Charité and among other stakeholders in the Berlin University system to develop and sustain a specific Gender in Medicine programme. Besides VRZ, the Board of the Center includes the adjunct speaker, Dr. Patricia Ruiz Noppinger, professor of the molecular basis of sex differences, and two other professors from Charité. The Center has around 70 members, from different scientific disciplines and institutions in medicine and from non medical disciplines, all of whom are more or less involved in a topic related to gender in medicine. Twenty of those members are teachers from different disciplines within medicine. The 70 members of the Center are represented in a Council of 13 members (7 professors, 4 research assistants, 1 student, 1 other collaborator). In addition to this, there is a scientific advisory committee, with national and international representatives. Through the establishment of these different organizational bodies, the Center has been able to involve important stakeholders from a variety of different fields (health and biomedical research, medical education, health care and health policy).

The position of VRZ is largely financed by the German Heart Center and the Cardiovascular Research Center. Funding for other staff, researchers and research projects must be found externally.

### **The approach to research**

During the time of the interview the research programme of GiM consisted of 7 basic research projects, 3 clinical research projects, 1 prevention research project, 1 health care research project and 1 research project directed towards the integration of attention to sex and gender related factors in medical education. Of these 13 projects, 8 were focusing on sex- and gender specific mechanisms related to cardiovascular diseases and 4 on autoimmune diseases (e.g., MS, rheumatoid arthritis, allergy, HIV). The project on medical education is of a more general nature. While GiM does not have a document describing the overarching scientific framework for studying the gender dimension in biomedical research, there are a number of general insights that play a role in the research programme.

According to VRZ an 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. Secondly, good research in ‘gender medicine’ is much more than “just counting men and women” according to 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. Giving an example from her own field of research VRZ said: “I just went through all my literature to write a review on gender and diastolic heart failure. At first it seemed there was almost no information available. I only found a few epidemiological studies that just counted men and women. In all the papers on the mechanisms of diastolic heart failure I have been able to find more relevant literature, however. But this is only because I know about the sex specific mechanisms that are involved in diastolic heart failure: for instance I know that some proteins are regulated by estrogens. So I continued my search by looking for literature on these topics. As a researcher you have to be able to make those links. That is what researchers do or should do.” Supporting researchers in finding the sex and gender related concepts, categories and relationships that may be relevant to their research questions is therefore one of the important tasks of GiM. 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.

Another task of the research group at GiM is to make existing evidence on sex- and gender related mechanisms of health and disease available to health care providers. This is done through the publication of systematic reviews of the literature or by organizing meetings for professionals on specific topics.

### **Training facilities**

Each year, the GiM members are giving a series of lectures, seminars, and courses to students in medicine on 'gender medicine' and related topics. They are also involved in educational programmes of related disciplines such as the Masters Health and Society and Molecular Medicine. Furthermore, the Center organizes a lecture series for a wider public, on broader issues. For example, the 2005-2006 series of lectures was related to the topic: Sex- Gender-Geschlecht: Ist Medizin geschlechtsneutral? The series included contributions by scientists from a variety of different disciplines, such as cultural sciences, biomedicine, sociology, molecular biology, sociobiology and public health. Furthermore, GiM organizes a yearly symposium, the so-called "Berlin Symposium on Gender Research in Medicine." These symposia are meant stimulate interest in research in the field of 'gender medicine' and to disseminate information on new research data and current debates on sex and gender differences in health research among (young) researchers, the 70 GiM members, and others who are interested.

### **Ongoing research**

Information on the specific content of the studies that are carried out under the auspices of GiM can be found at the website of the Center (<http://www.charite.de/gender>).

### **Achievements**

Within a relatively short period, GiM has been able to establish a research programme which has produced new insights regarding sex specific mechanisms in disease, the impact of sex and gender specific factors for clinical practice and on health services and prevention. It has also been able to attract professors and researchers with excellent research records in their own field of research. This facilitates the quality of the research that is conducted at the Center. The Center has played a key role in organizing the First International Conference on Gender Specific Medicine, in Berlin in 2006, and it continues to play a role in international cooperative efforts to advance 'Gender Medicine'. For instance, two of the 10 scientific reviews that were prepared for the expert meeting that is organized by GenderBasic in January 2007 are written by members of GiM.

### **Financing**

The GiM research programme relies mostly on external funding. The Center has been able to acquire funding for all of its current research projects from a number of (health) research funding organizations in Germany. Moreover, VRZ participates in the EU funded Network of Excellence, "Eugeneheart", which deals with the transition from hypertrophy to heart failure. The University of Goettingen is responsible for the over all coordination of this project, and VRZ coordinates one part of the project: the gender task force. However, finding external funding also involves complications that may be related to the fact that 'gender medicine' is a new area within biomedicine. For instance, in 2006 VRZ submitted a proposal to the German Science Foundation. The aim of the proposed project was to investigate a number of biological mechanisms of sex differences in clinical syndromes by means of an interdisciplinary biomedical approach. The project consisted of a series of subprojects that would be conducted by scientists from different biomedical subspecialties (e.g. molecular genetics, clinical chemistry, pharmacology, endocrinology, nephrology, cardiology, cardiovascular surgery, bioinformatics and biometrics). The proposal was rejected because "they did not feel that sex and gender differences was a relevant issue" according to VRZ. "One of the main reasons for this rejection was that the research group did not publish enough in gender. But all the scientists involved have published a lot. They are all eminent scientists. 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. For that reason, for reviewers of the proposal, it might have been difficult to identify that sex differences is indeed a common theme in the literature the research proposal was built on." So the German Science Foundation does not acknowledge the study of sex and gender differences as such as a relevant theme or common denominator for studying diseases. VRZ also said "I don't know where else I should apply for this type of research in Germany. There are hardly any gender funds for basic research." Indeed, gender research in the field of health is generally concerned with the investigation of a combination of socio-economic, cultural, psychosocial or psychological mechanisms that are related to health and disease. Gender research in basic biological and clinical mechanisms of health and disease is still a new area.

### **European cooperation**

GiM has a close cooperation with other Centers of Gender Medicine in Europe (Karolinska) and in the United States. VRZ is a partner in a large EU funded project (see above), through which the Center collaborates with other European Centers of Excellence in Health Research (e.g. INSERM and the Karolinska Institute).

### **Relevant topics for a future European gender sensitive health research agenda**

In the interview with VRZ there was little time to discuss suggestions for gender sensitive research that might be needed in the EU in the near future. However, in the course of the interview some issues were mentioned. GiM and several other researchers who are involved in 'gender medicine' in Europe think it is very important to organize a European network of researchers in 'gender medicine'. Such a network should have two aims: 1. To find out which gender issues are most relevant for a future research agenda and 2. To write a book on the state of the art of evidence concerning a number of these selected issues. To this end a project proposal has been submitted to the EU. "This proposal shows very well what we think should be done in terms of networking and research at a European level", according to VRZ. At the time of the interview a second version of this proposal was still under review. With respect to collaborative research with small or medium size companies, VRZ suggested that a lot more basic research in 'gender medicine' is needed to be able to collaborate with biotech companies. Nevertheless, there are several ideas. For instance VRZ said "if you work on artificial hearts you find out that most of the available implants are far too big for women. In the data base for artificial harts only 10 percent of the available hearts are fit for women. The others are too big. So this is an example of an issue we might be able to work on with European companies."

### **In Sum**

In 2003 Charité has founded a Center for Gender in Medicine. This Center has been able to develop a research programme on sex- and genderspecific differences that combines basic, clinical, prevention, and health services research. A number of conditions have facilitated the creation of this Center. 1. The Center was an extension of a VRZ's Chair in cardiovascular diseases in women, and the research programme could be built on her earlier research in this area. 2. The creation of the Center was supported by people in high-level positions at Charité. Through its organizational structure, the Center has ensured itself of the participation and support of a wide range of stakeholders. Each of these factors was not only important for creating a Center but also important for sustaining it. 3. The Center has been able to attract researchers with excellent track records in basic, clinical and health research and it has been able to find funding for personnel costs and projects. 4. The Center has been able to organize relevant local, national and international cooperation. 5. The creation of the Center has allowed researchers to develop an interdisciplinary approach to sex- and gender related mechanisms in health and disease. 6. So far, most of the research is carried out by scientists from different sub disciplines within biomedicine. 7. The Center regularly publishes research reports in scientific journals, which is an indicator of the scientific value of the chosen approach. The Center wants to make it possible for researchers who work within different biomedical research traditions (basic, clinical, prevention, health services) to work towards a common goal: to achieve a better understanding of sex-and gender related mechanisms of diseases. However, this approach has also raised questions from research funding organizations. An important question was what do interdisciplinary projects on sex- and gender related mechanisms in health and disease have in common, if different disciplines use different conceptualizations and categories for investigating sex- and gender differences? Thus, the development of a common conceptual model remains a challenge.



## Conclusions

This 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.

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).

The reasons for taking these initiatives varied. In the INSERM research programme on pathologies of the nervous system, the initiative to focus on sex and gender differences was taken, because this approach was already an intrinsic part of the prevailing research practices. The approach did not require an educational programme for the research team, or major adaptations of the research methods used in the project and of the available datasets. The initiatives to establish Centers of Gender (in) Medicine were taken because it was observed that there was often a lack of systematic attention to the impact of sex and gender specific factors the prevailing biomedical research practices. These Centers were established to create better conditions for paying attention to those factors in research.

Whereas the establishment of the Centers of Gender (in) Medicine, required good planning and lobbying, the implementation of the INSERM initiative 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 for 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.

The selected strategies for promoting attention to the gender dimension varied: In Montpellier attention to sex and gender factors was integrated in the “normal” research programme. In Stockholm and in Berlin specific research programmes had been developed that researchers could join and both institutions organized specific training activities for researchers. In addition to this, the Stockholm Center also had its own research-funding programme that was used to stimulate bottom up research on sex and gender related aspects of health of excellent quality.

According to the definition of the European Commission, attention to the gender dimension in the content of research comprises both sex and gender issues and requires a clear distinction between the two concepts. 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, behaviors and values that society ascribes to men and women on a differential basis.

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 opinion, 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). Some people may argue that the development of such a framework is not useful whereas much research is inductive and utilizes the terminology that fits the research. However, others may argue that there is a need for clarity regarding these concepts, not only for researchers themselves, but also for reviewers of research proposals, or research reports. Conceptual clarity might also help to convince research-funding bodies in individual member states.

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.

## Appendix: Selected quotes on salient issues

### 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 reports: "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."

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."

For instance in endocrinology, one of JAG's own areas of interest, the study of sex differences has opened many up new possibilities and insights, and will thereby remain an important focus.

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."

### Specific (research, national) contexts

#### *INSERM: epidemiology context*

KR: "There are many women working at INSERM. Women usually bring women's issues with them and there is no trouble in having female health oriented projects."

KR: "People often confuse a gender sensitive approach to research with feminist issues."

#### *SWEDEN: funding of gender research*

KSG: "So we are not only biologists but also interested in gender."

KSG "Also, when I was talking about 'gender medicine' medical doctors would often think that I was a communist, a die hard feminist, member of the anti men movement, and they would stop listening. So it took a lot to make them listen."

ZWH: "One aspect is that in Sweden 'gender research' is associated with a feminist view. At Karolinska, we are also looking at biological differences, and this has had a lot of resistance."

ZWH: "The 'gender researchers' don't like our biological approach. In their view gender research mainly involves the study of social and power relationships."

ZWH: "Thus we are looking at biological differences as well as social differences, I mean to everything from molecules to society, in a scientific way."

KSG: "The Centre has not received funding for its activities from any of the national research funding agencies in Sweden, neither from those funding gender research nor from those funding biomedical research."

ZWH: "But what I am a little concerned about is that this (i.e. the policy of the Swedish Research Council to concentrate on a few areas) is concentration at the exclusion of many other areas that are relevant."

### **Connections made between the gender dimension and promoting women's participation**

KR: "There are many women working at INSERM. Women usually bring women's issues with them and there is no trouble in having female health oriented projects."

JAG: "The strategy group has found a way around this (affirmative action). We have asked all the departments to give the names of their best female scientists and their CV's. This has been distributed to several experts. Subsequently, they have selected the best scientists on the basis of their CV's."

The introduction of this measure has been "a bit sensitive" according to JAG "because the women also have to accept that they are perhaps in need for more support (i.e coaching) than males."

JAG: "The reason that we believe in a 50/50 representation of male/female scientists is not only because of the fairness principle per se, although this is a good reason in and of itself. We also believe that women scientists can contribute to science in a special way. Perhaps, they can add new aspects to science. Women have perhaps another way to look at things than men do. So we think an equitable representation of women in science will also increase the intellectual potential or the creative potential of science itself."

### **Remarks made on conceptual issues / models / further insights**

According to KR, a gender sensitive approach does not require major adaptation of the existing research methodology.

According to KR recording sex (and gender?) differences has become "an intrinsic part" of the epidemiological methods used in population-based research.

KR: "I think the main thing is that we have a multi disciplinary group.

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KSG: "Another aspect of the Centre's scientific approach is that most research is conducted by multidisciplinary teams."

KSG: "We are working with biological determinants of health and also social and psychological determinants, but we have not elaborated these relationships properly in a model. We use these variables in our research projects."

ZWH: "We have hypotheses about some of the mechanisms and we are testing these." Indeed, as ZWH puts it, one has to say this approach is becoming very clearly established in all areas of biomedicine."

According to VRZ the understanding of cardiovascular diseases in women required a comprehensive, multi-disciplinary research programme on sex- and gender specific-mechanisms leading to cardiovascular diseases, which should include basic, clinical, epidemiological, prevention and health care studies.

According to VRZ an 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."

## Views on FP7

JAG: “So I really hope that FP7 will still pay as much attention to the study of sex and gender differences as FP6 did or that it will maybe even expand the attention to these issues. But then it comes to the political level.”

JAG: “One reason is that ‘gender medicine’, the study of sex and gender differences, has already proven to have “scientific value in its own right.” For instance in endocrinology, one of JAG’s own areas of interest, the study of sex differences has opened many up new possibilities and insights, and will thereby remain an important focus.

ZWH: “The fact that much of the research funded by the EU in FP7 will be curiosity driven and not centrally determined seems to me an excellent development and a big change from FP5 and FP6. This is becoming similar to the established practice at the NIH in the US. But if this change means that attention to gender issues, which is now very well established, at least in America, would be unselected or negatively selected this would be a very serious mistake. So hopefully the panels judging the applications in relevant areas will be instructed to look for the presence of attention to gender issues.”

ZWH & JAG feel that studying sex and gender differences adds to the quality of their science. To this background, in their view the presence of attention to sex and gender differences should remain a quality criterion for evaluating research proposal in FP7. They also expressed concern, however, that there may be less of a focus on this issue, in this programme.

VRZ: “So the German Science Foundation does not acknowledge the study of sex and gender differences as such as a relevant theme or common denominator for studying diseases. VRZ also said “I don’t know where else I should apply for this type of research in Germany. There are hardly any gender funds for basic research.”

## Suggestions for interesting research areas from a sex and gender sensitive perspective

KR: “What we now know on hormonal changes and hormonal influences is rather poor. I think this is a central area that might have implications for other research. We need to know more about that. On the basis of an inconclusive study in the USA, the Women’s Health Initiative (WHI), today HRT has practically been withdrawn. But in fact we don’t know enough about what hormones do. We always assume that they regulate the sexual part, but they also have an enormous influence throughout the brain, and we just don’t know enough about it (hormonal changes over the life span, ageing m/f, brain research).”

KR: “And the other thing is that we have reduced HRT simply as a technique to reduce a few menopausal symptoms. But it is really more fundamental than this. Estrogen receptors are in the hippocampus and the forebrain, the parts of the brain that deal with memory and cognition. And you should ask yourself, why is it that women don’t have certain problems until their fifties, such as Alzheimer’s disease, and certain mood disorders, and then suddenly the incidence of these problems explodes?”

ZWH believes that neuroscience is also such an area. “There is overwhelming evidence on sex differences in the brain. So I believe neuroscience should be an important focus. And I don’t just mean pain. For instance autism is seven times more common in men than in women whereas depression is more common in women than men. So there is overwhelming evidence for biological differences in the brain, which leads to differences in behavior, diseases and society.”

## Networks

JAG: [...] “to create a network of European biomedical universities. This network could have two major tasks. The first is concerned with research. The network could make an inventory of sex and gender related questions that are relevant in ‘gender medicine’ in Europe, make a programme of how these questions may be addressed, and it could also conduct some preliminary research. The second task would be to make an inventory of which policy measures are effective in enhancing attention to the gender dimension in science at a country and EU level.”

VRZ: “European network of researchers in ‘gender medicine’. Such a network should have two aims: 1. To find out which gender issues are most relevant for a future research agenda and 2. To write a book on the state of the art of evidence concerning a number of these selected issues.”

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