Gendered Innovations: harnessing the power of sex and gender analysis for research and innovation
Ineke Klinge

Associate professor of Gender Medicine, Maastricht University

Chair H2020 Advisory Group on Gender, European Commission
Definition of Terms

- **SEX**: biological qualities; male/female/intersex

- **GENDER**: cultural attitudes & behaviours; masculine feminine

- **WOMAN-MAN**: sex and gender plus other cultural factors interact in a person
Gendered Innovations...

1) develop state-of-the-art **Methods** of sex and gender analysis

2) provide **Case Studies** to illustrate how sex and gender analysis leads to discovery
Sex and Gender Interact

![Diagram showing the interaction between sex and gender with factors like nutrition, lifestyle, and sex hormones](image-url)
Most research is done in males

Percentage of articles reporting sex of cells used in the experiments

<table>
<thead>
<tr>
<th>Journal</th>
<th>Articles (n)</th>
<th>Unspecified</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulation</td>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J Am Coll Cardiol</td>
<td>(n = 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eur Heart J</td>
<td>(n = 7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circ Res</td>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterioscler Thromb Vasc Biol</td>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovasc Res</td>
<td>(n = 20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J Mol Cell Cardiol</td>
<td>(n = 20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Am J Physiol Heart Circ Physiol</td>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J Heart Lung Transplant</td>
<td>(n = 4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J Cardiovasc Pharmacol</td>
<td>(n = 4)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

% Articles Reporting Sex of Cells
Methods of sex and gender analysis

1. Rethinking research priorities and outcomes
2. Rethinking concepts and theories
3. Formulating research questions
4. Analyzing sex
5. Analyzing gender
6. Analyzing how sex and gender interact
7. Analyzing factors intersecting with sex and gender
8. Engineering innovation processes
9. Designing health and biomedical research
10. Rethinking standards and reference models
11. Participatory research and design
12. Rethinking language and visual representations
**Sex and Gender Analysis Lead to Gendered Innovations:**

- **Stem Cells: Analyzing Sex**
- **Osteoporosis Research in Men: Rethinking Standards and Reference Models**
- **Pregnant Crash Test Dummies: Rethinking Standards and Reference Models**
- **Animal Research: Designing Health & Biomedical Research**
- **Heart Disease in Women: Formulating Research Questions**
- **Water: Participatory Research and Design**
- **Machine Translation: Analyzing Gender**
- **The Genetics of Sex Determination: Rethinking Concepts and Theories**
- **Assistive Technologies for the Elderly**
Case studies

*On biomedicine*
- Stem cells
- Heart disease in women
- Osteoporosis in men
- Risk factors for NCD’s

*On health technologies*
- Assistive technologies for the elderly
Stem cell research

Magnified Muscle Fiber Developed from XX and XY Stem Cells
After two weeks' development in mdx mice

XX STEM CELLS

Magnified Muscle Fiber Developed from XX and XY Stem Cells
After two weeks' development in mdx mice

XY STEM CELLS

These micrographs show muscle fibers produced from XX and XY MDSCs and demonstrate that XX MDSCs induce "more efficient skeletal muscle generation" than their XY counterparts based on the number of dystrophin-positive muscle fibers produced for a given number of donor cells. Muscles were harvested after two weeks of development in mdx mice. Dystrophin-containing muscle fibers are stained red, indicating that they arose from transplanted stem-cells, as mdx mice lack a functional dystrophin gene and develop a syndrome similar to muscular dystrophy in humans. Nuclei are stained blue. Reproduced with permission from Deasy et al., 2007.
Analyzing sex

- reporting the sex of research subjects or users;
- recognizing differences that exist \textit{between} but also \textit{within} groups of females and males, and identifying potential \textit{overlap} between groups;
- collecting and reporting data on factors intersecting with sex in study subjects or users/consumers, such as age, socioeconomic status, and ethnicity;
- analyzing and reporting results by sex; and
- reporting null findings. This final step is important: Researchers should report when sex differences (main or interaction effects) are not detected in their analyses to reduce publication bias and improve meta-analyses.

NIH to balance sex in cell and animal studies
Heart disease in women

Coronary Angiograms for Patients with Chest Pain
Women are more likely to have minor or no obstruction

**Diffuse atherosclerosis**
Most often seen in younger women with IHD

**Obstructive atherosclerosis**
Most often seen in men and older women

Adapted with permission from (K. Lance Gould, 1999).
Osteoporosis in men

Osteoporotic Fracture Probability by Age and Sex
Risk shown for patients with $T \leq -2.5$

- WOMEN
- MEN

Data from United Kingdom
Adapted from Kanis et al., 2008b
# Osteoporosis in U.S. Women and Men

<table>
<thead>
<tr>
<th></th>
<th>WOMEN</th>
<th>MEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Age of Onset</td>
<td>65 years</td>
<td>75 years</td>
</tr>
<tr>
<td>Lifetime Incidence of Osteoporotic Fracture</td>
<td>25%</td>
<td>13%</td>
</tr>
<tr>
<td>Fraction of Hip Fractures Due to Osteoporosis</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>Criteria Used to Diagnose</td>
<td>$T \leq -2.5$ or Fragility Fracture</td>
<td>$T \leq -2.5$ or Fragility Fracture</td>
</tr>
</tbody>
</table>

Data from Burge et al., 2007
Risk factors for NCD’s

Cumulative Life Course Risk Factors for Non-Communicable Disease (NCD)
Highlighting the influence of sex and gender-related factors

Accumulated Risk of Developing Non-Communicable Diseases

GENDER-RELATED SOCIAL FACTORS

Established adult behavioral risk factors

SEX-RELATED BIOLOGICAL FACTORS

Mortality

Maternal nutrition
Birth weight
Growth rate

Socioeconomic status

Obesity

Smoking
Physical inactivity

Diseases

ADULT LIFE

FETAL LIFE | CHILDHOOD | ADOLESCENCE

Adapted from Darton-Hill et al., 2004
The diagram above illustrates how researchers might analyze a three-way interaction between gender-related factors, sex-specific biology, and various biological mechanisms involved in human food intake and processing. Gender-related food intake is translated into different sex-specific base metabolisms, gene expressions, and dietary responses, thereby making nutrigenomics a pervasive Gendered Innovation. As such, it exemplifies the relationship between the Gendered Innovation (GI1) discussed above and Gendered Innovations 2a, 2b, and 2c discussed below.
Exploring markets for assistive technologies for the elderly
Sex and Gender Analysis
Enhances all phases of research

Setting Research Priorities
Making Funding Decisions
Establishing Project Objectives
Developing Methodologies
Gathering & Analyzing Data
Evaluating Results
Developing Patents
Transferring Ideas to Markets
Drafting Policies
Canadian Institutes of Health requirements

- The questions are:
- Are sex (biological) considerations taken into account in this study? (Y/N)
- Are gender (socio-cultural) considerations taken into account in this study? (Y/N)
- If YES, please describe how sex and/or gender considerations will be considered in your research design. (maximum of 2,000 characters)
- If NO, please explain why sex and/or gender are not applicable in your research design. (maximum of 2,000 characters)


- In assessing return on investment, the researchers looked at disease incidence, direct medical expenditure, quality-adjusted life, and net economic return between 2003 and 2012. The analysis found that the guidance provided by the WHI clinical trial results led to:

- 76,000 fewer cases of cardiovascular disease (coronary heart disease, coronary artery bypass graft/percutaneous transluminal coronary angioplasty, and stroke)
- 4.3 million fewer combined hormone therapy users
- 126,000 fewer breast cancer cases
- 145,000 more quality-adjusted life years
- Direct medical expenditure savings of $35.2 billion

- The researchers calculated the total net economic return of the trial, which cost $260 million in inflation-adjusted dollars, at $37.1 billion.
Gendered Innovations research agenda; osteoporosis

- **Use gender analysis to optimize osteoporosis prevention.** Many risk factors and protective factors are gendered. A prevention campaign might focus on increasing physical activity and on smoking cessation, recognizing that women are more likely to be physically inactive and men are more likely to smoke tobacco.

- **Develop reference models focused on how fracture risk is influenced by biological sex and gendered behaviors.** The U.S. Preventive Services Task Force has concluded that "evidence is lacking, of poor quality, or conflicting" regarding osteoporosis screening for men (USPSTF, 2011).

- **Work to educate the public about the true incidence of the disease and to promote bone-healthy lifestyles in women and men (NIH, 2010).** The gendered beliefs of physicians may also contribute to the perception that osteoporosis is a woman's disease, resulting in osteoporosis in men being "substantially underdiagnosed, undertreated, and underreported" (Qaseem et al., 2008; Geusens et al., 2007).
Gendered Innovations research agenda on NCD’s

- Information for observational studies (to correlate behavioral and dietary variables, for example) is generally obtained through questionnaires. More research is needed to learn whether women and men provide equally accurate data. Better knowledge of the food consumption will allow researchers to better determine the effects of social environments on various populations and the sex-specific biological outcomes of different patterns of food consumption.

- Randomized intervention studies designed to investigate female and male responses to specific diets need to include both women and men. Moreover, measurements should include potentially informative biomarkers provided by current omic technologies (e.g., transcriptomics, epigenomics, proteomics and metabolomics), in addition to traditional risk factors.

- Studies exploring the effects of food consumption should be designed with two time frames in mind: chronic effects (i.e., long-term effects of diets on biomarkers and disease) and acute effects (i.e., postprandial fat challenges, known to be very different between men and women).
Gendered Innovations research agenda on assistive technologies

- Researchers are developing new assistive technologies to support independent living for the elderly and to lighten the burdens of caregivers. Through participatory research and design with both the elderly and their caregivers, designers have gained key insights for developing assistive products that are useful to a broad user base. Involving users and stakeholders in the design process enhances outcomes. Building machines based on sex and gender analysis of demographic data will be important for the development of the next generation of assistive technology.
EUGenMED: roadmap for the implementation of sex and gender in biomedicine and health research

- **FP7 project 2013-2015**
- We will produce an innovative roadmap for implementation of Sex and Gender (S&G) in biomedicine and health research. This will improve the treatment of major chronic diseases such as infarction, heart failure, diabetes, rheumatic disease, etc. in women and men and research in these areas.
- We will develop the roadmap in 6 meetings with key stakeholders in European Gender Medicine and Gender Research in the biomedical field. We will design recommendations, guidelines and teaching materials for the implementation of Sex & Gender research for target audiences, doctors, medical associations, teachers, students, researchers, industry, health policy makers, funding agencies and politicians.
EUGenMed kickoff-off press release

- **8 April 2014, Brussels**—In a one day kick-off conference, the European Gender Medicine Project (EUGenMed) partners met with eighty experts and key stakeholders and assessed the status quo of Gender Medicine (GM) in Europe. The kick-off conference marked the first of a series of project meetings under the DG Research and Innovation-funded Framework Seven Programme project to be held in 2014 and 2015 that will culminate in the development of a roadmap for the further implementation of sex and gender (S&G) in biomedical sciences and health research in Europe.

- **Patricia Reilly, Member of Cabinet for Commissioner Geoghegan-Quinn, DG Research & Innovation** delivered the keynote address at the kick-off conference, highlighting the importance of the project and its objectives, “Research addressing sex and gender in biomedical sciences and health research is a novel and highly promising field. Interaction of S&G related mechanisms leads to different manifestation of diseases such as infarction, heart failure, diabetes and rheumatic disease in women and in men. Research in this area will lead to better targeted and therefore more efficient treatment strategies than the previous ‘one-size fits all” approach and will increase opportunities for prevention and healthy life expectancy.”
EUGenMed workshops 2014-2015

- Sex and gender differences in clinical medicine and clinical pharmacology
- Sex and gender aspects of public health and prevention
- Sex and gender aspects in basic biomedical research
- Sex and gender in medicines regulation and medical education

- Roadmap conference
Alliantie for Gender & Health

- A unique collaboration of relevant stakeholders such as policymakers, medical specialists, health insurance companies, knowledge institutes (SCP, CBS), women’s organizations, gender researchers & scientists

- The Alliance strives for acknowledging relevant differences between women and men in health and health care in order to secure optimal health for both men and women.

- In collaboration with ZonMW a so called “knowledge agenda” will be produced shortly, leading up to a research programme Gender & Health at ZonMW

http://www.zonmw.nl/nl/actueel/nieuws/detail/item/programma-gender-gezondheid-van-start
Gendered Innovations added value

Add value to research and engineering by ensuring excellence and quality in outcomes and enhancing sustainability

Add value to society by making research more responsive to social needs

Add value to business by developing new ideas, patents, and technology
Thank you for your attention

Questions?

i.klinge@maastrichtuniversity.nl


http://www.eugenmed.eu