Gender and Health
Knowledge Agenda
Contents

Preface 3

Part I Background
Introduction 6

Chapter 1 Knowledge 10
Chapter 2 Recent international developments 15
Chapter 3 Knowledge Agenda: process and structure a 18

Part II Knowledge Agenda
Focus on the client 23

Theme 1 Collate and apply existing knowledge 25

Theme 2 Life stages 28
a Childhood and youth 29
b Adulthood and social participation 33
c Ageing 38

Theme 3 Healthcare consumers 44
a Lifestyle and health promotion 44
b General healthcare 46
c Drug treatments 51

Theme 4 Conditions and problems 54
a Cardiovascular disease 54
b Physical and psychological violence 62
c Diabetes 66
d Migraine 69
e Unexplained physical symptoms 72
f Psychological and psychiatric conditions 75
g Rheumatism 79
h Conditions specific to women and sexual conditions 82

Theme 5 Sex- and gender-aware research methodology 89

Final remarks National Gender and Health Knowledge Programme 93

Part III Appendices
Contributors 96

Notes 98

This publication is a translation of the Dutch Gender and Health Knowledge Agenda, and reflects the situation in the Netherlands (May 2015).
I am proud to present to you the Gender and Health Knowledge Agenda, which has been drawn up on behalf of the Gender & Health Alliance, in collaboration with a large number of experts in the healthcare sector and academia. It was supported by the Ministry of Education, Culture and Science. Clearly, we cannot ignore the questions set out in this Knowledge Agenda. Since research and practice still fail to take adequate account of differences between men and women in terms of health, illness and treatment, there is great potential here to improve the quality of care for women, and reduce costs at the same time. Some of the knowledge gaps can be addressed in current grant programmes. For example, every researcher should consider at the outset of every project whether it involves any sex-specific elements. If so, this should be properly reflected. Done systematically, this will in itself produce a significant improvement. In addition, a separate knowledge programme needs to be set up to address the more general questions. This Knowledge Agenda offers a broad overview of the gaps in the knowledge that might serve as a basis for such a programme.

The development of this Knowledge Agenda is part of a broader process towards a knowledge programme that is being overseen by the Gender & Health Alliance. The programme will require a coordinated approach to research, training and implementation on matters of gender and health. Many experts have contributed to this Knowledge Agenda. I should like to thank them personally for their great efforts, their critical insight and their unfailing willingness to cooperate.

Henk J. Smid, ZonMw director
The Hague, May 2015
Part I

Background
A common principle of healthcare in the Netherlands is that everyone should receive quality care, irrespective of age, sex, sexual preference, socioeconomic circumstances or cultural background. Current efforts to reduce health differences between men and women are a direct result of this principle.

Differences between men and women

There are many similarities between men and women, but when it comes to health and illness they also differ in many respects – biological, psychological, social and cultural. As a consequence, the healthcare offered to men and women should also differ, where necessary. This extends much further than differences in care occasioned by differences in terms of genitals, breasts and matters specific to women, such as pregnancy, birth, hormones, the menstrual cycle and menopause. For example, cardiovascular disease is one of the leading causes of death among women, partly because the signs are different and doctors do not always recognise them. Though women live longer than men, their quality of life tends to be poorer, particularly in their final years. ‘Men die quicker, but women get sicker’ is an oft-quoted saying. Life expectancy for women is 83.5 years longer than men. But men enjoy seven years more free of chronic illness. On average, men are more positive about their state of health than women. In the period 2011–2013, for example, almost 83% of men and just over 78% of women said their health was ‘good or very good’. This difference is the result not only of underlying objective differences in health, but also of differences in lifestyle and socioeconomic status, and of the way in which men and women assess their own health.

Health differences

Women have poorer health than men. They are for example more likely to experience comorbidity and psychological problems such as depression and anxiety disorders. Over 15% of women and 10% of men reported problems with their hearing, sight and/or mobility in the period 2011-2013. Women work fewer hours, sickness
absence is slightly higher among working women than among working men and in total women incur higher healthcare costs than men. For example, according to the National Medical Register, hospital admissions per 10,000 are over 20% higher among women than among men. Even excluding hospital admissions related to pregnancy, childbirth and postnatal care, the difference is still 10%. Above the age of 60, more men are admitted to hospital, particularly in connection with cancer and cardiovascular disease.

Besides cost savings and people's right to appropriate, good-quality care, efforts to ensure greater social participation by women are another important reason for focusing on the determinants of women's health and aspects of health and healthcare that are specific to women.

**Focus especially on women: making up lost ground**

Gender-sensitive healthcare focuses on quality of care for both men and women. It requires a multidisciplinary approach tailored to the individual healthcare consumer (i.e. multidisciplinary both within healthcare and within the field of medicine, psychology, sociology etc.) within his or her specific environment, taking into account all sex- and gender-related factors. This means that a comprehensive knowledge programme must focus on matters specific to women and to men. Men have a shorter life expectancy, for example, are more likely to die of cancer and are more likely to have an addiction disorder. However, there are at least two reasons to focus initially on health research specific to women and the implementation of the results in any future knowledge programme. Firstly, a lot of health research currently uses only male test subjects and test animals, or no clear distinction is made as regards the sex of the test subject or animal. As a result, scientific knowledge concerning factors specific to women lags behind. Secondly, women incur higher healthcare costs than men and working women work fewer hours and have higher rates of sickness absence than working men. This means that more gender-specific healthcare offers potential to improve the quality of care and reduce costs. However, in order to achieve this, it will be necessary to make up lost ground.

This is not to say that any future knowledge programme will focus exclusively on women. This Knowledge Agenda repeatedly highlights the fact that there is a need for research into gender differences on various matters. It is a matter of gender- or sex-specific differentiation between men and women. However, choices will have to be made in the knowledge programme, to ensure the limited resources available are used in the best possible way. The need to make up lost ground on women's health will be an important factor, with the aim of achieving healthcare that is better tailored to the biological, psychological, cultural and social characteristics, situational contexts and behaviour of different healthcare consumers.
Government policy

In its Equal Opportunities Letter (Hoofdlijnenbrief Emancipatiebeleid) of May 2013 the Ministry of Education, Culture and Science refers to ‘women and health’ as a new policy theme that warrants exploration. A year earlier ZonMw had published a survey entitled ‘Women Are Different’, on the need for research, development and implementation to achieve more sex-specific quality healthcare. In the Equal Opportunities Letter health minister Jet Bussemaker indicated she would like to find explanations for the differences in health between women and men, with a view to the potential need for different interventions. Like pioneers in the field, the present Government is keen to enhance the knowledge and awareness of stakeholders as regards the need for ‘gender-aware’ healthcare, and to help develop such a system. The health ministry has therefore launched an alliance to explore the potential for enhancing gender-awareness and -sensitivity in healthcare. The Gender & Health Alliance has now commenced its work, under the name WOMEN Inc. This Knowledge Agenda is the work of the Alliance’s Research Working Group. The aim is to improve quality of life for both men and women, and reduce costs where possible.

In its efforts to bring about gender-aware healthcare, the Ministry of Education, Culture and Science is collaborating with the Ministry of Health, Welfare and Sport and the Ministry of Social Affairs and Employment. In 2000 the health ministry drew up a policy programme on gender and health. In its Strategic Knowledge Agenda 2020 (January 2012) the ministry states that the healthcare sector should focus more on a segmented approach based on type of healthcare consumer. With this in mind, the ministry supports the work of the Gender & Health Alliance – in close collaboration with the Ministry of Education, Culture and Science – as evidenced among other things by the letter from the health minister to the House of Representatives (dated 28 October 2014) concerning the incorporation of gender-sensitive aspects of healthcare into medical training.

Gender & Health Alliance

The Gender & Health Alliance has set itself the challenge of ensuring that the current physical and mental healthcare system takes greater account of sex and gender. Differentiation must be introduced where necessary. In other words: where the unequal treatment of men and women would achieve better quality of care. The Alliance is not calling for special gender-sensitive healthcare, but for gender-sensitivity to be integrated into ordinary healthcare. This Knowledge Agenda suggests the direction research might take in order to achieve this goal, and must be seen in relation to other Alliance activities in the Awareness and Communication and Education Working Groups.
Diversity and intersectionality

Sex/gender is only one of the many distinctions that can be drawn in the overall group of healthcare consumers.\textsuperscript{13, 14} Differences according to age, ethnicity, socioeconomic circumstances and sexual preference are also important, for example. Women of non-Western origin up to the age of 60 are more likely (17%) to have problems with their hearing, sight and/or movement than ethnically Dutch women (9%). Problems with mobility (11%) and sight (9%) occur almost twice as often among non-Western women as among ethnically Dutch women. There is no difference in terms of hearing problems. Non-Western women are less likely to have a long-term illness (53%) than ethnically Dutch women (57%). They have fewer problems with joint wear in their hips and knees (just over 5% as opposed to almost 8%) and are less likely to have or have had cancer.\textsuperscript{15}

Altogether, this reveals a great deal of diversity, including among women – and men – as a group. There are in fact sub-categories of sub-categories. The many distinctions that can be drawn (male-female, homo-hetero, high-low socioeconomic status) can also be regarded as continuums rather than divisions. All these factors can also be mutually influencing. An intersectional approach is based on continuums that can have an impact on each other.\textsuperscript{16, 17, 18}

Terminology/definitions

The Knowledge Agenda distinguishes between sex and gender. Sex refers to the biological differences between men and women. Gender refers to a social and cultural process whereby men and women are assigned different roles and behaviours, including interaction with their psychological aspects. Since healthcare is not only concerned with biological differences, but also different behaviour and the social context in which healthcare consumers live, the term gender-sensitive healthcare is used in this document. This term refers to skills, such as a gender-sensitive approach by physicians in their diagnosis, treatment and manner towards patients. As such, this Knowledge Agenda also refers to gender-sensitive diagnosis, care and treatment. Any reference to sex concerns only biological differences. This Knowledge Agenda focuses on both sex- and gender-sensitive aspects of health and healthcare.
Awareness, knowledge development, and the collation and dissemination of existing and new knowledge are important elements of any policy geared to reducing health differences between men and women. In recent years a considerable body of knowledge has become available internationally on differences between men and women in relation to specific conditions. However, this knowledge has not been adequately incorporated into healthcare in the Netherlands. There are also many important gaps in our knowledge of sex- and gender-based differences in health, particularly aspects of health that are specific to women.

Differentiation

Nowadays, the healthcare sector increasingly takes account of specific groups of healthcare consumers, and differences in terms of age, socioeconomic status, genetic profile, origin, sexual preference and sex are increasingly determining what specific interventions and therapies are employed. This has become possible thanks partly to new knowledge (which in turn has resulted from modern information technology and biotechnology), greater awareness and assertiveness on the part of various groups of healthcare consumers and better collaboration between policymakers, practitioners and researchers. The emphasis on quality and efficiency and efforts to achieve a long, healthy and above all socially active life for all groups in society have for example all paved the way for a more differentiated approach. The health ministry’s Strategic Knowledge Agenda 2020 also refers to these developments. In short: we know more, we are able to do more and policymakers, care providers and healthcare consumers want more.

Potential benefits

Knowledge of gender-sensitive healthcare is therefore important if we are to better recognise and treat illness in men and women. This assumes that the knowledge will be applied in medical training, the purchasing policies of healthcare insurers, preventive action by local authorities, and in the health policy of central government. Together, these changes will have a positive impact on the health of women,
helping to improve their quality of life, reduce their disease burden, perhaps reduce sickness absence and costs to society, and possibly ensure that women participate more in society.

**Current knowledge based mainly on research involving men**

Women are often diagnosed and treated in accordance with guidelines drawn up on the basis of research on men.\(^{19,20}\) Courses have been developed to give guideline developers the tools they need to systematically integrate sex and gender into guidelines, but this does not yet occur to an adequate extent.

On the assumption – conscious or otherwise – that the results of health research are gender-neutral, female test animals are often excluded from fundamental research in order to prevent distortion of results due to hormonal differences, for example. In daily medical practice this eventually results in late or incorrect diagnoses, a greater disease burden and inadequate treatment, particularly for female patients, which in turn results in unnecessary illness, rising healthcare costs and – in extreme cases – avoidable deaths.\(^{21}\)

Similarly, for many years drug treatments have been tested only on men (often young men), although they are often absorbed, distributed and excreted differently and at a different rate by the male and female body. As a result many drug treatments are prescribed to women in standard doses based on research on male subjects, unnecessarily putting them at risk of overdose or underdose.

Furthermore, studies that do involve women often draw no distinction between the sexes and/or sub-groups. This too leads to unnecessary health problems and rising healthcare costs.

**Both differences and similarities**

To achieve the objective of ‘appropriate, good-quality care for all’ we will need a lot of knowledge about the great diversity that exists among healthcare consumers. Although, to date, healthcare and health research has largely assumed that ‘one size fits all’, the importance of individual differences is growing, given the desire to provide ‘tailor-made care’, or ‘personalised medicine’. This means that, as well as similarities, scientific research must also systematically study the differences between and within research populations. This Knowledge Agenda aims to gather more knowledge about female populations.

**Current situation**

Research into the difference between men and women in healthcare is nothing new. Large amounts of data are available, particularly on epidemiology and the uptake of healthcare. On the other hand, however, less is known about how men and women seek care and about the extent to which the sex differences we see impact on this behaviour.
Less is also known about the underlying causes of sex differences and aspects of prevention, diagnosis and the efficiency of treating ‘generic’ conditions that are specific to women. Equally important questions remain regarding pharmacotherapy – as we have said, drug treatments are usually tested on men – and the relationship between women’s health and issues like social participation, the effects of violence and healthy ageing. This is not to say that women-specific health research will be starting in a vacuum. The number of publications on these issues is growing steadily, both nationally and internationally. For instance, a sex-/gender-specific search filter has been developed, and in 2014 an interactive database of sex- and gender-specific medical literature was launched. Unfortunately, good reviews on gender and health tend to be lacking.

Implementation

This Knowledge Agenda highlights the current gaps in the knowledge of gender- and women-specific aspects of health and healthcare in a large number of areas. The aim of the Agenda is to provide direction for a new knowledge programme specifically concerned with gender and health for women. It is essential that both new and existing knowledge be applied in healthcare practice, guidelines, policy and training. To ensure that knowledge is implemented in this way, it is important that the knowledge programme explicitly create opportunity. Awareness-raising, pooling and dissemination of existing knowledge is just as important as developing and implementing new knowledge. Given the difficulty of implementing existing knowledge concerning gender-sensitive healthcare, research will be needed to identify the factors hampering the practical implementation of knowledge. Part II, theme 1 takes a more detailed look at the collation and application of existing knowledge.

International initiatives

The World Health Organization has officially declared women’s health an ‘urgent priority’. The US Department of Health and Human Services has recommended that more attention be given to sex and gender in research, treatment and the development of new technologies. The EU/US Gendered Innovations project makes scientists aware of the important of male-female differences in research, and its website has many practical tips for reflecting these differences in medical and scientific research. Europe has EUGenMed (European Gender Medicine Project), in which a large group of stakeholders are developing an innovative roadmap for the implementation of sex and gender in biomedical and health research. There is also a growing focus on the position of women in the world of science. One example is the European Platform of Women Scientists, which lobbies to improve the position of female scientists. International developments are examined in further detail in chapter 2.
ZonMw

A large proportion of health research in the Netherlands is funded under ZonMw programmes. One of the basic principles of these programmes is that diversity should be reflected, and therefore also differences between men and women in terms of health outcomes, as well as the factors behind these differences. Knowledge of sex- and gender-related factors in health and healthcare is therefore being developed in a number of programmes.

Back in 2000–2004, the ZonMw programme, M/F, commissioned by the Ministry of Health, Welfare and Sport explored the sex factor in healthcare. The goal of the programme was to implement insights gained in sex-specific medical care in the healthcare system and in policy. ZonMw funded a total of 30 projects on six different themes: basic medical training, policy on quality, regional healthcare policy, patient/consumer policy, self-help for women and scientific research. The programme succeeded in laying the foundations for sex-specific medical care. It was however found that those working in the field did not always recognise the need for more gender-sensitivity in healthcare.25,26

ZonMw’s current Pregnancy and Childbirth programme is helping reduce avoidable maternal and infant deaths and illness associated with childbirth (perinatal mortality and morbidity).27 One of the main priorities is to promote healthy pregnancy and childbirth in deprived areas (prevention). Professionals involved in pregnancy and childbirth are working together in multidisciplinary consortia, covering the entire range from informal care through to tertiary care. The programme explicitly addresses women-specific issues associated with pregnancy and childbirth, particularly as regards prevention.

ZonMw has now launched its fifth Health Promotion and Disease Prevention Programme.28 It will supply knowledge to help meet the objectives of the National Prevention Programme (NPP). The NPP Alles is gezondheid... (‘All is Health...’) will not only determine the implementation agenda for the next few years, it will also define the framework for long-term research programming. The fifth Health Promotion and Disease Prevention Programme is an important part of research programming. It comprises the following sub-programmes: Upbringing & Education, Healthy Neighbourhoods and Environments, Working is Healthy, Disease Prevention in Healthcare and Early Detection. Though sex and gender are not separate themes as such, given the focus on risk groups, they are included in project proposals where relevant. Gender differences are also addressed in other ZonMw programmes, including Efficiency Studies, Young People and the National Care of the Elderly Programme.
Broad spectrum

Gender-sensitive healthcare requires an approach that takes account of a broad spectrum of biological, medical, psychological and social factors. In some subject areas, this requires a multidisciplinary and integrated approach. Integrated implies that the whole person must be considered – including his or her environment. Multidisciplinary means that professionals from various specialisms both within and outside healthcare work together. As been said, various theoretical perspectives exist within the area of gender and health research. In *Social Science & Medicine* (2012), Springer, Hankivsky & Bates identify a relational, an intersectional and a biosocial approach. Each perspective introduces certain requirements as regards the approach to research. If data from several theoretical gender perspectives are studied (theoretical triangulation), this could considerably enhance our understanding of health problems, for example as regards menstrual and menopausal problems or unexplained physical symptoms, anxiety and eating disorders or ageing in women. Part II, theme 5 looks in greater detail at the methodology of sex- and gender-aware research.
The relationship between gender and health is attracting interest all over the world. The idea that women-specific healthcare lags further behind is universally accepted. In recent years a number of initiatives have therefore been launched to help make up the lost ground. For example, leading universities (Charité Berlin, Karolinska Institute Stockholm) have established centres for Gender in Medicine, major international journals have devoted special editions to the subject, and the number of scientific papers and manuals on the subject is growing rapidly. A brief overview of the most important international initiatives in research into gender and health is given below.

**WHO**

The World Health Organization has deemed avoidable health differences wrong and unfair, and as a result it has dubbed women’s health an ‘urgent priority’. The 2009 report ‘Women and Health: today’s evidence, tomorrow’s agenda’ makes a powerful plea for gender-sensitive healthcare worldwide. Research, registration and monitoring are important tools.

**United States**

A number of initiatives exist in America that are designed to foster research into gender and health. The Office for Research on Women’s Health was established as long ago as 1990, partly in order to ensure that women are included in clinical trials. In its Strategic Plan 2020 the US Department of Health and Human Services defines six goals for gender and health, and sets out steps towards achieving them. Stanford University’s Gendered Innovations website, launched in 2009, is an important initiative designed to provide scientists and engineers with practical methods of sex- and gender analysis in science and technology (see also Europe below).
Canada

The Canadian Institute of Gender & Health (IGH) is an important international leader, promoting research into gender and health. Thanks to the work of the IGH, since 2010 all research applications at the 12 Canadian Institutes for Health Research (CIHR) must consider sex and gender. The IGH has also developed a large amount of educational material, including ‘What a Difference Sex and Gender Make. A Gender, Sex and Health Research Casebook’. It is also developing online training for researchers and evaluators.

Europe

Research

The European Commission has also indicated that it regards the gender dimension of research as important. Since 2000 it has funded a series of projects in this field: Gender Impact Assessments FP5 (2000–2001); Gender Action Plans (FP6 2002–2006); GenderBasic (FP 7 2005–2007) and Gendered Innovations (2010–2013). EUGenMed (European Gender Medicine Project), running from 2013 to 2015, is the most recent project in which gender experts have joined forces with a highly diverse range of stakeholders (research institutions, policymakers, journals, grant providers, the education sector, the pharmaceutical industry, NGOs, patients’ associations, politicians) to develop an innovative roadmap to implement sex and gender in biomedical and health research, guidelines and medical training in Europe. One of its key aims is to underline and disseminate existing knowledge of gender and health, concerning subjects such as prevention, biomedical research and medication. The Netherlands is an active contributor to the programme.

Policy

The European Commission’s wide-ranging research and innovation programme Horizon 2020 – which covers the funding of health research – states in much stronger terms than its predecessors FP6 and FP7 that sex and gender must be integrated into all stages of research and innovation. This underlines the importance the Commission attaches to the subject of sex and gender in biomedical and health research.

Training

From 2010 to 2012 seven European universities collaborated, in a project entitled EUGIM (European Curriculum in Gender Medicine) to ensure medical training takes more account of the sex and gender aspects of health and healthcare. A flexible Gender Medicine training module was developed which can easily be incorporated into existing Bachelor’s and Master’s programmes. The EUGenMed project also focuses on medical training.
Networks
COST Network genderSTE is a targeted network of policymakers and experts that is designed to change institutional cultures and achieve better integration of sex and gender analysis into research and innovation.37

Another initiative funded by the EU is GENDER-NET ERA-NET, in which twelve European and American policy organisations collaborate to achieve equality between men and women by means of structural change in the broad field of research and innovation.38

Individual European countries are also taking initiatives designed to focus more attention on gender in research and development. The Irish Research Council, for example, included in its 2013–2020 Gender Strategy & Action Plan conditions intended to ensure that researchers give the sex and/or gender dimension a clear role in their studies. Norway, Sweden and Iceland are drawing up a joint gender programme.39

The Gender and Health knowledge programme will tie in as well as possible with international initiatives and use existing knowledge and infrastructure.
Chapter 3
Knowledge Agenda: process and structure

The aim of the Knowledge Agenda is to set the direction for a new national Gender and Health knowledge programme. The goal is to identify the main gaps in the knowledge, and define the shape of the programme. A broad look has of course been taken at knowledge already available, to prevent subjects about which we already have adequate knowledge from being included in the Knowledge Agenda. The same applies to subjects on which research is currently underway.

General terms

The subjects identified as knowledge gaps in the Agenda have been described in general terms, divided into overall categories. Reviews will need to be conducted as part of the knowledge programme to provide more differentiation and details.

Interviews

The Gender and Health Knowledge Agenda has been compiled with the help of members of the Gender & Health Alliances’ Research Working Group. They are all experts on gender differences in their own subject area. Interviews were conducted with all working group members to establish what is already known, and where there are gaps that require further research. Furthermore, a small number of experts from outside the working group were consulted where necessary. The findings of the interviews were recorded in reports on which the interviewees gave their comments. This Knowledge Agenda was written on the basis of these reports and sources in the specialist literature. The experts were given the opportunity to provide comments and additional information on their own subjects, and these were incorporated into the draft version.
Invitational conference

An invitational conference was held in February 2015 at which dozens of experts discussed the draft Knowledge Agenda. They indicated which knowledge gaps deserve priority in the Gender & Health knowledge programme, based on the criteria. These priorities are listed in a box in the sections on the individual themes below.

Criteria

The range of subjects that lend themselves to research on gender and health is virtually limitless. After all, gender plays a role in all facets of healthcare (for both healthcare consumers and care providers), the preventive medicine sector and health research. To provide direction for a future knowledge programme, choices therefore have to be made. Important considerations include the potential for quality improvement, cost reduction (direct and indirect), scope and potential for implementation/valorisation. The following criteria were determined on this basis.

1. Extent of disease burden and potential for improving quality of life; this concerns matters such as severity, chronicity, duration and mortality.
2. Degree of prevalence; priority should be given themes affecting large groups of clients.
3. Implementability of research results; the ultimate goal is to improve healthcare practice through research, i.e. to contribute to preventive measures, diagnosis, treatment and/or counselling.
4. The level of healthcare costs and potential for reducing them.
5. Social relevance, including the degree of social participation, working hours and sickness absence.

Data from www.volksgezondheidenzorg.info and other sources were used in applying these criteria.

Prioritisation

The Knowledge Agenda highlights a large number of knowledge gaps. According to the experts consulted, these knowledge gaps comply in broad terms with the above criteria. Further prioritisation is required to define the scope of the future knowledge programme. Knowledge syntheses will be needed to gain a good idea of what knowledge is already available, so that it can be used as a basis for making choices. Reviews are available on some subjects (e.g. cardiovascular disease), but this is not yet the case for most subjects.
Structure

The above process produced five main themes for this Knowledge Agenda, which have been divided into sub-themes where necessary.

**Theme 1** Collate and apply existing knowledge

**Theme 2** Life stages
   a. Childhood and youth
   b. Adulthood and social participation
   c. Ageing

**Theme 3** Healthcare consumers
   a. Lifestyle and health promotion
   b. General healthcare
   c. Drug treatments

**Theme 4** Conditions and problems
   a. Cardiovascular disease
   b. Physical and psychological violence
   c. Diabetes
   d. Migraine
   e. Unexplained physical symptoms
   f. Psychological and psychiatric conditions
   g. Rheumatism
   h. Conditions specific to women and sexual conditions

**Theme 5** Sex- and gender-aware research methodology

These themes are examined in more detail in part II. Where knowledge gaps require new research (themes 2 to 5), it is explicitly a matter of ‘developing and implementing’ new knowledge. Both theme-specific gaps and gaps that touch upon several different themes are mentioned in all the theme sections (the latter are therefore described under more than one theme heading).
Part II
Knowledge Agenda
Focus on the client

When it comes to improving the quality of care, many subscribe to the motto ‘focus on the client’, but in actual fact it tends to be difficult to put into practice in healthcare and research. ‘Focus on the client’ requires multidisciplinary collaboration that is sometimes difficult to achieve in a healthcare system that is divided into different disciplines that to a great extent operate separately and which, despite all the progress in this area, are still largely isolated from other fields.

The Gender & Health Alliance’s Research Working Group is calling for improvements in quality through a multidisciplinary approach, both in practice and in research. This follows directly from the use of the term gender, which refers to a social and cultural process whereby men and women are assigned different roles and behaviours, including interaction with their psychological aspects. The principle of ‘focus on the client’ therefore means that both in diagnosis and in prevention, counselling and treatment, symptoms and the effects of interventions and therapies are seen in conjunction with all kinds of biological, social and cultural factors.
The figure below is a schematic representation of the possible associations between all kinds of conditions and problems, including in relation to factors like cultural background, psychological wellbeing and work.

**Multidisciplinarity**

In this context, the term multidisciplinary can be defined in three different ways: (1) collaboration between healthcare disciplines, (2) collaboration between healthcare and other fields such as the social welfare sector, youth care services and/or the employment sector and (3) collaboration between practitioners (and patients), policymakers and researchers. The Research Working Group regards all these forms of collaboration as important to achieving an actual ‘focus on the client’. In specific terms, this means that these forms of multidisciplinarity will have to be a leading element of any future Gender and Health knowledge programme, including the awarding of funding for research and implementation.
Theme 1
Collate and apply existing knowledge

A considerable body of knowledge has become available internationally on differences between men and women, but it is not always applicable in the Dutch context. Even research performed in the Netherlands has rarely resulted in changes to training and guidelines. It is therefore important that existing knowledge in several areas of health be disseminated.  

Gap between research, practice and policy

A lot of the knowledge that now exists is not sufficiently applied in daily healthcare practice. This is also true of gender-sensitive healthcare. There are several reasons for this. Too much sex-specific knowledge ‘gets stuck’ in scientific publications, and so does not lead to changes to guidelines and the behaviour of doctors and other healthcare professionals. Care providers are often insufficiently aware of new sex- and gender-relevant insights, partly because they are often difficult to find. Furthermore, the subject of gender-sensitive healthcare does not enjoy high status among healthcare professionals and scientists, despite the growing interest in personalised medicine (tailor-made treatment attuned to the individual characteristics of the client). Medical training and refresher training also pay little attention to gender-sensitive care. This is reflected in the care women are currently offered.

Promote implementation

The Gender & Health Alliance has set itself the challenge of ensuring not only that new knowledge is developed, but also that existing knowledge is better implemented in healthcare and policy. Effective implementation not only requires knowledge, it also requires acceptance, adoption and application of that knowledge in the field. This in turn requires a better understanding of factors that can promote or hamper acceptance. Research into these factors – and application of the results – in the Gender and Health knowledge programme could boost the development of effective strategies for the implementation of gender and health knowledge.
Reviews

As remarked in chapter 1, a better overview of the existing national and international knowledge on gender and health is a key prerequisite for the implementation of knowledge on the subject. In this context it is important that more reviews are published, pooling the knowledge available and making it accessible to practitioners.

Implementation in Gender and Health knowledge programme

Around 25% of the resources available to the future Gender and Health knowledge programme will be used for the further implementation of existing knowledge on gender and health. It will therefore be a knowledge programme, rather than only a research programme. All the experts consulted highlighted the importance of implementation to actually bring about changes in healthcare practice. This requires both research into effective implementation strategies, and an infrastructure that promotes the implementation of existing and new knowledge.

Knowledge gaps

- Reviews of existing (national and international) knowledge of gender- and women-specific aspects of the themes set out in this Knowledge Agenda, including identification of where knowledge is lacking. The reviews should consider the likely impact on both quality of life and healthcare costs.
- Research into and development of effective strategies to promote implementation of knowledge about gender and health, targeting both practitioners (professional associations, treatment providers) and policymakers (public authorities, insurance companies).
- Analysis and amendment of existing guidelines and diagnostic questionnaires to reflect gender- and women-specific factors for which there is sufficient evidence, including amendment of the guidance for guideline development to ensure that it reflects gender factors.
- The establishment of three academic collaborative centres, creating an infrastructure (Dutch Gender Medicine Community) in which researchers, practitioners and policymakers automatically work together and integrate their efforts. It is important that the divisions in healthcare be removed and that different professions and specialisms and other relevant fields work together. An academic collaborative centre could serve as a centre of expertise, promoting exchange of knowledge.
- Pooling and publication of knowledge concerning gender- and women-specific physical and mental healthcare on a single national online platform.
- Implementation of new and existing knowledge of gender- and women-specific healthcare (physical and mental) in existing health platforms.
– Inclusion of gender-sensitive care in the exit qualifications for medical training and refresher training.
– Incorporation of existing knowledge of gender differences into information material for patients.
– Comparative studies of existing legislation, institutes and other infrastructure in the Netherlands and those in other countries as regards gender and health.
– Public-private partnership with pharmaceutical companies and healthcare insurance companies focusing on gender and health.

The participants at the invitational conference identified the following gaps as deserving top priority.
– Reviews of existing (national and international) knowledge of gender- and women-specific aspects of the themes set out in this Knowledge Agenda.
– Changes to guidelines and guideline development.
– Establishment of academic collaborative centres.
– Pooling and publication of knowledge concerning gender- and women-specific physical and mental healthcare on a single national online platform.
– Inclusion of gender-sensitive care in the exit qualifications for medical training and refresher training.
– Comparative studies of existing legislation, institutes and other infrastructure in the Netherlands and those in other countries as regards gender and health.
– Public-private partnership with pharmaceutical companies and healthcare insurance companies focusing on gender and health.
‘Focus on the client’ also means that problems and symptoms will be considered in relation to people’s situation in life. This differs from one individual to another, and depends partly on a woman’s stage of life. In childhood and youth, it is mainly a matter of growing, learning and forming an early identity. Adults experience ‘life in full flow’, form relationships, perhaps start a family, and participate fully in society. Elderly people can still participate in society, though not generally in the form of paid work. Increasingly, elderly people face physical (and sometimes psychological) problems and impairment.

The developments women undergo during their life can be regarded from different perspectives, as shown in the table below: biological, psychological, pedagogic and sociological. Most health problems can occur at any point in life. Nevertheless, each stage of life has its own (often mutually interacting) health risks and problems.
Theme 2a
Childhood and youth

Major differences exist between girls and boys, in terms of their biology, hormones, development and consumption of healthcare. Studies and policy documents still fail to properly recognise these differences, even though they are highly relevant. For example, the Advisory Committee on Health Research (RGO) report ‘Children and Disease’ draws no distinction between boys and girls, either in its content or in the table that presents figures on incidence, prevalence and healthcare costs.41 Nor indeed does it mention the fact that differences exist. This is apparently an area that requires more attention, where potential health benefits could be gained. Fortunately, in the past few years there has been a growing focus on the health differences between boys and girls, and more knowledge is becoming available.

Differences

There are of course biological differences between boys and girls. The (male) Y-chromosome becomes active as early as the sixth week of pregnancy, prompting the male genitals to develop. The development of the brain also proceeds differently under the influence of testosterone, even in the foetus. For example, the right half of a boy’s brain generally develops better than the left half. Testosterone causes the immune system to develop less well.
Boys develop differently from girls. Differences lie, for example, in the development of the brain and the hormones. On average, boys mature slightly more slowly than girls: a boy’s brain is mature after 25 years, while a girl’s brain matures some two years earlier. A boy’s immune system is slightly weaker initially, and in their first two years they tend to be ill slightly more often than girls. Physical growth tends to proceed more slowly and irregularly in boys than in girls. Boys often have growth spurts, whereas girls grow more steadily. Boys’ emotional and cognitive development also proceeds more slowly and irregularly. In terms of language development, boys lag some twelve to eighteen months behind girls. Girls enter puberty between 9 and 14, whereas in boys puberty commences between the ages of 10 and 17.

Sexual development, leading to fertility and menstruation, begins during adolescence. It involves many radical changes to the body, which have a whole range of physical and psychosocial effects. Girls are better able to control impulses from the central nervous system. Their more highly developed frontal cortex allows them to suppress their impulses. Over the past thirty years, it has generally been assumed that sex-specific behaviour stems from our upbringing. However, research has shown that brain development differs even in the womb, and therefore has a great impact. On this basis, one might conclude that boys and girls simply think entirely differently. Nevertheless, upbringing does influence the brain, which continues to develop as the child learns. We cannot rule out the possibility that a stereotypical approach to children influences the brain to such an extent that girls’ and boys’ brains will show growing differences.

Physical complaints

Perceived good health declines the older children become, from 96% in children under the age of 12 (in the assessment of their parents/carers), to 92% in youngsters aged 12–18 and 90% in young people between the ages of 18 and 25. Girls are slightly less positive than boys (92% as opposed to 94%). This concurs with the results of the 2009 HBSC study of young people’s health perceptions. Among children aged 12 to 15 there is virtually no difference between boys and girls; 81% to 91% say they enjoy good or very good health. This is still the case for 87% of boys at the age of 16, but the percentage has fallen to 71% among girls by this time.

Physical symptoms are the most common reason for visiting the doctor, particularly among girls. In terms of physical health problems, tension headaches, migraine, stomach pain, constipation and fatigue are the most common reason for consulting one’s general practitioner.

A total of 88 out of every 1000 0-19-year-olds visit the doctor in response to physical symptoms, ranging from 3.3% per 1000 for migraine to 24 per 1000 for constipation. Headache, stomach ache and migraine are most common among girls aged 10 to 19.
Psychological and social problems

Generally speaking, young people in the Netherlands are happy. Overall, pupils at primary school tend to be happier than high school pupils, and more girls than boys are unhappy during adolescence. Behavioural problems manifest themselves differently in boys than in girls. Boys often become troublesome to those around them: they shout and (sometimes) break things. Girls are more likely to cause difficulties for themselves: they become depressed, develop eating disorders or self-harm. Thirty per cent of boys aged 16 drink more than ten alcoholic drinks on one day at the weekend, while 9% of girls do so. Alcohol consumption among girls is increasing, and they are less able to cope with the effects than boys. The number of girls aged 15 to 19 admitted to accident and emergency departments with alcohol poisoning saw a 101% increase in the period 2000–2010. The increase among boys was 66%. Problematic gaming occurs mainly among boys (7% as opposed to 0.9% of girls); problematic use of social media is however more common among girls (8.6% as opposed to 3.7% of boys). Problematic use of social media is associated with poor performance at school, a reduction in social activity not involving the internet and feelings of depression, for example. ADHD and autism are much more common among boys and, partly for this reason, are more often overlooked in girls than in boys. Autism spectrum disorders manifest themselves differently in women than in men. Women often display compensation mechanisms in terms of social interaction and communication, as a result of which behavioural observation provides inadequate insight into the presence of problems. Parents and teachers, and also psychologists and psychiatrists, are less likely to recognise mild symptoms in girls. Boys with ADHD display impulsive and troublesome behaviour. Girls are regarded as hyperactive and excessively talkative, but not necessarily as troublesome, as a result of which professional help is not always sought. Both boys and girls are more at risk of sexual abuse if they grow up with only one biological parent. Girls are more at risk than boys, particularly if they live with a stepfather. Sexual abuse is more likely to occur in families where the mother is absent, either literally or emotionally, for example if the mother works outside the home, or suffers from addiction or illness. Female genital mutilation is a medically unnecessary procedure performed on the external sexual organs. It involves cutting away all or part of the external female genitals. It is not known how often female genital mutilation actually occurs in the Netherlands. In 2005 the Council for Public Health and Health Care (RVZ) estimated the figure at 50 cases a year. The long-term TRAILS study involving 2300 children and young people in the northern Netherlands has found that girls with psychological problems are more likely to use care services than boys with psychological problems. The data show that at the age of 10–11 20% of youngsters use care; the figure rises to 32% by the
age of 19. The increase is accounted for mainly by girls, and most of the care provided is general healthcare, such as GP consultations. ZonMw’s programmes for young people address differences in psychosocial development between boys and girls where necessary. Where possible, parts of this Knowledge Agenda will be incorporated into the new programming.

**Knowledge gaps**

- Concerted collaboration between the various disciplines and research groups for the investigation of ‘differences between girls and boys in terms of health and illness’.
- Differences between boys and girls (young people) in terms of headache and migraine.
- Influence of the hormonal cycle on the development and health of girls.
- Causes of the sharp increase in GP consultations by girls.
- Effective interventions to reduce addiction to social media among girls.
- Gender-related methods to curb the development of obesity, diabetes and cardiovascular risk factors in children (particularly following gestational diabetes).
Theme 2b
Adulthood and social participation

Our adult years are devoted largely to participating in society. Besides having a family (in all its various forms), most people are also involved in paid work, voluntary work or, sometimes, informal care. Many health problems – some of them women-specific – can manifest themselves during adulthood. These problems are addressed under theme 4: conditions and problems. In this section, we shall consider only the relationship between social participation and health.

Participation

Social participation is regarded as very important in our society. Work and other forms of social participation and health impact on each other. The literature suggests that the impact of social participation on health is not clear-cut. Work (including voluntary work) generally has a positive effect on health, but the effect can be negative in the event of work-related illness, or if work exacerbates existing health problems. Conversely, a person’s health has an impact on their labour market participation and other forms of participation. Health problems have a particularly negative impact on participation if they cause impairment. Poor health has a negative impact on participation in work (one hour a week or more) and other activities (voluntary work and club memberships).
The fact that women are more likely to have impairments and report poorer health therefore has a negative impact on their participation in the labour market and other areas of society. Research on health and labour participation has found that the negative impact of poorer health is greater among women of Turkish and Moroccan origin than among women of Dutch origin.

Poor health can negatively impact labour market participation in a number of ways: it can prevent people from ever joining the workforce (in the event of serious illness/impairment), it can cause sickness absence and incapacity for work, unemployment and (insofar as still possible) early retirement. It should be noted that there is another hidden effect of health on women’s labour market participation (particularly in the case of older women), which is not revealed by the research referred to here because it includes all jobs from just one hour a week. Many women work part-time, and the reason for this is often poor health, particularly when it comes to older women. Research has also found that older, highly educated women (in all categories of workers) are more likely to report fatigue and exhaustion related to their work. Women who worked fewer than 25 hours a week were found to be less likely to report such problems than women who worked more hours, or full-time. This led the researchers to conclude that these women work part-time to limit their total burden (from work, care of children/home and informal care) and thus protect their health.

There is a possibility that the current changes to the care system will increase the demand for informal care and therefore also the pressure on women. Many women in the Netherlands have a paid job, but their average number of working hours is low.

Some jobs tend to be specific to men, while others are more commonly held by women. Men are more likely to work in sectors involving heavy physical labour (such as construction). However, the working conditions in some sectors where many women work, such as healthcare, cleaning and temping, are also unfavourable. A lot of the work these women do is emotionally and/or physically demanding. Overall, slightly more men than women do physically demanding work and slightly more women do emotionally demanding work. Furthermore, women are more likely than men to work in jobs where they have little say over how, when and in what order they do their work, and they are more likely to encounter sexual harassment and abuse at work. More women than men work in low-paid sectors (and therefore earn proportionally less) and are more likely to do work that can be done part-time, so they are able to combine work and care responsibilities. It is also known that women are often paid less for the same work.

Women are slightly more active than men when it comes to voluntary work and informal care. They also do a larger share of caring for children and relatives/friends/neighbours than men. Among men and women with young children the total number of hours of activity is highest among the men.
Labour participation, sickness absence and incapacity for work

Many Dutch women are in paid employment, but they work relatively few hours. Work generally contributes to good health and, partly for this reason, it is desirable that people should work. The talents of women are important for society, both sociologically and economically, to help fund the welfare state, for example. It is also important that women are better represented on the workfloor and in senior positions to ensure work is distributed more evenly.

Even though women’s labour market participation rate and number of working hours are lower than those of men, they are almost as likely as men to claim incapacity for work benefits. The double burden on women who combine work and family causes more incapacity only among single mothers. Women with young children are however more likely to be absent (for short periods) due to illness than men with young children.

In 2013 the sickness absence rate was 3.6% for men and 4.4% for women. Sickness absence has fallen in the past two years, particularly among women, who in 2013 had their lowest rate since 2008. The difference in the male and female rate of sickness absence is greatest in the 25 to 35 age group. Although the sickness absence rate excludes pregnancy and maternity leave, it is likely that women in this age group have a higher rate because of illness during pregnancy or as a result of complications during childbirth. The higher rate of sickness absence among women – irrespective of age, almost across the board – is also due to the fact that a relatively large number of women work in healthcare and education, where sickness absence rates are relatively high.

Partly because the influx of women into the labour market in the Netherlands happened fairly late (in the 1980s), the average age of women in the labour force is slightly lower than that of working men. This means that, since the average age of female workers is rising, we can expect to see sickness absence among women rise further over the coming years, which will inevitably have an impact, including greater costs to society.

Differences between women in terms of education, age and cultural background have a major impact on the way the relationship between work and health affects them. Turkish and Moroccan women, for example, have a higher risk of incapacity for work, and their labour participation rate has fallen. Despite higher levels of education, sickness absence among young women is still higher than that of their male peers, particularly in connection with psychological problems.

Part-time work used to be associated mainly with motherhood, but it now appears to be the norm for all women. Furthermore, the second phase of the economic crisis mainly impacted on jobs in the public sector and the service industry, including the healthcare sector. Women are overrepresented in these sectors.
Knowledge gaps

Links with other themes

– Gender differences (and the potential for reducing them) in the relationship between psychological problems (stress, anxiety, depression, burn-out) and sickness absence/incapacity for work.
– Relationship between work-related stress in women and cardiovascular disease, partly in light of their double responsibilities (home/family and work).
– Connection between sexual problems and pelvic floor dysfunction, and their implications for women's functioning in society.
– How female workers, managers and occupational health doctors regard and deal with conditions specific to women such as fertility problems or menstrual/menopausal problems.
– Poverty among elderly (immigrant) women in relation to health, healthcare and informal care.
– Contraception methods and their impact on women’s participation in society.
– Cycle- and reproduction-related problems in women and their impact on social participation.
– The implications of menstrual and menopausal problems for social participation, including working hours and sickness absence among women.

Specific to adulthood and social participation:

– Gender differences (and the potential for reducing them) in social participation, working hours, sickness absence and incapacity for work in relation to health, underlying factors and the costs to society.
– Gender differences (and the potential for reducing them) in the way managers and workers deal with participation, sickness absence and incapacity for work in relation to health.
– Multidisciplinary research into the consequences of double responsibilities (work, family and informal care) for the health, status and social participation of women, partly in connection with the current transitions in the healthcare system and the fact that more women work in the healthcare profession.
– Gender differences (and the potential for reducing them) in occupational medicine (both practitioners and workers).
– Health differences between women working part-time and full-time.
– The impact of sexual harassment and physical abuse on work in relation to labour participation, working hours, sickness absence and incapacity for work.
– Relationship between sickness absence and incapacity for work and lack of control in jobs commonly done by women.
– Gender differences in sickness absence and incapacity for work in relation to health (and the potential for reducing these differences) related to factors like socioeconomic status, level of education, age and cultural background.
– Factors that help women's reintegration into the work process after treatment for breast cancer.
– Health and overburden as a reason for women to leave the work process (e.g. to prevent illness and incapacity) and the health implications of not working.
– Relationship between working conditions and the health of women (including at a later age).

The participants at the invitational conference identified the following gap as deserving top priority.
– Multidisciplinary research into the consequences of double responsibilities (work, family and informal care) for the health, status and social participation of women, partly in connection with the current transitions in the healthcare system and the fact that more women work in the healthcare profession.
One of the key challenges in healthcare, where the gender aspect has also been seriously overlooked, is ageing, particularly ‘healthy ageing’. On average, women live longer than men, but men and women enjoy an equal number of years in good health. The number of years that women spend in good health is not increasing. In short, during their extra years of life women have a reduced or poor quality of life, despite the fact that a large proportion of the health budget is spent on chronic diseases affecting older women. At a later age men and women differ in terms both of the incidence of illness and the nature and number of conditions they experience simultaneously (multimorbidity). Women have different illnesses than men and they are less likely to be life-threatening. Multimorbidity is also more common in women.

The proportion of over-75s with impairments is much higher among women than among men, not only because women live longer than men. Even taking account of the age profile of the group of men and women over 75, impairment among women is more prevalent than among men. Just over 41% of men report at least one long-term condition, as opposed to over 53% of women. The older a person, the more likely they are to report two or more chronic conditions. Illnesses of which women are relatively more likely to die include psychological and behavioural disorders (particularly dementia), diseases affecting the skin and
subcutaneous tissue (generally infected pressure sores and other infections) and
diseases affecting the muscles and joints (osteoporosis, osteoarthrosis and arthritis).
More than twice as many women as men die of these diseases, particularly at
a very advanced age.68

Women are disproportionately affected by stroke. Strokes rarely occur in the under-
60s. The incidence of stroke increases sharply with age among the elderly. In every
age group the incidence among women is lower than among men, until they reach
a very advanced age. Nevertheless, more women die of stroke in the Netherlands
than men, because there are relatively more older women, stroke affects older
women in particular, and the likelihood of surviving a stroke diminishes in this age
group. Sex differences have been observed in the risk profile, clinical presentation,
response to treatment, pathological mechanism (intrinsic and hormonal
mechanisms) and pathophysiological implications.

Causes

A number of studies have explored the question of why women live longer than
men. Explanations that have been advanced relate to differences in lifestyle factors
(e.g. smoking and drinking), more high-risk behaviour on the part of men, physically
more demanding work, stress levels and violence (murder). As the emancipation of
women progresses (more smoking, more and more demanding or more stressful
work), the difference in life expectancy is expected to diminish, at least in part.
It also seems that the hormone oestrogen keeps a woman’s body in better condition,
possibly enabling the immune system to function properly for longer. The difference
in life expectancy between men and women, to the benefit of the latter, has been
seen in almost every country in the world for many years. It is therefore highly
likely that it is partly caused by a biological difference between the sexes.
This might involve factors related to the genes and factors related to the sex
hormones. One important gene-related factor is the inactivation (random or
selective) of one of the two X-chromosomes which occurs in all female cells. As a
result, dysfunctional genes can be repressed and favourable genes expressed.
Sex hormones can have an impact in two ways: via structural effects that occur
during critical periods in the development of the human body (as in the foetal
period, early childhood and puberty) and via temporary effects that occur when
hormone levels rise and then cease when they fall again. The differences that thus
emerge between men and women lead to more favourable outcomes in women in
terms of immune function, oxidative stress reactions and antioxidant status, the
lipoprotein metabolism, storage of fats and metabolism, the stress response via
the hypothalamic-pituitary-adrenal axis (HPA) and the capacity of female cells to
retain their integrity under the influence of various stressors. A combination of
these factors may contribute to women’s longer life expectancy.69

Oestrogen deficiency after menopause is the most likely cause of conditions like
loss of bone density, cardiovascular disease (incl. brain haemorrhage), cognitive
disorders and Alzheimer’s disease, depression, prolapse and incontinence in
women.70 Utrecht-based gynaecologist Bart Fauser mentioned women-specific
ageing in his inaugural lecture in 2005, because it has a biological cause that applies only to the female sex. A woman’s entire system is different. Ovarian function is not limited to reproduction; it plays a key role in a woman’s overall state of health and wellbeing throughout her life, from embryo to death. Health in old age is determined to a large extent by inability to perform certain daily activities (quality of life). Older women experience more impairment than older men. The fact that women are more likely to have multimorbidity only partially explains this. Even when men and women have the same number of medical conditions, the impairment women experience appears to be more severe and even when the conditions (causing the impairment) are of the same type, the impairment women experience tends to be greater. It may be that the severity of the condition is greater in women, or that other factors, such as social factors, that play a role in the perception of impairment, are more prevalent among women or have a different impact on women than on men. Little research has been done on this to date.

Current situation

The number of elderly people increases every year and conditions that used to be fatal are increasingly becoming chronic, thanks to better healthcare. This is increasing the pressure on the healthcare system and the associated costs to society. Dementia is a growing problem among the elderly. Despite varying results from different studies, dementia appears to be just as prevalent among men as among women. Hereditary factors appear to play a greater role in causing dementia in men, while in women oestrogen is a major factor. Men with dementia have a shorter lifespan and a higher rate of mortality than women. Poverty – an important risk factor for health problems – is a much greater problem among older women, particularly migrant women, than among men. Women have smaller pensions, and migrant women not only often have no occupational pension, they also do not have a full entitlement to a state pension. This means that they have to live on social assistance or less. This is an overlooked yet very serious problem, in terms of uptake of healthcare, decentralisation, informal care and the increase in dementia among migrants. This is certainly the case if subsequent generations also have poor access to the labour market, and families therefore have inadequate financial buffers.

Women with early menopause are more likely to face health problems. Women are living longer and longer, but the onset of menopause occurs at the same age. Women will therefore spend a growing proportion of their life in the post-menopausal phase (currently more than a third). This presents huge challenges given the growing focus on quality of life, alongside longevity. Menopause (end of ovarian function) does not occur in men, although men’s testosterone level does gradually fall as they grow older.
Prompt recognition, diagnosis and hospital treatment of stroke are crucial to a good prognosis for stroke victims. However, there is a greater delay in the admission of female stroke victims to hospital, possibly because their symptoms are more often atypical than they are in men. As a result, women themselves and their doctors are less likely to recognise them as being caused by stroke. The classic symptoms include paralysis down one side, defective speech, coordination and spatial orientation, and memory problems. Atypical symptoms include pain, headache, dizziness and confusion. Very few studies have examined the symptoms that occur in women and whether they present differently than in men. The studies that have been performed show a varying picture: sometimes women tend to present with atypical symptoms, and sometimes there is no difference in the symptoms experienced by men and women. Women are given thrombolysis treatment less frequently than men. This is also true of the Netherlands, where this has been attributed to the greater delay in admitting female stroke victims to hospital. The majority of clients with stroke are given only supporting therapy. There is a need for safe and effective treatment options.

In recent years it has become increasingly clear that women-specific ageing not only has implications for women’s health and healthcare, but also for the labour market, sickness absence and women’s important contribution to informal care. For this reason, too, the debate on ‘length of life’ should be more about ‘quality of life’, or rather ‘the number of years with good quality of life’.

As the population ages and the pressure on the healthcare system grows, the need for informal care is increasing, all the more so given the current changes to healthcare. The burden tends to be particularly high on informal carers who are still caring for their own children (most of whom are women – known as the sandwich generation), and can lead to psychological problems. Female informal carers generally employ a care strategy, while male informal carers tend to use a support strategy. A support strategy would appear to work better for both carer and elderly recipient than a care strategy. Grandparents also act as informal carers, helping to care for their grandchildren.

Current research

Internationally, research into ‘healthy ageing’ has mushroomed, with a particular emphasis on improving elderly people’s quality of life. The issue is approached from a social, technological, prevention and healthcare perspective. In Europe, the European Innovation Partnership Active and Healthy Ageing is exploring the issue. Fourteen European countries and Canada have launched the Jointing Programming Initiative ‘More Years, Better Lives – The Potential and Challenges of Demographic Change’ to better coordinate knowledge programmes. The EU Joint Programme ‘Neurodegenerative Disease Research’ (JPND) is an innovative research initiative launched in order to tackle the growing challenges of neurodegenerative disease. Gender is one of the focal points of these international programmes.
In the Netherlands, the ‘Memorabel’ dementia research and innovation programme (administered by ZonMw), part of the Delta Plan for Dementia, is working to improving the quality of life and care of dementia patients. Collaboration with a new gender and health programme would bring huge added value.

**Knowledge gaps**

**Links with other themes**
- Better recognition and treatment of post-menopausal women with cardiovascular disease relative to the care usually provided, including the possible link with diastolic heart failure.
- Gender differences (and ways of reducing them) in dementia and other cognitive disorders (both diagnosis and treatment).
- Assessment of long-term health risks in women who experience early versus late menopause, particularly cancer, cardiovascular disease, cognition, Alzheimer’s disease, depression and other psychological problems.
- Long-term follow-up on health of women in relation to age at menopause (normal or premature).
- Cardiovascular disease in relation to ageing in women. Women live longer than men and cardiovascular disease occurs mainly at a later age. There are earlier signs, but little basic knowledge exists about diastolic heart failure and factors specific to women, for example. This group is set to grow to large proportions, and a major intervention study is needed.
- Hormone replacement therapy for women after menopause (premature or otherwise).
- Relationship between women-specific ageing and social participation.
- Poverty among older women, particularly migrant women, in relation to health, healthcare and informal care.
- Psychological problems related to menopause and other relevant life stages.
- Relationship between the incidence of aneurysm, tendency of blood vessel wall to tear and localisation of the aneurysm, and the likelihood of subarachnoid haemorrhage in older women.

**Specific to ageing**
- Multidisciplinary research into gender differences in genetic, biological, social and psychological mechanisms of ageing, distinguishing between the third and fourth ages.
- Multidisciplinary research on the link between women-specific biological, social, psychological and epigenetic aspects of multimorbidity at an advanced age.
- Influence of reduced oestrogen levels on emergence of health problems as women age.
- Other factors that explain older women’s reduced quality of life.
- Potential for improving ‘healthy ageing’ among women.
Gender differences in the impact of ageing processes on mobility (musculoskeletal system).

Risk assessment to establish which women develop severe problems during and after menopause.

Gender differences in presenting complaint and clinical symptoms of stroke and link to delay in call for assistance and diagnosis.

Gender differences in outcomes of stroke (from which older women generally die, or retain many residual symptoms).

Study of whether gender-specific criteria should be applied in determining which (invasive) modes of treatment are used for stroke.

Effective interventions for timely diagnosis of stroke in women.

The participants at the invitational conference identified the following gaps as deserving top priority.

Multidisciplinary research into gender differences in genetic, biological, social and psychological mechanisms of ageing, distinguishing between the third and fourth ages.

Multidisciplinary research on the link between women-specific biological, social, psychological and epigenetic aspects of multimorbidity at an advanced age.
A healthy lifestyle can reduce the risk of disease and other medical conditions, and can have a strong impact on the outcome of treatment. Well-known factors like not smoking, getting enough exercise, safe sex, moderate alcohol consumption and a healthy diet are the subject of many health promotion programmes. Men and women can have a major influence on their own health, and reduce their risk of cardiovascular disease, diabetes and cancer by making healthy choices. In some areas, major differences exist in the lifestyles of men and women.

**Figures**

In 2013, 23% of the Dutch population aged 12 and over smoked occasionally, and 18% smoked every day. More men (26%) than women (20%) are smokers. This applies to all age groups. Men are also more likely to be ex-smokers than women (43% as opposed to 35%). In 2013 the average number of cigarettes smoked by smokers aged 15 and over was approximately 13 per day. There is virtually no difference between the figures for men and women (COR, 2013). Almost 7% of Dutch men over the age of 19 drink more than the maximum recommended two alcoholic drinks every day. More than 6% of women over 19 drink more than the maximum recommended one alcoholic drink a day. Two out of three Dutch people aged 19 and over comply with the Dutch standard for healthy exercise applying to adults. On average, men are more likely than women to meet the three different exercise standards that exist. In 2012 the Netherlands had approximately 1.3 problem users of opiates per 1000 head of population aged between 15 and 64. This equates to around 14,000 individuals. 86% are men and 14% are women. In 2012 53% of men and 44% of women were overweight. Men are more likely to be overweight than women, though women are more likely to be obese. The obesity rate among men is 11%; among women it is 14%.
Dutch adults eat only small quantities of fruit and vegetables. The Health Council recommends 200 grammes of vegetables and two pieces of fruit a day. Among adults up to the age of 69, 10% of women and 6% of men eat the recommended amount of fruit. They eat even fewer vegetables: 5% of men and women eat the recommended amount.\textsuperscript{86, 87}

Originally Dutch women and women of Western origin are more likely to smoke than non-Western women: just over 24% as opposed to almost 20% in 2011–2013. The proportion who are slightly overweight is the same, but at over 14%, more non-Western women are severely overweight than women from other groups (8%).\textsuperscript{88}

**Health promotion**

Health promotion is high on the agenda of policymakers, NGOs and care providers. Under the National Prevention Programme (NPP *Alles is gezondheid*...), which includes the fifth ZonMw Health Promotion and Disease Prevention, all kinds of parties in society agree measures and take joint action designed to spark a trend towards better health and more vitality in the population. However, sex and gender aspects of health promotion activities, such as measures to prevent women smoking just as much as men, are still given too little consideration. That is why this Knowledge Agenda calls in several places for sex and gender factors to be taken into account more in disease prevention and health promotion.

**Knowledge gaps**

**Link with other themes**
- Lifestyle programmes that take account of specific gender-related factors and are more effective (and cost-effective) than the usual programmes.
Theme 3b
General healthcare

Healthcare consumers – both men and women – encounter a range of care and assistance providers in the healthcare system and other related fields. In many cases, their general practitioner will be their first port of call, but they may turn to a district nurse, social worker, psychologist, nurse practitioner (mental healthcare), physiotherapist or member of a community welfare team or health clinic. The GP is a general specialist. He or she will often have known the patient for many years, be aware of the specifics of their circumstances and family situation, and will where possible coordinate all care, both somatic and psychosocial. The GP is accessible and available to answer any questions on health; consultation is free at point of contact. GPs can also give advice on disease prevention and lifestyle. Basic care as provided by GPs therefore extends to all the themes dealt with in this Knowledge Agenda.

Healthcare consumers may expect the same standard of care from all providers irrespective of their sex, or the sex of the practitioner or therapist. In practice, however, sex and gender differences can have an impact on the care offered. Care provision is not gender-neutral.

Accessible care means that ‘people requiring care have access to care provision in good time and without encountering any major obstacles’. There are several aspects to accessibility: affordability, physical accessibility, timeliness of acute and non-acute care, accessibility according to need, availability of staff and freedom of choice. Gender differences can exist in relation to all these aspects.

The freedom to choose one’s GP, including the choice of a male or female doctor, is mainly of importance to women. One in four of the women on the NIVEL consumer panel would prefer to choose, and the majority would opt for a female GP. The younger the respondent, the greater their sex preference. When it comes to symptomatic examination and sexual problems, the figure can be as high as 36%, with women almost always expressing a preference for a female GP. Women who consult a gynaecologist also prefer a female practitioner to a male one. This sex preference is explained largely by women’s client-oriented style of communication.

Help-seeking behaviour

Men and women differ in their views on health and illness. Women report more health problems than men. These differences appear to be caused by differences in the way in which men and women notice and interpret how their body functions. Furthermore, men and women deal with problems (health and other) that influence their help-seeking behaviour in different ways.

In 2011 83% of women consulted their GP at least once. Of those women, 30% had one or two consultations that year, and on average they consulted their GP on 6.1 occasions. Among men, 72% had consulted their own GP at least once, 41% once
or twice, and they had had an average of 4.7 GP consultations. Women experience more health problems and visit a doctor for all groups of conditions more often than men. The underlying causes are not always known, nor are the implications for the health of men and women. The relative difference is greatest in the case of conditions affecting the urinary tract. In 2011 12% of women visited their GP for this reason, as opposed to 4% of men. People of non-Western origin visit the GP more often for all problems than the originally Dutch population. Health problems where the differences are particularly great include anaemia and diabetes. Non-Western ethnic minorities consult their GP less for conditions affecting the ears and the cardiovascular system.

In all ethnic groups women consult their GP more often than men. The difference is greatest among people of Turkish origin. The male-female differences per type of condition are virtually the same in nearly all ethnic groups. The difference for conditions affecting the urinary tract is clearly smaller among non-Western groups, however, mainly because men of non-Western origin consult their GP relatively often for such conditions.

The number of hospital admissions is 20% higher among women than among men. After correction for admissions linked to pregnancy and childbirth, the difference is still 10%. Differences in the number of admissions between men and women are greatest in relative terms for diseases affecting the urinogenital system, diseases of the nervous system and senses, and diseases affecting the muscles and joints. Women are admitted to hospital for these conditions 50% more often than men. Men are 1.4 times more likely to be admitted to hospital for diseases of the cardiovascular system. Men and women are equally likely to be admitted for relatively common illnesses affecting the digestive system.

Communication

Men and women communicate differently and this is reflected, among other things, in the way in which healthcare consumers present and explain their symptoms to their GP (or fail to do so). For instance, men are more inclined than women to deny health problems (including psychological problems), or to think of their own solution. Women experience and report more health problems. Whether women make ‘unnecessary’ use of healthcare services in some cases and/or men make ‘insufficient’ use of them is unclear. Clients with cancer have been found to be most concerned about the expertise and the behaviour, actions and manner of doctors and nursing staff. Men and women find different aspects of this important. Women are more concerned about ‘waiting times’, ‘the manner of nurses’, ‘support, advice and counselling’ and ‘continuity of care’.

Studies have found that women are more vigilant in terms of their health than men. They are more likely to undergo necessary tests and are generally more willing to have worrying potential cancer symptoms investigated. Nevertheless, there are symptoms that even the most alert of women can overlook because they appear to be part of the normal functioning of a woman’s body. Care providers
should explore how men and women perceive, interpret and present physical problems, and tailor their actions accordingly by establishing what assistance is actually being requested. Help-seeking behaviour can lead to a delay in presentation of problems to the healthcare system in both women and, more especially, men.

Prevention

A GP or other doctor and/or nurse practitioner assesses the risk that a healthcare consumer will, for example, develop COPD, cardiovascular disease, diabetes etc. on the basis of factors like sex, age, socioeconomic status, smoking, alcohol consumption, weight and physical activity. Lifestyle advice and counselling are increasingly becoming part of basic healthcare. Interestingly, men who smoke consult their GP less often than men who do not, whereas the opposite applies to women.99, 100 There are also indications of gender-related risk factors that GPs should monitor. For instance, women who suffer pre-eclampsia during pregnancy at a later age have a greater chance of developing cardiovascular disease or diabetes.101, 102, 103

Male GPs do more in the way of active prevention, are more likely to call people in for a consultation, for example. Female GPs appear to be more active in terms of case finding when a patient visits the GP-surgery. This is consistent with the longer average consultation times with female GPs.104

Sex of the doctor

The sex of the doctor appears to play an important role in both communication with the client and the choices the doctor makes in terms of the patient’s care. Female doctors communicate in a more client-oriented manner than their male counterparts.105, 106 During consultations, female doctors explore the client’s psychosocial circumstances in more depth, pay more attention to emotions and feelings, adopt a more positive tone, facilitate collaboration with the client on an equal footing, and encourage clients to participate more in medical decisions. When it comes to more task-oriented communication – often regarded as a more male form of communication – no differences between the sexes are seen in doctor-client relationships. This type of communication involves things like establishing the patient’s medical history and explaining the diagnosis and policy. Male and female doctors sometimes also make different choices when it comes to diagnosis and treatment.

For the same set of symptoms, male doctors are more likely to perform a rectal examination on male clients than their female counterparts; female GPs are more likely to perform a vaginal examination.107, 108, 109 Apparently, psychological barriers exist when it comes to asking people of the opposite sex intimate questions or performing intimate procedures on them. This might mean that such procedures are not performed, as a result of which the doctor will be less skilled in these matters, and fewer relevant findings will be made.
Male GPs and internal medicine specialists are more likely to prescribe psychopharmaceuticals, sedatives and analgesics, and in higher doses, than their female counterparts.\textsuperscript{110,111}

Doctors are more likely to interpret women’s health complaints as psychosomatic than men’s complaints; male doctors are more likely to regard tranquillisers as indicated and female doctors are more inclined to talk about the problem. Female clients are prescribed tranquillisers more commonly than male clients, and more often by male doctors than by female ones. Male doctors are also more likely to offer menopausal women hormone replacement therapy; they are also more likely than their female colleagues to prescribe protease inhibitors to HIV-positive clients, be they male or female. Sometimes the situation and life stage of the doctor him-/herself appears to play an even more specific role. For instance, women with menopausal problems are more likely to be prescribed hormone therapy by female GPs who are themselves of menopausal age than by male GPs or by younger female GPs.

Knowledge gaps

Links with other themes

– Development and implementation of professional GP association (NHG) guidelines with a focus on recognising violence as an underlying factor in medical problems.
– Possibility of an automated dosage system for medication. The system would include client-specific factors (such as sex, weight, age, genetic information) and would determine the correct dose on the basis of a combination of factors.
– The effectiveness and cost-effectiveness of treatment for depression whereby GPs ask systematic questions about partner violence and adapt their policy accordingly.
– The influence of doctors’ manner of communication (categorised by sex) on matters of sexuality.

Prevention

– Gender-related risk factors in lifestyle.
– Underlying causes of women’s more frequent consultations with their GP and other practitioners – compared with men – and the implications for care of and the health and life expectancy of women and men.
– Gender differences in help-seeking behaviour and possible ways of influencing it.
– Gender differences in lifestyle counselling: costs, benefits and impact on disease burden of gender-sensitive interventions with a focus on preventing smoking.
– Gender-related referral behaviour by GPs and other practitioners (M/F) for male and female healthcare consumers.
– Gender factors in relation to timely GP diagnosis of all serious conditions.
Sex of client and doctor

- Gender differences in expectations, wishes and satisfaction in relation to unequal access to total care, examined from perspective of client (female).
- Gender differences in communication between doctor (M/F) and healthcare consumer (M/F) and strategies for reducing negative effects of these differences.
- Gender-related actions by GPs and other practitioners (M/F) when diagnosing and treating conditions such as Parkinson’s, diabetes, cancer, COPD and incontinence, and the effectiveness (and cost-effectiveness) of such actions compared with the usual care.
- Ways of making doctors (M/F) aware of their gender-related actions and strategies in order to promote uniformity in the quality of care.

The participants at the invitational conference identified the following gaps as deserving top priority.

- Gender differences in lifestyle counselling: costs, benefits and impact on disease burden of gender-sensitive interventions with a focus on preventing smoking.
- Gender differences in expectations, wishes and satisfaction in relation to unequal access to total care, examined from perspective of client (female).
**Theme 3c  
Drug treatments**

Great benefits can be achieved by taking more account of gender differences when researching and prescribing drug treatments. Differences between men and women affect the use and effect of medication in many ways. Women not only use more medication, they are also more likely than men to experience side effects.\(^{112}\)

**Current situation**

Until the end of last century women (and, in many cases, female test animals) were systematically excluded from drug trials.\(^{113, 114}\) This was based on the assumption that women’s hormonal cycle or use of the contraceptive pill would impact on the research results. Another reason for not including women in drug trials is the risk if they turn out to be pregnant during the trial. The reality is, however, that women have a hormonal cycle and many women take the contraceptive pill. It is therefore in fact important to know what impact the hormones have on the effect of medication. The risks of using medication during pregnancy should also be more thoroughly investigated.\(^{115}\) Though the pharmacokinetics of new substances are almost always described separately for men and women, the pharmacodynamic effect (the treatment effect) is almost never described in this way.\(^{116, 117}\) The specific effect on women of a huge number of existing medications is simply unknown. Patient information sheets distinguish between adults and children, but not between men and women, though this is certainly necessary, given the differences. Research proposals still fail to present arguments in support of excluding women (whether pregnant or not).

Differences in the physiology of men and women mean that drugs are absorbed and excreted by the body in different ways and at different rates.\(^{118}\) Factors that play a role in this include – as far as is known – body weight, fat percentage and metabolic rate. Body weight certainly plays a key role. Women tend to be lighter than men, though to date this has never been taken into account in dosages. Women also use more different medications more frequently and for longer, and have a greater chance of experiencing side effects than men.\(^{119, 120, 121, 122}\) Multiple use of medications by women, much more so than by men, cannot only be explained by use of the contraceptive pill. Even after menopause women use more medicines (more frequently). This means that it is also important to take the age factor into account in research.

We still know far too little about the specific effect of certain medications (and combinations of medications) used by women (in various distinct groups), some of them in different hormonal phases. Research focused on sex and gender could therefore yield great health benefits and possibly also cost savings, particularly if the focus were initially on commonly used medications, such as treatments prescribed for chronic conditions. We also know too little about gender aspects of drug use.
Current research

ZonMw’s Rational Pharmacotherapy programme (GGG) aims to ensure existing medication is used more effectively, safely and efficiently. It focuses on improving pharmacotherapy, both at the level of the medication and in terms of the use of medication in daily healthcare practice. A number of specific studies focusing on use of medication (e.g. antidepressants) by pregnant women are currently underway as part of the programme. It is important that the theme of gender and health be further integrated into current programmes such as this.

Legislation

Legislation to allow new medication to be marketed is drawn up at European level. It is desirable that gender differences be incorporated into such legislation, but this will have to be tackled at European level. The international ICH guidelines on this matter have been translated into legislation in the United States; in Europe the EMA is of the opinion that this is not necessary.\textsuperscript{123,124} It would be wise to investigate whether there is now support for this, perhaps by organising an international conference.

Knowledge gaps

Links with other themes
- Sex-specific aspects of psychopharmaceuticals (including therapy compliance, lifestyle factors).
- Gender differences in the effects and side effects of medication for cardiovascular disease.
- Gender differences in the interaction between different medications for cardiovascular disease.
- Possibility of an automated dosage system for medication. The system would include client factors (incl. sex, weight, age, genetic information) and would determine the correct dose on the basis of a combination of factors.
- Gender differences in the effects of medication for rheumatism.

Specific to drug treatments
- Sex differences in the way (including degree and rate) in which medicines are absorbed, converted, transported and excreted by the body.
- Gender differences in the way healthcare consumers deal with medication.
- Identification of medications commonly used by specific groups of women (e.g. in their fertile years or post-menopause), often simultaneously.
- Risks associated with and safe use of commonly prescribed medications during pregnancy, breastfeeding and various hormonal phases.
- Side effects in women of commonly used medications (and combinations of medications) and adaptation of information sheets (e.g. antidepressants, antihypertensive drugs, diabetes medication).
– Regulatory study: review of proportion of medication approved in the EU in recent years whereby sex-specific analyses were performed, and differences with the US, where such analyses are mandatory.
– Interaction between medications commonly used by specific groups of women.
– Adjustments to doses based on gender differences.
– Changes to information sheets based on gender differences.

The participants at the invitational conference identified the following gaps as deserving top priority.

– Risks associated with and safe use of commonly prescribed medications during pregnancy and breastfeeding.
– Side effects in women of commonly used medications (and combinations of medications) and adaptation of information sheets (e.g. antidepressants, antihypertensive drugs, diabetes medication).
Cardiovascular disease is a leading example of a set of conditions on which differences between men and women have a bearing. These differences are expressed in all aspects of cardiovascular disease, as regards the underlying defect, the impact of hormones and practical issues such as symptoms, diagnosis and treatment.

There has been a sharp fall in the number of deaths from cardiovascular disease in the Netherlands over the past few decades. Fifty years ago one in two Dutch people died of cardiovascular disease; the figure is now one in four. This is due both to better primary prevention thanks to progress in the treatment of dyslipidemia (high cholesterol), hypertension and diabetes, and to major improvements in the treatment of cardiovascular disease itself thanks to angioplasty, bypass operations and better secondary prevention.

On the other hand, however, lifestyle-related risk factors such as obesity and lack of exercise are on the increase. The total number of smokers has fallen, but the proportion of young women smoking has risen.

High blood pressure is the second most common chronic condition in women (17%) after migraine, and it is the most frequently reported chronic condition among men (14%). Older women in particular are more likely than men to have high blood pressure. Interestingly, the fall in the number of deaths from cardiovascular disease has been greater among men than among women. In some groups of women, such as female diabetes sufferers, there has been no improvement at all in the mortality rate from cardiovascular disease. This underlines the need for the differences between men and women to be given full consideration.

Sex differences are a common factor across the entire range of cardiovascular disease, in terms of epidemiology, pathophysiology, diagnosis and treatment. Current cardiovascular care takes insufficient account of this fact. There are important differences between the sexes, not only in terms of the underlying defects, but also in communication styles and psychosocial factors. The still prevalent notion that women have a low risk of cardiovascular disease is very outmoded.
Current research

In 2014 three national multidisciplinary studies were launched, all of them subsidised by the heart research charity Hartstichting. The first is the Queen of Hearts project on risk markers and their relationship with diastolic heart failure in women. The second is the CREW project, a multidisciplinary study into the relationship between women-specific risk factors such as PCOS, pre-eclampsia and migraine, and cardiovascular disease (both arterial and venous). Finally, the WOMB study is investigating the influence of lifestyle on pregnancy, mother and child. These studies are largely restricted to women of reproductive age.\textsuperscript{130}

Epidemiology

Before menopause women are less likely to have cardiovascular disease than men of the same age. The situation is reversed at a later age. Oestrogens inhibit the development of atherosclerosis in young women. Extensive studies have shown that administering hormones after menopause has no protective effect in terms of vascular ageing, and can in fact be harmful at an advanced age.\textsuperscript{131, 132}

Causes

The classic risk factors for cardiovascular disease, such as smoking, hypertension, diabetes and dyslipidemia (high cholesterol) apply to both men and women. There are however subtle yet important differences between men and women in terms of the impact of these factors.\textsuperscript{133} Diabetes is for example a greater risk factor for cardiovascular disease in women than in men. Smoking at a young age is also relatively more risky for women than for men; male smokers have their first heart attack six years earlier than male non-smokers, but female smokers tend to have a heart attack 14 years sooner than their non-smoking counterparts.\textsuperscript{134} Smoking in combination with use of the contraceptive pill gives women over the age of 35 an increased risk of cardiovascular disease.

Besides the classic risk factors, there are also gender-sensitive risk factors. For women, they are often related to complications during pregnancy (such as pre-eclampsia/HELLP syndrome, pregnancy-induced hypertension and premature birth), or they are related to reproduction and reproductive problems such as the menstrual cycle, PCOS and very early menopause (<40th year). Women who suffer from migraine with aura have an increased risk of cardiovascular disease. It has been demonstrated that men who experience erectile dysfunction at an early age (<40th year) have a greatly increased risk of cardiovascular disease.

There is growing evidence that the ageing of the blood vessels follows a different pattern in men and women, with inevitable implications for health problems, examination and treatment.
Prevention

More knowledge is required to identify risk factors and develop adequate preventive interventions. For instance, research among women aged 45 and over has shown that prescribing acetylsalicylic acid to prevent a first heart attack (primary prevention) has no effect.\textsuperscript{135} This has however been proved effective in men with an increased cardiovascular risk profile. Since guidelines do not adequately reflect our progressive understanding of cardiovascular disease, women with chest pain are still prescribed anticoagulants, often in combination with antacids to treat (unnecessarily!) stomach problems that occur as a side effect.

Diagnosis

Since GPs and cardiologists do not practise sufficient gender sensitivity, they overdiagnose younger women, and underdiagnose post-menopausal women (and therefore undertreat symptoms and risk factors). This not only results in poorer care, it also leads to wastage and higher costs. It is also by no means clear that the current diagnostic potential and cut-off values of various tests are appropriate for both men and women.

Women dominate two important clinical pictures in cardiology: microvascular angina (chest pain without clogging of the main arteries) and heart failure with preserved ejection fraction. Both share (at least partially) an underlying mechanism, i.e. dysfunction in the small vessels of the cardiac muscle. Current imaging techniques are unable to properly capture these small vessels, as a result of which women with symptoms are often simply discharged. It is known that these clinical pictures, if symptomatic, are associated with reduced survival rates, and current antianginal medication is not entirely effective. Such defects are also seen in men, albeit to a lesser extent. The largest group is however women with heart failure as a result of diastolic dysfunction (so the heart muscle can still contract, but the chambers do not fill properly), mainly post-menopausal women. It is not clear why this occurs and why it is most common in women. There are two further clinical pictures that include temporary heart failure as a result of a large reduction in the strength of contraction in the cardiac muscle: peripartum cardiomyopathy (CM) and Takotsubo cardiomyopathy (known as Broken Heart Syndrome). Both appear to be related to a sudden dramatic increase in adrenalin as a result of stress during childbirth (peripartum CM), or after experiencing strong emotion (Takotsubo CM).
**Treatment**

There is growing evidence that gender differences have important implications for the criteria for angioplasty, bypass surgery or implantation of a defibrillator, and for the timing of such treatment for women. The delay between symptoms and treatment is longer for women than for men. Women with a dilated abdominal aorta have been found to be more at risk of tearing at the same diameter as men with this condition. However, guidelines do not give different cut-off values for surgery to be performed on men and women. Sex-specific research into peripheral vascular disease is also still in its infancy.

**Knowledge gaps**

**Link with other themes**

- Cardiovascular disease combined with diabetes in women. This comorbidity gives rise to many problems, absence from work, and mortality. Causes of higher rates of cardiovascular death among women with diabetes compare to men with diabetes.

- Relationship between stress and differences in development of cardiovascular disease in men and women. One example is Broken Heart Syndrome (a form of acute heart failure caused by extreme stress, which manifests itself as an acute myocardial infarction). This syndrome is ten times more common among women than among men. This type of acute coronary syndrome (ACS) is affecting a growing group of clients.

- Gender differences in the relationship between dementia and cardiovascular disease.

- Relationship between the combination of pregnancy and psychological problems (including postnatal psychological problems) and cardiovascular disease.

- Unexplained physical symptoms in women in relation to cardiovascular disease.

- Lifestyle programmes that take account of specific gender-related factors and their effectiveness (and cost-effectiveness) compared with the usual programmes.

- Relationship between work stress and cardiovascular disease in women, taking account of their double responsibilities (home/family and work).

- Cardiovascular disease in relation to ageing in women. Women live longer than men and cardiovascular disease occurs mainly at a later age. There are earlier signs, but little basic knowledge exists about diastolic heart failure and factors specific to women, for example. This group is set to grow to large proportions; a major intervention study is needed.

- Effects and side effects of medication for cardiovascular disease in women. For example, gender differences in the interaction between different anticoagulants administered for cardiovascular disease and differences in factors leading to haemorrhage.
Gender differences in the interaction between different medications for cardiovascular disease.

Better recognition and treatment of post-menopausal women with cardiovascular disease relative to the care usually provided, including the possible link with diastolic heart failure.

Assessment of long-term health risks in women who experience early versus late menopause, particularly cancer, cardiovascular disease, cognition, Alzheimer’s disease, depression and other psychological problems.

Incidence of type 2 diabetes, obesity and cardiovascular risk factors in the years following childbirth in mothers who have had gestational diabetes, including the possible influence of ethnic background.

Relationship between physical and psychological violence and conditions like cardiovascular disease, unexplained physical symptoms (chronic pain) and gynaecological problems.

Relationship between childbirth (peripartum CM) and poor contractility of the left ventricle.

Implementation of knowledge on increased risk of cardiovascular disease in female smokers who take the contraceptive pill. Many women are unaware of the increased risk and doctors are doing too little to inform them.

Assessment of migraine as a cardiovascular risk factor and possible gender differences in this area. Migraine as part of gender-specific cardiovascular risk prediction models.

Relationship between migraine- and pregnancy-related cardiovascular complications, such as pre-eclampsia and the secondary headache associated with this.

The pathophysiology and gender-specificity of the increased risk of stroke in female clients with migraine.

The extent to which the frequency of migraine attacks impacts on the cardiovascular risk profile of women, and necessary changes to current treatments.

Difference between migraine with aura and migraine without aura as a cardiovascular risk factor among women.

Relationship between the incidence of aneurysm, tendency of blood vessel wall to tear and localisation of the aneurysm, and the likelihood of subarachnoid haemorrhage in older women.

Epidemiology

Cardiovascular risk in women with premature menopause, e.g. resulting from preventive ovariectomy, radiotherapy/chemotherapy, or natural causes.

Cardiovascular disease among female migrants; this is a growing population with many risk factors.
Causes

- Gender differences in the classic risk factors for cardiovascular disease (such as smoking and diabetes).
- Consideration of gender differences in cardiovascular risk management and the effectiveness (and cost-effectiveness) of this compared with the usual care.
- Cause of death after myocardial infarction. More women than men die after a myocardial infarction, despite receiving similar treatment. It is not clear why this is so.
- The relationship between a woman’s hormonal cycle and the development of cardiovascular disease.
- The relationship between pregnancy (and complications in pregnancy) and cardiovascular disease (both as an independent risk factor and because they increase the likelihood of classic risk factors like diabetes and hypertension).
- Other sex-specific risk factors for cardiovascular disease (e.g. migraine, lifestyle, genetic differences between men and women).
- Gender differences in vascular dysfunction in terms of etiology, risk factors and diagnosis.
- Relationship with autoimmune disorders: women with autoimmune disorders are more likely to develop cardiovascular disease. The underlying mechanism is not sufficiently known.
- Gender differences in the impact of cancer treatment on cardiovascular disease. This might include the damage caused by breast cancer treatment and gender differences in the development of hypertension, possibly caused by oncological medication that raises blood pressure.
- Risk factors, symptoms and early diagnosis of microvascular coronary dysfunction (angina, MCD) in women. MCD in the absence of obstructive coronary artery disease (CAD) is a specific cardiological problem among middle-aged women who have heart problems with no demonstrable narrowing of the coronary artery. These women are not catered for by current cardiological care.
- Gender differences in the relationship between early vascular dysfunction and the risk of cardiovascular disease, including in relation to the role of genetics and epigenetics and inflammation, implications for the older age group and a possible link with dementia.
- Gender differences in the interaction between cancer and cardiovascular disease.
- Incorporation of lifetime risk of cardiovascular disease for men and women in guidelines, questionnaires and tables.
- Possible gender differences in cardiac surgery in the Netherlands.
- Causes of increased cardiovascular risks for women after menopause.
- Role and precise action mechanism of oestrogen in protecting women prior to menopause.
- Timing and role of hormone replacement therapy in menopausal women.
Prevention
– Specific lifestyle factors in women and the implications for cardiovascular disease and other conditions. For prevention, it is also important to focus more on the differences between individuals and groups. How can women be encouraged to take more exercise and avoid obesity? How can effective anti-smoking programmes be developed for young women? How many women aged over 35 smoke and take the pill, greatly increasing their risk of cardiovascular disease? What benefit could be had from approaching these women proactively, helping them to stop smoking or encouraging them to use a different form of contraceptive?
– Better tools to distinguish between women at high and low risk.
– Cardiovascular prevention strategies for women with high cardiovascular risk (e.g. diabetes, smoking or pre-eclampsia).

Diagnosis
– Scientifically proven cost-effective tools (e.g. blood tests, ultrasounds, non-invasive examination) for recognising different forms of cardiovascular disease in women at different stages of life both better and earlier (early diagnosis). Work is currently underway on a blood test that can help diagnose diastolic heart failure at an early stage.
– Investigate whether the existing tests and values apply to women. For instance, a recently developed test shows that a unisex test can miss women who have had a myocardial infarction (who are then wrongly discharged). A more sensitive and cost-effective test for women would identify this group more effectively.

Treatment
– Gender differences in criteria for treatment options.
– Effective communication with female healthcare consumers, partly to encourage them to take control (e.g. by measuring their own blood pressure).
– Tools and their effectiveness/cost-effectiveness relative to ordinary care, for good diagnosis and treatment of diastolic heart failure in post-menopausal women. Women and elderly people are currently undertreated.
– Identify malpractice resulting from a failure to take a gender-sensitive approach to cardiology, using data from healthcare insurance companies, and identify potential for reducing this.
– Effective treatment of women with microvascular angina and heart failure with preserved ejection fraction.
– Gender differences in cardiac arrhythmia (atrial fibrillation is more common in elderly women than in men; causes symptoms/high rates of admission/use of anticoagulants and risk of haemorrhage).
– Gender differences in stroke (which kills many elderly women or leaves them with lots of residual problems).
The participants at the invitational conference identified the following gaps as deserving top priority.

- Knowledge synthesis of existing applicable knowledge of cardiovascular disease in women and methods of knowledge sharing.
- Gender differences in vascular dysfunction in terms of etiology, risk factors and diagnosis.
- Gender differences in the link between mental stress and cardiovascular disorders.
**Theme 4b**

Physical and psychological violence

Gender differences play a big role in violent crime. Even though gender-neutral terms like domestic violence or partner/family violence are used nowadays, and even though there are many different groups of victims (the elderly, children, women, men, gay men and women etc.), in practice the vast majority of perpetrators are men and victims women.\(^\text{140, 141, 142}\) Women are also more likely to encounter serious forms of violence, and are more likely than male victims to seek medical assistance.\(^\text{143, 144}\) Gender also plays an important role in the factors underlying violence.\(^\text{145}\)

It is known that experiencing violence has major psychological and physical consequences for victims in the short term and in later life.\(^\text{146, 147}\) However, many questions remain about this issue. We do not for example know what proportion of healthcare and other costs to society are generated by family, sexual or other violence. It seems likely it will be considerable, however, given the severity and prevalence of violence.
Current situation

A great deal of research is performed, particularly on family and sexual violence (and the prevalence of this phenomenon) in the general population. Time and again studies produce shocking figures. For example, a recent study by the European Union found that 33% of women in the EU have encountered partner violence at some time, and that they generally seek assistance in a medical setting. The 2014 report ‘Violence against women: an EU-wide survey’ makes it clear that 10% of Dutch women have been raped, 11% have encountered sexual violence from a partner or ex-partner, and 20% have been physically assaulted by a partner or ex-partner.  

Concern for recognising violence and the role of care providers has grown in the healthcare system – and in other sectors – over the past decade. Legislation that came into force in 2013 obliging professionals to report domestic violence and child abuse also applies to medical professionals. Doctors’ association KNMG has developed a reporting code and a step-by-step plan for dealing with child abuse and domestic violence. This is a rather legalistic document which provides limited guidance and is currently inadequately underpinned by scientific evidence. Violence often has a lifelong impact on victims’ health and wellbeing. They are more likely to consult their GP, have more chronic complaints and use more painkillers, and depression is five times more common among women who have experienced violence than among women who have not. Quite a lot is known about the implications of violence for the psychological health of victims; much less is known about its impact on physical health. International studies have estimated that a GP sees an average of one or two women a week who have health problems related to partner violence. This group is often not recognised as such. Abused women have been found to visit their GP almost twice as often for unexplained physical symptoms. Only 0–3% of the women who come with symptoms related to partner violence are recognised as victims. Not only must medical care providers recognise and raise the issue of violence, it is also important to prevent the immediate and delayed medical effects and the transfer of violence to the next generation (generally neglect and sexual violence); prevention of transgenerational transmission, in other words. When women do seek medical assistance, it is generally a matter of secondary and tertiary prevention in a high-risk group.


Knowledge gaps

**Link with other themes**
- Link between sexual problems and experience of sexual violence in childhood and partner violence in adulthood, and the treatment of these problems.
- Relationship between physical and psychological violence and conditions like cardiovascular disease, unexplained physical symptoms (chronic pain) and gynaecological problems.
- Retraumatisation of sexual violence during internal medical gynaecological procedures.
- Development and implementation of professional GP association (NHG) guidelines with a focus on recognising violence as an underlying factor in medical problems.
- Integrated approach to psychological problems (incl. anxiety, depression, substance abuse) as a result of violence, including all the different sex-specific roles, family situation and mutual interaction (the family as a system).
- Relationship between women-specific problems and experience of violence and/or views on gender roles.
- Connection between pelvic floor dysfunction and sexual violence.

**Specific to physical and psychological violence**
- Prevalence of clients with experience of violence seeking help in the medical sector and their help-seeking behaviour. Where do they seek help, and for what problems?
- Insight into the healthcare needs and healthcare costs of victims of family and sexual violence.
- Insight into social costs resulting from familial and sexual violence. Figures for women who are unable to work as a result, and therefore claim social security benefit.
- Interaction between violence and social class.
- Research into integrated multidisciplinary gender-sensitive interventions for prevention, treatment and education to prevent violence and its effects, and the effectiveness (incl. cost-effectiveness) of these interventions compared with the usual care.
- Fundamental research into gender differences in terms of impact of violence on physical and neuroimmunological processes and relationship with development of physical symptoms (explained or unexplained).
- Definition of the most vulnerable groups and necessary interventions to prevent violence and its effects.
- Improvement in the recognition of victims of family and sexual violence in the healthcare system, many of whom report other (often unexplained or psychological) symptoms.
- The role of culture, context and household in family and sexual violence.
- The influence of family and sexual violence on the development of sexual and gender identity.
– Cost-effective interventions aimed at preventing and treating the effects of violence that prevent transgenerational transmission to children who grow up in violent families.
– Integrated approach to family and sexual violence, including all the different sex-specific roles, family situation and mutual interaction (the entire family system), and improvements to effective help.

The participants at the invitational conference identified the following gaps as deserving top priority.
– Research into integrated multidisciplinary gender-sensitive interventions for prevention, treatment and education to prevent violence and its effects, and the effectiveness (incl. cost-effectiveness) of these interventions compared with the usual care.
– Fundamental research into gender differences in terms of the impact of violence on physical and neuroimmunological processes and relationship with development of physical symptoms (explained or unexplained).
– Definition of the most vulnerable groups and necessary interventions to prevent violence and its effects.
Diabetes mellitus is a highly prevalent condition with ramifications in many areas. One important issue is how to translate study results from other countries to the situation in the Netherlands and to our healthcare system.

**Epidemiology**

Around 100,000 individuals in the Netherlands have type 1 diabetes mellitus; around 800,000 have type 2 diabetes. The incidence of gestational diabetes is around 5–8% in the Netherlands (20,000-30,000 clients a year). Type 1 diabetes is associated with a mortality risk two to three times higher in meta-analyses, with a higher figure for women. Type 1 diabetes leads to a loss of 8–13 years of life. The reason for the increased mortality rate among women is not known exactly. Mortality is also higher among women for type 2 diabetes, and here comorbidity plays an important role.

In terms of morbidity, macrovascular complications are more common in clients with every type of diabetes, and account for both higher morbidity and higher mortality. A clear gender difference is seen here, with a higher incidence of abnormalities in female clients. The reason for this is most probably multifactorial. When it comes to microvascular complications, nephropathy is most closely related to mortality (kidney failure and microvascular defects); it is also an important cause of morbidity, along with retinopathy and neuropathy. We are learning more and more about the influence of gender on the likelihood of complications, such as the increased rate of neuropathy among men, and higher rates of nephropathy in women with a specific gene mutation.

Clients with type 1 diabetes lose years at a productive working age and organ complications reduce their productivity. The number of diabetes-related days of sickness absence is also higher. Past research by NIVEL has shown that clients with diabetes experience more problems at work. The extent to which this is the case and whether gender differences play a role (and if so, how) is not certain.

**Prevention**

Prevention of type 2 diabetes depends greatly on a healthy lifestyle. Existing lifestyle programmes often pay little attention to gender-related factors. Gestational diabetes is associated with maternal and foetal/neonatal morbidity. Trials for the prevention of gestational diabetes have not enjoyed any clear success (a VU university medical centre study as part of the ZonMw pregnancy and birth programme). It is becoming increasingly clear that these women have a higher incidence of type 2 diabetes in the first few years after childbirth and an increased risk of diabetes, hypertension, obesity and lipid metabolism disorders (metabolic
The children also have an increased risk of obesity, hypertension and type 2 diabetes, for which the effects of the altered intra-uterine environment is held responsible, alongside genetic factors and environmental factors in childhood.

**Treatment**

Little is known about gender differences in the effects of treatment for diabetes (types 1 and 2). Besides ‘hard’ technical medical data and economic data, quality of life also plays a key role. The disease burden is determined by chronic organ complications and the degree of blood sugar regulation. It is quite possible that gender has an impact on this, but this remains unclear. Good information on this matter, coupled with practical tools, could be a great help for clients.

Gestational diabetes is an expression of a genetic predisposition to develop type 2 diabetes, triggered by pregnancy hormones. Treatment consists of dietary advice and, if that fails to achieve the blood sugar targets, insulin treatment. Some 30% of women with gestational diabetes are treated with insulin. Exercise can have a positive impact on glucose regulation, though it is not yet known whether this can delay or even preclude the need for insulin treatment. This could reduce the disease burden for the sufferer and lower medical costs.

**Knowledge gaps**

**Link with other themes**
- Incidence of type 2 diabetes, obesity and cardiovascular risk factors in the years following childbirth in mothers who had gestational diabetes, including the possible influence of ethnic background.
- Lifestyle programmes that take account of specific gender-related factors and are more effective (and cost-effective) than the usual programmes.
- Cardiovascular disease combined with diabetes in women. This comorbidity gives rise to many problems, absence from work, and mortality. Causes of higher rates of cardiovascular deaths among women with diabetes compare to men with diabetes.

**Epidemiology**
- Impact of gender and the mechanisms behind it on increased morbidity and mortality among clients with type 1 (and type 2) diabetes.
- Presence of gender differences in factors restricting labour market participation and labour productivity as a result of diabetes types 1 and 2, and potential for improving the situation.

**Prevention**
- Gender-related factors affecting the development of a healthy lifestyle.
– Strategies for reducing the incidence of insulin treatment for gestational diabetes (this would produce savings: on the costs of insulin, blood sugar monitoring, medical care). Particular attention should be paid to increasing physical activity.
– Methods for reducing the incidence of diabetes after childbirth.
– Gender-related methods for reducing the development of obesity, diabetes and cardiovascular risk factors in children (particularly following gestational diabetes).
– Effective exercise programmes for pregnant women with gestational diabetes to prevent or delay the transition to insulin treatment and their effectiveness (including cost-effectiveness) compared with the usual programmes.
– Sex differences in preferences for lifestyle interventions (particularly exercise) among clients with type 2 diabetes in the GP population. Are there sex differences in the effects of exercise programmes and in implementation/process outcomes?
– Optimisation of prevention and care/after-care of women with gestational diabetes.

**Treatment**
– Impact of gender and degree of influence over quality of life and disease burden for diabetes patients, including improvement strategies.
– Gender-related evaluation methods (questionnaires).
– Effective interventions for reducing cardiovascular disease (and its impact) in women with diabetes.

*The participants at the invitational conference identified the following gaps as deserving top priority.*
– Optimisation of prevention and care/after-care of women with gestational diabetes.
– Effective interventions for reducing cardiovascular disease (and its impact) in women with diabetes.
Various disorders of the central and peripheral nervous system have different clinical presentation in men and women. Migraine is the most common of them, and the differences between men and women are particularly striking. Some 12% of the Dutch population have an average of two migraine attacks a month, each of which lasts 1–3 days. A quarter of migraine clients – around 3% of the population – have one or more attacks a week (chronic migraine). The World Health Organization classes the disease migraine – i.e. repeated migraine attacks – among the top ten most disabling diseases; migraine comes in third place for women; it takes seventh place when both men and women are considered. The major loss of working days and high prevalence of migraine also make it one of the most costly brain diseases to society.

Besides the direct impact of the attacks themselves, migraine is also an important cardiovascular risk factor, particularly in women. Recent data in fact suggest that migraine contributes more to cardiovascular risk than traditional factors like diabetes, obesity and smoking.

**Current research**

Both the LUMC and Erasmus MC teaching hospitals are intensively researching the impact of female sex hormones on migraine. The CREW project, mentioned above in section 4d on cardiovascular disease, is studying migraine as part of the women-specific cardiovascular risk profile.

**Epidemiology**

Between puberty and menopause migraine is three times more common among women than among men of the same age. Outside that period, differences in prevalence are much smaller, or entirely absent, which suggests that female sex hormones play a key role. This hypothesis is supported by the observations that girls start having migraine attacks around puberty (see theme 1a: Childhood and youth), women often suffer migraines when menstruating, and that in the second and third trimester of pregnancy and while breastfeeding they are often completely absent, only to return again with full force afterwards.

**Causes**

The precise cause of migraine is not known. It is known that genetic factors play an important role and that exogenous and endogenous modulating factors (such as sex hormones) have a strong impact on the risk of an attack. The interactions between genes and sex hormones is a key topic of research at the LUMC and Erasmus MC.
**Diagnosis**

No diagnostic biomarker has yet been found for migraine. Diagnosis is based on precise and extensive anamnesis, with questions concerning validated diagnostic criteria drawn up by the International Headache Society.\(^{164}\)

**Treatment**

Mild migraine attacks can sometimes be treated with ‘ordinary’ painkillers and rapidly absorbed NSAIDs. Better results are often achieved with triptans. Roughly speaking, these medications have sufficient effect in 40% of clients. Unfortunately, the effect is not adequate in the remaining 60%.

Besides medication that suppresses attacks, an attempt can be made to prevent attacks using prophylactics like certain beta-adrenoreceptor antagonists, sodium valproate, topiramate, flunarizine, methysergide, pizotifen and candesartan. The effect mechanism of these prophylactics is unknown, however, and they are often disappointing in terms of their efficacy (a 50% reduction in the frequency of attacks can be achieved in 50% of clients). They also often have many side effects. Currently, no distinction is drawn in the treatment of male and female clients, though this might well be a way to achieve health benefits. Sometimes women can attempt to prevent attacks by taking (or indeed discontinue) the contraceptive pill, though the results are generally disappointing. Female clients themselves have many questions about the relationship between hormones and migraine.

**Knowledge gaps**

**Link with other themes**

- Differences between boys and girls in terms of migraine and headache.
- Assessment of migraine as a cardiovascular risk factor and possible gender differences in this area. Migraine as part of gender-specific cardiovascular risk prediction models.
- The pathophysiology and gender-specificity of the increased risk of stroke in female clients with migraine.
- The extent to which the frequency of migraine attacks impacts on the cardiovascular risk profile of women, and necessary changes to current treatments.
- Difference between migraine with aura and migraine without aura as a cardiovascular risk factor among women.
- Gender differences in comorbidity of depression, anxiety disorders and epilepsy with migraine.
- The relationship between menarche, pregnancy, the menstrual cycle and menopause and the onset or cessation and the severity, frequency and perceived pain of migraine.
- Sex hormones other than oestradiol that are relevant to the pathophysiology of migraine.
– Interaction between female sex hormones and neuropeptides involved in migraine.
– The effect of the contraceptive pill in women with migraine.
– Safe and adequate treatment of migraine during pregnancy.
– Relationship between migraine- and pregnancy-related cardiovascular complications, such as pre-eclampsia and the secondary headache associated with this.

**Causes**
– Underlying factors that cause the higher prevalence of migraine among women.
– Possible interaction between genetic and epigenetic factors involved in migraine and female sex hormones (and fluctuations in those hormones).

**Treatment**
– Gender differences in the effects and side effects of migraine medication.
Theme 4e
Unexplained physical symptoms

Unexplained physical symptoms, also known as somatic symptom disorder (SSD), involve persistent complaints that are not objectively measurable and for which no disease mechanism can be defined using current medical knowledge. Such symptoms can lead to a considerable disease burden and impair people’s day-to-day functioning in society. The symptoms often include fatigue, gastrointestinal problems and all kinds of pain. Such complaints lead to a high level of sickness absence and therefore high costs to society. Common complaints that are also severe and long-lasting are grouped together under various names, such as chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), chronic pelvic pain (CPP), chronic pain syndrome (CPS), repetitive strain injury (RSI), fibromyalgia and whiplash.

Existing research into unexplained physical symptoms pays little attention to gender differences. Though sex differences in prevalence receive a mention, they are not generally investigated or specified any further. Kroene and Spitzer (1998) investigated the impact of psychiatric comorbidity on the high prevalence of unexplained physical symptoms among women. They found depression and anxiety to be the main predictors of unexplained physical symptoms, though the gender factor was also found to have a major impact.
Research has scientifically proven the effectiveness of two treatments for unexplained physical disorders: cognitive behavioural therapy (CBT) and graded exercise training (GET). The empirical findings underline the need to focus on a complex biopsychosociocultural model, because biological, psychological, social and cultural factors can all play a role.

A review that considered whether female hormones have an impact on chronic pain syndrome found that the menstrual cycle has an impact on the severity of symptoms in chronic pain syndrome.

**Epidemiology**

Up to 40% of consultations with internal medical specialists, neurologists and gynaecologists concern physical symptoms for which no adequate somatic explanation can be given, if at all. Severe chronic unexplained physical symptoms are less common (prevalence 2.5%). At least some three-quarters (70–90%) of healthcare consumers with SSD are women. Women experience and report physical symptoms more readily than men and often tend to ascribe them to physical causes (somatisation). A notably high proportion of women with unexplained physical symptoms have also been sexually abused.

**Causes**

Characteristically, no clear medical cause can be indicated for unexplained physical symptoms. Psychologists propose explanations related to the cognitive and emotional information processing system. Pathophysiological models tend to assume that stress-related pain and fatigue symptoms indicate a disruption of the central nervous system, the hormone system and/or the immune system, or a disruption in the communication between these control systems. Increasingly, explanations are being sought in a combination of medical, psychological, social and cultural factors that might play a role in the emergence and persistence of SSD.

**Diagnosis and treatment**

Given the diversity of unexplained physical symptoms, diagnosis depends on the various diagnostic models use in the various disciplines.

Treatments of proven effectiveness and other treatment programmes and protocols are generally described in sex-neutral terms. A number of qualitative studies do however offer sex-specific suggestions for those caring for female clients with complaints for which there is no medical explanation.165
Knowledge gaps

Link with other themes
– Unexplained physical symptoms in women in relation to cardiovascular disease.
– Relationship between physical and psychological violence and conditions like cardiovascular disease, unexplained physical symptoms (chronic pain) and gynaecological problems.
– Gender differences in the relationship between, for example, chronic fatigue and other unexplained physical symptoms and psychological and psychiatric problems.

Epidemiology
– More information on the scale of and symptoms experienced by clients (mainly female) with unexplained physical symptoms, specified by age, class, ethnicity, regional differences, transgenerational problems, gender roles and gender attitudes, including the costs to society.

Causes
– Multidisciplinary research (including genetic research) into gender-specific factors involved in specific unexplained physical symptoms.
– Underlying processes (including psychological factors) that explain how and why the menstrual cycle and post-menopausal hormonal status have an impact on unexplained physical symptoms.
– Research into common assumptions about sex differences in the neurological and psychological control systems.
– Relationship between unexplained physical symptoms and alcohol, smoking, painkillers, drugs, medication and/or physical activity.

Treatment
– Monitoring of women who have received treatment to establish long-term effects (including in terms of social participation and healthcare costs).
– Approach to unexplained physical symptoms, including a focus on differences in professional practices and communication, specified by the sex of both the attending physician and the client, and the effectiveness (including the cost-effectiveness) of this compared to the usual care.

The participants at the invitational conference identified the following gaps as deserving top priority.
– Multidisciplinary research into gender-specific factors involved in specific unexplained physical symptoms.
– Approach to unexplained physical symptoms, including a focus on differences in professional practices and communication, specified by the sex of both the attending physician and the client, and the effectiveness (including the cost-effectiveness) of this compared to the usual care.
**Theme 4f**

**Psychological and psychiatric conditions**

The differences between men and women are becoming increasingly apparent when it comes to mental health problems. The Statistics Netherlands health survey (2010–2012) shows that some 13% of women and girls and 9% of men and boys aged 12 and over are in poor psychological health. They may for instance be nervous, down, agitated, sombre and/or unhappy. Women are twice as likely as men to become depressed. Anxiety disorders are also more common among women. Another striking finding is that ten times as many women as men are treated for eating disorders. Men, on the other hand, are more troubled by addiction and are more likely to be treated by forensic psychiatrists. Biological differences between men and women are a key cause, though psychological and social factors also play a role.

The underlying causes of differences in prevalence are difficult to determine. Perhaps more even than in somatic healthcare, in mental healthcare there appears to be a complex interaction between biological, psychological and social factors, whereby the roles of care provider (M/F) and healthcare consumer must also be taken into consideration. For instance, men are perhaps less inclined to talk about negative feelings than women, leading to underdiagnosis among men.

On the other hand, it may be that care providers are more likely to consider a female client depressed than a male client. In other examples, aggression (often passive-aggressive behaviour) is less well recognised in women, and eating disorders are too often overlooked in boys and men.

There are many relevant sex and gender differences in the risk factors, perception, manifestation, severity and presentation of psychological disorders and lack of wellbeing, and possibly also in treatment outcomes, which interestingly are often gender-neutral.

**Epidemiology**

Although we know a great deal about differences in prevalence between men and women, the data are not always up-to-date or fully reliable. Much depends on the research procedures and methods used and whether matters like under- and overdiagnosis have been taken into account.

**Causes**

There is still a lot we do not know about the underlying and external mechanisms associated with psychological problems and the differences in this respect between men and women, in terms both of sex- and gender-related vulnerability factors and of exposure to sex- and gender-related stressors. Many questions also remain about the interaction between the two in terms of their effect on the development and persistence of psychological disorders and milder forms of lack
of wellbeing, such as work stress, relationship and family problems, and work-life interference. Differences in attachment (and attachment styles) and the psychological capacities associated with this, particularly autonomy problems, can have a bearing on this. Other factors that can have an effect include being the victim of sexual, familial and other violence, and possibly excessive burden, especially among women, as a result of combining work and care responsibilities (family, informal care). Forms of gender role stress (sex-specific stress resulting from an inability to meet certain gender role expectations), and differences in coping styles and emotion regulation can also be relevant.

**Prevention**

Prevention of psychological problems is a complex matter, and is still in its infancy, particularly when it comes to potential sex-specific factors.

**Diagnosis**

The entire process of self-recognition of problems, seeking assistance and diagnosis by the care provider includes gender-sensitive elements about which too little is known.

We know little about the relationship between the diagnosis of depression in women by their GP and partner violence (current or past). GPs often diagnose depression and treat it in accordance with the GPs’ association standard, following the ‘stepped-care’ model, but rarely identify partner violence as a background factor, as a result of which treatment will be less effective.

**Treatment**

We also have insufficient understanding of sex and gender aspects of treatment for psychological and psychiatric disorders. Psychotherapy and cognitive behavioural therapy are rarely, if ever, used in a gender-sensitive manner, and medication is often tested exclusively on men.

**Knowledge gaps**

**Link with other themes**
- Gender differences in the relationship between, for example, chronic fatigue and other unexplained physical symptoms and psychological and psychiatric problems.
- Sex-specific aspects of psychopharmaceuticals (including therapy compliance, lifestyle factors).
- Relationship between work stress combined with (double) care responsibilities and psychological and psychiatric conditions.
- Gender differences in the relationship between dementia and cardiovascular disease.
- Psychological problems related to menopause and other relevant life stages.
- Integrated approach to psychological problems (incl. anxiety, depression, substance abuse) as a result of violence, including all the different sex-specific roles, family situation and mutual interaction (the family as a system).
- The effectiveness and cost-effectiveness of treatment for depression whereby GPs ask systematic questions about partner violence and adapt their policy accordingly.
- Gender differences (and the potential for reducing them) in the relationship between psychological problems (stress, anxiety, depression, burn-out) and sickness absence/incapacity for work.
- Gender differences (and ways of reducing them) in dementia and other cognitive disorders.
- Assessment of long-term health risks in women who experience early versus late menopause, particularly cancer, cardiovascular disease, cognition, Alzheimer's disease, depression and other psychological problems.
- Relationship between stress and differences in development of cardiovascular disease in men and women. One example is Broken Heart Syndrome (a form of acute heart failure caused by extreme stress, which manifests itself as an acute myocardial infarction). This syndrome is ten times more common among women than among men. This form of acute coronary syndrome (ACS) is affecting a growing group of clients.
- Relationship between the combination of pregnancy and psychological problems (including postnatal psychological problems) and cardiovascular disease.
- Relationship between work stress and cardiovascular disease in women, taking account of their double responsibilities (home/family and work).
- Gender differences in the relationship between depression and anxiety disorders and migraine.

**Causes**
- The influence of gender role stress (inability to meet gender-related demands, some of which are changing) on wellbeing and psychological functioning.
- Gender differences in attachment and attachment-related factors, including their implications for the emergence of psychological problems.
- Relationship between psychological problems in women and their impact on care responsibilities (e.g. childcare) and on other members of the family.
- Interaction between sex/gender and other relevant diversity factors such as ethnic background and their links with psychological disorders and lack of wellbeing (and their treatment).
- Gender differences in emotion regulation and the link with psychopathology.

**Prevention**
- Effectiveness of gender-sensitive interventions for psychological and psychiatric complaints in terms of prevention, 'lifespan', with a focus on diversity in the broad sense.
Diagnosis
– Gender differences among healthcare consumers in the early recognition and discussion of psychological and psychiatric problems and the effectiveness (and cost-effectiveness) of this compared with the usual care.
– Gender differences between GPs and other basic healthcare workers (M/F) when it comes to recognising and diagnosing psychological and psychiatric problems.
– Failure to identify, or late identification of symptoms that are not necessarily expected because they do not comply with the stereotypical image; e.g. depression, anxiety disorders, eating disorders and burn-out in men; aggression problems and alcohol abuse in women.
– Identification of gender bias in diagnostic tools commonly used in the Netherlands.

Treatment
– Gender differences in the effects of interventions and after-care and their effectiveness (and cost-effectiveness) compared with the usual care. There are differences in emphasis as regards views on the effectiveness of cognitive behaviour therapy. The literature, which is often gender-neutral, suggests that CBT is equally effective in both sexes; i.e. it reduces symptoms (generally in only half of clients, however). Since many psychological complaints, like anxiety and depression, occur twice as often in women as in men, on balance many more women are affected by its limited effectiveness.

The participants at the invitational conference identified the following gaps as deserving top priority.
– Effectiveness of gender-sensitive interventions for psychological and psychiatric complaints in terms of prevention, ‘lifespan’, with a focus on diversity in the broad sense.
– Gender differences between GPs and other basic healthcare workers (M/F) when it comes to recognising and diagnosing psychological and psychiatric problems.
Complaints affecting the muscles and joints are common. They account for around a third of the complaints for which clients consult their GP (back and joint pain). At 10%, twice as many women as men have impaired mobility. Wear and tear on hips and knees are the third most common chronic condition in women. The differences between men and women are particularly pronounced in the over-60 age group. Some of the complaints affecting the muscles and joints are caused by rheumatic diseases. It is generally quite difficult for GPs to recognise rheumatic conditions at an early stage because physical examinations will not reveal many anomalies in blood test results and x-rays at this stage. Little is known about gender differences in the prevention, diagnosis and treatment of joint and muscle disorders other than rheumatism.

Epidemiology

A number of rheumatic diseases are more common among women than among men. They include rheumatoid arthritis and systemic lupus erythematosus (SLE). Generally speaking, a GP will recognise them in time, because it is known that women have a greater risk of developing these diseases. It is an entirely different story when it comes to axial spondyloarthritis (formerly known as Becherew’s disease), which is more common among men. This disease occurs in around 1–2% of the population and often begins at a young age, around 25. The main symptom is back pain, particularly during the night, which can lead to hours of stiffness in the morning that subsides only in the course of the day due to movement. X-rays often show inflammation of the sacroiliac joints (sacroilitis) and extra bone formation and deformation of the spine. It often takes several years before the effects become visible.

It used to be thought that axial spondyloarthritis (axial SpA) was ten times more common in men than in women, but over the years it has become clear that the disease occurs much more often in women than initially believed and that the ratio of male-female sufferers is now 3:1. This is because knowledge of all symptoms of the disease has increased, and milder cases can now also be identified.

Diagnosis

The general impression is that severe x-ray changes associated with axial SpA, such as ossification of the sacroiliac joints and stiffening of the spinal column, occur more readily and in more serious forms in men than in women. This sometimes leads to an assumption in practice that though women experience more pain, there is either nothing actually wrong with them or they have ‘soft-tissue rheumatism’. Unfortunately, it has been found that women can have a very severe progressive form of the disease with deformations at an early age, sometimes
requiring spinal surgery. It is therefore very important that severe progressive forms of this disease in women and the factors that play a role in it are identified. For adequate treatment, it is important that rheumatic conditions are identified at an early stage and that clients are referred to a rheumatologist in good time. Starting treatment early can prevent irreversible damage to joints. Unfortunately, many GPs (and rheumatologists) are unaware of recent insights into the common occurrence of SpA among women, and the diagnosis is often missed. The diagnostic ‘delay’ is therefore much longer in women than in men.\(^\text{186}\) Besides the fact that the attending physician is simply less likely to consider diagnosing axial SpA in a woman than in a man, differences in physical build might also play a role. Women tend to be more supple, i.e. have a more flexible back than men, so it is sometimes more difficult to interpret impaired movement during a physical examination. Barely any research has been done into these differences, which are frequently seen in practice.

Recent research has shown that clients with axial spondyloarthritis frequently have problems working. Over 40% of clients experience major problems with work participation, in terms both of sickness absence and of performance at work, even before they are diagnosed.\(^\text{187}\) This results in a double problem for women, who are diagnosed later, and thus increases their likelihood of losing their place in the labour market. There has been barely any research on the effects of underdiagnosis of axial SpA in women and its implications for social participation.

**Treatment**

It appears that women respond less well to biologicals (TNF inhibitors), as a result of which they are more likely to stop taking them or switch to another, more expensive form of medication.\(^\text{188}\) The reason behind this and its impact on healthcare costs have yet to be properly investigated.

Given the fact that axial SpA occurs at a young age, problems often arise in association with pregnancy. Medication like nonsteroidal anti-inflammatory drugs (NSAIDs), which is highly effective in combating pain and morning stiffness, has to be discontinued as soon as a woman becomes pregnant – and preferably before. This results in a lot of pain. The disease also appears to become much more active in many sufferers during pregnancy (with higher values for blood inflammatory markers), as a result of which heavy medication (like prednison) is often needed to bring the disease back under control.\(^\text{189,190}\) This situation contrasts with other rheumatic diseases like rheumatoid arthritis, which often (in 70% of cases) abate during pregnancy, even after medication is no longer administered. In clinical practice, axial SpA is often seen to grow worse during pregnancy, though data on frequency are scarce and there is no clarity as to the most effective treatment.
Knowledge gaps

Link with other themes
– Gender differences in the effects of rheumatism medication.

Epidemiology
– Sex differences in muscle and joint complaints in GP practice, including differences in comorbidity and progression/prognosis.
– Gender differences in epidemiology, prevention, diagnosis and treatment of muscle and joint complaints other than rheumatism.

Diagnosis
– Implementation of existing knowledge concerning prevalence of SpA among women.
– Identification of severe progressive SpA among women, including factors that might be of influence.
– Methods of reducing underdiagnosis of rheumatism and muscular conditions in women, and the effectiveness (and cost-effectiveness) of this compared with the usual care.
– Gender differences in the auto-immune system and auto-immune diseases.
– Implications of SpA (and underdiagnosis) for work participation and the working life of women.

Treatment
– Gender differences in the effects of medication.
– Progression and adequate treatment of SpA in pregnant women.
– Sex differences in the uptake of healthcare (frequency of contact, extra tests, referrals, medication) among patients with rheumatism in the GP population.

The participants at the invitational conference identified the following gaps as deserving top priority.
– Methods of reducing underdiagnosis of rheumatism and muscular conditions in women, and the effectiveness (and cost-effectiveness) of this compared with the usual care.
– Gender differences in the auto-immune system and auto-immune diseases.
Theme 4h
Conditions specific to women and sexual conditions

A wide range of gynaecological, women-specific and sexual conditions exist. In line with the criteria described in chapter 3 this Knowledge Agenda mainly considers complaints associated with the menstrual cycle, fertility problems, pelvic floor dysfunction, problems associated with the menopause and pain during intercourse (genito-pelvic pain).
Hormones play a key role in a woman’s life. The menstrual cycle and, later in life, the menopause have a major impact on her wellbeing and quality of life. The prevalence of fertility problems has increased in recent years, partly as a result of the fact that women are starting a family later. Women are not sufficiently aware of the fact that they are less fertile above the age of 35 and that fertility treatment entails health risks.
Pain during sexual intercourse is generally caused by a lack of arousal in the woman, often combined with insufficient pleasure and a limited ability to achieve orgasm. Genito-pelvic pain is common, but many women think they are the only one to suffer it and are embarrassed at the fact. Such complaints can persist for years while the woman fails to seek or receive adequate help, and have a major impact on quality of life.
The medical platform VrouwMC.nl, which focuses entirely on women, provides accessible and scientifically accurate information on these and many other issues specific to women.

**Current research**

See chapter 1 for information on ZonMw's Pregnancy and Childbirth programme.

**Epidemiology**

It is often difficult to draw a line between normal and abnormal menstrual and menopausal complaints. A certain degree of discomfort can be ‘expected’. However, for this very reason, women’s complaints are often inadequately recognised and are not always taken seriously. Reliable prevalence data on these complaints are therefore unavailable. Their implications in terms of absence from work are also unknown.

Conditions specific to women such as endometriosis and myoma are common (these two conditions affect at least 10% of women). Endometriosis is a benign condition that occurs when the uterine tissue (endometrium) adheres to other structures or organs outside the womb. This is generally the ovaries, fallopian tubes and the tissue lining the abdominal cavity. The most common symptoms are chronic pelvic pain, painful menstruation and infertility.

Polycystic ovary syndrome (PCOS) is the most common hormonal disorder in women. Five to ten per cent of the female population of childbearing age experience PCOS symptoms.\(^{191}\)

Pelvic floor dysfunction occurs in more than 70% of women aged between 45 and 85.\(^{192}\) This includes both hypotonicity (weak pelvic floor muscles) and hypertonicity (tight pelvic floor muscles). Both types of pelvic floor dysfunction are associated with incontinence (urinal and faecal) and vaginal prolapse.\(^{193,194}\) Pelvic floor hypertonicity is also associated with genito-pelvic pain and chronic pelvic pain. There are no reliable figures on the prevalence of genito-pelvic pain (vulvodynia, dyspareunia, vaginismus, unexplained abdominal and pelvic pain in women and scrotal pain, glans penis pain, and unexplained abdominal and pelvic pain in men) in the Netherlands. International estimates of the lifetime prevalence of genito-pelvic pain in women range between 14 and 34% for young women, and 6.5 to 45% for older women; prevalence among men ranges from 5 to 15%.\(^{195}\)

One in a hundred women experience premature menopause (POF) and stop menstruating before their 40th year.

We know too little about the mechanisms behind the development of cancer. There are relevant biological differences, and differences in behaviour can also play a role. It is suspected that a complex interaction between hormonal and chromosomal regulation, the immune system and oxidative stress response has an impact on the development of tumours.
Causes

Research has been done into the most common causes of menopausal problems and menstrual complaints like premenstrual syndrome, dysmenorrhoea, menstrual migraine and heavy menstrual blood loss. Pain during sexual intercourse is caused mainly by penetration in the event of an overactive pelvic floor, or by insufficient arousal in the woman. Pelvic floor dysfunction due to weak pelvic floor muscles is generally caused by pregnancy and birth, sometimes combined with denervation of the pelvic floor as the woman grows older or due to the extra burden resulting from other conditions. Pelvic floor dysfunction due to hypertonicity or overactivity in the pelvic floor muscles can be associated with stress (including post-traumatic stress), past sexual trauma, overburden, and anxiety and depression. At a later age these women are often diagnosed with chronic fatigue or fibromyalgia. Despite pelvic floor overactivity and pain during coitus, the majority of women continue to have intercourse, suffering pain in the process. This is partly down to a desire to be ‘normal’ and to avoid a negative response from their partner.

Prevention

The prevalence of fertility problems and pain during sexual intercourse could be reduced by more, and more effective, public information. Too many problems associated with menstruation and menopause remain undiscussed, and therefore untreated, partly because many women assume that their complaints are simply ‘part of being a woman’, even though treatment could give them major health benefits. A lot of knowledge is available about problems connected with menstruation, pregnancy, menopause and sexuality. Unfortunately, this information does not always reach the women affected.

Treatment

In recent years commonly administered hormone therapies have been a regular subject of debate. Long-term hormone therapy is rarely prescribed, partly because of the increased risk of breast cancer. Myoma are frequently occurring benign tumours on the wall of the uterus. Infertile clients with myoma are often referred for surgery, if no other factors adversely affecting fertility have been identified, even though there are no scientific arguments in support of this line of treatment. Further research is needed. Myoma that cause problems, such as pain and heavy blood loss, must be treated. The UMCU teaching hospital has set up an egg bank, by analogy with the sperm bank, in order to treat fertility problems. There is however a shortage of donors, and waiting times are long. Conventional medicine does not offer an appropriate solution for all complaints and women often seek solace in alternative/complementary medicine. Current monocausal treatments for genito-pelvic pain have little effect, and there is
often a delay in diagnosis, resulting in major economic costs. Multidisciplinary treatment protocols are needed for these complaints, and their effectiveness must be assessed.

**Knowledge gaps**

**Link with other themes**
- The implications of menstrual and menopausal problems for social participation, including working hours and sickness absence among (older) women.
- Retraumatisation of sexual violence during internal medical gynaecological procedures.
- Link between sexual problems and experience of sexual violence in childhood and partner violence in adulthood, and the treatment of these problems.
- Connection between sexual problems and pelvic floor dysfunction, and their implications for women's functioning in society.
- Better recognition and treatment of post-menopausal women with cardiovascular disease compared with the care usually provided, including the possible link with diastolic heart failure.
- Connection between pelvic floor dysfunction and sexual violence.
- How female workers, managers and occupational health doctors regard and deal with conditions specific to women such as fertility problems or menstrual/menopausal problems.
- Relationship between women-specific ageing and social participation.
- Relationship between women-specific problems and experience of violence and/or views on gender roles.
- The influence of doctors’ manner of communicating (categorised by sex) about sexuality with clients.
- Relationship between childbirth (peripartum CM) and poor contractility of the left ventricle.
- Implementation of knowledge concerning increased risk of cardiovascular disease in female smokers who take the contraceptive pill. Many women are unaware of the increased risk and doctors do too little to inform them.
- Assessment of long-term health risks in women who experience early versus late menopause, particularly cancer, cardiovascular disease, cognition, Alzheimer’s disease, depression and other psychological problems.
- Incidence of type 2 diabetes, obesity and cardiovascular risk factors in the years following childbirth in mothers who had gestational diabetes, including the possible influence of ethnic background.
- Contraception methods and their impact on women’s participation in society.
- Cycle- and reproduction-related problems in women and their impact on social participation.
- Long-term follow-up on health of women in relation to age at menopause (normal or premature).
- Hormone replacement therapy for women after menopause (premature or otherwise).
– Relationship between the combination of pregnancy and psychological problems (including postnatal psychological problems) and cardiovascular disease.
– Relationship between physical and psychological violence and conditions like cardiovascular disease, unexplained physical symptoms (chronic pain) and gynaecological and sexual problems.
– Psychological problems related to menopause and other relevant life stages.
– The relationship between pregnancy, the menstrual cycle and menopause and the severity, frequency and perceived pain of migraine.
– Sex hormones other than oestradiol that are relevant to the pathophysiology of migraine.
– Interaction between female sex hormones and neuropeptides involved in migraine.
– The effect of the contraceptive pill in women with migraine.
– Safe and adequate treatment of migraine during pregnancy.
– Relationship between migraine- and pregnancy-related cardiovascular complications, such as pre-eclampsia and the secondary headache associated with this.

**Epidemiology**
– Reliable data on the prevalence of complaints before, during and after menstruation and menopause.
– Reliable data on the prevalence of pain problems and genito-pelvic pain.

**Prevention**
– Effective interventions to make prospective parents aware of the risks and problems of pregnancy at a later age.
– Effective interventions to improve women’s awareness of the potential for healthy conception. There is much to be gained in terms of preventing complications during pregnancy and better ‘children outcomes’ if women take better care of their health before they become pregnant (insofar as not already covered in ZonMw’s Pregnancy and Childbirth programme).
– Effective interventions to make clear to men and women at a young age that penetration during sex can only be painless if both the man and the woman are aroused.
– Effective interventions to encourage women to ask doctors for help in reducing menstrual and menopausal complaints. A particular focus on ethnic minority women would be desirable.
– Factors that influence girls’ and women’s choice of contraceptive, and factors that play a role in contraceptive failure. What side effects do girls and women experience with different contraceptives?
– Relationship between fertility problems (and acceptance of such problems) and perception of illness.
Diagnosis
- Methods for timely diagnosis (by GP and specialist) of abnormal blood loss during menstruation and other conditions, including endometriosis, polycystic ovary syndrome and their effectiveness (and cost-effectiveness) compared with the methods commonly used.
- Methods for timely diagnosis (by GP and specialist) of abnormal menopausal complaints and their effectiveness (and cost-effectiveness) compared with the methods commonly used.
- Methods for timely diagnosis of genito-pelvic pain (including pain during sexual intercourse in women) and their effectiveness (and cost-effectiveness) compared with the methods commonly used.

Causes
- Research into the causes of pelvic problems and their link with pregnancy, childbirth and menopause.
- Reliable data on the link between pelvic floor dysfunction and stress (including post-traumatic stress), past sexual trauma, overburden, and anxiety and depression.
- Impact of cancer (particularly breast cancer) and cancer treatment on things like sexuality and relationships, fertility, pregnancy, breastfeeding and contraception, including a multidisciplinary approach involving gynaecologists, oncologists and sexuologists.

Treatment
- Research into the side effects of current contraceptives.
- Alternatives to hormonal contraceptives and hormone replacement therapy during menopause (and the risks associated with them), including the potential offered by complementary medicine and the effectiveness (and cost-effectiveness) of this compared with conventional healthcare.
- Awareness-raising and public acceptance of egg donation.
- Multidisciplinary treatment for genito-pelvic and sexual problems in women and the effectiveness (and cost-effectiveness) of this compared with the usual care.
- Research into the causes of and effective interventions for common conditions affecting women, such as PCOS (approx. 10% of all women), endometriosis and myoma.
- Knowledge and consideration of the impact of the menstrual cycle on pharmacokinetics and general conditions, such as migraine, epilepsy and mental state.
- Ovarial damage and fertility preservation in women with cancer.
- Chronic abdominal and pelvic pain in GP practice: prevention, progress, duration, GP approach, uptake of healthcare and effectiveness of a future care protocol, and the effectiveness (and cost-effectiveness) of this compared with usual healthcare practice.
The participants at the invitational conference identified the following gaps as deserving top priority.

– Connection between sexual problems and pelvic floor dysfunction, and their implications for women’s functioning in society.
– Contraception methods and their impact on women’s participation in society.
– Cycle- and reproduction-related problems in women and their impact on social participation.
The development of gender-sensitive healthcare will require a revolution in thinking about scientific medical research. Our present medical knowledge is based mainly on men, and has been amassed mainly through research on men and male test animals. This applies not only to drugs testing, but to the entire range of health research, with the exception of research into conditions specific to women. Knowledge gathered through research conducted only on men has led to under- and overdiagnosis in women, and incorrect doses of medication (based on physiology, height, weight), with the inevitable consequences. It is vital that a distinction be drawn between outcomes in men and women if we are to achieve gender-sensitive care and treatment.

Everyone is different

Efforts in Western society to achieve equal rights and opportunities for and equality between all people can lead to a misconception that all people are the same. Nothing could be further from the truth: everyone is different. This realisation is gradually taking hold in healthcare, too.

The advent of more diversified healthcare can be seen as a valuable alternative to care based on the universal ‘one size fits all’ model. This means that health research must seek ways of giving adequate consideration to the many differences between people.

From binary to intersectional

If health research distinguishes at all between different groups, the division is generally binary (male/female), with sub-categories within the two groups (e.g. young/old, high and low socioeconomic status) and possibly further subdivision of these categories (e.g. gay/straight, ethnically Dutch/ethnic minority). These binary divisions can be interpreted in unidimensional or multidimensional ways: in other words, exclusively biological or social, or biosocial and/or psychosocial and/or sociocultural. This produces a static classification that may provide a certain basis for policy, but does not do justice to the variation that is relevant to healthcare.
It is not only differences between men and women that are relevant. Research will also have to reflect the variation in the significance and health effects of sex/gender categories within differences in ethnicity, age, class, sexual preference.

It is clear that differences in sex, gender, age, income, sexual preference and ethnicity cannot be seen in isolation, but are in fact mutually influencing. How they interfere with each other is not a foregone conclusion, but a subject for theoretical debate and empirical research.

A fairly recent – more dynamic – perspective taken in healthcare is the intersectional approach, in which these differences are seen as a continuum rather than a dichotomy, and as multidimensional rather than one-dimensional. For instance, women might have a high or low ‘score’ for oestrogen, behaviour, female roles and female values. Furthermore, this perspective acknowledges the fact that these continuums imply social inequalities that manifest themselves in terms of sex, age and class discrimination, hetero-dominance and/or cultural (generally ‘white’) privilege. The term ‘intersectional’ indicates that these continuums can in fact intersect in all kinds of ways, partly depending on the context in which the differences occur. Intersections can therefore change with the situation, and over the course of time. An intersectional approach such as this not only better reflects the identity of healthcare consumers and the dynamics of their life, it also allows health risks, prospects of recovery, health skills and resilience to be estimated more accurately. In short, it increases the opportunity for tailoring care.

The implications of this intersectional perspective for research methodology are a subject for further research in themselves. In many cases the use of several research methods and types of data (known as methodological and data triangulation) is advisable, in order to optimise the validity, generalisability and usability of research results.

**Generalisability**

It is thus clear that different approaches can be taken in order to incorporate sex differences and gender-aspects into health and healthcare research. A binary approach in which sex differences are considered in the research is the minimum option. Unfortunately, even this occurs only rarely. This casts doubt on the extent to which a lot of existing, current and forthcoming research can be generalised to women. The development of an intersectional approach taking account of diversity therefore requires a powerful boost in research and in practice. It would probably lead to an expansion in statistical generalisations to include other forms of generalisation (in the context of qualitative research, Smaling distinguishes between inductive, analogue and communicative generalisation, for example).
Multidisciplinary approach

To place the entire person at the centre of healthcare practice, rather than only his or her medical condition, it is necessary to focus on the social, cultural and psychological aspects of health and lack of health, as well as the biological. This requires a multidisciplinary approach to research, involving non-medical disciplines too (e.g. psychology, sociology, cultural anthropology).

Research methods

Twelve ‘methods of sex and gender analysis’ applicable to health research have been developed as part of the European Gendered Innovations project. These methods apply to the entire research process, from problem definition to policy recommendations. Besides sex and gender, they also consider ‘intersecting factors’ of a biological or sociocultural nature. The GI project distinguishes the following phases and aspects that require consideration:

- **Problem definition**: operationalisation of gender, which aspects of gender seem relevant in view of risk, protection, diagnosis and treatment (or decision not to treat). This concerns biology, psychology, behaviour, ethical standards, social institutions.
- **Data collection**: inclusion of women, criteria, numbers, specific groups. Implementation of guidelines (e.g. CIOMS) for inclusion of women.
- **Data analysis**: stratified analysis, qualitative, quantitative, interactions.
- **Reporting**: on differences and lack of differences.

Types of research

Currently, there are more examples of good qualitative research than of quantitative research, and more involving epidemiology than intervention. Given the tradition of evidence-based research, there is an urgent need for designs for qualitative analysis on gender and health.

Principles for new research

The following aspects should be considered in all phases of research:
- Generalisability of outcomes.
- Avoiding exclusion of invisible groups.
- Focus on empowerment factors at individual, institutional and cultural level.
- Connecting the micro- and macro-level (incl. identity, social status).
- Revealing similarities (including unexpected ones).

Further details will have to be added in each area of research.
Methodological learning network

The possibility of setting up a special advisory committee as part of the Gender and Health knowledge programme is being considered. Researchers would be able to consult the committee in order to optimise their methodological approach, prior to and during the research. This would form part of a methodological learning network that would also be available to other ZonMw research programmes.

Knowledge gaps

- Development and implementation of methods for sex and gender analysis.
- Development of a model of health determinants and identification of appropriate qualitative and quantitative methods.
- Implementation of guidelines for inclusion of women (e.g. CIOMS).
- Further analysis of gender aspects in existing data.
- Operationalisation of sex/gender, masculinity and femininity, including guidelines and policy for embedding gender in research and analysis.
- Identification of added value of intersectional approach.
- Identification of statistical procedures that fully reflect the intersectional approach.
- There is a need for guidelines that reveal the extent to which women are included in scientific health research. These guidelines should be applied when awarding research grants.

The participants at the invitational conference identified the following gaps as deserving top priority.

- Operationalisation of sex/gender, masculinity and femininity, including guidelines and policy for embedding gender in research and analysis.
- Implementation of methods for sex and gender analysis.
- Identification of added value of intersectional approach.
- Identification of statistical procedures that fully reflect the intersectional approach.

The following conditions were defined for the awarding of grants under any future Gender and Health knowledge programme.

- Methodological conditions will be defined in each call, including pre-defined gender-specific criteria for the awarding of grants.
- Researchers must work with practitioners and policymakers in multidisciplinary communities/consortia or academic collaborative centres.
- Participation in methodological learning network. All project managers will share knowledge of methodology during the course of the research.
Final remarks

National Gender and Health Knowledge Programme

The purpose of this Knowledge Agenda is to give direction to a future National Gender and Health knowledge programme. This Agenda mentions a large number of subjects that might be included in such a programme. Nevertheless, further clustering, definition and prioritisation will be needed. Budgets are under strain and clear choices will have to be made.

In this respect, it is important that the choices made under the national knowledge programme cater directly for the needs and wishes of clients and women themselves. With this in mind, it would seem wise to establish an advisory committee including representatives of patients and patient associations.

One major problem associated with the subject of gender and health lies in the fact that a lot of knowledge is fragmented, and there is insufficient awareness and practical implementation of existing knowledge. In this regard, it is important that any future knowledge programme tie in with the work of the Gender & Health Alliance’s Awareness and Communication and Education Working Groups. The Research Working Group would therefore recommend a broad-based multi-year knowledge programme with two major components:

1. implementation of existing knowledge and
2. development and implementation of new knowledge.
Part III
Appendices
 Contributors

Dr. Y. (Yolande) Appelman, interventional cardiologist, VU University Medical Centre Amsterdam

Prof. M. H. J. (Marrie) Bekker, professor of clinical psychology, University of Tilburg

M.H. (Marjolein) Blüm, MSc, Gender & Health Alliance WOMEN Inc. Coordinator

Dr. A.M.E. (Annelies) Bos, gynaecologist, subspecialist in reproductive medicine and endocrinology, Woman and Baby Division, UMC Utrecht

J.J.W.H. (Jeroen) Crasborn, MSc, physician, senior adviser on healthcare strategy at Achmea

Prof. C.J.M. (Bart) Fauser, professor of reproduction & gynaecology/medical department head, Woman and Baby Division, UMC Utrecht

T.S. (Tidde) Goldhoorn, LLM, senior policy officer on medication and medical technology, Ministry of Health, Welfare and Sport

I.H.A. (Ingrid) van Hattem, public health policy officer, Ministry of Health, Welfare and Sport

Dr. I.E. (Irene) van der Horst-Bruinsma, rheumatologist, VU University Medical Centre Amsterdam

Prof. G.T. (Ineke) Klinge, Gender Medicine, Institute of Gender in Medicine (GiM)/Charité, Universitätsmedizin, Berlin; Chair H2020 Advisory Group on Gender, European Commission.

Dr. E.T.M. (Ellen) Laan, health psychologist, NVVS sexuologist, senior university lecturer, Sexuology and Psychosomatic Obstetrics and Gynaecology department, AMC Academic Medical Centre

L. (Leonie) Leliveld, MSc, senior policy officer on public health, health differences, Ministry of Health, Welfare and Sport

Prof. A.L.M (Toine) Lagro-Janssen, general practitioner, Radboud university medical centre, emeritus professor of women’s studies, medical sciences, primary care medicine

Dr. S. H. (Sylvie) Lo Fo Wong, general practitioner, senior researcher, Radboud university medical centre, women’s studies, medical sciences, primary care medicine

Prof. H.E.M. (Angela) Maas, MD PhD FESC, professor of cardiology for women, Radboud university medical centre, Nijmegen
Dr. A. (Antoinette) Maassen van den Brink, senior university lecturer, Erasmus MC, pharmacologist
Prof. J. (Janneke) van Mens-Verhulst, former professor of women’s healthcare
J.G.F. (Ans) Merens, MSc, scientific officer, Care, Emancipation and Time Use Research Sector, Netherlands Institute for Social Research (SCP)
Dr. C.J. (Clara) Moerman, epidemiologist and senior researcher, Hogeschool Windesheim Flevoland, Almere
Dr. G. (Greta) Noordenbos, senior researcher and university lecturer, clinical psychology, Leiden University
N.L.W. (Nico) van Oosten, MSc, senior adviser at Movisie
Dr. J.E. (Jeanine) Roeters van Lennep, internal medicine practitioner specialising in vascular medicine, Erasmus MC, Rotterdam
W.J. (Wilna) van Rossum, MSc, policy officer on macroeconomic issues and the labour market, Ministry of Health, Welfare and Sport
H.M. (Hester) den Ruijter, MSc, researcher specialising in cardiovascular disease in women, Laboratory for Experimental Cardiology, UMC Utrecht
Dr. H.W. (Harold) de Valk, internal medicine specialist/endocrinologist, UMC Utrecht
I.J. (Jannet) Vaessen, MSc, director of WOMEN Inc.
Dr. E. (Els) Veenis, senior policy adviser on emancipation, Ministry of Education, Culture and Science
Dr. P. (Petra) Verdonk, university lecturer, Department of Metamedicine, EMGO Institute, School of Medicine
Dr. L.E. (Loes) Visser, hospital pharmacist/trainer at Apotheek Haagseziekenhuizen and senior university lecturer in pharmacoepidemiology, Erasmus MC
Dr. L.E. (Laura) Voorrips, statistical researcher, CBS Statistics Netherlands
Dr. M.M. (Hedwig) Vos, general practitioner, V&V Huisartsen, Leiden University Medical Center, Huisartsenkring Haaglanden, Radboud university medical centre, women’s studies, medical sciences, primary care medicine
Notes


26 http://www.zonmw.nl/nl/programmas/programma-detail/zwangerschap-en-geboorte/algemeen/


30 http://www.cihr-irsc.gc.ca/e/44082.html

31 http://www.cihr-irsc.gc.ca/e/8673.html


34 http://www.eugenmed.eu/

35 http://gender.charite.de/en/education/eugim/

36 http://gender.charite.de/en/education/eugim/

37 http://www.genderste.eu/

38 http://www.gender-net.eu/?lang=en


CBS Gezondheidsenquete 2013.


CBS Gezondheidsmonitor GGDS, CBS and RIVM (2012).

CBS Gezondheidsmonitor GGDS, CBS and RIVM (2012).


125 www.hartstichting.nl


134 Movisie Factsheet on domestic violence: facts and figures November 2009.


159 Cahill, Nat Rev Neurosci. 2006; 7: 477.
191 Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group.
192 Messelink, B., Benson, T., Bergmans, B., Bo, K. Standardization.
198 Warren, J.W., Langenberg, P., Claauw, D.J. (2013). The number of existing functional somatic syndromes (FSSs) is an important risk factor for new, different FSSs. J Psychosom Res; 74: 12-7.


204 Gendered Innovations. How Gender Analysis contributes to Research


In: Praktijkgericht kwalitatief onderzoek: problemen en perspectieven.

ZonMw is the Dutch national organisation for health research and healthcare innovation. As an intermediary between science and society, ZonMw works to improve disease prevention, healthcare and health by stimulating and funding research, development and implementation. ZonMw supports knowledge enhancement, quality and innovation in health research and in healthcare. The organisation covers the entire spectrum, from fundamental health research to healthcare practice – from preventive and curative healthcare to youth care services. ZonMw’s main commissioning bodies are the Ministry of Health, Welfare and Sport and the Netherlands Organisation for Scientific Research.

Editor Marcel Senten
Coordinator Margo van den Berg
Assistant Anne Toppen
English translation Sue McDonnell
Design Katja Hilberg
Illustrations Heleen van den Thillart
Printed by Quantes

Published July 2015
The Gender and Health Knowledge Agenda summarises the gaps in our knowledge of gender and health, and serves as a basis for new research programming, including a future National Gender and Health knowledge programme. The agenda has been drawn up in collaboration with a large number of healthcare experts, the Gender & Health Alliance's Research Working Group. It was supported by the Ministry of Education, Culture and Science.

By exploring the differences between men and women in terms of health, illness and treatment more, and more effectively, we have the potential to improve quality of life and, at the same time, reduce waste and healthcare costs. This Knowledge Agenda is of interest to primary healthcare professionals, nurses, medical specialists, healthcare managers, health insurers, policymakers, researchers and health economists. In short: to anyone who is concerned with health and illness.