



Expert Views

Gender Medicine

Women's Health, Gaps in Care,
and (Re)Insurance Solutions

SCOR
The Art & Science of Risk

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What is Gender Medicine?

Gender medicine, also known as gender-sensitive or gender-specific medicine, is a relatively new discipline in medicine. Gender medicine considers the existing differences in health and illness between the sexes and attempts to consider the biological and socio-cultural differences between men and women in diagnoses, medication, therapy, and prevention, to close the gap in healthcare for women and to ensure the best possible treatment for women and men.

In previous decades, research findings were based on studies conducted mainly on male probands, which led to deficits in healthcare information concerning women. Gender medicine first developed in the United States, with the first centers for gender medicine in Europe, including the Institute for Gender Research in Medicine (GIM) in Berlin, beginning early in the 21st century.

It is important to be aware of the biological differences between men and women. These go far beyond height and weight, so treating women like smaller, lighter men leads to sub-optimal treatment results. Significant differences are present, for example, in the hormonal balance, the immune system, and the cardiovascular system, as well as in the psychological area.

It is obvious that changing hormone levels within a woman's monthly cycle, particularly estrogen and progesterone, have an influence on the effectiveness of medication. In addition, hormone levels change completely with the onset of menopause, which must also be considered. As sex hormones have a lifelong effect on activation and organizational tasks within all organs, they play an important role at every stage of life.

There are also differences between men and women when it comes to mental health. For example, on average across all ages, almost two-thirds of depression occurs in women. Digital platforms have shown that the duration of treatment for depression is approximately 10% longer for women, regardless of the type of therapy. However, significantly more men commit suicide than women.

Differences in the immune system are also remarkable. Because the genes responsible for this are mainly located on the X chromosome, women have 'double' information here compared to men. As a result, women have a better immune defense and are less susceptible to infections than men.

Men also tend to suffer somewhat more severely from flu-like infections, also jokingly referred to as severe male flu. The price that women pay for their better immune defense is the higher incidence of autoimmune diseases. The stronger immune defense is therefore also more frequently directed against the body's own cells. Four out of five autoimmune diseases affect women.



Gap in the Treatment of Cardiovascular Diseases in Women

Especially interesting is the gap in care for women with cardiovascular diseases. Although it is the most common cause of death in both sexes, mortality after a heart attack is significantly higher in women than in men for several reasons.

First, women are underrepresented in many cardiovascular studies and thus important research results are still awaited. In addition, the symptoms of a heart attack are almost always described in the literature as chest pain radiating to the left arm, as is usually observed in men. As a result, symptoms in men are identified very easily, so that emergency medical treatment can be quickly provided. In men, classic coronary heart disease, which is usually caused by blockages in the large coronary vessels, can be easily diagnosed using imaging techniques.

In women, on the other hand, the symptoms tend to be non-specific: often there are diffuse complaints such as abdominal, back and neck pain, dizziness, fatigue, and headaches. Neither the women themselves nor their families and, unfortunately, often not even the doctors treating them, suspect a heart attack. A recent study by PricewaterhouseCoopers (PwC) showed that 85% of the participants were unaware of the differences in the symptoms of a heart attack in men and women.

Ischemic heart diseases in women are more often caused by spasms or dissections of the smaller coronary vessels, which are more difficult to detect using imaging techniques. Premenopausal women have a low risk of heart disease due to the protective effect of estrogen. However, this risk increases significantly after menopause.

Biological differences between men and women also lead to a divergence in the efficacy of medications for treating cardiovascular diseases. For example, active ingredients can be broken down at different rates by the liver due to different metabolisms between the sexes, or the efficacy is influenced by the hormonal situation. For example,

beta blockers have a longer and stronger effect in women, because their bodies break them down more slowly. The situation is different for the blood-thinning agent ASA (e.g., in the drug aspirin). ASA is significantly less effective at inhibiting platelet clumping in women than in men.

There are also differences in emergency care. A study of the pre-hospital phase of severe heart attacks showed that in 2002, men arrived at the emergency room after just 180 minutes, while women took 240 minutes. Even in 2019, women were still admitted to hospital half an hour later than men who suffered a heart attack.

A mortality study on the risk of death after heart attack was presented at the European Society of Cardiology (ESC) Heart Failure Congress 2023 in Prague. The researchers analyzed the risk of death at two points in time after ST-segment elevation myocardial infarction (STEMI):

- After 30 days, 11.8% of women and 4.6% of men had died. The risk of death was thus 2.57 times higher for women than for men.
- After five years, 32.1% of women and 16.9% of men were no longer alive, which corresponds to a mortality risk for women that is almost twice as high.

However, it should also be noted that women suffer from a heart attack on average 10 years later than men. However, the advanced age at which a heart attack occurs is associated with an increased likelihood of additional risk factors or concomitant diseases, as well as a higher mortality rate. This must be considered in the study results.

Overall, although atherosclerotic cardiovascular disease is the leading cause of death in women, cardiovascular health is often neglected. Insufficient assessment of cardiovascular risk in women and missed or delayed diagnosis are major contributors to this neglect. It is imperative to identify and treat modifiable cardiovascular risk factors in women earlier.



Behavioral Differences Between the Sexes

As for behavioral differences between the sexes, men are more active, smoke a little more often, and consume more alcohol. Women on average pay more attention to their diet and sleep.

To determine how men and women benefit from exercise, data from more than 400,000 people were evaluated from 1997 to 2019. The result was astonishing: men achieve the maximum reduction in mortality risk by doing around 300 minutes of exercise per week. Women, on the other hand, only need around 140 minutes. This means that for women, even relatively little training can lead to a positive effect.

Men smoke slightly more than women. However, the female body reacts differently to tobacco than the male body does. The female vascular system and blood clotting mechanisms function differently, which increases the risk of a blood clot forming, which can lead to a thrombosis, stroke, heart attack, or peripheral arterial disease. A study of 2.4 million smokers found that women are 25% more likely to suffer from this condition than men. Women also tend to develop cardiovascular disease at a younger age, even if they only smoke a few cigarettes a day.

Given that tobacco use among women has increased significantly in recent decades, the prevalence of chronic obstructive pulmonary disease (COPD) among women has also risen dramatically. Women now suffer from COPD at least as often as men. However, they appear to be more susceptible to the respiratory effects of tobacco smoking, developing COPD at an earlier age and with a greater degree of lung dysfunction with a given amount of tobacco use.

Between 1980 and 2000, the annual rate of COPD mortality increased by 291% in women, compared to only 60% in men. Gender differences in COPD are increasingly being recognized in relation to susceptibility to the disease, disease phenotype, radiological appearance, and response to drug therapy.

Despite the behavioral differences described above and the fact that men are more likely than women to be obese, to have high cholesterol and high blood pressure, the leading causes of death are the same for both sexes: cardiovascular disease and cancer.



Women are Underrepresented in Clinical Studies

In clinical studies, systematic investigations are carried out to test the safety and effectiveness of new medications or treatments. The testing of medications on humans before their authorization takes place in three phases, with sick individuals only being involved from the second phase onwards when the effectiveness is being tested.

Women are often underrepresented in clinical research, which has led to a lack of data on how drugs and treatments specifically affect women. In the past, women have been excluded from clinical trials for several reasons:

Safety concerns

In the 1960s, after the Thalidomide tragedy, women of childbearing age were excluded from clinical studies in Germany for many years. At that time, many pregnant women had taken the sedative Thalidomide, which in numerous cases led to severe malformations in newborn children.

Biological variability

Women's hormone levels fluctuate much more than men's. The female sex hormones fluctuate over the course of the monthly cycle and are produced in greater or lesser amounts depending on the phase of the cycle. In addition, there are hormonal changes during menopause. Furthermore, the inclusion and exclusion criteria for participation in studies, such as blood pressure values, are determined only in men.

Legal and ethical concerns

Women are born with one to two million eggs and do not produce any new ones during their lifetimes. Men constantly produce new sperm. If a drug under investigation has negative effects on fertility, this would be much more dramatic in women.

In addition, women of childbearing age are at risk of damage to the embryo or fetus by the

drug under investigation. For this reason, women participating in studies must use two independent contraceptive methods to prevent pregnancies during the research phase.

Historical bias

In the past, the exclusion of women was also based on the lack of understanding that women react differently to medications; therefore, dosages used to treat smaller, lighter men are not always optimal for women. In addition, women are subject to hormonal fluctuations that can influence study results.

A significant turning point in the inclusion of women was in 1993, when the US National Institutes of Health (NIH) passed the Revitalization Act. This law required the appropriate inclusion of women and minorities in NIH-sponsored clinical trials. Since 2004, the German Medicines Act has required that clinical studies investigate possible differences between women and men. However, for older medications that have been approved for a long time, there is hardly any data regarding gender-specific efficacy.

Current guidelines suggest that women should be represented in studies at least in proportion to how they are affected by certain health conditions. This goal is not met for serious diseases such as cardiovascular diseases and some cancers. Of 40 drugs approved by the U.S. Food and Drug Administration (FDA) for both sexes in 2019, nearly half had less than 50% female representation.

In phase 1 clinical trials – when a drug is tested on humans for the first time – only men usually participate. It is therefore initially easier to study how a new drug behaves in the body in men. In the preceding animal experiments, drugs are also tested on male animals. The reason for this is that the female animals are used for reproduction, and here too the hormonal cycles influence the results.



The proportion of women in phases 2 and 3 in Germany is between 30% and 80%. Within the EU, the proportion of women is roughly the same as their proportion in the respective patient group.

However, despite a higher proportion of women suffering from the diseases being studied, they only make up one-third of participants in studies on cardiovascular drugs.

Drug Effects are Different in Women

Pharmacokinetics describes the behavior of a drug in the human body, which essentially consists of the four processes of absorption, distribution, metabolism, and elimination. Gender-specific differences in pharmacokinetics affect all four processes. Some important points are:

- **Resorption (absorption of the active ingredient into the body):** Women often have slower gastric emptying than men, which can affect the absorption of medication.
- **Distribution (distribution in the body):** On average, women have a higher body fat percentage than men. Since many drugs are lipophilic (fat-soluble), they can accumulate more in the fatty tissue of women.
- **Metabolism (metabolization):** Enzymes that are responsible for breaking down drugs show gender-specific differences in their activity. For example, women often have a higher activity of the CYP3A4 enzyme, which is expressed in the gastrointestinal tract and liver and is mainly involved in the metabolization of large and lipophilic molecules and can thus accelerate the breakdown of certain drugs.
- **Elimination (excretion from the body):** Kidney function, blood flow, and liver enzyme activity can differ between the sexes, which affect the excretion of medication.
- **Hormonal influences:** In addition, female and male sex hormones such as estrogen, progesterone and testosterone influence the metabolism of drugs. Hormonal fluctuations, such as those that occur during the menstrual cycle, pregnancy, or menopause, can significantly affect the pharmacokinetics of drugs.

The differences outlined above can lead to women and men reacting differently to the same medication, which can affect the appropriate dosage and treatment results. Some studies assume that women are at almost double the risk of suffering from side effects compared to men. Women are also more at risk of experiencing severe side effects that require a stay in hospital. One reason for this lies in the differences in drug metabolism described above.

Because many medications were originally tested on male subjects, the prescribed dosage may not always be optimal for women. Plus, women more often than men take several medications at the same time which also impacts drug effectiveness. Different medications can lead to interactions that cause further problems.

Sociocultural influences also play a role. Women are more likely to report side effects and seek medical help, which can lead to a higher detection rate of intolerances.



The Role of the Reinsurer

At the beginning of 2024, SCOR launched a project with PwC that aims to draw attention to weaknesses in gender-specific medicine. To date, joint events have been held on this topic in Zurich, Paris, and Monte Carlo (Rendezvous de Septembre). The feedback showed that the participants had a basic knowledge of the differences in disease symptoms and the effects of medication but that they are unaware of the implications of the predominantly gender-neutral treatment in the medical field.

In addition to raising awareness of the biological and sociocultural differences between men and women, SCOR would also like to promote research and teaching in gender-sensitive medicine to better understand biological differences and ensure fair treatment. Discussions are planned with various pharmaceutical companies in this regard.

Reinsurers – and insurers – can apply their expertise in various areas to ensure that women receive appropriate support. Product development offers a wide range of creative possibilities. To close gaps in coverage for women, life insurance products specifically for women have been developed in some countries. These include critical illness insurance that either only pays out when cancer occurs or also pays out when serious illnesses occur that primarily affect women. Severe gynecological surgery often also triggers the benefit payment, regardless of the stage of the cancer. SCOR has helped develop such insurance in Asia.

Furthermore, coverage has been created in Scandinavia that focuses on menopause and the resulting health complaints and physical changes in women. The insurance covers medical consultations as well as access to therapies and medications that are not covered by health insurance in some countries.

Together with SCOR, the start-up HV/LD offers this coverage through an employer. The focus here is not only on support and alleviating complaints

but also on reducing sick days. In addition to the services listed above, policyholders have access to a digital platform that contains information on all aspects of women's health.

As mentioned earlier, women are more prone to mental illnesses than men. These findings are also reflected in the portfolios of companies which offer disability insurance. It therefore makes sense to provide policyholders with preventive services in this area. This not only helps prevent future claims but also allows policyholders to perceive insurance companies as health conscious and supportive partners.

In recent years, SCOR has developed from being purely a risk carrier to being a prevention partner in mental health and uses new technologies to constantly improve its services. Prevention and early detection are becoming increasingly important in today's world. That is why SCOR also cooperates with companies such as ifeel and Humanoo to have a positive influence on physical and mental health. Various prevention measures have already been integrated into insurance products in collaboration with the relevant start-ups.

The services mentioned above not only cover the area of prevention but can also be made available to policyholders in the event of a claim, through coaching and rehabilitation services.



Status Quo and Outlook

In the last three decades, important steps have been taken with consideration of gender differences in medicine. In addition, legal regulations came into force to take women into account in research. Finally in 2021, the first professorship in gender-sensitive medicine in Germany was established at the medical faculty of the University of Bielefeld.

In 2023, Jill Biden, as First Lady of the United States, also committed herself to the topic of gender medicine. In this context, she pointed out that research into women's health has always been underfunded and the topic underrepresented.

Despite the measures already implemented, medicine is still in its infancy when it comes to ensuring gender-specific, needs-based treatment. Many diseases that only affect women, such as endometriosis, have hardly been researched, and there are no therapies. It is not enough to treat women as smaller men or to include mammograms in the product range for men's health.

Gender-specific aspects should therefore be included in medical studies. The European Commission plans to integrate the gender dimension into research and teaching by 2025 with 'Horizon Europe'. However, to enable evidence-based teaching, there should also be priorities in drug research in the future that consider gender aspects in pharmacokinetics and dynamics, toxicology, quality of life, and the sustainable use of health-related resources. This will provide better data and better results for both sexes. Stronger governance and oversight by regulatory authorities, as well as the engagement of the scientific entrepreneurial community, are needed to advance more gender-equitable pharmaceutical research, reporting, regulation, and commercialization.

Broader support is needed to advance gender equality in leadership and decision-making positions in pharmaceutical research and regulation. Medicines and therapies should be tailored to the target group. This also makes sense for the economy, to leverage efficiency reserves in healthcare and to secure the labor force of both men and women.

In 2025, SCOR will continue to address this issue and contribute to reducing the treatment gap in women.

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