

Female Sex Hormones and Health Outcomes in Women with Specific Focus on Asthma

Akademisk avhandling

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av Guo-Qiang Zhang

Fakultetsopponent:
Professor Klaus Bønnelykke
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Avhandlingen baseras på följande delarbeten

- I. **Zhang GQ**, Chen JL, Luo Y, Mathur MB, Anagnostis P, Nurmatov U, Talibov M, Zhang J, Hawrylowicz CM, Lumsden MA, Critchley H, Sheikh A, Lundbäck B, Lässer C, Kankaanranta H, Lee SH, and Nwaru BI. Menopausal hormone therapy and women's health: an umbrella review. *PLoS Medicine* 2021;18(8):e1003731.
- II. **Zhang GQ**, Basna R, Mathur MB, Lässer C, Mincheva R, Ekerljung L, Wennergren G, Rådinger M, Lundbäck B, Kankaanranta H, and Nwaru BI. Exogenous female sex steroid hormones and new-onset asthma in women: a matched case-control study. In Manuscript, 2022.
- III. **Zhang GQ**, Basna R, Mathur MB, Lässer C, Mincheva R, Ekerljung L, Wennergren G, Rådinger M, Lundbäck B, Kankaanranta H, and Nwaru BI. Age at menarche and menopause and new-onset asthma in women: a matched case-control study. In Manuscript, 2022.

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Abstract

In humans, gender differences exist across a wide spectrum of diseases. For example, women are more likely to develop Sjogren's syndrome, systemic lupus erythematosus and autoimmune thyroid disease than men. On the other hand, men are more likely than women to develop coronary heart disease, Parkinson's disease and severe coronavirus disease 2019. Asthma is a heterogenous respiratory disease, affecting 1–18% of the population in different countries. For decades, an age- and gender-related switch in asthma has been reported across different continents. Before puberty, asthma is more common in boys than in girls. However, from adolescence and into adulthood, asthma becomes more common in women than in men. These observations have led to the hypotheses that female sex steroid hormones (estrogens and progestogens) may play an important role in the pathogenesis of these diseases. This thesis aims to investigate the role of female sex hormones in women's health, with a particular focus on asthma. In Paper I, we conducted an umbrella review, which synthesizes the evidence from previously published systematic reviews and meta-analyses, to obtain a comprehensive picture around the effects of menopausal hormone therapy (MHT) in menopausal women. Overall, we found that MHT had a complex balance of benefits and risks on diverse health outcomes. For instance, besides the alleviation of menopausal symptoms, use of MHT was associated with decreased risks of bone fracture, diabetes mellitus, esophageal cancer, gastric cancer and colorectal cancer, but increased risks of stroke, venous thromboembolism, gallbladder disease, breast cancer and ovarian cancer. The overall quality of the included systematic reviews was only moderate to poor. In Paper II, we conducted a matched case-control study to determine the effects of hormonal contraceptives and MHT on the risk of developing asthma in women. We found that use of hormonal contraceptives may reduce the risk of asthma in women, whereas use of MHT may increase the risk in menopausal women. In Paper III, we conducted a matched case-control study to investigate the effects of age at menarche and menopause on asthma risk. We found that early age at menarche was associated with an increased asthma risk. The relation of age at menopause to asthma risk in menopausal women was uncertain. In conclusion, female sex hormones can influence diverse health outcomes in women. The umbrella review provides a comprehensive tool for clinicians and patients to evaluate the trade-offs between the benefits and risks associated with MHT use in menopausal women. Further epidemiologic studies or clinical trials of female sex hormones and asthma across different populations are warranted to replicate our findings. Further mechanistic studies are needed to identify potential sex hormone-driven asthma endotypes as well as novel therapeutic targets, thereby providing the foundation for more individualized asthma prevention and treatment strategies.

Keywords: asthma, Bayesian estimation, case-control, causal inference, estrogens, female sex hormones, hormonal contraceptives, menarche, menopausal hormone therapy, menopause, meta-analysis, multiple imputation, progestogens, systematic review, umbrella review, women

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