PROJECT PROPOSAL

2023 Academic Entry Year – Cohort 2

Supervisory Team

Primary Supervisor

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Project Details

Title: Ethnic inequalities in mental and physical multimorbidity in women before, during and after the menopause transition: modulatory effects of physical activity

Summary: Menopause, both natural and surgical, are associated with increased risk of developing chronic diseases, such as cardiovascular disease and osteoporosis. This increased risk is associated in part with the menopause-associated loss of estrogen. Endogenous estrogen confers multiple beneficial effects on numerous systems, including the cardiovascular, immune, metabolic, and skeletal systems, and the brain. Accordingly, loss of estrogen due to menopause is associated with evolution of a proatherogenic lipid profile, insulin resistance, obesity, osteoporosis, hypertension, and increased prevalence of anxiety and depression. These conditions may present individually, but with increasing age, they more commonly cluster. The health consequence of clustering, or multimorbidity (MM), are not clear. However, MM is an important predictor of poor health outcomes and is associated with decreased life expectancy. Other factors that are thought to play a role on developing MM in women include ethnicity. However, the impact of ethnicity on MM in women across the menopause transition are not well described. In our study we will examine ethnic inequalities in mental and physical MM in women before, during and after the menopause transition, and we will investigate the modulatory effects of physical activity levels on MM. We aim to identify high-risk groups who may benefit from lifestyle interventions to help improve MM outcomes.

Theme(s) the project most closely aligns to: Multimorbidity

How the PhD project and training would be appropriate for NMAHPs or GPs: Conducting research in women, including within the local community of Leicester, will facilitate increased clinical and medical expertise in a population that are currently under-investigated and overlooked. It will also support clinical development of the candidate to be able to identify how to improve services for the benefit of these patients. Application of this knowledge will further facilitate new areas of academic and clinical investigation post-doctoral, leading the candidate to new and continued collaborations and networking between endocrinological, biological, psychological and social clinicians and researchers. Academic development of the candidate will be supported through the learning and guidance on how to critically evaluate scientific research findings, and how to articulate and disseminate their work via varied communication methods, including conference presentation, written articles, and verbal communications with colleagues and external stakeholders.

How the project addresses health inequalities: Women present with a unique hormonal profile that is associated with inequalities in the aetiology, presentation, treatment and prognosis of chronic disease states, such as cardiovascular disease, compared with men. Further ethnic inequalities are also observed with cardiovascular disease for both men and women. However, when clusters of chronic disease occur, as commonly occurs with increasing age, interactions between the co-morbidities and the resultant effects on health are less well understood. In women, menopause identifies a time of increased risk for the development of multiple chronic diseases, or multimorbidity (MM). Specifically, the menopause transition has recently been recognised as a window of marked increase in the development and progression of chronic diseases. As such, this 'window' is deemed to be an important opportunity for intervention to potentially modulate MM in women. However, ethnic inequalities in the physical and mental MM in women are unknown. The efficacy of the modulatory effects of physical activity, a recommended lifestyle intervention for women to maintain their health, on MM during this window are also unclear. Thus, the proposed project aims to examine ethnic inequalities in MM in women before, during and after the menopause transition, and to investigate the modulatory effects of levels of physical activity. Identification of ethnic disparities in these investigations will help identity high-risk groups that

may benefit from early (reproductive) health-related assessments. Such investigations have real world implications for the quality of life and management of MM risk, and it's future burden, in women.

Aim: This project aims to examine ethnic inequalities in mental and physical MM in women before, during and after the menopause transition. It also aims to investigate whether lifestyle behaviours, such as physical activity, modulates these inequalities.

Background: Menopause is an important stage in women's lives, affecting many physical and social changes. The average age of menopause is 51 years, but there is considerable inter-individual variation, ranging between 40 and 60 years (Maas et al., 2021) with variation due in part to ethnic and cultural differences (Morabia et al, 1998). Beyond reproduction, estrogens exert favourable effects on metabolic and cardiovascular health in women, including lipid metabolism, insulin resistance, vascular reactivity, cardiac remodelling, and blood pressure (Miller et al., 2008). Further, estrogens also modulate the immune system, which influences both vascular function and ageing (Klein et al., 2016). Accordingly, the loss of estrogen in association with menopause is associated with increased risk of individual chronic diseases and multimorbidity (MM) (Sehl et al., 2018). The coexistence of two or more chronic diseases are well described in women after menopause, including, but not limited to, cardiovascular disease, osteoporosis, arthritis, depression, insulin resistance, dyslipidaemia, and obesity (Maas et al., 2021; Lobo et a., 2014). Surgical menopause (e.g., bilateral oophorectomy) before age 50 years is also associated with a 4.5-fold increased risk of developing cardiovascular disease (Lobo et al., 2014) and 24% higher risk of accelerated development of MM (Rocca et al., 2017) versus age-matched women going through natural menopause at ~51 years of age. Premature menopause, occurring before the age of 45 yrs, is also associated with a 7-fold higher risk of cardiovascular disease (Lobo et al., 2014) and 3-fold higher risk of MM versus women having gone through menopause in their early 50 s (Xu et al., 2020). Thus, menopause, contributes importantly to individual disease states, such as cardiovascular disease, as well as the development of MM in women (Lobo et al., 2014; Xu et al., 2020). An epoch in women's lives when hormonal changes are particularly marked is the menopause transition, or perimenopause. It is identified as a period of accelerated risk for the development and progression of vascular dysfunction and CVD (Lobo, 2014), and increased prevalence of MM with CVD (Puri et al., 2022). Importantly, perimenopause and the first 10 years after menopause (eg before the age of 60 years) has been identified as an important window for intervention in health management for women (Lobo, 2014). However, the efficacy of this window for interventions aimed at decreasing MM risk are unknown. It is also unknown if ethnic inequalities exist in MM presentation during this 'window'. Further, the modulatory effects of physical activity on MM during this 'window' are also unknown. In view of physical activity being a recommended lifestyle behaviour for postmenopausal women to help maintain healthy weight and improve cardiorespiratory fitness (Maas et al., 2021; Eigendorf et al., 2019), the modulatory effects of exercise on MM during perimenopause and the recent years after menopause among ethnically diverse groups of women may be of particular relevance to the evolution and management of the future burden of MM in women.

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