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Protocol

An Exploration of the Mental Health impact among Menopausal Women: The MARIE Project Protocol (International Arm)

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Abstract

Introduction: Menopause is characterised by the ending of the menstrual cycle as part of a natural process. However, menopause can also be caused due to other health conditions such as premature ovarian failure or cancers that may have led to a oophorectomy or a radical hysterectomy. The physiological and psychological mechanisms linked to menopause across all age groups, races and ethnicities is not well understood. The paucity of data could reduce advancement of optimal clinical practice leading to reduce quality of life for women. To better explore and assess menopause we have designed the Menopause Mental Health Rating (MARiE) tool.

Methods: We will conduct a prospective mixed methods study in women and trans-men≥18 years old that are experiencing perimenopause, menopause or post-menopause. The development phase of the MARiE tool will involved a systematic review and in depth exploration of the range of symptoms experienced during menopause as part of a co-production workshop with thirty women. This was used to design the quantitative questionnaire, MARiE tool and the qualitative topic guides. This will include the Hospital Anxiety and Depression Scale, Insomnia Severity Index Scale, Menopause Rating Scale, Greene Climacteric Scale, Health related quality of life, Quebec Pain Disability Scale, and Burnout Assessment Tool. The MARiE tool will be clinically reviewed for face validity and completed by thirty women with confirmed menopause.

Ethics Approval: Research Ethics approval reference for this study in the UK is 22/EE/0159. Country specific approvals, as required have been obtained. Any additional countries that may take-part in the project after this article has been published will be included in the main manuscript.

Dissemination: The study findings will be made available using a peer review publication journal, workshops and conferences.

Keywords: Women's health, Mental health, Menopause, Psychology

List of Abbreviations: MARiE: Menopause Mental Health Rating; GOF: Goodness of Fit

Introduction

Menopause is the cessation of menstruation [1]. The menopause transition is distinguished by hormonal fluctuations and linked to a diverse array of physiological and psychological symptoms that could lead to comorbidities such as cardiometabolic diseases or mental health conditions [1,2]. The nature and severity of these issues could differ across women and trans-men which could have a bidirectional relationship with societal factors such as cultural practices within different geographical regions, ethnicities and races [2,3]. Typically, women begin to experience these menopausal symptoms in their late 40s, and they can persist for 5 to 8 years although this could extend beyond this period. This is referred to as natural menopause. However, surgical or medical menopause could impact people at any age, as it is a direct result of an oophorectomy or a hysterectomy due to conditions such as a cervical cancer, endometriosis or uterine fibroids [2-4]. The Nuffield Health Survey, which encompassed 3,725 menopausal women in the UK, revealed that 47% of these women reported experiencing symptoms of depression, while one-third of them encountered feelings of anxiety [4,5]. Additionally, sleep disturbances, encompassing difficulties in falling asleep and recurrent awakenings, affected up to one-third of women going through the menopausal transition, which could further exacerbate their mental health issues. It is estimated that approximately 20% of women in this transition phase seek medical help from their primary care physicians due to symptoms of depression or anxiety, underscoring the seriousness and impact of this issue. The Study of Women's Health Across the Nation (SWAN) has identified various contributing factors that make women more susceptible to depression during this period [5]. These factors include discomfort related to physical symptoms such as hot flashes, pre-existing mental health conditions, a lack of adequate social support, psychosocial stressors, health and lifestyle behaviors, and demographic characteristics. However, the increased risk of depression and anxiety observed in this population cannot be fully explained by these factors alone [6,7]. Evidence from studies that adjust for these variables indicates a lingering, elevated risk. It is becoming increasingly evident that the clinical manifestation of depression and anxiety in women undergoing the menopausal transition differs from that in women not experiencing these biological changes [7]. This phenomenon is associated with a wide spectrum of symptoms, including fatigue, diminished energy levels, low self-esteem, feelings of isolation, cognitive impairment, reduced libido, weight gain, muscle aches, and back pain [8]. Mood changes observed in women during the menopausal transition are pre-

dominantly characterized by irritability, paranoia, and anger, as opposed to women of reproductive age who typically exhibit sadness and a low mood. The causation of mental health issues during the menopausal transition is multifaceted, encompassing biological, psychological, and social factors [7-9]. Hormonal fluctuations in the hypothalamic-pituitary-gonadal axis directly impact brain function. Gonadal hormones play a significant role in regulating brain metabolism, enhancing cerebral blood flow, reducing inflammation, and promoting neuronal regeneration and nerve growth factor [10,12]. These biological factors interact with psychosocial elements that arise during this life stage, including perceptions of aging, the cessation of reproductive capabilities, changing roles in the workplace and family, physical ailments, and stressful life events [11-14]. The available evidence strongly reinforces the idea that mental health issues during the menopausal transition have a distinct origin and display specific clinical characteristics [15]. This underscores the necessity for a specialised tool designed to investigate and assess the impact of menopause on both the physical and psychological health during this phase.

Methods

Aims and Objectives

This project aims to investigate the mental health impact of menopause by evaluating both the physiological and psychological aspects through several distinct work stream packages. The focus of this protocol is on (WP) 2, which consists of two components: work packages WP2a and WP2b. The primary objective of WP 2 is to comprehensively explore menopause across diverse populations globally and to further validate our novel menopause assessment tool known as the Menopause Mental Health Rating (MARiE). This tool was developed through a synthesis of existing research data, clinical expertise, and collaborative efforts as part of the broader women's health program, ELEMI.

Study Design

The MARIE project uses a multifaceted approach where WP2a uses a prospective mixed-methods study design aimed at gathering information using existing clinically validated questions. The administration of these questions will be followed by a study-specific topics guide developed to assess participant experience to further strengthen the understanding and evaluation of the menopause.

Data Collection

Participants will complete the validated questionnaires online. The overall questionnaire includes the Hospital Anxiety and Depression Scale (HADS), Insomnia Severity Index Scale (ISIS), Menopause Rating Scale (MRS), Greene Climacteric Scale (GCS), Health-Related Quality of Life (HRQoL), Quebec Pain Disability Scale (QPDS), Marital Satisfaction Scale (MSS) and the Burnout Assessment Tool (BAT-12). These questionnaires will be completed at baseline (days 1) and at day-30 following informed consent. A subset of participants will complete a qualitative interview at day-60 using the topics guide. The qualitative interviews will be audio-recorded and transcribed in full by the local teams. Early interviews will be reviewed by the research team to assess whether any modifications to the topic guides are necessary. The anticipated duration for interviews is approximately 45 minutes, although the duration may vary for each participant. The interviews will be transcribed by the researchers, and the transcripts will be reviewed for accuracy. Subsequently, they will be de-identified and uploaded into NVivo software for the purpose of data coding and retrieval. WP2b will commence as a feasibility study following the completion of WP2a. Work Package 2b is focused on validating the MARiE assessment tool in a broader participant population.

Study Population & Recruitment

This study protocol will be used in India, Sri Lanka, Malaysia, Pakistan, Brazil, Nigeria, Singapore and Ghana. Some aspects of the data collection will be aligned to the local requirements and cultural practices. The eligibility criteria for WP2a and WP2b include women and trans-men, aged 18 years or older, and have either undergone natural or surgical menopause or they are currently undergoing the peri-menopausal or post-menopausal phase. Participants should be willing and able to provide electronic consent and have access to a digital device to complete the online questionnaires and interviews. Recruitment efforts will be extended through various social media platforms, including Twitter, LinkedIn, local hospital websites, Instagram, and Facebook to reach potential participants. Participants will also be recruited through menopausal and family physician clinics by local clinical research teams. As this study is open to rural and urban principalities, participants will be provided with material in their preferred local languages.

Informed Consent

Informed consent will be obtained electronically through the Qualtrics XM platform for WP2a and WP2b. Participants will receive comprehensive information about the study. Eligible individuals who provide their consent will then be officially enrolled in the study. Participants will have the option to withdraw from the study at any time before submitting their questionnaire. However, once the questionnaire is submitted, it will not be feasible to identify the participant for data withdrawal, unless they have previously provided contact details that can be used to identify and withdraw their data. In such cases, any data that has already been collected with the participant's consent will be retained, but no additional data will be gathered, and no further research procedures will be conducted in relation to that specific participant.

Data Analysis

Quantitative data will be collected through online questionnaires utilising the Qualtrics XM platform. Each participant will be assigned a study ID, and no personally identifiable information will be recorded. Data will be extracted from the Qualtrics XM platform and imported into statistical software packages like SPSS and STATA for graphical representation and analysis. Data collection and analysis will be intertwined. If data saturation is reached, the interview focus may shift to other groups to enable more comprehensive exploration where appropriate.

WP2a: We will present descriptive statistics for continuous variables based on the data's distribution, using means (SD) or medians (IQR) as appropriate. For categorical data, we will provide statistics in the form of frequencies and proportions. In cases where data doesn't follow a normal distribution, non-parametric techniques such as the Kruskal-Wallis test and Mann-Whitney U-test will be employed. Additionally, for categorical variables and to explore associations between demographic data and responses related to mental health and well-being, we will use either the Chi-square or Fisher's exact test. Pearson's correlation analysis will be applied to measure the strength of linear relationships between variables.

WP2b: Pearson's correlation analysis will be used to assess the strength of linear relationships between variables. We will also evaluate the goodness-of-fit of latent class models for categorical responses through Pearson and likelihood-ratio chi-squared tests. Following this, we will employ a factor model, using confirmatory factor analysis with the Maximum Likelihood approach, to explore the covariance fit of the tested factor models. Model selection will be based on Goodness-Of-Fit Indices (GOF), considering various indices, both absolute and relative fit. All interviews will be conducted via a secure online platform, specifically a password-protected Zoom teleconference. These interviews will be audio-recorded and transcribed in their entirety. Data collection and analysis will be conducted in an integrated manner, employing a framework methodology that utilises an indexing coding approach to organize the data and facilitate interpretation.

Author's Contributions

GD and PP conceptualised and developed the MARiE project as part of the ELEMI program. GD and JQS designed the statistical analysis plan. GD wrote the first draft of the protocol manuscript. All authors critically appraised and commented on the protocol manuscript. All authors read and approved the final manuscript.

Competing Interests Statement

PP has received a research grant from Novo Nordisk and other, educational from the Queen Mary University of London, other from John Wiley & Sons, other from Otsuka, other from Janssen, outside the submitted work. All other authors report no conflict of interest. The views expressed are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, the Department of Health and Social Care or the Academic institutions. AF has no competing interests to declare.

Data Availability Statement

The authors will consider sharing the dataset gathered upon receipt of reasonable requests.

References

1. Siobán D Harlow, Margery Gass, Janet E Hall, Roger Lobo, Pauline Maki, et al. (2012) Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. Menopause 19(4): 387-395.
2. Roberts H, Hickey M (2016) Managing the menopause: An update. Maturitas 86: 53-58.
3. Hill K (1996) The demography of menopause. Maturitas 23(2): 113-127.
4. Kessler RC (2003) Epidemiology of women and depression. J Affect Disord 74(1): 5-13.
5. Bromberger JT, Kravitz HM (2011) Mood and menopause: findings from the Study of Women's Health Across the Nation (SWAN) over 10 years. Obstet Gynecol Clin North Am 38(3): 609-625.
6. (2023) Nuffield Health Survey: One in Four with menopause symptoms concerned about ability to cope with life.
7. Joffe H, Massler A, Sharkey KM (2010) Evaluation and management of sleep disturbance during the menopause transition. Semin Reprod Med 28(5): 404-421.
8. Soares C (2004) Perimenopause-related mood disturbance: an update on risk factors and novel treatment strategies available. In: Meeting Program and Abstracts. Psychopharmacology and Reproductive Transitions Symposium. American Psychiatric Publishing.
9. Li Y, Yu Q, Ma L, Sun Z, Yang X (2008) Prevalence of depression and anxiety symptoms and their influence factors during menopausal transition and postmenopause in Beijing city. Maturitas 61(3): 238-242.
10. Cohen LS, Soares CN, Vitonis AF, Otto MW, Harlow BL (2006) Risk for new onset of depression during the menopausal transition: the Harvard study of moods and cycles. Arch Gen Psychiatry 63(4): 385-390.
11. Parry BL (2020) Towards improving recognition and management of perimenopausal depression. Menopause. 27(4): 377-379.
12. Gibbs Z, Lee S, Kulkarni J (2015) The unique symptom profile of perimenopausal depression Clinical Psychologist 19(2): 76-84.
13. Epperson CN, Amin Z, Ruparel K, Gur R, Loughead J (2012) Interactive effects of estrogen and serotonin on brain activation during working memory and affective processing in menopausal women. Psychoneuroendocrinology 37(3): 372-82.
14. Gayathri Delanerolle, Rema Ramakrishnan, Dharani Hapangama, Yutian Zeng, Ashish Shetty, et al. (2021) A systematic review and meta-analysis of the Endometriosis and Mental-Health Sequelae; The ELEMI Project. Women's Health (Lond) 17: 17455065211019717.
15. Delanerolle G, Yang XJ, Cavalini H, Kurmi OP, Røstvik CM, et al. (2023) Exploratory systematic review and meta-analysis on period poverty. World J Meta-Anal 11(5): 196-217.