ARIC STUDY MANUSCRIPT PROPOSAL # 714

1. a. Full Title: Effect of menopausal status on mood: The influence of demographic and psychosocial characteristics

b. Abbreviated Title (Length 26): Menopause and mood

2. Writing Group (list individual with lead responsibility first): Kelly J. Rohan, Patricia M. Dubbert, Cecil Burchfiel, Sharon Wyatt, Edward Meydrech, Gail Hughes

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3. Timeline: Data analysis will begin following Publications Committee approval. We expect to begin manuscript preparation immediately and to submit the manuscript for publication within 9 months of proposal approval.

4. Rationale:

   Menopause-related changes in mood and well-being are important women’s health issues. Some reviews have concluded that incidence of Major Depressive Episode among women across the life span are analogous to plasma levels of estrogen with peaks during childbearing and perimenopausal years\(^1\). A few prospective studies have found elevated levels of clinical depression\(^2\) and depressive symptoms\(^3\) among perimenopausal women relative to menopausal and premenopausal women.

   Recently, several large-scale studies and national surveys have attempted to clarify any relations between menopausal status and affective symptoms. Analysis of the NHANES data revealed a significant relative risk of Major Depression during perimenopause and natural menopause based on Center for Epidemiological Studies Depression Scale- (CESD-) criteria, but these became nonsignificant after controlling for depression history\(^4\). The Massachusetts Women’s Study also found that perimenopause was associated with elevated rates of clinical depression defined by CES-D scores\(^5\). Among women who were not clinically depressed at the initial assessment, those who went from premenopause to perimenopause or who remained perimenopausal had higher rates of depression 27 months later than those who remained premenopausal or postmenopausal. In the Healthy Women
Study, postmenopausal and premenopausal women did not differ on the Beck Depression Inventory scores, but perimenopausal women self-reported more depressive symptoms than premenopausal controls\textsuperscript{5}.

Several studies have examined whether mood-menopause relations differ depending on type of menopause [i.e., occurring naturally, surgically induced, or including bilateral oophorectomy (BSO)]. Effects of initiation of hormone replacement therapy (HRT) on mood are also of interest. Results of the Healthy Women Study revealed no differences between hysterectomy, BSO and HRT, BSO only, and premenopausal women on self-reported depressed mood, psychosomatic symptoms, anxiety, or anger\textsuperscript{7}. The NHANES study found no differences in depressive symptoms, general well-being, or sleep between women who underwent surgical menopause with and without BSO\textsuperscript{4}. In a meta-analysis of 26 studies assessing the effects of HRT on menopausal depressed mood, estrogen only or in combination with androgen exerted moderate to large effects (reduced depressive symptoms) in pre-treatment to posttreatment and treatment to control comparisons\textsuperscript{8}.

Thus, current findings suggest that some women may experience negative mood changes with onset of perimenopause. Differences across studies may reflect differences in methodology (e.g., how perimenopause is defined and which dependent measures are used). In addition, some factors appear to moderate the effects of menopausal status on mood, including history of clinical depression\textsuperscript{4}, exercise participation\textsuperscript{9}, duration of menopause\textsuperscript{10}, and initiation of HRT\textsuperscript{8}.

Although reviews emphasize the importance of examining race and SES as moderating factors in menopausal experience\textsuperscript{11}, no reports using large-scale survey data have done so. Although race and SES could serve as markers for different educational and cultural influences on response to hormonal change, surprisingly, studies that sampled across race and SES (e.g., NHANES and the Massachusetts Women Study) have not examined these moderating variables in relation to menopausal mood changes. Because ARIC sampled African American and Caucasian women from various SES groups, sufficient power to conduct such analyses could be attained. Unlike other large surveys, the ARIC database contains other possible moderating variables such as physical activity level, social support, antidepressant medication use, smoking behavior, alcohol consumption, and various medical conditions. In addition, ARIC used unique psychosocial measures (i.e., vital exhaustion and anger), not previously assessed through the menopausal transition.

The proposed study will examine the relation between menopausal status and psychosocial dimensions in a biethnic sample (i.e., African American and Caucasian). Women varying in hormonal status [premenopausal, perimenopausal, postmenopausal (natural or surgical; with or without BSO, with or without HRT)] will be included as participants. Several moderating variables will be considered: race, SES, HRT use, physical activity level, social support, antidepressant medication use, cigarette smoking, alcohol consumption, and presence of health conditions (DM, cancer, CHD, stroke). Research questions include:

1. Will the findings of increased negative affect at perimenopause be replicated in the ARIC data, which included novel mood and psychological measures?
2. Will any moderating variables of the mood-menopausal status relation emerge?
Will type of menopause (surgical vs. natural) or initiation of HRT differentially impact mood across the menopausal transition?

5. **Main Hypotheses:**

The primary hypothesis is that perimenopausal status will be related to higher self-reported vital exhaustion and trait anger. Low SES, physical inactivity, poor social support, no HRT, smoking, excessive alcohol consumption, and presence of medical conditions are expected to emerge as moderating factors, associated with greater depressive symptoms.

6. **Data (variables, time window, source, inclusions/exclusions):**

The Vital Exhaustion Scale and State-Trait Anger Expression Inventory (from the Health and Life Profile) will be used as dependent measures. Menopausal status can be inferred from answers to questions regarding regularity of menstruation, and, in particular, changes in self-reported menstrual status between visits. Other variables of interest include ethnicity, income, age, hormone use, social support, physical activity, antidepressant medication use, smoking behavior, alcohol consumption, and prevalent health conditions.

7. **Analyses:**

In defining menopausal status, we will use the menopause-derived variable developed and used by Nabulsi et al. (1993)\(^\text{12}\) in their investigation of HRT and cardiovascular risk factors among postmenopausal ARIC participants. This variable is categorical: primary amenorrhea, premenopause, perimenopause, natural menopause (no menstruation during the past 2 years, including women who underwent hysterectomy, leaving one or two ovaries intact, and were age 55 or over), surgical menopause (no menstruation in the past 2 years and bilateral oophorectomy), and unknown ovarian status. Women classified as primary amenorrhea and unknown ovarian status will be excluded from our analyses. Whereas Nabulsi et al. (1993) used baseline ARIC data, we are interested in classifying women into menopausal status categories at Visits 2, 3, and 4 as well coding changes in menopausal status between these visits.

Vital Exhaustion: Hypotheses regarding vital exhaustion (assessed at Visit 2 only) will be evaluated through cross-sectional analyses. Consistent with the approach of Nabulsi et al. (1993), we plan to conduct an analysis of covariance (ANCOVA) using vital exhaustion as the dependent variable and Visit 2 menopausal status as the independent variable, controlling for age. Several moderating variables will be included: race, SES (Visit 1 education and income), and physical activity (Visit 1 leisure, sports, and work-related). Other moderating variables concurrently assessed at Visit 2 include hormone use (estrogen, progestin, or combination), social support, tobacco use (cigarette, cigar, or pipe smoking), alcohol consumption, antidepressant medication use, and prevalent health conditions (DM status, cancer at any cite, and coronary heart disease).
Trait Anger: The above analysis will be repeated using Visit 2 trait anger as the dependent variable. However, because trait anger was assessed at Visits 2 and 4, a longitudinal statistical approach is also appropriate. Specifically, we plan to examine changes in trait anger as a function of change in menopausal status. With change in trait anger from Visit 2 to 4 as the dependent variable, we will conduct an ANCOVA using change in menopausal status from Visit 2 to 4 as the independent variable, controlling for age. Moderators will include race, SES, physical activity (Visit 3 leisure, sports, work-related), and Visit 2 social support. Other possible moderating variables will be entered, including hormone use, tobacco use (cigarette, cigar, or pipe smoking), alcohol consumption, antidepressant medication use, and prevalent health conditions (DM, cancer, CHD, and stroke). Given that the ARIC cohort was 45 to 64 years old at Visit 1, it is unlikely that many women will remain premenopausal across all visits. Thus, data for any women classified as premenopausal at Visit 4 will be excluded from this longitudinal analysis.
References


