



Review Article

Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS): A cohort profile



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ABSTRACT

The Women's Health Clinic (WHC) at Mayo Clinic in Rochester, Minnesota, has provided consultative care to women with menopausal and sexual health concerns since 2005. Clinical information on the 8688 women seen in the WHC through May 2017 who gave consent for the use of their medical records in research is contained in the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS). Initially, DREAMS was created to improve the clinical care of women, but it has become a valuable research tool. About 25% of the DREAMS women have been seen in the WHC 2 or more times, allowing for passive longitudinal follow-up. Additionally, about 25% of the DREAMS women live in the 27-county region included in the expanded Rochester Epidemiology Project medical records linkage system, providing additional information on those women. The cohort has been used to investigate associations between: caffeine intake and vasomotor symptom bother; recent abuse (physical, sexual, verbal, and emotional) and menopausal symptoms; specific menopausal symptoms and self-reported view of menopause; and obstructive sleep apnea risk and vasomotor symptom severity and the experience of vasomotor symptoms in women older than 60 years. A study nearing completion describes a clinical series of over 3500 women presenting for sexual health consultation by sexual function domain and by decade of life. Other studies under way are determining correlates with sexual health and dysfunction. Planned studies will investigate associations between the experience with menopause and the risk of disease.

1. Introduction

The Women's Health Clinic (WHC) at Mayo Clinic in Rochester, Minnesota, was established in July 2005 as a consultative practice specializing in the management of menopause and female sexual health concerns. At that time, the status and safety of menopausal hormone therapy were uncertain. The results of the Women's Health Initiative trials had been published in 2002, and subsequently, women had difficulty obtaining prescriptions for menopausal hormone therapy or were seeking alternatives. Furthermore, gaps existed in the treatment of

sexual health concerns of women, who not uncommonly also had menopausal symptoms. The WHC was established to address these unmet clinical needs. A data registry of women seen for consultation was established concurrently with the WHC and subsequently named the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS). Although the initial use of the registry was to inform and improve clinical care, the registry also provided research opportunities.

Understanding the health and well-being of midlife women is critical for providing individualized care to women as they age. This focus is particularly salient with the increased life expectancy for women [1],

Abbreviations: ACE, adverse childhood experiences; BOSS, big one-stop shop; DREAMS, Data Registry on Experiences of Aging, Menopause, and Sexuality; FSFI, female sexual function index; MHQ, menopause health questionnaire; OSA, obstructive sleep apnea; REP, Rochester epidemiology project; VMS, vasomotor symptom; WHC, Women's Health Clinic

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Questionnaire	Period When Questionnaire Was Administered			
	July 2005-April 2015	May-December 2015	January-December 2016	January-May 2017
Menopause Health Questionnaire (MHQ) ^a	Only women referred for menopause consultation			
Female Sexual Function Index (FSFI) ^{a,b}	Only women referred for sexual health consultation		All women	
Menopause Rating Scale (MRS) ^{a,b}			All women	
Kansas Marital Satisfaction Scale ^{a,b}			All women	
Female Sexual Distress Scale—Revised (FSDS-R) ^{a,b}			All women	
Alcohol Use Disorders Identification Test (AUDIT) ^{a,b}			All women	
Patient Health Questionnaire depression scale (PHQ-9) ^{a,b}			All women	
Generalized Anxiety Disorder (GAD-7) ^{a,b}			All women	
STOP-Bang Questionnaire ^a		All women		
Adverse Childhood Experiences (ACEs) ^a		All women		
Gratitude Questionnaire (GQ-6) ^a		All women		
Mindful Attention Awareness Scale (MAAS) ^a		All women		
Perceived Stress Scale (4-item version) (PSS-4) ^a		All women		
Pittsburgh Sleep Quality Index (PSQI) ^a				All women
Brief Resilience Scale (BRS) ^a				All women
Perceived Stress Scale (10-item version) (PSS-10) ^a				All women
Linear Analogue Self-Assessment (LASA) of quality of life (single item) ^a				All women

Fig. 1. Timeline for Administration of Questionnaires. Footnote a indicates that questionnaire was administered to all women seen for initial consultation and annually to those returning for clinical care. Footnote b indicates that questionnaire was administered to all women seen for subsequent visits (> 2 weeks and < 1 year since the initial or annual visit). STOP-Bang indicates Snoring? Tired? Observed? Pressure? Body mass index > 35? Age > 50? Neck size large? Gender male?

because one-third of a woman’s life may occur after menopause [2]. The menopausal transition—a normal physiologic change for most women—is nothing short of a sentinel event marking the loss of ovarian follicular function and the beginning of the postmenopausal phase [3]. It is an opportunity to assess the risk of diseases highly prevalent in postmenopausal women, to review preventive strategies, and to provide counseling and education to women with the goal of reducing the burden of chronic diseases of aging, especially cardiovascular disease [4]. Evidence is accumulating related to sex-specific differences in cardiovascular disease risk and the associations between factors such as polycystic ovary syndrome, diseases of pregnancy (eg, gestational diabetes and preeclampsia), natural and iatrogenic premature menopause, and the timing of the onset and persistence of vasomotor symptoms (VMSs) and future cardiovascular disease [5–11].

Identifying factors in midlife (or earlier) that predict sex-specific risk for disease may allow for more effective screening and prevention strategies. For example, hot flashes and night sweats (VMSs) are the most common symptoms experienced by women in the menopausal transition. Previously considered an annoyance to be endured, VMSs are now known to vary among women in the timing of onset and the duration and, in some women, to indicate neurovascular dysregulation

and be a predictor of cardiovascular disease risk [9,12,13]. In addition, research is only beginning to unravel associations among stress, resilience, mood, sleep, obesity, substance use, abuse history, and the menopausal experience.

Female sexual dysfunction, another common concern in midlife women, is underdiagnosed and undertreated even though it seriously affects a woman’s quality of life and well-being [14–16]. The compelling need for future research to guide the diagnosis and management of female sexual dysfunction cannot be overemphasized.

Because knowledge relating to the care of midlife women is limited, well-designed observational studies can provide invaluable information to address clinical questions that cannot be addressed through randomized controlled studies. In addition, observational studies may provide preliminary data for the design of randomized controlled clinical trials (when they are possible) to address treatment interventions and efficacy.

2. Who is in the cohort and what information is collected?

At the WHC, one of the largest menopause and women’s sexual health clinics in the United States, about 2000 unique patients are seen

in over 3000 patient visits annually. Primary indications for consultation in the WHC include questions or concerns about hormonal and nonhormonal management of menopausal symptoms and concerns about sexual health (including desire, arousal, orgasm, and pain). Although some women are seen for consultation only once, many return for follow-up and ongoing care for these specific issues.

All women seen for clinical care in the WHC are asked to give permission for their personal health information to be used in research. Only a small percentage of women (about 6%) decline participation. A set of questionnaires is administered to each woman as part of her clinical care along with an intake form that includes demographic information, pertinent past medical history (including history of cancer, reproductive and gynecologic history, and a family history), and information on sexual orientation and gender identity. In addition, an extensive medical record abstraction is in progress for the entire cohort to obtain data about menopausal status (premenopausal, perimenopausal, or postmenopausal), including menopausal type (spontaneous, induced, or primary ovarian insufficiency) and timing (premature, age < 40 years; early, age 40–45 years; and normal, age > 45 years), and the use of medications that might affect menopausal symptoms (eg, hormonal therapies, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, gabapentinoids, and oxybutynin). The Table summarizes the cohort demographic data.

The specific questionnaires administered to women have changed since the WHC was established in 2005. Initially, the Menopause Health Questionnaire (MHQ), a clinical tool from the North American Menopause Society, was completed by women presenting for menopause consultation, and the Female Sexual Function Index (FSFI) was completed by women presenting for sexual health consultation. However, beginning in May 2015, the same set of questionnaires was administered to all women presenting for consultation in the WHC. The primary reason for this change was our clinical recognition and understanding of the overlap between menopausal and sexual health concerns and of the factors influencing these concerns in women. Since then, adjustments in the questionnaires administered in the WHC have been based on clinical need (Fig. 1). All questionnaires and the intake form are completed by women at the time of initial consultation and annually by those who return for subsequent visits; a subset of questionnaires is administered at each follow-up visit (if > 2 weeks but < 1 year since the initial or annual visit). To date, 8688 unique women have been included in the cohort. Of these women, 14.7% resided in Olmsted County, Minnesota, and 78.1% lived in Midwestern states (Table 1) [17].

3. Are women followed longitudinally?

Women return for consultative clinical care in the WHC as needed, and since its inception in 2005, 74.8% of women have been seen once, 19.8% have been seen twice, and 5.5% have been seen 3 or more times. This allows for passive longitudinal study of women who return for follow-up. There is also the potential to follow women who have been seen previously in the WHC through research initiatives (eg, through mail or telephone interviews or an invitation to undergo an in-person visit or a test).

Additional passive longitudinal follow-up is possible because women in DREAMS may also be part of the Rochester Epidemiology Project (REP) medical records linkage system [18,19]. An initial query indicated that approximately 14.7% of women in DREAMS resided in Olmsted County, Minnesota, and 25.8% of women in DREAMS resided in the 27-county region included in the expanded REP, adding considerably to the information available on each woman [20,21]. Other local and regional databases, such as the Mayo Clinic Cohort Study of Oophorectomy and Aging [17], the Mayo Clinic Study of Aging [22], and the Mayo Clinic Biobank [23], provide additional opportunities for future study of the women who are in more than 1 study cohort. Upon initial query, about 16% of women in the DREAMS cohort have

Table 1
Demographic Characteristics of Women in the Dreams Cohort, July 2005 Through May 2017

Characteristic	Value ^{a,b}
Age, y	
Mean (SD)	52.5 (10.9)
Median (range)	52.7 (11.6–115.8)
Q1, Q3	46.8, 59.0
Body mass index ^c (n = 5328)	
Mean (SD)	26.7 (6.0)
Median (range)	25.4 (11.6–65.9)
Q1, Q3	22.3, 29.8
Marital status, No. (%)	
Divorced	646 (7.4)
Legally separated	32 (0.4)
Widowed	198 (2.3)
Married	6914 (79.6)
Life partner	30 (0.3)
Single	830 (9.6)
Unknown	38 (0.4)
Race	
White	8026 (92.4)
Black or African American	99 (1.1)
American Indian or Alaskan native	28 (0.3)
Asian	113 (1.3)
Pacific Islander, Guamanian, or Chamorro	10 (0.1)
Other	124 (1.4)
Unknown or choose not to disclose	288 (3.3)
Ethnicity	
Not Hispanic or Latino	7606 (87.5)
Hispanic, Latino, or other Spanish culture	199 (2.3)
Unknown or choose not to disclose	883 (10.2)
Education	
Eighth grade or less	18 (0.2)
Some high school, but did not graduate	54 (0.6)
High school graduate or general equivalency diploma	879 (10.1)
Some college or 2-y degree	2454 (28.2)
Graduate of a 4-y college	2337 (26.9)
Postgraduate studies	2267 (26.1)
Unknown	679 (7.8)
Employment	
Employed	4140 (47.7)
Self-employed	892 (10.3)
Full-time homemaker	1052 (12.1)
Retired	1104 (12.7)
Student	75 (0.9)
Work disabled	262 (3.0)
Unemployed	427 (4.9)
Other	124 (1.4)
Unknown	612 (7.0)
Have you ever felt the need to cut down on your alcohol consumption?	
No	7236 (83.3)
Yes	602 (6.9)
Unknown	850 (9.8)
Do relatives or friends worry or complain about your alcohol consumption?	
No	7734 (89.0)
Yes	106 (1.2)
Unknown	848 (9.8)
Do you currently smoke or use other tobacco products?	
No, I never used any	1773 (20.4)
No, I quit all use	884 (10.2)
Yes	208 (2.4)
Unknown	5823 (67.0)
Residency	
Minnesota	4107 (47.3)
Iowa	652 (7.5)
Illinois	569 (6.5)
Wisconsin	450 (5.2)
Michigan	264 (3.0)
North Dakota	138 (1.6)

(continued on next page)

Table 1 (continued)

Characteristic	Value ^{a,b}
Indiana	124 (1.4)
Kansas	124 (1.4)
Missouri	125 (1.4)
South Dakota	113 (1.3)
Nebraska	78 (0.9)
Ohio	45 (0.5)
Other US state	1672 (19.2)
Outside the United States	227 (2.6)
Residence in Olmsted County, Minnesota	1281 (14.7)
Residence in 27-county region ^d	2243 (25.8)

Abbreviations: DREAMS, Data Registry on Experiences of Aging, Menopause, and Sexuality; Q1, first quartile; Q3, third quartile.

^a Data are for 8688 women unless noted otherwise.

^b Categorical data are presented as number of women (percentage of sample).

^c Calculated as weight in kilograms divided by height in meters squared.

^d Residence in the 27-county region in Minnesota and Wisconsin included in the expanded Rochester Epidemiology Project.

consented to be part of the Mayo Clinic Biobank and have provided blood samples for DNA and serum/plasma research.

4. Ethical approval

DREAMS was approved by the Mayo Clinic Institutional Review Board. Because the data collection is historical, women do not need to provide study-specific informed consent but rather a general consent to allow use of their medical records for research (in compliance with Minnesota legal requirements).

5. Validation of data entry and data storage

Patient-provided information is entered manually into DREAMS at the time of the clinical visit to ensure that the data are available in real time for clinical use. To validate the data-entry process, we compared the data entered in the database with the original paper questionnaires and intake forms for 20 randomly selected women. The average number of errors across all items and all instruments was 0.8% for the questionnaires and 3.1% for the intake forms. In the near future, data will be entered electronically by the patient at the time of the visit. DREAMS is contained within Mayo Clinic's Big One-Stop Shop (BOSS), an electronic data capture system designed to support all aspects of data registry and study management within 1 comprehensive system. BOSS provides a way to capture patient-specific information while providing automated data security and monitored access logging.

6. Key findings and publications

DREAMS allows for an integrated analysis of the menopausal experience, female sexual concerns, and the correlates of these variables. Initial studies from the database have focused on the experience of menopause, particularly on the variables affecting the self-reported severity and bother of VMSs, the most commonly reported menopausal symptoms.

Although women have routinely been counseled to avoid caffeine as a lifestyle management strategy to reduce VMSs, the medical literature contained surprisingly little data supporting this recommendation and even provided conflicting evidence [24,25]. In 2014, we examined the association between caffeine intake and menopausal symptom bother with an analysis of data from 1806 women older than 40 years [26]. Compared to women who did not use caffeine, caffeine users had higher mean VMS bother scores after adjustment for smoking and menopausal status ($P = 0.027$). These findings provide some support for the recommendation that women with bothersome VMSs avoid caffeine intake. Future studies with more detailed information on caffeine intake

may further elucidate differences in symptoms according to menopausal status.

Abuse (physical, sexual, verbal, or emotional) is a common, underreported problem that affects women irrespective of age, race, education, and socioeconomic status [27]. It is also associated with adverse health outcomes, including poor mental health [28]. We observed that, during their interviews, women presenting for consultation in the WHC commonly reported a history of abuse. Therefore, we investigated the experience of abuse in our cohort and, subsequently, the association between recent abuse and menopausal symptoms.

The first study [29], published in 2016, included 1389 women (mean age, 55 years) seen between 2005 and 2010. Those women were queried about physical, sexual, and verbal or emotional abuse in the previous year and whether they had received counseling. In that study, 7% of women reported experiencing verbal or emotional abuse in the previous year, 1% reported physical abuse, and less than 1% reported sexual abuse. The majority of women (69%) reporting verbal or emotional abuse indicated that they had received counseling.

The second study [27], which examined the association between recent abuse and VMS bother, reported on 3740 women seen in the WHC between January 2006, and October 2014. Again, nearly 7% of women (with partial participant overlap with the first study) reported experiencing abuse in the preceding year, and nearly all (96%) reported that they had experienced verbal or emotional abuse. There was a significant positive association between self-reported abuse in the preceding year and total menopausal symptom bother scores ($P < 0.001$). The findings remained similar in multivariate analyses after adjusting for demographic and substance use characteristics. These findings are relevant because women with a history of abuse may report more bothersome menopausal symptoms, and providers should be prepared to ask about abuse. The study also extends the existing literature on childhood abuse and VMS bother [30]. A recent report [31] noted an association between a history of childhood or adult abuse and risk for bilateral salpingo-oophorectomy performed before the natural age of menopause, even in the absence of a clear ovarian indication. Therefore, to better understand the association between the menopausal experience and a history of abuse, we added the Adverse Childhood Experiences (ACE) questionnaire to our data collection instruments in 2015.

In a study of the effect of specific menopausal symptoms on women's self-reported views of menopause, we found that mood symptoms and weight gain, although less common than VMSs, had a greater association with a negative view of menopause [32]. In addition to managing VMSs, targeting these specific issues may improve women's psychological well-being and experience during menopause. Because a number of the nonhormonal options for management of VMSs (eg, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, and gabapentin) may cause weight gain, an open dialogue about therapeutic options for VMS management is needed.

Although the mean duration of VMSs in midlife women is 7–9 years, in some women these symptoms persist for 10 years or more [13,33–35]. In our clinical experience, a large proportion of women seeking care for management of bothersome VMSs were in their seventh decade of life or older. Indeed, 18.6% of women presenting to the WHC for menopausal symptom management from January 2006 through October 2014 were 60 years or older, and 41% of those women reported moderate or severe VMS bother [36]. We have also observed that postmenopausal women referred for management of VMSs, particularly nocturnal VMSs with concomitant sleep disturbance, often have undiagnosed obstructive sleep apnea (OSA). Differentiating sleep disturbances related to VMSs from those due to a primary sleep disorder is difficult; however, despite its association with cardiovascular disease risk, OSA in women is underdiagnosed and undertreated [37,38]. Even though OSA and VMSs have been independently associated with cardiovascular disease risk [39], an association between OSA and VMSs has not been previously described and a manuscript is in press

describing our findings [40].

The DREAMS cohort also allows for questions about female sexual function to be addressed, including basic information about age-related differences in the domains of female sexual function (arousal, desire, orgasm, satisfaction, and pain) and the effect of substance abuse, mood, marital satisfaction, and other factors on those domains. Since 2005, over 3500 women have presented to the WHC for concerns about their sexual health. We are completing studies to define sexual health concerns according to decade of life and sexual function domain and the associations between alcohol intake, female sexual function, and sexual distress.

7. Conclusions

7.1. Future directions

To date, published studies from DREAMS have focused on questions arising during the course of clinical practice. Findings from preliminary studies have raised additional research questions and prompted development of plans for further investigation. Women's Health Internal Medicine at Mayo Clinic in Arizona has begun collecting data with the same set of questionnaires from women seen for menopause and sexual health consultations for inclusion in DREAMS, adding to the geographic, ethnic, and cultural diversity of the cohort. Intramural collaboration with clinical and basic science colleagues and experts from other medical centers, as well as passive longitudinal follow-up and linkage to other record systems will further enable DREAMS to be used to answer important clinical questions. In addition, future randomized controlled clinical trials would be possible with women selected from the cohort and appropriate institutional review board approval and patient consent.

7.2. What are the main strengths and weaknesses?

7.2.1. Strengths

The primary strength of DREAMS is the size of the well-defined cohort of women seeking care for female-specific issues. This registry provides opportunities to investigate associations between symptoms and risk factors and to develop hypotheses of possible correlates of diseases in women as they age. An additional strength is the linkage to the integrated electronic health record, the ability to use longitudinal care information with women who return for follow-up, and the ability to retrieve further longitudinal follow-up information for the women included in the REP [18–21]. Because clinical care questionnaires are administered at least annually to patients who choose to return, this cohort is followed longitudinally in a passive fashion.

It is also possible to gain additional information on this cohort of women through other databases, such as the Mayo Clinic Cohort Study of Oophorectomy and Aging [17] and the Mayo Clinic Study of Aging [22]. If the women participate in the Mayo Clinic Biobank [23], it is also possible, with appropriate study approvals, to use collected blood and DNA samples to investigate novel biomarkers or genetic risk factors for female-specific conditions.

7.2.2. Weaknesses

The women in our patient population were motivated to seek care in a subspecialty clinic at a tertiary care center and were primarily white, educated, married, and employed. Thus, given the absence of ethnic and socioeconomic diversity of the cohort, the generalizability of the findings may be limited. However, this may be mitigated, in part, by collaboration with colleagues in Women's Health Internal Medicine at Mayo Clinic, in Arizona who plan to include their patient population in the database. The potential for recall bias or selective reporting of information also exists because data from questionnaires administered to women reflect self-reported experiences and patients may decline to answer certain questions.

Contributors

SSF participated in the design and writing of the manuscript.
 EK participated in the design and writing of the manuscript.
 JMK provided critical review and editing.
 CLK provided critical review and editing.
 RS provided critical review and editing.
 JER provided critical review and editing.
 JMT provided critical review and editing.
 LTS provided critical review and editing.
 WAR participated in the design and writing of the manuscript.
 KSFH provided critical review and editing.
 KCM contributed statistical support.
 DRS contributed statistical support.
 VMM participated in the design and writing of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

DREAMS was approved by the Mayo Clinic Institutional Review Board. Because the data collection is historical, women do not need to provide study-specific informed consent but rather a general consent to allow use of their medical records for research (in compliance with Minnesota legal requirements).

Provenance and peer review

This article has undergone peer review.

Research data (Data sharing and collaboration)

Investigators interested in testing a specific hypothesis in collaboration with the DREAMS research team should send a brief outline of the intended project to Stephanie S. Faubion, MD (faubion.stephanie@mayo.edu).

References

- [1] National Center for Health Statistics, Table 14: Life Expectancy at Birth and at Age 65, by Sex: Organisation for Economic Co-operation and Development (OECD) Countries, Selected Years 1980–2014, (2017) <https://www.cdc.gov/nchs/data/hus/hus16.pdf#014>.
- [2] M.R. Jenkins, V.M. Miller, 21 st century women's health: refining with precision, *Mayo Clin. Proc.* 91 (6) (2016) 695–700.
- [3] J.L. Shifren, M.L. Gass, N.R.f.C.C.o.M.W.W. Group, The North American Menopause Society recommendations for clinical care of midlife women, *Menopause* 21 (10) (2014) 1038–1062.
- [4] M. Garcia, V.M. Miller, M. Gulati, S.N. Hayes, J.E. Manson, N.K. Wenger, C.N. Bairey Merz, R. Mankad, A.W. Pollak, J. Mieres, J. Kling, S.L. Mulvagh, Focused cardiovascular care for women: the need and role in clinical practice, *Mayo Clin. Proc.* 91 (2) (2016) 226–240.
- [5] L.J. Hwu, F.C. Sung, C.H. Mou, I.K. Wang, H.H. Shih, Y.Y. Chang, Y.L. Tzeng, Risk of subsequent hypertension and diabetes in women with hypertension during pregnancy and gestational diabetes, *Mayo Clin. Proc.* 91 (9) (2016) 1158–1165.
- [6] E.A. Jackson, S.R. El Khoudary, S.L. Crawford, K. Matthews, H. Joffe, C. Chae, R.C. Thurston, Hot flash frequency and blood pressure: data from the study of women's health across the nation, *J. Womens Health (Larchmt)* 25 (12) (2016)

- 1204–1209.
- [7] T. Muka, C. Oliver-Williams, S. Kunutsor, J.S. Laven, B.C. Fauser, R. Chowdhury, M. Kavousi, O.H. Franco, Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis, *JAMA Cardiol.* 1 (7) (2016) 767–776.
- [8] V. Regitz-Zagrosek, G. Kararigas, Mechanistic pathways of sex differences in cardiovascular disease, *Physiol. Rev.* 97 (1) (2017) 1–37.
- [9] R.C. Thurston, Y. Chang, E. Barinas-Mitchell, J.R. Jennings, R. von Kanel, D.P. Landsittel, K.A. Matthews, Physiologically assessed hot flashes and endothelial function among midlife women, *Menopause* 24 (8) (2017) 886–893.
- [10] R.C. Thurston, B.D. Johnson, C.L. Shufelt, G.D. Braunstein, S.L. Berga, F.Z. Stanczyk, C.J. Pepine, V. Bittner, S.E. Reis, D.V. Thompson, S.F. Kelsey, G. Sopko, C.N. Bairey Merz, Menopausal symptoms and cardiovascular disease mortality in the Women's Ischemia Syndrome Evaluation (WISE), *Menopause* 24 (2) (2017) 126–132.
- [11] W.M. White, M.M. Mielke, P.A. Araoz, B.D. Lahr, K.R. Bailey, M. Jayachandran, V.M. Miller, V.D. Garovic, A history of preeclampsia is associated with a risk for coronary artery calcification 3 decades later, *Am. J. Obstet. Gynecol.* 214 (4) (2016) e1–e8 519.
- [12] J.S. Silveira, R. Clapauch, M. Souza, E. Bouskela, Hot flashes: emerging cardiovascular risk factors in recent and late postmenopause and their association with higher blood pressure, *Menopause* 23 (8) (2016) 846–855.
- [13] P.G. Tepper, M.M. Brooks, J.F. Randolph Jr., S.L. Crawford, S.R. El Khoudary, E.B. Gold, B.L. Lasley, B. Jones, H. Joffe, R. Hess, N.E. Avis, S. Harlow, D.S. McConnell, J.T. Bromberger, H. Zheng, K. Ruppert, R.C. Thurston, Characterizing the trajectories of vasomotor symptoms across the menopausal transition, *Menopause* 23 (10) (2016) 1067–1074.
- [14] S.A. Kingsberg, M. Krychman, S. Graham, B. Bernick, S. Mirkin, The women's EMPOWER survey: identifying women's perceptions on vulvar and vaginal atrophy and its treatment, *J. Sex. Med.* 14 (3) (2017) 413–424.
- [15] S.R. Leiblum, P.E. Koochaki, C.A. Rodenberg, I.P. Barton, R.C. Rosen, Hypoactive sexual desire disorder in postmenopausal women: US results from the Women's International Study of Health and Sexuality (WISHeS), *Menopause* 13 (1) (2006) 46–56.
- [16] J.L. Shifren, B.U. Monz, P.A. Russo, A. Segreti, C.B. Johannes, Sexual problems and distress in United States women: prevalence and correlates, *Obstet. Gynecol.* 112 (5) (2008) 970–978.
- [17] W.A. Rocca, L. Gazzuola-Rocca, C.Y. Smith, B.R. Grossardt, S.S. Faubion, L.T. Shuster, J.L. Kirkland, E.A. Stewart, V.M. Miller, Accelerated accumulation of multimorbidity after bilateral oophorectomy: a population-based cohort study, *Mayo Clin. Proc.* 91 (11) (2016) 1577–1589.
- [18] J.L. St Sauver, B.R. Grossardt, B.P. Yawn, L.J. Melton 3rd, W.A. Rocca, Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester epidemiology project, *Am. J. Epidemiol.* 173 (9) (2011) 1059–1068.
- [19] W.A. Rocca, B.P. Yawn, J.L. St Sauver, B.R. Grossardt, L.J. Melton 3rd, History of the Rochester Epidemiology Project: half a century of medical records linkage in a US population, *Mayo Clin. Proc.* 87 (12) (2012) 1202–1213.
- [20] W.A. Rocca, B.R. Grossardt, S.M. Brue, C.M. Block-Goodner, A.M. Chamberlain, P.M. Wilson, L.J. Finney Rutten, J.L. St Sauver, Data resource profile: expansion of the Rochester epidemiology project medical records-linkage system (E-REP), *Int. J. Epidemiol.* (2017) in press.
- [21] J. St Sauver, B.R. Grossardt, L.J. Finney Rutten, V.L. Roger, M. Majerus, D.W. Jensen, S.M. Brue, C.M. Block-Goodner, W.A. Rocca, Rochester Epidemiology Project Data Exploration Portal (REP DEP) Preventing Chronic Diseases, (2017) in press.
- [22] R.O. Roberts, Y.E. Geda, D.S. Knopman, R.H. Cha, V.S. Pankratz, B.F. Boeve, R.J. Ivnik, E.G. Tangalos, R.C. Petersen, W.A. Rocca, The Mayo Clinic Study of Aging: design and sampling, participation, baseline measures and sample characteristics, *Neuroepidemiology* 30 (1) (2008) 58–69.
- [23] J.E. Olson, E. Ryu, K.J. Johnson, B.A. Koenig, K.J. Maschke, J.A. Morrisette, M. Liebow, P.Y. Takahashi, Z.S. Fredericksen, R.G. Sharma, K.S. Anderson, M.A. Hathcock, J.A. Carnahan, J. Pathak, N.M. Lindor, T.J. Beebe, S.N. Thibodeau, J.R. Cerhan, The Mayo Clinic Biobank: a building block for individualized medicine, *Mayo Clin. Proc.* 88 (9) (2013) 952–962.
- [24] F. Pimenta, I. Leal, J. Maroco, C. Ramos, Perceived control, lifestyle, health, socio-demographic factors and menopause: impact on hot flashes and night sweats, *Maturitas* 69 (4) (2011) 338–342.
- [25] J. Kandiah, V. Amend, An exploratory study on perceived relationship of alcohol, caffeine, and physical activity on hot flashes in menopausal women, *Health (N. Y.)* 02 (09) (2010) 989–996.
- [26] S.S. Faubion, R. Sood, J.M. Thielen, L.T. Shuster, Caffeine and menopausal symptoms: what is the association? *Menopause* 22 (2) (2015) 155–158.
- [27] S. Vegunta, C. Kuhle, J.M. Kling, J.A. Files, E. Kapoor, P.S. David, J. Rullo, R. Sood, J.M. Thielen, A. Jatoi, D.R. Schroeder, S.S. Faubion, The association between recent abuse and menopausal symptom bother: results from the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS), *Menopause* 23 (5) (2016) 494–498.
- [28] C.P. Mouton, R.J. Rodabough, S.L. Rovi, R.G. Brzyski, D.A. Katerndahl, Psychosocial effects of physical and verbal abuse in postmenopausal women, *Ann. Fam. Med.* 8 (3) (2010) 206–213.
- [29] R. Sood, P. Novotny, S.S. Faubion, J.M. Thielen, L.T. Shuster, C.L. Kuhle, E. Kapoor, M. Marnach, B. Barrette, A. Jatoi, Self-reported verbal abuse in 1300+ older women within a private, tertiary women's health clinic, *Arch. Gerontol. Geriatr.* 66 (2016) 62–65.
- [30] R.C. Thurston, J. Bromberger, Y. Chang, E. Goldbacher, C. Brown, J.M. Cyranowski, K.A. Matthews, Childhood abuse or neglect is associated with increased vasomotor symptom reporting among midlife women, *Menopause* 15 (1) (2008) 16–22.
- [31] L. Gazzuola Rocca, C.Y. Smith, B.R. Grossardt, S.S. Faubion, L.T. Shuster, E.A. Stewart, W.A. Rocca, Adverse childhood or adult experiences and risk of bilateral oophorectomy: a population-based case-control study, *BMJ Open* 7 (5) (2017) e016045.
- [32] R. Sood, C. Kuhle, E. Kapoor, J. Rullo, J. Thielen, K. Frohmader, K. Mara, D. Schroeder, S. Faubion, A negative view of menopause: does the type of symptom matter? *Climacteric* 19 (6) (2016) 581–587.
- [33] N.E. Avis, S.L. Crawford, G. Greendale, J.T. Bromberger, S.A. Everson-Rose, E.B. Gold, R. Hess, H. Joffe, H.M. Kravitz, P.G. Tepper, R.C. Thurston, Study of women's health across the, duration of menopausal vasomotor symptoms over the menopause transition, *JAMA Internal Med.* 175 (4) (2015) 531–539.
- [34] E.W. Freeman, M.D. Sammel, R.J. Sanders, Risk of long-term hot flashes after natural menopause: evidence from the Penn Ovarian Aging Study cohort, *Menopause* 21 (9) (2014) 924–932.
- [35] P. Gartoulla, R. Worsley, R.J. Bell, S.R. Davis, Moderate to severe vasomotor and sexual symptoms remain problematic for women aged 60–65 years, *Menopause* 22 (7) (2015) 694–701.
- [36] P.S. David, J. Kling, S. Vegunta, S. Faubion, K. Mara, D. Schroeder, E. Kapoor, C. Kuhle, Moderate to severe vasomotor symptoms in women aged 60 years and older: results from the data registry on experiences of aging, menopause and sexuality (DREAMS), *Menopause* 23 (12) (2016) 1385.
- [37] H. Joffe, A. Massler, K.M. Sharkey, Evaluation and management of sleep disturbance during the menopause transition, *Semin. Reprod. Med.* 28 (5) (2010) 404–421.
- [38] F. Kapsimalis, M. Kryger, Sleep breathing disorders in the U.S. female population, *J. Womens Health (Larchmt)* 18 (8) (2009) 1211–1219.
- [39] T. Muka, C. Oliver-Williams, V. Colpani, S. Kunutsor, S. Chowdhury, R. Chowdhury, M. Kavousi, O.H. Franco, Association of vasomotor and other menopausal symptoms with risk of cardiovascular disease: a systematic review and meta-analysis, *PLoS One* 11 (6) (2016) e0157417.
- [40] C.C. Gao, E. Kapoor, M.C. Lipford, V.M. Miller, D.R. Schroeder, K.C. Mara, S.S. Faubion, Association of vasomotor symptoms and sleep apnea risk in midlife women, *Menopause* 25 (4) (2017) in press.