

Predictors of impact of vaginal symptoms in postmenopausal women

Mary M. Hunter, MN,¹ Sanae Nakagawa, MA,² Stephen K. Van Den Eeden, PhD,³
Miriam Kuppermann, PhD, MPH,² and Alison J. Huang, MD^{2,4}

Abstract

Objective: This study aims to identify factors associated with greater impact of vaginal symptoms on the functioning and well-being of postmenopausal women.

Methods: Postmenopausal women who reported vaginal dryness, itching, irritation, or pain with sexual activity completed the multidimensional Day-to-day Impact of Vaginal Aging (DIVA) questionnaire and underwent assessment of multiple sociodemographic and clinical factors that have the potential to influence the impact of vaginal symptoms. Multivariable linear regression analyses examined relationships between selected participant characteristics and DIVA scale scores assessing symptom impact on activities of daily living, emotional well-being, self-concept and body image, and sexual functioning.

Results: Among 745 symptomatic participants, the mean (SD) age was 56 (9) years, and 66% were racial/ethnic minorities. Women with comorbid depression reported greater impact of vaginal symptoms on all dimensions of functioning and well-being measured by the DIVA questionnaire (11%-22% estimated increase in impact scores associated with every three-point increase in Hospital and Anxiety Depression Scale scores). Women with urinary incontinence also reported greater impact of vaginal symptoms on activities of daily living, emotional well-being, and self-concept and body image (27%-37% estimated increase in impact scores). Age, partner status, frequency of sexual activity, general health, and body mass index also predicted greater impact on at least one domain.

Conclusions: Findings suggest that special efforts should be made to identify and treat vaginal symptoms in postmenopausal women known to have depression or urinary incontinence, as these women may experience greater impact of vaginal symptoms on multiple domains of functioning and quality of life.

Key Words: Vaginal dryness – Vulvovaginal atrophy – Depression – Urinary incontinence – Menopausal symptoms.

Up to a third of postmenopausal women experience vaginal dryness, soreness, itching, irritation, pain with sexual intercourse, and other symptoms associated with genitourinary syndrome of menopause.¹⁻⁴ The

magnitude of the impact of these symptoms on functionality and well-being is not well understood, although previous research from the CLOSER (Clarifying Vaginal Atrophy's Impact on Sex and Relationships), REVEAL (Revealing Vaginal Effects at Midlife), and REVIVE (Real Women's Views of Treatment Options for Menopausal Vaginal Changes) surveys has suggested that these symptoms may be associated with a negative impact on sexual activity, body image, and psychological well-being.^{2,5-10} Variations in perceptions of menopause and aging have been observed in differing racial and ethnic groups,^{11,12} and these perceptions may influence how vaginal symptoms are experienced. However, much of the work that has been performed to date has involved primarily white women; as a result, little is known about how their experiences may differ from the experiences of women of other groups.

One reason that research on the impact of menopause-related vaginal symptoms has been limited is that, until recently, no participant-reported measures of impact have been validated across diverse populations. To address this need, our research team developed a structured self-administered questionnaire to measure the impact of vaginal symptoms (such as dryness, irritation, itching, soreness, and pain) on multiple dimensions of functioning and well-being. Using

Received January 30, 2015; revised and accepted March 31, 2015.

From the ¹Department of Physiological Nursing, School of Nursing, University of California San Francisco, San Francisco, CA; ²Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California San Francisco, San Francisco, CA; ³Division of Research, Kaiser Permanente Northern California, Department of Urology, University of California San Francisco, San Francisco, CA; and ⁴Department of Medicine, University of California San Francisco, San Francisco, CA.

Funding/support: This research was supported by grant 1R03AG035207 from the National Institute on Aging; grant P50 DK064538 from the National Institutes of Diabetes, Digestive, and Kidney Diseases and the Office of Research on Women's Health; a Paul Beeson Career Development Award in Aging Research; grant 1K23AG038335 from the National Institute on Aging and the American Federation on Aging Research; and the resources of Kaiser Permanente Northern California. Financial disclosure/conflicts of interest: A.J.H. has received a grant from Pfizer Inc for unrelated research on vulvovaginal atrophy. S.K.V.D.E. has received grants from Takeda and Abbott Molecular for unrelated studies.

Address correspondence to: Mary M. Hunter, MN, Department of Physiological Nursing, School of Nursing, University of California San Francisco, 2 Koret Way, Box 0610, San Francisco, CA 94143. E-mail: mary.hunter@ucsf.edu

data from a large racially/ethnically diverse sample of postmenopausal women who reported at least one vaginal symptom, we sought to identify demographic and clinical factors associated with greater impact of vaginal symptoms on functioning and well-being as measured by this questionnaire. Our goal was to provide clinicians and women new insights into factors associated with postmenopausal women experiencing a negative impact of vaginal symptoms on quality of life. This knowledge could be used to guide the development of strategies for identifying and treating women at greatest risk.

METHODS

Study population

This research was conducted as an ancillary study to the Reproductive Risks of Incontinence Study at Kaiser (RRISK), a multiethnic cohort study of risk factors for urinary tract dysfunction in community-dwelling middle-aged and older women.¹³⁻¹⁵ Participants were female enrollees in Kaiser Permanente Northern California (KPNC), an integrated healthcare delivery system serving approximately 25% to 30% of the northern California population. To be eligible for the parent RRISK cohort, women had to have enrolled in KPNC by age 21 years and to have had at least half of any childbirth events at a KPNC facility. In addition, women of racial/ethnic minorities were oversampled to achieve a target composition of 40% non-Latina white, 20% Latina/Hispanic, 20% African American, and 20% Asian/Asian American. Approximately 20% of all participants were recruited from the KPNC Diabetes Registry to ensure robust participation by women with diabetes. No symptoms or complications of diabetes were required, nor were women required to have any symptoms of urinary tract dysfunction.

Data for this study were collected from November 2008 to April 2012 through study visits with 2,016 women conducted in participants' homes during the third wave of RRISK (RRISK3). During RRISK3 study visits, women who reported at least 6 months of spontaneous amenorrhea or who had undergone bilateral oophorectomy were asked whether they had experienced vaginal dryness, soreness, itching, irritation, or pain with sexual intercourse in the past month. For this ancillary study focusing on the impact of vaginal symptoms on the functioning and well-being of postmenopausal women, only those women reporting at least one vaginal symptom were included in the analyses. A written informed consent form was obtained from all participants before data collection, and all study procedures were approved by the institutional review boards of the University of California San Francisco and the Kaiser Foundation Research Institute.

The Day-to-day Impact of Vaginal Aging instrument

The multidimensional impact of vaginal symptoms on functioning and well-being was assessed using a structured, validated, self-administered instrument—the Day-to-day Impact of Vaginal Aging (DIVA) questionnaire. The DIVA instrument was designed to be a self-administered paper-

based questionnaire and has been validated in this same self-administered paper form. Development and evaluation of the psychometric properties of the DIVA instrument have been described in detail elsewhere.¹⁶ Briefly, questionnaire items were developed based on qualitative findings from focus groups of diverse symptomatic women and refined based on one-on-one cognitive pretesting interviews. After field testing in a larger sample of symptomatic postmenopausal women and exploratory and confirmatory factor analyses to confirm measure structure, the refined DIVA instrument consisted of four multi-item domain scales addressing major dimensions of functioning and well-being affected by postmenopausal vaginal symptoms: (1) activities of daily living (five items); (2) emotional well-being (four items); (3) self-concept and body image (five items); and (4) sexual functioning (nine items for a long version appropriate for sexually active women and five items for a shorter version appropriate for women without a recent history of sexual activity). The questionnaire addresses symptom impact in the 4 weeks before survey self-administration. Each scale was designed to be scored from 0 to 4, with higher scores indicating greater impact of symptoms on the relevant domain. Women participating in RRISK3 data collection who reported being postmenopausal and having at least one vaginal symptom were asked to complete the DIVA questionnaire at their RRISK3 study visit; 745 of 757 eligible participants (98.4%) completed the instrument. Because the term “genitourinary syndrome of menopause” was not widespread at the time of the study, the instrument did not use this term but instead referred to “vaginal dryness, itching, irritation, soreness, and pain during sexual activity.”

Measurements

Data collected from the RRISK3 cohort included multiple demographic, clinical, and contextual factors that had the potential to influence the impact of vaginal symptoms on functioning and well-being as measured by the DIVA instrument.

Demographic characteristics such as race/ethnicity, spouse/partner status, and educational attainment were assessed by self-administered questionnaires. Specifically, race/ethnicity was determined by asking participants to characterize themselves as non-Latina white, Latina/Hispanic, Black/African American, Asian/Asian American, or other. Spouse/partner status was assessed by asking women whether they had a spouse or sexual partner. Education level was categorized as “some college or less” or “completed college.”

Clinical characteristics such as general health status, comorbid conditions associated with vaginal symptoms, and body mass index (BMI) were assessed through a combination of interviewer-administered and self-administered questionnaires, medical records review, and physical examination. To assess general state of health, interviewers asked participants to rate their overall health status as *excellent*, *very good*, *good*, *fair*, or *poor*.¹⁷ Diabetes was assessed based on participant report of a past clinical diagnosis of diabetes; this

information was supplemented with a review of abstracted clinical records from KPNC indicating use of glycemic control medication or a fasting blood glucose level of at least 126 mg/dL.¹⁸ To assess urinary incontinence, interviewers asked participants whether they had experienced any urine leakage in the past month; those reporting leakage were further asked to clarify whether they had at least weekly leakage versus less frequent leakage. Depression symptoms were measured using the Hospital Anxiety and Depression Scale (HADS), a validated self-administered questionnaire assessing feelings of anxiety and depression in the past 4 weeks, including a seven-item depression subscale scored from 0 to 21.¹⁹ Hot flashes were assessed by asking participants whether they had experienced hot flashes in the previous month; women reporting hot flashes were further prompted to rate the bothersomeness of their symptoms on a five-point Likert scale ranging from *not at all* to *extremely*. Bilateral oophorectomy was assessed by asking participants whether they had had both their right and left ovaries removed. For determination of BMI, participants underwent a brief physical examination, including measurement of weight and height, by a trained study coordinator.

Self-administered questionnaires were also used to assess sexual activity, defined inclusively to include both partnered and unpartnered sexual activities.

Participants were first asked, "During the past 3 months, have you had any sexual activity, that is, any activity that is arousing to you, including masturbation?" Women reporting any sexual activity in the past 3 months were further asked about the frequency of their activity in the past 3 months. For this analysis, participants were categorized as being *not sexually active*, *active less than weekly*, or *active weekly or more*.

Use of medications that have a significant likelihood of affecting vaginal symptoms, including vaginal and systemic estrogens and selective serotonin reuptake inhibitors (SSRIs), was assessed by abstraction and review of electronic KPNC pharmacy data for participants who reported filling at least 80% of their prescriptions through a KPNC pharmacy. For participants who reported filling less than 80% of their prescriptions through a KPNC pharmacy, medication use was ascertained by a self-administered questionnaire.

Statistical analyses

Means, SDs, and percentages were calculated to describe the demographic and clinical characteristics of participants in the analytic sample. DIVA domain scales were described by means, SDs, observed ranges, and interquartile ranges. Univariable and multivariable linear regression models were developed to examine the associations of a priori selected demographic and clinical characteristics with scores for each of the DIVA domain scales. All models included the following demographic variables: race/ethnicity (non-Latina white, Latina/Hispanic, Black/African American, or Asian), age (analyzed in 5-y intervals), sexual activity (not sexually active, active less than weekly, active weekly or more),

spouse/partner status (yes or no), and completion of college (yes or no). Clinical variables included self-assessment of overall health (fair or poor vs good), BMI (<25, 25-29, ≥30 kg/m²), bilateral oophorectomy (yes or no), HADS score (analyzed in three-unit intervals), SSRI use (yes or no), diagnosis of diabetes (yes or no), urinary incontinence (weekly occurrence; yes or no), moderate or severe hot flashes (yes or no), current use of systemic estrogen (yes or no), and current use of vaginal estrogen (yes or no). Because scores for each of the DIVA scales had skewed distributions, we log-transformed them in linear regressions to meet the normality assumption. We reported unstandardized regression coefficients multiplied by 100 to provide an estimate of the percentage of change in DIVA domain scores associated with each participant characteristic in the model.

For analyses focusing on the activities of daily living, emotional well-being, and self-image and body concept domain scales, models included all DIVA respondents. For analyses focusing on sexual function, models were stratified by sexual activity status. We developed one set of models that were restricted to sexually active women and used the longer nine-item version of the DIVA sexual functioning scale. We developed another set of models that were restricted to non-sexually active women and used the shorter five-item version of the scale. All analyses were implemented by SAS version 9.3 (SAS Institute Inc, Cary, NC).

RESULTS

The mean (SD) age of participants was 56 (8.5) years (range, 41-81 y; Table 1). Participants formed a racially/ethnically diverse population (21% African American, 25% Latina, and 20% Asian). Less than half (40%) had completed college. Seventy-seven percent had either a spouse or a sex partner, and 62% reported being sexually active either with a partner or alone.

Twenty percent rated their overall health as fair or poor. Most women in this study were overweight or obese. Six percent had undergone bilateral oophorectomy. The mean HADS depression subscale score was 3.4. Twenty-seven percent had been diagnosed with diabetes. Thirty-seven percent reported at least weekly urinary incontinence. Twenty-six percent reported that they were at least moderately bothered by hot flashes. Almost 18% of participants took SSRIs, 9% used systemic estrogen, and 16% used vaginal estrogen.

In this community-based sample of women, the mean scores for all of the DIVA domain scales were less than 1.0 (on a scale of 0-4), reflecting a relatively low impact of vaginal symptoms on women's functioning and well-being (Table 2). The lowest scores were assigned to the activities of daily living (mean [SD], 0.3 [0.5]) and emotional well-being (0.3 [0.6]) scales, whereas the highest scores were assigned to the self-concept and body image scale (0.9 [1.0]). Among sexually active participants (n = 462), the mean (SD) score for the nine-item extended sexual functioning domain scale score was 0.9 (0.9); among non-sexually active participants, the mean (SD) score for the shorter five-item sexual functioning scale was 0.7 (1.0).

TABLE 1. Demographic and clinical characteristics of symptomatic postmenopausal women

Characteristic	Symptomatic postmenopausal women (N = 745)	Sexually active symptomatic postmenopausal women (n = 462) ^a
Demographic		
Age, mean (SD), y ^b	56.2 (8.5)	54.7 (7.9)
Non-Latina white	250 (34)	167 (36)
Latina/Hispanic	187 (25)	115 (25)
Black/African American	155 (21)	80 (17)
Asian/Asian American	153 (20)	100 (22)
College degree	295 (40)	213 (46)
Relationship		
Current spouse/sex partner	568 (77)	420 (91)
Any sexual activity in the past 3 mo	462 (62)	462 (100)
Sexual activity at least weekly	200 (27)	200 (43)
Clinical		
Fair/poor self-reported health	148 (20)	69 (15)
Body mass index <25 kg/m ²	206 (28)	140 (30)
Body mass index 25-29 kg/m ²	225 (30)	142 (31)
Body mass index ≥30 kg/m ²	311 (42)	177 (39)
Bilateral oophorectomy	42 (6)	24 (5)
Hospital Anxiety and Depression Scale depression subscale score, mean (SD)	3.4 (3.1)	2.9 (2.8)
Diabetes mellitus	200 (27)	113 (24)
Weekly urinary incontinence	265 (37)	153 (33)
Hot flashes ^c	190 (26)	120 (26)
Medications		
Any estrogen use	183 (25)	122 (27)
Systemic estrogen use	69 (9)	50 (11)
Vaginal estrogen use	114 (16)	72 (16)
Selective serotonin reuptake inhibitor use	130 (18)	71 (16)
Vaginal symptoms		
Dryness	567 (76)	375 (82)
Irritation	214 (29)	127 (28)
Itching	317 (43)	165 (36)
Soreness	106 (14)	66 (14)
Pain during sex	220 (30)	184 (40)

Data are presented as n (%) unless stated otherwise.

^aWomen were considered to be sexually active if they reported some sexual activity, either with or without a partner, in the past 3 months.

^bAge range was 41 to 81 years.

^cWomen were considered to have hot flashes if they reported being at least moderately bothered by hot flashes in the past month.

On multivariable analyses, DIVA domain scale scores reflecting the impact of vaginal symptoms on activities of daily living were higher among women who reported only fair or poor overall health, had higher BMI, had higher HADS depression subscale scores, or were experiencing urinary incontinence on at least a weekly basis (Table 3). Scores for the DIVA emotional well-being impact scale were lower

among women with a spouse or sexual partner and higher among women who did not have a college degree, had higher HADS depression subscale scores, or were experiencing urinary incontinence on at least a weekly basis. Scores for the DIVA self-concept and body image scale were lower among Latina/Hispanic women (compared with non-Latina white women), older women, and women with diabetes but higher among women who had higher HADS depression subscale scores and weekly incontinence.

Among women who were sexually active, scores for the long form of the DIVA sexual function impact scale were lower among Latina/Hispanic women (compared with those who were non-Latina white) but higher among women who reported less-than-weekly sexual activity, had higher HADS depression subscale scores, or reported at least moderately bothersome hot flashes (Table 4). Among women who reported no sexual activity in the past 3 months, scores for the short form of the DIVA sexual function impact scale were lower among women who were older and higher among women with a spouse or sexual partner.

DISCUSSION

In this large, racially/ethnically diverse, community-based sample of postmenopausal women with vaginal symptoms, we found that women experiencing depression or urinary incontinence reported a greater impact of vaginal symptoms on their functioning and well-being, compared with women without these comorbidities. These findings suggest that depression and urinary incontinence may magnify the effects of vaginal symptoms on women's activities, feelings, and relationships, and that postmenopausal women experiencing these comorbid problems may be in special need of evaluation and treatment.

Given that depression has been shown to intensify the quality-of-life impact of a wide variety of long-term health conditions (including urinary incontinence),²⁰⁻²² it is not surprising that it should also magnify the quality-of-life impact of postmenopausal vaginal symptoms. Nevertheless, depression was associated with not only greater impact of vaginal symptoms on women's emotional well-being but also impact on other domains (such as activities of daily living) that have less direct ties to emotional status. These findings suggest that comorbid depression has the potential to fundamentally change women's experience of symptoms (such as vaginal dryness) such that treatment of depression may be as

TABLE 2. Score distribution for the Day-to-day Impact of Vaginal Aging domain scales

Domain scale	Number of items	Participant sample	Mean (SD) score	Observed score range	Interquartile range
Activities of daily living	5	745	0.3 (0.5)	0-4	0-0.4
Emotional well-being	4	745	0.3 (0.6)	0-4	0-0.5
Self-concept and body image	5	742	0.9 (1.0)	0-4	0-1.2
Sexual functioning (longer form) ^a	9	462	0.9 (0.9)	0-4	0.2-1.4
Sexual functioning (short form) ^a	5	265	0.7 (1.0)	0-4	0-1.2

^aScores for the long form of the sexual functioning domain scale were calculated for sexually active women, whereas scores for the short form of the scale were calculated for non-sexually active women.

TABLE 3. Estimated percentage of differences in DIVA impact scores for activities of daily living, emotional well-being, and self-concept and body image domains associated with participant characteristics

Subscale domain	Estimated % difference (95% CI) in DIVA scale scores ^a		
	Activities of daily living domain (n = 715)	Emotional well-being domain (n = 715)	Self-concept and body image domain (n = 714)
Latina/Hispanic vs non-Latina white	-11.2 (-29.1 to 6.7)	-13.4 (-33.4 to 6.7)	-40.9 (-63.1 to -18.6) ^b
Black/African American vs non-Latina white	1.3 (-17.9 to 20.5)	-12.3 (-33.8 to 9.2)	-22.1 (-45.9 to 1.8)
Asian/Asian American vs non-Latina white	9.9 (-9.2 to 28.9)	17.2 (-4.2 to 38.5)	-11.1 (-34.8 to 12.7)
Age (for every 5-y increase)	-0.8 (-4.9 to 3.4)	-4.0 (-8.6 to 0.7)	-5.4 (-10.5 to -0.2) ^c
Less-than-weekly sexual activity	1.9 (-15.1 to 18.8)	9.7 (-9.3 to 28.7)	37.7 (16.6 to 58.8) ^b
Current spouse/sex partner	-4.3 (-22.0 to 13.3)	-24.2 (-44.0 to -4.5) ^c	1.6 (-20.3 to 23.5)
No college degree	13.1 (-1.4 to 27.7)	16.3 (0.04 to 32.6) ^c	-4.8 (-22.9 to 13.3)
Fair/poor general self-reported health	20.2 (2.0 to 38.5) ^c	-02.8 (-23.2 to 17.7)	14.0 (-8.6 to 36.6)
Body mass index (for every one-unit increase)	2.0 (1.0 to 3.1) ^b	0.4 (-0.8 to 1.5)	-0.9 (-2.2 to 0.4)
Bilateral oophorectomy	15.1 (-14.3 to 44.5)	24.8 (-8.1 to 57.8)	27.9 (-8.7 to 64.4)
Hospital Anxiety and Depression Scale depression subscale (for every three-unit increase)	11.4 (4.4 to 18.5) ^d	21.8 (13.9 to 29.7) ^b	20.8 (12.0 to 29.5) ^b
Selective serotonin reuptake inhibitor use	3.4 (-15.4 to 22.2)	8.9 (-12.1 to 30.0)	-1.0 (-24.4 to 22.4)
Diabetes mellitus	9.3 (-7.0 to 25.5)	5.9 (-12.3 to 24.1)	-35.2 (-55.4 to -15.0) ^b
Weekly urinary incontinence	34.1 (19.8 to 48.4) ^b	36.8 (20.8 to 52.8) ^b	26.7 (8.9 to 44.5) ^d
Hot flashes ^e	14.3 (-1.8 to 30.5)	6.8 (-11.2 to 24.9)	7.9 (-12.1 to 28.0)
Systemic estrogen use	18.1 (-5.4 to 41.6)	-7.6 (-34.0 to 18.7)	-19.3 (-48.7 to 10.2)
Vaginal estrogen use	0.6 (-18.2 to 19.3)	3.7 (-17.3 to 24.8)	21.1 (-2.2 to 44.4)

DIVA, Day-to-day Impact of Vaginal Aging.

^aValues greater than 0 indicate increased symptom impact associated with the predictor. Adjusted estimated percentage of differences was obtained from a multivariable regression model controlling for all predictors listed in the table.

^bP < 0.001.

^cP < 0.05.

^dP < 0.01.

^eWomen were considered to have hot flashes if they reported being at least *moderately* bothered by hot flashes in the past month.

important as treatment of vaginal symptoms in improving condition-specific quality of life.

In at least one prior study, vaginal symptoms such as dryness, itching, and irritation have been linked to urinary

incontinence in postmenopausal women.²³ Although this may reflect the contribution of lower estrogen levels to these syndromes, it may also be that women who simultaneously experience vaginal symptoms and urinary incontinence tend

TABLE 4. Estimated percentage of differences in Day-to-day Impact of Vaginal Aging impact scores for sexual function domain associated with participant characteristics, stratified by sexual activity status

Subscale domain	Estimated % difference (95% CI) ^a	
	Sexual function domain scale (long version for sexually active women) (n = 447)	Sexual function domain scale (short version for sexually inactive women) (n = 261)
Latina/Hispanic vs non-Latina white	-35.3 (-61.6 to -9.0) ^b	-25.5 (-67.8 to 16.7)
Black/African American vs non-Latina white	-25.4 (-54.0 to 3.1)	-27.3 (-72.0 to 17.3)
Asian/Asian American vs non-Latina white	-10.3 (-37.1 to 16.5)	-15.4 (-63.1 to 32.3)
Age (for every 5-y increase)	-2.4 (-8.8 to 3.9)	-17.4 (-26.6 to -8.2) ^c
Sexually active less than weekly vs sexually active weekly or more	35.9 (16.1 to 55.6) ^c	NA
Current spouse/sex partner	1.9 (-31.6 to 35.3)	36.2 (3.4 to 69.1) ^d
No college degree	3.1 (-17.5 to 23.7)	11.0 (-25.2 to 47.2)
Overall health fair/poor	-2.6 (-32.4 to 27.2)	1.6 (-35.6 to 38.8)
Body mass index (for every one-unit increase)	-1.0 (-2.6 to 0.7)	-0.2 (-2.5 to 2.1)
Bilateral oophorectomy	21.7 (-24.0 to 67.3)	49.4 (-16.0 to 114.7)
Hospital Anxiety and Depression Scale depression subscale score (for every three-unit increase)	16.2 (5.2 to 27.2) ^b	9.2 (-6.1 to 24.4)
Selective serotonin reuptake inhibitor use	7.5 (-21.0 to 36.1)	-15.3 (-57.6 to 27.0)
Diabetes mellitus	-16.9 (-41.3 to 7.5)	-19.8 (-57.5 to 17.8)
Weekly urinary incontinence	19.0 (-2.5 to 40.4)	20.8 (-11.5 to 53.2)
Hot flashes ^e	26.5 (3.1 to 49.8) ^{d,c}	11.1 (-27.8 to 50.1)
Systemic estrogen use	-12.0 (-44.4 to 20.4)	-11.2 (-77.5 to 55.1)
Vaginal estrogen use	15.4 (-11.6 to 42.4)	37.8 (-6.7 to 82.4)

NA, not applicable.

^aValues greater than 0 indicate increased symptom impact associated with the predictor. Adjusted estimated percentage of differences was obtained from a multivariable regression model controlling for all predictors listed in the table.

^bP < 0.01.

^cP < 0.001.

^dP < 0.05.

^eWomen were considered to have hot flashes if they reported being at least *moderately* bothered by hot flashes in the past month.

to experience a greater quality-of-life burden from the cumulative effects of these problems. This suggests that treatment of incontinence may also be an important component of vaginal symptoms treatment.

Despite prior research suggesting more severe vaginal symptoms, including painful intercourse, among women with diabetes,³ diabetes was not associated with higher impact scores for any of the DIVA domain scales in our multivariable models. With regard to sexual function, our findings are consistent with those of other studies, which found that women with diabetes and women without diabetes have similar levels of perceived sexual problems despite possible reduced vascular flow or neuropathy that might impact sexual function.^{24,25} It has been proposed that women with diabetes have a decreased interest in sexual activity for other reasons,²⁵ which might mask the specific impact of vaginal symptoms on their sexual function. Another possible explanation is that any effect of diabetes on the impact of vaginal symptoms may be mediated through other comorbid conditions (such as depression or incontinence) that were independently assessed in our models. On univariate analyses, we detected significant associations between diabetes and DIVA scores for the activities of daily living and emotional well-being domains (ie, an estimated 36% and 23% increase in impact scores, respectively); however, these associations did not persist in multivariable models that adjusted for other demographic and clinical factors, including comorbid depression and incontinence.

Among women who reported no recent sexual activity, older age was associated with lower sexual function impact scores, indicating that older women who are not sexually active may be less bothered by the impact of vaginal symptoms on their sexual function than are younger women who are not sexually active. This may reflect decreased expectations of regular sexual activity among older versus younger postmenopausal women. Nevertheless, sexually inactive women with a spouse or sexual partner had higher scores for the DIVA sexual function scale than those without a spouse or partner, suggesting that cessation of sexual activity because of vaginal symptoms may be seen as more of a problem when a spouse or sexual partner is affected.

Women who were sexually active on at least a weekly basis reported a lower impact of their vaginal symptoms on the self-concept and body image and sexual function domains. On one hand, frequent sexual activity may help protect postmenopausal women against developing more severe vaginal symptoms, including dyspareunia, for a variety of reasons such as improved clitoral and vulvar circulation,²⁶ supporting the “use it or lose it” exhortation first voiced by Masters and Johnson.^{26a} Alternatively, this finding may simply indicate that women with more bothersome vaginal symptoms may have less frequent sexual activity precisely because they are bothered.

Interestingly, Latina women tended to have lower impact scores for the DIVA self-concept and body image and sexual function domains compared with non-Latina white women. There has been very little study of the burden of vaginal

symptoms in postmenopausal women of diverse backgrounds, and it is difficult to know whether these findings are attributable to the severity of vaginal atrophy, perceptions of or expectations about vaginal symptoms, or discomfort in expressing the impact of symptoms. Although one prior study reported a lower prevalence of vaginal symptoms in Latina postmenopausal women, another reported a higher prevalence in comparison with non-Latina white women; however, neither of them explored differences in the perceived impact of symptoms on functioning or well-being.^{27,28}

We did not detect significant associations between use of vaginal or systemic estrogen and any DIVA scale scores in this cohort. In an observational cross-sectional study such as this one, the beneficial effects of a therapy may be masked by the phenomenon of confounding by indication, in which participants who are most bothered by symptoms are more likely to be prescribed treatment than those who are less bothered. For this reason, our findings cannot be interpreted as evidence that vaginal or systemic estrogen therapy does not improve the impact of vaginal symptoms on condition-specific functioning or well-being.

Limitations of this study include its cross-sectional design, which prevented us from examining longitudinal relationships between participant characteristics and symptom impact across time. In addition, overall DIVA impact scores were low in this community-based population of women, and our results may not be representative of women with very severe vaginal symptoms. Participants in this study did not undergo physical examination or laboratory testing to evaluate their vaginal symptoms, and we would not know whether women’s symptoms were a result of postmenopausal vaginal atrophy or a pathologic process. Furthermore, we were unable to take into account the premenopausal sexual history of participants (ie, history that might predict sexual function after menopause).²⁹

Our study population also consisted of long-time female enrollees in an integrated healthcare system in northern California, whose members have been shown to underrepresent the very poor and the very wealthy and to be slightly better educated than the northern California population at large¹⁵ but are otherwise similar to the population of the geographical area. The study population was enriched with women of racial/ethnic minorities, which may affect the generalizability of findings to women in other settings. Lastly, the study population was enriched with women with diabetes, resulting in a 27% prevalence of diabetes compared with 16% in those aged 45 to 63 years and 26% in those aged 65 to 74 years.³⁰ Therefore, the overall distribution of vaginal symptoms may be slightly different in this sample than in the general northern California population, although the fundamental relationships between depression, incontinence, and vaginal symptoms would be expected to be similar to the population at large.

CONCLUSIONS

Postmenopausal women commonly experience vaginal symptoms, and many fail to discuss their complaints with

healthcare providers for a variety of reasons.^{10,24} Our research suggests that special efforts should be made to identify and treat vaginal symptoms in women already known to have depression or urinary incontinence, as these women may experience greater impact of their symptoms on functioning and quality of life.

REFERENCES

- Dennerstein L, Dudley EC, Hopper JL, Guthrie JR, Burger HG. A prospective population-based study of menopausal symptoms. *Obstet Gynecol* 2000;96:351-358.
- Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med* 2005;118(suppl 12B):14-24.
- Huang AJ, Moore EE, Boyko EJ, et al. Vaginal symptoms in postmenopausal women: self-reported severity, natural history, and risk factors. *Menopause* 2010;17:121-126.
- Pastore LM, Carter RA, Hulka BS, Wells E. Self-reported urogenital symptoms in postmenopausal women: Women's Health Initiative. *Maturitas* 2004;49:292-303.
- McKenna SP, Whalley D, Renck-Hooper U, Carlin S, Doward LC. The development of a quality of life instrument for use with post-menopausal women with urogenital atrophy in the UK and Sweden. *Qual Life Res* 1999;8:393-398.
- Barlow DH, Cardozo LD, Francis RM, et al. Urogenital ageing and its effect on sexual health in older British women. *Br J Obstet Gynaecol* 1997;104:87-91.
- van Geelen JM, van de Weijer PH, Arnolds HT. Urogenital symptoms and resulting discomfort in non-institutionalized Dutch women aged 50-75 years. *Int Urogynecol J Pelvic Floor Dysfunct* 2000;11:9-14.
- Simon JA, Nappi RE, Kingsberg SA, Maamari R, Brown V. Clarifying Vaginal Atrophy's Impact on Sex and Relationships (CLOSER) survey: emotional and physical impact of vaginal discomfort on North American postmenopausal women and their partners. *Menopause* 2014;21:137-142.
- Wysocki S, Kingsberg S, Krychman M. Management of vaginal atrophy: implications from the REVIVE survey. *Clin Med Insights Reprod Health* 2014;8:23-30.
- Parish SJ, Nappi RE, Krychman ML, et al. Impact of vulvovaginal health on postmenopausal women: a review of surveys on symptoms of vulvovaginal atrophy. *Int J Womens Health* 2013;5:437-447.
- Beyene Y, Gilliss C, Lee K. "I take the good with the bad, and I moisturize": defying middle age in the new millennium. *Menopause* 2007;14:734-741.
- Avis NE, Zhao X, Johannes CB, Ory M, Brockwell S, Greendale GA. Correlates of sexual function among multi-ethnic middle-aged women: results from the Study of Women's Health Across the Nation (SWAN). *Menopause* 2005;12:385-398.
- Appa AA, Creasman J, Brown JS, et al. The impact of multimorbidity on sexual function in middle-aged and older women: beyond the single disease perspective. *J Sex Med* 2014;11:2744-2755.
- Thom DH, Brown JS, Schembri M, Ragins AI, Subak LL, Van Den Eeden SK. Incidence of and risk factors for change in urinary incontinence status in a prospective cohort of middle-aged and older women: the Reproductive Risk of Incontinence Study in Kaiser. *J Urol* 2010;184:1394-1401.
- Thom DH, van den Eeden SK, Ragins AI, et al. Differences in prevalence of urinary incontinence by race/ethnicity. *J Urol* 2006;175:259-264.
- Huang AJ, Gregorich SE, Kuppermann M, et al. Day-to-Day Impact of Vaginal Aging questionnaire: a multidimensional measure of the impact of vaginal symptoms on functioning and well-being in postmenopausal women. *Menopause* 2014;22:144-154.
- Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-483.
- Karter AJ, Ackerson LM, Darbinian JA, et al. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes registry. *Am J Med* 2001;111:1-9.
- Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67:361-370.
- Frick AC, Huang AJ, Van den Eeden SK, et al. Mixed urinary incontinence: greater impact on quality of life. *J Urol* 2009;182:596-600.
- Sung VW, West DS, Hernandez AL, Wheeler TL II, Myers DL, Subak LL; Program to Reduce Incontinence by Diet and Exercise (PRIDE). Association between urinary incontinence and depressive symptoms in overweight and obese women. *Am J Obstet Gynecol* 2009;200:557.e1-557.e5.
- Smith DJ, Court H, McLean G, et al. Depression and multimorbidity: a cross-sectional study of 1,751,841 patients in primary care. *J Clin Psychiatry* 2014;75:1202-1208.
- Jackson SL, Scholes D, Boyko EJ, Abraham L, Fihn SD. Predictors of urinary incontinence in a prospective cohort of postmenopausal women. *Obstet Gynecol* 2006;108:855-862.
- Bhasin S, Enzlin P, Coviello A, Basson R. Sexual dysfunction in men and women with endocrine disorders. *Lancet* 2007;369:597-611.
- Lindau ST, Tang H, Gomero A, et al. Sexuality among middle-aged and older adults with diagnosed and undiagnosed diabetes: a national, population-based study. *Diabetes Care* 2010;33:2202-2210.
- Thomas HM, Bryce CL, Ness RB, Hess R. Dyspareunia is associated with decreased frequency of intercourse in the menopausal transition. *Menopause* 2011;18:152-157.
- Masters W, Johnson V. *Human Sexual Response*. Boston: Little, Brown and Company; 1966.
- Green R, Polotsky AJ, Wildman RP, et al. Menopausal symptoms within a Hispanic cohort: SWAN, the Study of Women's Health Across the Nation. *Climacteric* 2010;13:376-384.
- Schnatz PF, Serra J, O'Sullivan DM, Sorosky JI. Menopausal symptoms in Hispanic women and the role of socioeconomic factors. *Obstet Gynecol Surv* 2006;61:187-193.
- Dennerstein L, Dudley E, Burger H. Are changes in sexual functioning during midlife due to aging or menopause? *Fertil Steril* 2001;76:456-460.
- National Diabetes Statistics Report, 2014. Available at: <http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf>. Accessed March 23, 2015.