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Convergent-divergent validity and correlates of the Day-to-Day Impact of Vaginal Aging domain scales in the MsFLASH vaginal health trial

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Introduction

Vaginal symptoms can adversely affect the physical, psychological, and sexual functioning of women. Although bothersome vaginal symptoms including dryness, soreness, and pain with intercourse may affect women of any age, the prevalence of these symptoms increases significantly with menopause. In a prospective population-based study, only 3% of reproductive-age women reported vaginal dryness, while 21% of women in the late menopause transition and 47% of women who were three years past menopause reported this symptom.[1, 2] A 2010 international survey of over 4000 postmenopausal women reported a 39% prevalence of some type of vaginal discomfort.[3]

Research on postmenopausal vaginal symptoms has been limited by the lack of sensitive and validated instruments that measure the multidimensional impact of these symptoms on functioning and well-being. The Day-to-Day Impact of Vaginal Aging (DIVA) instrument, a structured-item self-report questionnaire consisting of four domain-specific scales (activities of daily living, emotional well-being, sexual functioning, and self-concept and body image), was developed to fill this gap in postmenopausal vaginal health research.[4] Construct validity of the DIVA questionnaire was initially evaluated in an observational sample of

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postmenopausal women using factor analysis as well as testing for correlations between the four DIVA domain scales and a limited number of other self-report measures. However, this initial assessment of construct validity was limited by the relatively small number of other measures available for comparison and the absence of validated measures of female sexual function and tissue-specific markers of vaginal atrophy. Further, these preliminary analyses were conducted in a community-based sample of women with overall low impact scores on the DIVA domain scales, suggesting relatively low burden of postmenopausal vaginal symptoms.

In light of the limitations of earlier work, our study team sought opportunities for further exploration of construct validity of the DIVA measure. Recent incorporation of the DIVA scales into the National Institutes of Health's multicenter MsFLASH (Menopause Strategies: Finding Lasting Answers for Symptoms and Health) Vaginal Health Trial offered a unique opportunity to examine the convergent and divergent validity of the DIVA domain scales using a richer array of measures relevant to postmenopausal vaginal health and sexual function. The MsFLASH trial also provided an opportunity to use the DIVA questionnaire to identify demographic and clinical factors associated with greater impact of vaginal symptoms on functioning and well-being in a population of postmenopausal women with a more severe symptom burden.

Material and Methods

The MsFLASH Vaginal Health Trial was a 12-week randomized trial comparing the efficacy of vaginal estradiol or vaginal moisturizer versus placebo for treating postmenopausal vulvovaginal symptoms. Study design, participant recruitment, and eligibility criteria have been reported elsewhere.[5] Briefly, participants were women aged 45 to 70 years who had experienced their last menses at least two years previously and who reported either (1) moderate-to-severe symptoms of vulvovaginal itching, pain, irritation, or dryness at least weekly within the past 30 days, or (2) pain with intercourse at least once monthly. Exclusion criteria included use of systemic estrogen (prior 60 days) and vaginal estrogen, vaginal moisturizer, or "stimulatory" lubricant (prior 30 days). Additional exclusion criteria, which included current vaginal infection, current or past lichen sclerosis or lichen planus, and chronic premenopausal vulvovaginal symptoms, are listed in the study protocol, included as Supplement 1 in the main study report.[5] Participants were recruited at Kaiser Permanente Washington (Seattle) and the University of Minnesota (Minneapolis) between April, 2016 and February, 2017.

The DIVA Questionnaire

Participants were asked to complete the DIVA questionnaire, a structured-item measure consisting of four domain-specific scales, at baseline. These included a 5-item scale assessing the impact of vaginal symptoms on everyday activities, 4-item scale assessing impact on emotional well-being, 5-item scale assessing impact on self-concept and body image, and 5-item scale assessing impact on sexual functioning.[4] Although the original DIVA questionnaire also included a 9-item version of the sexual functioning scale appropriate for women with a history of recent vaginal sexual intercourse, the MsFLASH

trial incorporated only the shorter 5-item version appropriate for women regardless of history of recent intercourse. All items for all scales included 5-level Likert response options, with higher scores indicating greater symptom impact.

Convergent-Divergent Validity Measures

At baseline, participants also completed a variety of self-report measures in addition to undergoing physical exam/laboratory measures relevant to postmenopausal vaginal health. These measures, described below, were used to assess convergent-divergent validity of the DIVA domain scales and identify factors associated with symptom impact.

All participants identified their most bothersome vulvovaginal symptom at baseline as itching, pain, dryness, irritation, or pain with penetration, and then rated its severity on a scale of 0–3 (none-0, mild-1, moderate-2, or severe-3). Due to the eligibility criteria of the underlying trial, all women had to report at least one symptom that was at least moderate (2) in severity at baseline.

Frequency of sexual activity was determined from diary data collected during the first week of the trial. Specifically, women who reported sexual activity during this first-week diary were defined as being sexually active weekly. Sexual function was assessed using the Female Sexual Function Index (FSFI), a 19-item questionnaire scored from 2 to 36; with scores less than 26 conventionally used to indicate clinically significant sexual dysfunction.[6] Sexual distress was measured using the Female Sexual Distress Scale-Revised (FSDS) Item 1, which asks the respondent to indicate how often she has felt distressed about her sex life in the past 4 weeks (never-0, rarely-1, occasionally-2, frequently-3, or always-4).[7]

Depression symptoms were assessed using the Patient Health Questionnaire 8 (PHQ-8), an 8-item scale scored from 0–24, wherein scores of 10 or more indicate moderate-to-severe depression symptom burden.[8, 9] Anxiety was examined using the Generalized Anxiety Disorder 7 (GAD-7), a 7-item scale scored from 0–21, in which scores of 10 or greater correspond to moderate-to-severe anxiety.[10] Menopause-Specific Quality of Life (MENQOL) was assessed using the 29-item MENQOL instrument which measures the presence and bother of symptoms, feelings, and experiences in four domains related to menopause: physical (16 items), vasomotor (3 items), psychosocial (7 items), and sexual (3 items).[11] For this report, resulting MENQOL values were averaged to yield a separate score for each domain ranging from 1 to 8, with higher scores indicating more bother.

Tissue-specific measures of vaginal atrophy assessed at baseline included vaginal pH, for which higher pH corresponds to greater estrogen depletion, and vaginal maturation value (MV), in which lower proportions of superficial cells are associated with estrogen depletion and atrophic vaginal epithelium.[12] Vaginal pH was assessed using litmus paper applied at time of collection to vaginal fluid samples obtained from the upper third of the vagina during pelvic exams. Vaginal epithelial cell samples for assessment of MV were collected at baseline, using standard methods, to determine the percentage of parabasal, intermediate, and superficial vaginal epithelial cells, as well as calculate an overall MV.[5, 12] Blinded MV assessment was performed by certified research cytologists at Pathology Associates Medical Laboratories (PAML) in Spokane, Washington.

Baseline questionnaires also included items assessing current age, age at time of menopause, history of hysterectomy and oophorectomy, race and ethnicity, education, smoking, alcohol use, partner status, and presence and severity of other common midlife symptoms such as vasomotor symptoms and urinary incontinence. Body mass index (BMI) was calculated from weight and height measured by clinic staff at baseline.

Statistical Analyses

For this report, analyses focus on baseline data only in order to address symptom impact prior to administration of treatments. Participants who completed at least one domain scale of the DIVA questionnaire at baseline were included in the analytic sample. Descriptive statistics were first used to describe the distributions of variables, including DIVA domain scores and other self-report and physical or laboratory measures selected for assessment of convergent-divergent validity (Table 1). Visual inspection of histograms of DIVA domain scale scores was performed to assess for skewed distributions and confirm that no transformation of data was needed. Mean scores and observed score ranges for each of the DIVA domain scales were examined. Item-scale correlations were then calculated using Pearson coefficients, and internal consistency reliability for these scales was re-examined using Cronbach's alpha (Table 2).

To address our first objective, we developed *a priori* hypotheses about the strength of associations between DIVA domain scales and the construct validity measures described above, based on our review of past studies of the impact of postmenopausal vaginal symptoms (Appendix Table A). We anticipated moderate-to-strong correlations between scores on the DIVA emotional well-being scale and other measures of mood, and between scores on the DIVA sexual function scale and other sexual function measures. We did not expect to detect an association between DIVA domain scale scores and vaginal pH or MV, in part, because other research (including the MsFLASH trial) demonstrated that, although most postmenopausal women develop tissue-specific signs of vaginal atrophy without supplemental estrogen, vaginal pH and MV are not well-correlated with bothersome vaginal symptoms.

We then examined actual correlations between DIVA domain scales and other construct validity measures in the baseline MsFLASH Vaginal Health Trial population in order to test the above convergent-divergent validity hypotheses (Table 3). Pearson correlation coefficients of <0.20, 0.20–0.29, 0.30–0.39, and ≥0.40 were considered to indicate minimal, weak, moderate, and strong correlations between the DIVA domain scales and these validity measures, following the precedent of prior work.[4]

To address the second objective, we developed unadjusted and adjusted linear regression models of each DIVA domain scale to examine associations with demographic and clinical participant characteristics. Adjusted models included the following factors hypothesized to influence the impact of vaginal symptoms on one or more dimensions of functioning and well-being: most bothersome vulvovaginal symptom severity; type of most bothersome symptom (pain with penetration vs. another symptom); participant age; relationship status (married or in a marriage-like relationship vs. non-married); race (non-white vs white); sexual activity (weekly vs. less frequent); PHQ-8 depression score; GAD-7 score; urinary

incontinence (a few times a week vs. less); co-morbid vasomotor symptoms (moderate/severe vs. less bothersome or no symptoms), and BMI. Age at time of menopause was not included due to concern about the association of this variable with chronologic age. No stratification or adjustment for treatment assignment was performed, since models did not include post-treatment data.

Results

Of the 302 women randomized in the MsFLASH Vaginal Health Trial, 301 completed at least one DIVA domain scale at baseline and were included in this analysis. Demographic and clinical characteristics of the participants are presented in Table 1, with an emphasis on self-report and physical or laboratory measures relevant to the impact of vaginal symptoms on functioning and well-being. Mean age was 60.9 (SD 4.1) years, with the majority of women reporting 10 or more years since cessation of menses. Pain with vaginal penetration was identified as the most bothersome symptom (MBS) by the largest proportion of women at baseline (60.5%). Only 20.6% of women identified vaginal dryness as their MBS, although 94.7% of women reported vaginal dryness that was at least moderate in severity.

Score distribution, item-scale correlations, and internal consistency of DIVA domains

Within the baseline trial population, the full score range of 0.0 to 4.0 was observed for all DIVA domain scales except for the activities of Daily Living scale, which had an observed range of 0.0 to 3.2 (Table 2). Mean scores ranged from 0.5 for the activities of daily living scale to 2.5 for the self-concept and body image scale. Item-scale correlations were high (greater than 0.60) for all scales, and all four domain scales of the DIVA instrument demonstrated strong internal consistency reliability based on standardized Cronbach's alpha's >0.80 (Table 2).

Convergent-divergent validity of the DIVA domain scales

Using Pearson correlation coefficients of <0.20, 0.20–0.29, 0.30–0.39, and ≥0.40 to indicate minimal, weak, moderate, and strong correlations,[4] we confirmed multiple hypothesized associations between DIVA domain scales and selected validity measures. As anticipated, moderate correlations were detected between the DIVA emotional well-being scale and the PHQ-8 depression and GAD-7 anxiety scores (Table 3). Strong correlations were observed between the DIVA sexual functioning scale and scores on the FSFI, the FSDS, and the MENQOL sexual function domain. Strong correlations were detected between the DIVA emotional well-being scale and MENQOL psychosocial domain scores, as well as between the DIVA self-concept and body image scale and the FSFI, the FSDS, and the MENQOL sexual function domain.

Contrary to expectation, no significant correlations were detected between the DIVA activities of daily living scale and self-reported severity of women's most bothersome vulvovaginal symptom (MBS). However, significant correlations were detected between DIVA activities of daily living domain scores and self-reported severity of other vulvovaginal symptoms not directly related to sexual activity, such as itching and irritation (Pearson r's of .43 ($p< 0.001$) and 0.34 ($p<0.001$) respectively). As anticipated, no

significant correlations were detected between any of the DIVA domain scales and either vaginal pH or MV.

Demographic and clinical factors associated with DIVA domain scores

In adjusted linear regression models examining associations between participant characteristics and each of the four DIVA domain scales (Table 4), greater vulvovaginal symptom severity was associated with higher average impact scores for all DIVA domain scales except for the activities of daily living scale. Specifically, each 1-point increase in self-rated vulvovaginal symptom severity (on a 0–3 point scale) was associated with an estimated 0.3 point increase in DIVA emotional well-being score (95% confidence interval [CI] 0.1, 0.5), 0.5 point increase in DIVA sexual function score (95% CI 0.3, 0.7), and 0.4 point increase in DIVA self-concept and body image score (95% CI 0.1, 0.6), against an overall 0–4 point DIVA scale range. Women who reported that their most bothersome vulvovaginal symptom was pain with penetration reported lower impact of symptoms on the DIVA activities of daily living domain (average −0.3 point difference; 95% CI −0.5, −0.2) compared to women who identified a different vulvovaginal symptom as their most bothersome symptom. Non-white race was associated with greater perceived impact of vaginal symptoms on the DIVA activities of daily living domain (average 0.4 point score difference; 95% CI 0.2, 0.6). Compared to women with less frequent sexual activity, women who maintained at least weekly sexual activity reported lower average impact of vaginal symptoms on the DIVA sexual function (average −0.4 point score difference; 95% CI −0.7, −0.2) and self-concept/body image domains (average −0.3 point score difference; 95% CI −0.5, −0.0). Depression symptoms were associated with greater perceived impact on the activities of daily living scale (average 0.2 point DIVA score increase [95% CI 0.1, 0.3] for each 5-point increase in PHQ-8 score) and emotional well-being domains (0.4 point DIVA score increase [95% CI 0.2, 0.6] for each 5-point increase in PHQ-8 score). Vaginal pH and MV measurements were not included in these analyses because these laboratory values showed no correlation with any DIVA domain scale scores in earlier analyses (see Table 3).

Discussion and Conclusions

Our research addresses the need for psychometrically robust instruments to assess the impact of vaginal symptoms on functioning and well-being in postmenopausal women and guide evaluation of factors that influence vaginal symptom impact in this population. Using baseline data from the MsFLASH Vaginal Health Trial, we evaluated the convergent-divergent validity of four DIVA domain scales in postmenopausal women with a moderate to severe vulvovaginal symptom burden. The DIVA questionnaire scales demonstrated strong item-scale correlations and internal consistency reliability in each of the four domains. Correlations between DIVA domain scale scores and similar self-report measures largely conformed to expectations, supporting construct validity.

Of note, no significant correlations were observed between any of the DIVA domain scales and either vaginal pH or MV. This result reinforces the MsFLASH Vaginal Health Trial's prior conclusion that measurements of vaginal pH and MV have limited usefulness for

assessing symptom impact or for guiding treatment decisions if the goal of treatment is to improve vaginal symptom-related functioning and quality of life.[5, 13]

In addition to supporting the convergent-divergent validity of the DIVA scales, our analyses identified demographic and clinical participant characteristics associated with either greater or lesser impact of vaginal symptoms in MsFLASH trial participants. Specifically, findings suggest that greater frequency of sexual activity is associated with lower impact of vaginal symptoms, while depression symptoms are associated with worse symptom impact, consistent with findings from prior research in women with milder vaginal symptoms.[14]

While it is not surprising that women with recent sexual activity reported lower impact of vaginal symptoms on sexual function, there is more than one possible explanation for this finding. It is reasonable to assume that women who experience more vaginal discomfort during sexual intercourse may avoid intercourse, and this could largely explain the correlation. On the other hand, a number of researchers have suggested that frequent sexual activity is associated with greater sexual well-being and may contribute to an improvement in sexual function.[15–17] Given that our study, like prior research, is cross-sectional and observational, we cannot draw definitive conclusions about causality.

Our finding that depression symptoms were associated with greater symptom impact in the activities of daily living and emotional well-being domains aligns with other research showing that depression intensifies the impact of numerous health conditions on functioning and well-being.[14, 18] At the same time, disruptive vaginal symptoms have the potential to exacerbate symptoms of depression, creating the potential for a bidirectional relationship. This further evidence linking depression symptoms to postmenopausal sexual health provides one more reason to screen for and address depression.

Strengths of the study include the multicenter sample of symptomatic women and rich array of validated measures available for assessing the DIVA questionnaire. Generalizability is limited by eligibility restrictions for the underlying randomized trial. Estrogen use prior to washout period before enrollment could also have exerted residual effects on vaginal symptoms, pH or cytology, although all participants were required to have at least moderately severe vulvovaginal symptoms at baseline regardless of prior estrogen use.

Generalizability may also be limited by the fact that close to 60% of participants reported pain with penetration as their most bothersome complaint. This may explain the lack of observed correlation between self-reported severity of women’s most bothersome symptom and their scores on the DIVA day-to-day activities domain, which does not address problems related to sexual activity. Research using the DIVA instrument in a population of women who do not experience pain with penetration as their most bothersome complaint may produce different results.

Additionally, we do not yet have enough evidence to know whether the magnitude of score differences detected in our analysis constitute clinically relevant differences. Overall, the observed DIVA score differences of 0.2 to 0.5 may be modest in comparison to the overall 0 to 4 point scale range, which points to the need for further research to define minimal clinically important differences in DIVA domain scores.

Nevertheless, this analysis from the MsFLASH Vaginal Health Trial provides important evidence regarding the DIVA instrument's psychometric properties, lending support for its use in epidemiologic and therapeutic research. We also anticipate that the DIVA questionnaire could be used in clinical practice to assess the impact of vulvovaginal symptoms before or after treatment. In this way, it could help clinicians gauge whether clinical treatments were having a beneficial effect on patients' functioning and well-being. Our findings point to factors that may influence or be influenced by the multidimensional impact of postmenopausal vaginal symptoms, such as frequency of sexual activity and comorbid depression, which may guide clinicians and researchers seeking to improve the sexual health of postmenopausal women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Conflict of Interest:

Funding for this research was provided by the National Institutes of Health/National Institute on Aging. Dr. Reed receives research funding from Bayer. Dr. Mitchell has served as a consultant for Scynexis Inc, and receives research funding from Merck. Dr. Huang has previously received funding from Pfizer Inc. and Astellas Pharma through research grants awarded to the University of California San Francisco to conduct research unrelated to this report. All other authors report that they do not have any potential conflicts of interest

Appendix

Appendix A.

Hypothesized correlations between DIVA domain scales and other measures assessing related convergent-divergent constructs at baseline

	DIVA Domain Scales			
Other Measures	**Activities of Daily Living**	**Emotional Well-being**	**Sexual functioning**[a]	**Self-concept & body image**
Most bothersome symptom severity	++	++	++	++
Patient Health Questionnaire-8 (PHQ-8) depression	+	++	+	+
Generalized Anxiety Disorder-7 (GAD-7) score	+	++	+	+
Female sexual function index	.	+	++	+
Female sexual distress scale	.	+	++	+
Menopause-Specific Quality of Life (MENQOL) measures				
Physical	.	.	.	.
Psychosocial	.	++	.	+
Sexual function	.	.	++	.
Vasomotor	+	+	+	+
Vaginal pH	.	.	.	.

	DIVA Domain Scales			
Other Measures	**Activities of Daily Living**	**Emotional Well-being**	**Sexual functioning**[a]	**Self-concept & body image**
Vaginal maturation **value** (<5% superficial cells)	.	.	.	.

++ = moderate-to-strong correlation; + = weak correlation; . = minimal correlation

[a]For the DIVA sexual function scale, only sexually active participants were included.

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Table 1.

Baseline demographic and clinical characteristics of the MsFLASH Vaginal Health Trial participants (n=301)

Participant characteristic	**N**	**%**
Age, years		
< 55	4	1.3%
55 – 59	124	41.2%
60 – 64	111	36.9%
≥ 65	62	20.6%
Years since menopause, mean (SD)	11.8	(6.8)
Surgical menopause	36	12.0%
Race/ethnicity		
White	267	88.7%
African American	12	4.0%
Other/unknown	22	7.4%
Education		
≤ High school diploma/GED	11	3.7%
School after high school	89	29.6%
College graduate	200	66.4%
Current smoking	6	2.0%
Alcohol drinks / week		
0	89	29.6%
>0 - <7	149	49.5%
≥ 7	63	20.9%
Marital status		
Never married	14	4.7%
Divorced / widowed	30	10.0%
Married or marriage-like relationship	257	85.4%
Sexual activity in the past week[a]	117	38.9%
Vaginal pH ≤ 5	39	13.0%
Vaginal Maturation Value (MV), mean (SD)	30.3	(21.2)
Most bothersome symptom		
Vulvar and/or vaginal itching	20	6.6%
Vulvar and/or vaginal soreness	14	4.7%
Vulvar and/or vaginal irritation	19	6.3%
Vaginal dryness	62	20.6%
Pain with vaginal penetration	182	60.5%
Most bothersome symptom severity (range 0–3), mean (SD)	2.5	(0.6)
Any moderate-severe symptom		
Vulvar and/or vaginal itching	165	54.8

Participant characteristic	N	%
Vuvar and/or vaginal soreness	230	76.4
Vulvar and/or vaginal irritation	219	72.8
Vaginal Dryness	285	94.7
Pain with penetration	253	84.1
Urinary incontinence at least a few times a week	86	28.6%
Patient Health Questionnaire-8 (PHQ-8) depression score		
None (0–4)	213	70.8%
Mild (5–9)	70	23.3%
Moderate/Severe (≥10)	18	6.0%
Generalized Anxiety Disorder-7 (GAD-7) score		
None (0–4)	203	70.8%
Mild (5–9)	70	23.3%
Moderate/Severe (≥10)	18	6.0%
Female Sexual function Index (FSFI) score, mean (SD)	15.5	(6.4)
Female Sexual Distress Scale-Revised (FSDS-R), frequency of distress about sex life		
Never/Rarely	45	15.0%
Occasionally	99	32.9%
Frequently/Always	156	51.8%
Menopause-Specific Quality of Life (MENQOL) score, mean (SD)		
Physical	3.0	(1.2)
Psychosocial	2.6	(1.3)
Sexual function	4.9	(2.0)
Vasomotor	2.7	(1.9)

[a]Sexual activity in the past week was assessed at the end of the first week of the trial.

Data were missing for 5 participants for years since menopause, 1 for surgical menopause, 1 for education, 7 for sexual activity in the past week, 5 for vaginal pH ≤ 5, 33 for MV, 4 for most bothersome symptom and severity, 3 for urinary incontinence severity score, 49 for FSFI, 1 for FSDS-R, 3 for MENQOL psychosocial, 5 for MENQOL sexual function, and 1 for MENQOL vasomotor.

Table 2.

Descriptive statistics, item-scale correlations, and internal consistency reliability for the Day-to-day Impact of Vaginal Aging (DIVA) domain scales at baseline

Domain scale	Number of items	Number of subjects	Observed range[a]	Mean (SD) score[b]	Item-scale correlation range	Cronbach's alpha[c]
Activities of daily living	5	300	0.0 – 3.2	0.5 (0.6)	0.67 – 0.82	0.82
Emotional well-being	4	301	0.0 – 4.0	1.1 (0.9)	0.79 – 0.87	0.84
Sexual functioning [d]	5	300	0.0 – 4.0	2.4 (1.0)	0.66 – 0.82	0.83
Self-concept and body image	5	301	0.0 – 4.0	2.5 (1.1)	0.81 – 0.88	0.90

Data were missing for 1 woman for the DIVA emotional well-being scale and 1 woman for the DIVA sexual functioning scale.

[a] Possible score range was 0 to 4 for all DIVA domain scales, with higher scores indicating greater impact c symptoms.

[b] Mean domain scale scores were obtained by averaging the scores of all individual contributing items.

[c] Internal consistency reliability was assessed using standardized Cronbach's alphas, with thresholds of ≤0.60, 0.61–0.70, 0.71–0.80, and >0.80 interpreted as indicating poor, moderate, good, and excellent reliability, respectively.

[d] Analyses were performed using the short-version of the DIVA sexual functioning scale, consisting of five items appropriate regardless of whether women had recently had sexual intercourse.

Table 3.

Observed correlations between Day-to-Day Impact of Vaginal Aging (DIVA) domain scales and other measures assessing related convergent-divergent constructs at

	DIVA Domain Scales							
Measure	**Activities of daily living**		**Emotional well-being**		**Sexual functioning**		**Self-concept and body image**	
	R	**p-value**	**R**	**p-value**	**R**	**p-value**	**R**	**p-value**
Most bothersome symptom severity rating	0.07	0.24	0.26	<0.001	0.29	<0.001	0.25	<0.001
Patient Health Questionnaire-8 (PHQ-8) depression score	0.26	<0.001	0.39	<0.001	0.08	0.18	0.20	<0.001
Generalized Anxiety Disorder-7 (GAD-7) score	0.17	0.004	0.37	<0.001	0.06	0.28	0.20	<0.001
Female Sexual Function Index (FSFI) score	−0.08	0.22	−0.28	<0.001	−0.56	<0.001	−0.45	<0.001
Female Sexual Distress Scale (FSDS) score	0.16	0.004	0.45	<0.001	0.50	<0.001	0.55	<0.001
Menopause-specific Quality of Life (MENQOL) domain score								
Physical	0.32	<0.001	0.32	<0.001	0.14	0.01	0.29	<0.001
Psycho-social	0.30	<0.001	0.47	<0.001	0.13	0.02	0.28	<0.001
Sexual function	0.20	<0.001	0.39	<0.001	0.47	<0.001	0.42	<0.001
Vasomotor	0.22	<0.001	0.16	0.006	0.11	0.05	0.10	0.08
Vaginal pH	−0.07	0.22	−0.08	0.19	−0.01	0.88	0.02	0.77
Vaginal Maturation Value (MV)	0.11	0.08	0.11	0.08	−0.05	0.40	−0.04	0.55

R = Pearson correlation coefficient

Table 4.

Estimated differences (95% CI) in Day-to-Day Impact of Vaginal Aging (DIVA) scores associated with participant characteristics and other measures, adjusted model

Measure	DIVA Domain Scales							
	Activities of daily living		Emotional well-being		Sexual function		Self-concept and body image	
	Difference (95% CI)	p-value	Difference (95% CI)	p-value	Difference (95% CI)	p-value	Difference (95% CI)	p-value
Most bothersome vaginal symptom severity, 1-point difference	0.1 (0, 0.2)	0.08	0.3 (0.1, 0.5)	0.002	0.5 (0.3, 0.7)	<0.001	0.4 (0.1, 0.6)	0.001
Most bothersome symptom: Pain with penetration vs. other symptom	−0.3 (−0.5, −0.2)	<0.001	0 (−0.3, 0.2)	0.68	0 (−0.3, 0.2)	0.86	0.1 (−0.1, 0.4)	0.30
Age, 5-year difference	0 (0, 0.1)	0.31	−0.1 (−0.2, 0)	0.08	−0.1 (−0.2, 0)	0.21	0 (−0.2, 0.1)	0.85
Married, marriage-like relationship vs. non-married	0 (−0.2, 0.2)	0.78	−0.2 (−0.5, 0)	0.09	0.2 (−0.1, 0.6)	0.14	0.1 (−0.3, 0.4)	0.67
Non-white vs. White	0.4 (0.2, 0.6)	<0.001	0.2 (−0.1, 0.5)	0.31	0 (−0.3, 0.4)	0.88	0 (−0.4, 0.4)	0.95
Sexual activity in the past week [a]	0.1 (−0.1, 0.2)	0.39	−0.1 (−0.3, 0.1)	0.38	−0.4 (−0.7, −0.2)	<0.001	−0.3 (−0.5, −0)	0.03
Patient Health Questionnaire-8 (PHQ-8) depression, 5-point difference	0.2 (0.1, 0.3)	0.001	0.4 (0.2, 0.6)	<0.001	0.1 (−0.1, 0.3)	0.42	0.2 (−0.1, 0.4)	0.14
Generalized Anxiety Disorder-7 (GAD-7) score, 5-point difference	0 (−0.1, 0.1)	0.48	0.2 (0, 0.3)	0.02	0 (−0.2, 0.1)	0.75	0.2 (0, 0.4)	0.10
Urinary incontinence a few times a week vs. less	0.1 (−0.1, 0.2)	0.43	0 (−0.2, 0.3)	0.71	0 (−0.2, 0.3)	0.74	−0.1 (−0.4, 0.2)	0.51
Moderate/severe vasomotor symptoms vs. less bothersome/no symptoms	0.1 (0, 0.3)	0.04	0.1 (−0.1, 0.3)	0.37	0.2 (0, 0.5)	0.07	0.2 (0, 0.5)	0.09
Body Mass Index, 5-kg/m^2 difference	0 (0, 0.1)	0.24	0 (−0.1, 0.1)	0.75	0 (−0.2, 0)	0.22	0 (−0.2, 0.1)	0.48

Data are presented as beta coefficients, which correspond to DIVA domain scale score differences between subgroups defined by other measures, with each model adjusted for remaining measures.

[a] Sexual activity in the past week was defined as reporting sexual activity on the first week sexual activity diary.