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Menopause Characteristics and Subjective Symptoms in Women with and without Spinal Cord Injury

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Abstract

Objective—Examine menopause transition characteristics and symptom bother in women with spinal cord injury (SCI).

Design—Prospective cohort (four data collection periods across four years).

Setting—Community.

Participants—Sixty-two women with SCI (injury levels C6 through T12, non-ambulatory and > 36 months post-injury; 86.1% retention) and 66 women without SCI (92.9% retention) with intact ovaries, not using hormone therapy and between the ages of 45 and 60 years volunteered. 505 observations were collected and analyzed.

Interventions—None.

Main outcome measures—Age at final menstrual period (FMP); transitions through menopause status classifications; and menopause symptom bother (vasomotor, somatic, psychological symptoms).

Results—The number of women transitioning through a menopause status classification over the course of the study did not significantly vary by group ($p = 0.263$) nor did age at FMP ($p = 0.643$). Women with SCI experienced greater bother of somatic symptoms (a sub-scale, $p \leq 0.001$), bladder infections ($p \leq 0.001$), and diminished sexual arousal ($p = 0.012$). Women without SCI had significantly greater bother of vasomotor symptoms ($p = 0.020$). There were no significant group by

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menopause status interactions; main effects for menopause status were only significant for vasomotor symptoms and vaginal dryness.

Conclusions—Results suggested that women with SCI experience greater symptom bother in certain areas, but that patterns of symptom bother across menopause and transition through menopause and age at FMP is similar to their peers. Larger studies are needed to examine menopause outcomes with respect to level of injury and completeness of injury. These findings provide a framework that women with SCI and their health care providers can use to address the menopause transition and highlights the importance of multidisciplinary involvement to maximize health and well being during this transition.

Keywords

menopause; spinal cord injuries; paraplegia; quadriplegia; women

Longer life spans of women in the general population suggest many years of life lived postmenopausally and life expectancy after spinal cord injury (SCI) among women suggests that those who sustain SCI in young adulthood or early midlife can also expect to live a number of years postmenopausally.^{1, 2} However, little is known about this transition in these women as the majority of studies in the SCI literature use male samples and from which aging in persons with SCI has been conceptualized.² Menopause research itself has gained momentum only in the last several decades and the majority of studies on menopause have been conducted with Caucasian women drawn from clinic populations^{3, 4} with little to no representation of women with disabilities.⁵ Decision making with respect to the use of hormone therapy or other interventions to manage symptoms, for example, is hampered by a lack of knowledge about their experience and how they make such decisions.⁶ Becker et al.⁷ found that women with disabilities want more information about the use of hormone therapy in menopause; however there have been no clinical trials of interventions to support such decisions. Understanding the menopause transition in women with SCI can make a meaningful contribution to this gap in understanding. Spinal cord injury is not a progressive disease, although its secondary effects may have progressive effects on health. The onset of injury is often a distinct event and there is no evidence to suggest that after an initial period of amenorrhea that post-injury menstruation is altered due to injury.⁸ For women injured in adulthood, after full maturation of the hypothalamic-pituitary-ovarian axis, the transition through menopause can be expected to progress normally.

A model of menopause in the context of spinal cord injury

We have proposed a model of menopause in the context of SCI⁹ reflecting the general hypothesis due to the effects of injury (e.g., temperature dysregulation, neurogenic bowel and bladder, altered sexual response), women with SCI will experience greater severity of symptoms. This model posits that the *pattern* of symptom bother across the menopause will be similar (with peaks during peri-menopause and early postmenopause), but that the *magnitude* of severity for symptoms most closely related to the effects of SCI will be greater for women with SCI.

Vasomotor symptoms, characterized by hot flashes, are the hallmark of menopause and experienced by a majority of women (50–80%^{10, 11}). In women with SCI, vasomotor problems may be exacerbated by thermoregulatory and blood pressure dysfunction.² Sleep disturbance is a common complaint in menopausal women with estimates ranging from 38%¹² to 42%.¹³ In menopausal women with SCI, sleep disturbance has ranged from 20% for those with pre-injury FMP and 43% with post-injury FMP.¹⁴ Sexual interest and frequency tends to decline during menopause with painful intercourse resulting from vaginal dryness due to declines in estrogen.¹⁵ For women with SCI, sexual dysfunction is associated with a diminished sexual

response,¹⁶ and problems with pain, bleeding, vaginal dryness, positioning, spasticity and autonomic dysreflexia.¹⁴ Fatigue has been associated with menopause in American women¹⁷ and cross-culturally.¹⁸ In SCI, fatigue also can be quite common¹⁹ and interfere with functioning²⁰ and self-care.²¹ Depression has been associated with menopause, though its link with estrogen is equivocal.²² The proportion of postmenopausal women with SCI who have reported problems with emotional lability, depression and anxiety has been reported as high as 50%.¹⁴ In general, rates of psychological disturbance in persons with SCI are higher than expected in the general population,²³ although these findings are not always consistent when examined by gender.²⁴

Purpose

The purpose of this study was to examine transitions through menopause status and experience of symptoms (“bother”) in women with SCI compared to their non-SCI peers. We hypothesized that, compared to women without SCI, women with SCI will experience their FMP at the same age and the proportion of women who transition through menopause statuses over the course of the study will be similar by group (hypothesis 1). Our general hypothesis was that women with SCI would report greater symptom bother than women without SCI, but that the pattern of bother across the menopause transition would be similar. Specifically, we hypothesized that women with SCI will have greater bother of vasomotor symptoms (hypothesis 2), somatic symptoms (i.e., somatic symptom sub-scale and symptoms of bladder infections, vaginal dryness, sleep problems, and fatigue; hypothesis 3), diminished sexual arousal and sexual activity (hypothesis 4) and psychological symptoms (e.g., anxiety, depression, worry; hypothesis 5).

METHODS

Participants

This prospective cohort study involved women with and without SCI with a recruitment goal of 60 women in each group. Eligible women were between 45 and 60 years, had intact ovaries and did not use hormone therapy. Women with SCI had injury levels C6 through T12, were primarily non-ambulatory and > 36 months post-injury. Three institutions across the U.S. specializing in SCI care participated in this study; both women with and without SCI were recruited from research registries, clinics and by posting announcements in each institution’s medical centers. The study was approved by each institution’s Institutional Review Board and conducted between 2004 and 2008.

Data collection and measures

Self-report surveys were collected four times, approximately nine months apart, over the duration of the four year study. Assignment of menopause status for menstruating women was based on menstrual cycle characteristics using a prospective menstrual diary²⁵ collected for three months prior to each survey collection. For each monthly diary, women marked the day of the month when bleeding occurred and rated the heaviness of blood flow (spotting to heavy). If no bleeding occurred during a particular month or the menstrual period, this was indicated. Bleeding patterns were used to define menopausal status:⁴ pre-menopause = normal menstrual cycles; peri-menopause = irregular cycles (<21 or >35 days); early postmenopause = first five years after the FMP; and late postmenopause = years thereafter.

The *Mid Life Symptom Checklist* (MLSC)²⁶ was used to examine the subjective experience of vasomotor, somatic and psychological symptoms. Respondents rated 46 items for bother in the previous four weeks on Likert scales ranging from 1 (not at all) to 5 (extremely). The vasomotor sub-scale includes hot flashes and night sweats; the somatic sub-scale includes pain,

incontinence and bladder infections, gastrointestinal discomfort and sexual arousal; the psychological sub-scale includes depressed mood, anxiety, concentration and fatigue. Internal consistency (Cronbach alpha; time 1) high for somatic ($\alpha = 0.879$, 30 items) and psychological ($\alpha = 0.887$, 14 items) subscales; the correlation for the two items of the vasomotor subscale was modest ($r = 0.299$, $p \leq 0.001$).

Statistical analysis

Women completing at least three data collection times were included in the analysis. Because menopause status was integral to testing hypotheses, women completing only one or two data collections were excluded. Descriptives and univariate analysis were used to describe demographic and menopause transition characteristics (hypothesis 1). To examine whether there were significant group differences (controlling for age at study entry) in the proportion of women who transitioned from one menopause status to another, we first used ordinal regression with a five-level outcome: no change, pre-menopausal to peri-menopausal, peri-menopausal to early postmenopause, early to late postmenopause and late postmenopause. However, this approach failed ($X^2 = 19.27$, $p = 0.004$; $df = 6$) the assumption of parallel lines (this assumption refers to factors in the model being equivalent across levels of the dependent factor). We then tested the same model using multinomial regression, which requires less stringent assumptions.

Linear mixed models (LMM) were used to analyze repeated measures data (hypotheses 2, 3, 4 and 5). Six covariance structures were considered for each outcome: compound symmetry, compound symmetry heterogeneous, autoregressive, autoregressive heterogeneous, Toeplitz and Toeplitz heterogeneous. Schwarz's Bayesian Criteria (BIC) was used to identify the best model fit.²⁷ Nine outcomes were modeled in separate LMM analyses to test hypotheses 2, 3, 4 and 5. Because we were interested in the interaction of group (with SCI vs. without SCI) and menopause status classification on each outcome, each model was tested in a hierarchical fashion. The model of main effects only was tested; then the interaction term was added. If the interaction was not statistically significant, the interaction was dropped and the main effects model retained. In this analysis we were most interested in the effect of group and the interaction of group and menopause status on outcomes. Time (categorical for the four data collection periods) was included in the model to control for its effects, but was not of interest in this particular analysis. For each outcome, the main effects model was *group + menopause status + time* and the interaction model was *group + menopause status + time + (group $\times$ menopause status)*. Achieved power for using LMM to test group comparisons (two levels) accounting for within group effects (four levels), interaction of group by menopause status, and $\alpha = 0.05$ was estimated using Power Analysis and Sample Size System (PASS) 2008. SPSS® 16.0 was used to conduct all statistical analyses.

RESULTS

Participant characteristics

Of the 72 women with SCI who were enrolled, 60 completed all four data collection times and two completed three data collection times (86.1% retention); of the 71 women without SCI who were enrolled, 61 completed all four data collection times and five completed three data collection times (92.9% retention). Reasons for missing follow up periods were primarily surveys that were not returned and women who could not be reached via telephone or mail to complete follow ups. A total of 505 observations were collected and analyzed. There were no significant differences in retention rates between groups and the recruitment goal was met. Achieved power was estimated to be 93% (95% CI: 86%, 97%). Demographic and injury characteristics are given in table 1.

Hypothesis 1: Menopause transitions and age at FMP

At study entry, there were no significant differences between women with and without SCI for menopause status (table 2). Transitions between menopause statuses over the course of the study occurred in 54 (42.1%) women (26 women with SCI and 28 without SCI) with no significant group differences ($X^2 = 0.033$, $p = 0.856$; $df = 1$). Specific transitions between each menopause status did not significantly vary between groups ($X^2 = 5.24$, $p = 0.263$; $df = 4$). Fourteen women experienced their FMP during the course of the study (5 women with SCI, 7 women without SCI) with no significant group differences for age at FMP (see table 2). These results fully supported hypothesis 1.

Symptom bother ratings, averaged across all time periods for each outcome for each group, are given in table 3. Estimates for model testing are given in table 4; when factors were significant for any outcome, results are also displayed graphically.

Hypothesis 2: Bother of vasomotor symptoms

Contrary to expectations, women with SCI had significantly less bother of vasomotor symptoms than women without SCI. There also was a significant effect of menopause status on vasomotor symptoms such that women in early postmenopause were significantly more bothered than those in late postmenopause. There was no significant interaction effect. Thus, hypothesis 2 was partially supported by a lack of significant interaction effect; while there was a significant group difference, it was in the reverse as expected (figure 2).

Hypothesis 3: Bother of somatic symptoms

Women with SCI had significantly greater bother of overall somatic symptoms (figure 3) and bladder infections (figure 4), but there were no significant group differences for vaginal dryness, sleep problems, or fatigue. There was a main effect of menopause status on vaginal dryness (figure 5) with bother ratings increasing across the menopause transition. There was no menopause status effect on bladder, sleep problems or fatigue. There were no significant interactions for any of the somatic outcomes. Thus hypothesis 3 was partially supported by some significant group differences and no interaction effect. The lack of a significant main effect of menopause status for all but vaginal dryness suggested a lack of specificity of these symptoms for menopause in this sample.

Hypothesis 4: Bother of diminished sexual arousal and sexual activity

Women with SCI had a significantly greater bother of diminished sexual arousal than women without SCI. There also was a main effect for menopause status such that peri-menopausal women had greater bother of diminished sexual arousal compared to late postmenopausal women (figure 6). There were no significant group or menopause status main effects for bother of diminished sexual activity. For both outcomes there was no significant interaction of group by menopause status. Thus hypothesis 4 was partially supported by the group difference for arousal and no interaction effect for either outcome. The significant main effect of menopause status for diminished sexual arousal suggests some specificity for menopause in this sample, but not for sexual activity.

Hypothesis 5: Bother of psychological symptoms

There was no significant main effect for group or menopause status or interaction effect for bother of psychological symptoms. Thus hypothesis 5 was partially supported only by a lack of interaction effect of group by menopause status. The lack of significant main effect for menopause status suggested a lack of specificity of psychological symptoms for menopause in this sample.

DISCUSSION

Results suggest that in some ways women with SCI experience greater symptom bother, but that patterns of symptom bother across menopause and transition through menopause is similar to their peers. In this study, the age at FMP was similar to women without SCI in this sample as well as the general population of American women (51 years). The age at FMP of women with SCI is several years later than reported by Jackson et al.,¹⁴ who also found age at FMP was not significantly different for those had their FMP before or after injury. An underestimation bias of recall of the age at FMP has been found in previous research²⁸ and may explain these differences to some extent. Transitions through menopause stages over the course of the study also were similar for women with and without SCI.

With respect to symptom outcomes, there were fewer group differences than hypothesized. As expected, bother of somatic symptoms, bladder infections and diminished sexual arousal were significantly greater among women with SCI and most closely related to the effects of SCI. For somatic symptoms and bladder infections, there was no effect of menopause status suggesting that these symptoms are not particularly specific for menopause; rather, for this sample, these are most likely due to the presence of SCI and not menopause. Significant main effects for menopause status for vasomotor symptoms and vaginal dryness in this sample are consistent with declines in estrogen in menopause^{10, 29–31} and suggest some specificity for menopause for this sample.

Bother of diminished sexual arousal was significantly higher for women with SCI than women without SCI. This was expected given a diminished sexual response after injury, such as the ability to achieve orgasm.¹⁶ This is also consistent with other findings that sexual desire is significantly lower in women with SCI compared to age-matched peers with a substantial decline in desire after injury compared to pre-injury levels.³² In our study there also was a significant main effect for menopause status consistent with the literature on sexual arousal and menopause.³³ This finding suggests that for menopausal women with SCI in this study, diminished sexual arousal is likely attributable to the injury and menopause.

Unlike arousal, bother of diminished sexual activity was similar between both groups and across the menopause transition. This is consistent with other findings that many women with SCI engage in sexual activity after injury.^{14, 32} The lack of main effect for menopause status is also consistent with other findings that frequency of intercourse is not associated with menopause status when controlling for demographic characteristics and partner status,³⁴ although this is not a consistent finding.³⁵ Sexual arousal and activity are important issues for all women during the menopause transition and unfortunately our data are limited to address the reasons for these differences and similarities in bother ratings between women to distinguish between the effects of injury on physiology of sexual functioning and the opportunity for engaging in sexual activity and other related social factors.

Vasomotor symptom bother was significantly higher for women without SCI, contrary to expectations. It may be that women with SCI are simply less bothered by them (although we did not measure their frequency or intensity) or attribute them solely to the effects of SCI. It may also be the case that phrasing of “bother” accounts, in part, for this difference. Women with SCI may more often contend with temperature dysregulation, for some long before the menopause transition begins, and vasomotor symptoms may become less noticeable or bothersome.

The lack of a main effect for menopause status on six out of nine outcomes points to the lack of specificity for menopause of general somatic symptoms, sleep problems, fatigue, sexual activity and psychological symptoms. The lack of group differences for psychological symptoms in this study is somewhat surprising given the literature on high rates of

psychological co-morbidity among persons with SCI.²³ However, much of this literature is conducted in predominantly male samples and our previous work suggests men, not women, may be more vulnerable to depression, for example than their peers in the general population.³⁶ A lack of specificity for menopause among many symptoms commonly associated with the menopause transition has been found in previous research comparing midlife women and their male peers.³⁷ Our findings suggest that in planning future menopause studies with this population should carefully select those symptoms most closely aligned with menopause.

By modeling not only main effects of menopause status but also the interaction of group by menopause status, we are able to examine the contribution of SCI to the experience of menopause. The interaction captures the extent to which the *pattern* of symptom bother (e.g., peaks and valleys or stable) across the menopause transition is consistent between groups. This finding strongly supports the element of the conceptual model positing that *whatever* the effects of menopause status on the experience of symptom bother, it will be largely the same for women with and without SCI. Difference in the *degree or magnitude* of symptom bother between groups reflected in the conceptual model was only partially supported by results. This suggests that despite the injury, women with SCI in this sample do not differ much from their peers as we might expect for these experiences. It is likely that other domains of midlife, such as family responsibilities, work demands, or caring for aging parents, affect high rates of sleep problems and fatigue in women, irrespective of the presence of disability.

Clinical implications

Findings from this study provide the start of an empirical framework that women with SCI and their health care providers can use to address menopause issues as they arise in midlife. Our results suggest that changes a woman with SCI may begin to experience in midlife such as hot flashes, vaginal drying or diminished sexual arousal are likely to be related both the menopausal transition and SCI. Moreover, even if some symptom outcomes did not vary between groups, this does not mean that the *impact* of certain symptoms will also be similar or that interventions to manage symptoms will be equally efficacious without further empirical investigation. These issues highlight the need for multidisciplinary involvement and good communication of gynecological and psychiatry providers.

Study limitations

Women who participated in this study were primarily well educated and Caucasian, one of the major limitations of menopause research in general and likely due to the areas of the country where this research was conducted. Retrospective surveys introduce recall bias which can inflate or minimize subjective ratings. The symptom scale itself may be limited in its specificity for symptoms related to menopause, though this is a common limitation in many menopause studies. Measurement of hot flashes did not include frequency or intensity which limits the extent to which we can interpret the effect of this symptom. We did not collect information about the extent to which symptoms were present or has resolved prior to study entry. The use of menstrual diaries for the assignment of menopausal status is limited by the interpretation of the menstrual patterns by investigators and age at FMP prior to study entry may also be inaccurate in some cases. Finally, there was not adequate power to test outcomes with respect to level or completeness of SCI or include factors such as the influence of education, ethnicity and socioeconomic status.

Future Directions in Research

Given only partial support for our conceptual model, further examination and modification is warranted. Larger studies with adequate power are needed to examine outcomes with respect to level of injury and completeness of injury. No studies have yet to be conducted on the efficacy of interventions to treat menopause symptom bother in this population. There may also be a

benefit to examining symptom profiles using techniques like cluster analysis as such profiles may point to important intersections of SCI and menopause not captured using a group comparisons and may assist in clinical decision making. This study's findings related to sexual arousal and activity raise a number of interesting questions related to midlife women with SCI and their sexuality that can be pursued. Adaptation to health conditions related to SCI is another key dimension not addressed in this study, but with important implications for understanding symptom experience and the impact of the menopause transition. Finally, this study presents a methodological and conceptual foundation for future investigations for other women with disabilities.

Conclusions

By including both women with SCI and their peers without SCI and using a prospective design, we are able to gain a greater understanding of the experience of menopause among women with SCI. While there were significant differences for symptoms most closely aligned with injury, transitions through menopause status, age at FMP and similar patterns of symptoms across the transition suggest that in important ways, women with SCI experience menopause similarly to their peers without SCI. Our results point to a number of areas for new research to pursue to fill gaps in knowledge to maximize the health and well being of women with SCI along the lifespan.

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Hypothesis 1
(transition through menopause status and age at FMP similar)

Figure 1.
Conceptual Model of Symptom Bother in the Context of SCI

Figure 2.
Vasomotor symptoms

Figure 3.
Somatic sub-scale

Figure 4.
Bladder infections

Figure 5.
Vaginal dryness

Figure 6.
Sexual Arousal

Table 1

Demographic and injury characteristics

	Women with SCI (N = 62)	Women without SCI (N = 66)	Test, p value; df; [95% C.I.]
Current age (M ± SD)	51.82 ± 4.42	51.75 ± 4.10	$t = 0.10, p = 0.920; df = 126;$ C.I.: -1.41, 1.56
Caucasian (%)	52 (83.3)	60 (90.9)	N.S.
Married (%)	33 (53.2)	35 (53.0)	N.S.
Some college or more (%)	57 (91.9)	64 (97.0)	N.S.
Employment (full or part-time; %)	35 (56.5)	62 (93.9)	$\chi^2 = 24.47, p < 0.001; df = 1$
Body mass index (M ± SD)*	25.4 ± 5.58	27.95 ± 6.01	$t = -2.50, p = 0.013; df = 126;$ C.I.: -4.60, -0.542
Years post injury (M ± SD)	30.76 ± 12.29	N.A.	N.A.
Age at injury (M ± SD) [†]	31.26 ± 11.73	N.A.	N.A.
Level of injury (tetraplegia, paraplegia; %)	21 (33.9) and 42 (66.1)	N.A.	N.A.
Completeness of injury (complete, incomplete; %)	37 (59.7) and 19 (30.6) [‡]	N.A.	N.A.

* Averaged across all time points

[†] One outlier dropped (injured at birth)

[‡] Missing data for six women with SCI

N.S. = not significant

N.A. = not applicable

Table 2**Menopause Status Distributions and age at FMP**

	Women with SCI N = 62	Women without SCI N = 66	Significance
Menopause status at study entry			
Pre-Menopausal (N, %)	18 (29.5)	11 (16.7)	$\chi^2 = 2.94, p = 0.401,$ $df = 3$
Peri-Menopausal (N, %)	13 (25.4)	18 (27.3)	
Early postmenopausal (N, %)	21 (35.5)	27 (40.9)	
Late postmenopausal (N, %)	9 (15.5)	10 (15.2)	
Transitions during study period			
No change (N, %) [§]	28 (45.2)	30 (45.5)	$\chi^2 = 5.24, p = 0.263,$ $df = 4$
Pre-menopause to peri-menopause (N, %)	14 (22.6)	8 (12.1)	
Peri-menopause to early postmenopause (N, %)	5 (8.1)	7 (10.6)	
Early postmenopause to Late postmenopause (N, %)	7 (11.3)	14 (21.2)	
Late postmenopause (N, %)	8 (12.9)	7 (10.6)	
Age at FMP (M $\pm$ SD; N)	50.06 $\pm$ 5.8; N = 37	49.47 $\pm$ 5.6; N = 44	$t = 0.465, p = 0.643;$ $df = 79; 95\% \text{ C.I.: } -1.936, 3.118$

[§]No change refers only to pre-menopausal, peri-menopausal and early postmenopausal classifications; late postmenopause status cannot change and is shown in the last category.

Table 3

Mean bother ratings and frequency* of symptom outcomes

Symptom outcome*	Women with SCI Mean bother rating (SD) Frequency (%)				Women without SCI Mean bother rating (SD) Frequency (%)			
	Pre-menopause	Peri-menopause	Early PM	Late PM	Pre-menopause	Peri-menopause	Early PM	Late PM
Vasomotor (subscale)	2.36 (0.9) NA	2.83 (1.3) NA	3.15 (1.5) NA	2.73 (1.2) NA	2.83 (1.1) NA	3.48 (1.6) NA	3.73 (1.8) NA	2.85 (1.4) NA
Somatic (subscale)	55.90 (13.3) NA	50.17 (16.2) NA	53.72 (14.5) NA	57.13 (1.6) NA	42.13 (8.3) NA	44.57 (10.4) NA	45.25 (10.8) NA	44.26 (10.5) NA
Psychological (subscale)	23.9 (8.9) NA	25.03 (8.3) NA	26.3 (8.4) NA	31.16 (9.8) NA	25.22 (5.8) NA	24.12 (6.9) NA	24.82 (7.6) NA	23.74 (7.3) NA
Bladder infections	1.67 (1.0) 44.9	1.91 (1.1) 42.4	1.86 (1.1) 45.9	1.68 (1.0) 40.0	1.0 (0.0) 0.0	1.11 (33.6) 9.6	1.10 (0.4) 6.7	1.03 (0.2) 3.4
Vaginal dryness	1.30 (0.6) 24.2	1.42 (0.8) 27.3	1.69 (0.9) 45.9	1.73 (1.1) 41.7	1.30 (0.7) 21.7	1.47 (0.8) 32.9	2.05 (1.3) 49.5	20.3 (1.3) 54.2
Sleep problems	2.33 (1.0) 75.8	2.35 (1.1) 74.4	2.26 (1.1) 68.2	2.90 (1.0) 86.0	2.17 (1.0) 69.6	2.42 (1.2) 69.9	2.35 (1.1) 76.9	2.32 (1.1) 74.6
Fatigue	2.48 (1.0) 90.9	2.49 (1.1) 83.3	2.65 (1.1) 63.5	3.10 (1.0) 96.0	2.48 (0.7) 95.7	2.53 (1.2) 75.3	2.46 (1.0) 88.5	2.32 (1.0) 78.0
Diminished sexual arousal	2.59 (1.5) 60.2	2.01 (1.3) 47.4	2.39 (1.4) 63.5	3.17 (1.6) 74.0	1.57 (0.8) 43.5	1.92 (1.0) 58.9	2.01 (1.1) 52.9	2.09 (1.3) 54.2
Diminished sexual activity	2.59 (1.5) 63.6	2.03 (1.3) 44.9	2.43 (1.4) 62.4	2.65 (1.4) 62.0	1.70 (1.1) 39.1	1.92 (1.1) 50.7	2.07 (1.3) 49.0	2.40 (1.5) 59.3

* Aggregated across all time periods; frequencies of bother ratings 2 ("a little") and above only Bladder infections, vaginal dryness, sleep problems, fatigue, diminished sexual arousal and activity ratings range from 1 (not at all) to 5 (extremely); PM = postmenopause; NA = sub-scale scores do not have frequency ratings

Table 4

Effects of Group, Menopause Status, Time and Group by Menopause Status on Symptom Bother

Outcome (Compound symmetry covariance structure used for each outcome)	Group* (without SCI is referent) <i>Estimate (SE) / p val.</i> [C.I.]	Menopause Status* (Late postmenopause is referent) <i>Estimate (SE) / p val.</i> [C.I.]	Time* (Time 4 is referent) <i>Estimate (SE) / p val.</i> [C.I.]	Group × Menopause Status* <i>Estimate (SE) / p val.</i> [C.I.]
Vasomotor subscale	-0.306 (0.14) / 0.020 [-0.585, -0.287]	Early Postmenopause 0.324 (0.14) / 0.032 [0.058, -0.027]	0.877	0.284
Somatic subscale	0.691 (0.15) / ≤0.001 [0.380, 0.996]	0.921	0.223	0.625
Psychological subscale	0.093	0.663	0.043 [†]	0.399
Bladder infections	0.823 (0.13) / ≤0.001 [0.567, 1.08]	0.696	0.497	0.904
Vaginal dryness	0.187	Pre-Menopause -0.507 (0.18) / 0.007 [-0.872, -0.141] Peri-Menopause -0.460 (0.15) / 0.003 [-0.758, -0.161]	0.923	0.669
Sleep problems	0.684	0.400	0.179	0.518
Fatigue	0.145	0.551	0.116	0.507
Diminished sexual arousal	0.379 (0.15) / 0.012 [0.085, 0.673]	Peri-Menopause -0.351 (0.16) / 0.026 [-0.659, -0.043]	0.458	0.249
Diminished sexual activity	0.131	0.230	0.320	0.359

* Estimates represent the change in outcome variable with one unit change in predictor; estimates are presented in the outcome units (z-scores); C.I. = 95% confidence interval for the difference; significant post-hoc testing is bolded; only p-values (Type III fixed effects) are reported for non-significant estimates

[†] Type III F test for fixed values was significant, but within category testing was non-significant