

Supplementary Table 1. [Elements-Questions](#) related to menopause in the CLIMB Epidemiologic Survey.

Q7. Have your ovaries been surgically removed?		<input type="checkbox"/> ONE <input type="checkbox"/> BOTH	<input type="checkbox"/> NO	____/____ (Month/Year)	Reason:			
Q8. Has your uterus been surgically removed?		<input type="checkbox"/> YES	<input type="checkbox"/> NO	____/____ (Month/Year)	Reason:			
Q9. When was your last menstrual period?		____/____ (Month / Year of last period)						
Q10. Do you think you have started menopause?		<input type="checkbox"/> YES		<input type="checkbox"/> NO <i>Please move to next page</i>				
Q11. Was the onset of menopause associated with the following?		Radiation	<input type="checkbox"/> YES Date of radiation ____/____		<input type="checkbox"/> NO			
		Chemotherapy	<input type="checkbox"/> YES Name: _____ Date ____/____		<input type="checkbox"/> NO			
Q12. When did you first experience symptoms of menopause?		Hot flashes (month/year):			____/____			
		Irregular menstrual periods (month/year):			____/____			
Q12. Have you ever taken hormone replacement therapy (HRT) for menopausal symptoms? If YES, please fill in details below for each type.				<input type="checkbox"/> YES	<input type="checkbox"/> NO <i>Please move to next page</i>			
Hormone Therapy (HRT)	Brand Name (Fill in)	Route of administration (choose: gel, cream, patch, pill, suppository)					Start date (Month/Year)	Stop Date (Enter "Current" if still taking)
Estrogen		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Estrogen+Progesterone		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Testosterone		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Raloxifene (Evista)		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Phytoestrogens (soy estrogens)		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Black cohosh		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____
Other:		<input type="checkbox"/> gel	<input type="checkbox"/> cream	<input type="checkbox"/> patch	<input type="checkbox"/> pill	<input type="checkbox"/> suppository	____/____	____/____

Supplementary Table 2. Comparison of demographic and clinical characteristics between survey respondents and CLIMB subjects fulfilling study inclusion criteria who [chose not to, or](#) did not yet, complete the survey.

	Completed survey	Did not complete survey	p-value
N	724	486	
Age at last clinic visit (mean (SD))	49.3 (11.4)	46.9 (11.8)	<0.001
Age at first symptom (mean (SD))	33.7 (9.9)	32.6 (10.1)	0.052
White (%)	93.0	91.0	0.23
Hispanic (%)	3.6	5.8	0.087
EDSS (median (range))	2 (0, 9.5)	2 (0, 9)	0.89
Disease category (%) (CIS, RR, SP, PP, PR)	4.6 / 77.1 / 14.2 / 3.0 / 1.1	4.1 / 77.0 / 15.4 / 2.3 / 1.2	0.89

At the time of the study (7/1/2014), 60% CLIMB subjects had completed the survey.

Supplementary Table 3. Demographic and menopause characteristics of study subjects contributing to the primary inflection point analyses.

	Natural menopause	Surgical menopause
N (% total in table)	101 (35.4)	23 (9.4)
Age at last clinic visit, years (mean (SD))	55.9 (4.7)	50.8 (4.5)
Age at first symptom, years (mean (SD))	38.3 (8.5)	33.7 (6.7)
White (N (%))	99 (98.0)	21 (91.3)
Hispanic (N (%))	1 (1.0)	1 (4.3)
Disease category (CIS, RR, SP, PP, PR) (N (%))	3, 80, 13, 2, 1 (3.0, 80.8, 13.1, 2.0, 1.0)	0, 17, 5, 0, 1 (0.0, 73.9, 21.7, 0.0, 4.3)
EDSS at last clinic visit (mean, (SD))	2.2 (2.0)	2.8 (2.4)
Reported age at menopause, years (mean (SD))	51.0 (4.1)	45.3 (5.6)
Ever-use any form of HRT (N (%))	8 (8.2)	2 (14.3)
Ever-use systemic E or E+P HRT within 3 years of menopause (N (%))	5 (5.2)	2 (14.3)
<u>Follow-up time pre-menopause (mean (SD))</u>	<u>5.3 (3.2)</u>	<u>5.5 (3.6)</u>
<u>Follow-up time post menopause (mean (SD))</u>	<u>5.0 (3.1)</u>	<u>5.5 (3.3)</u>

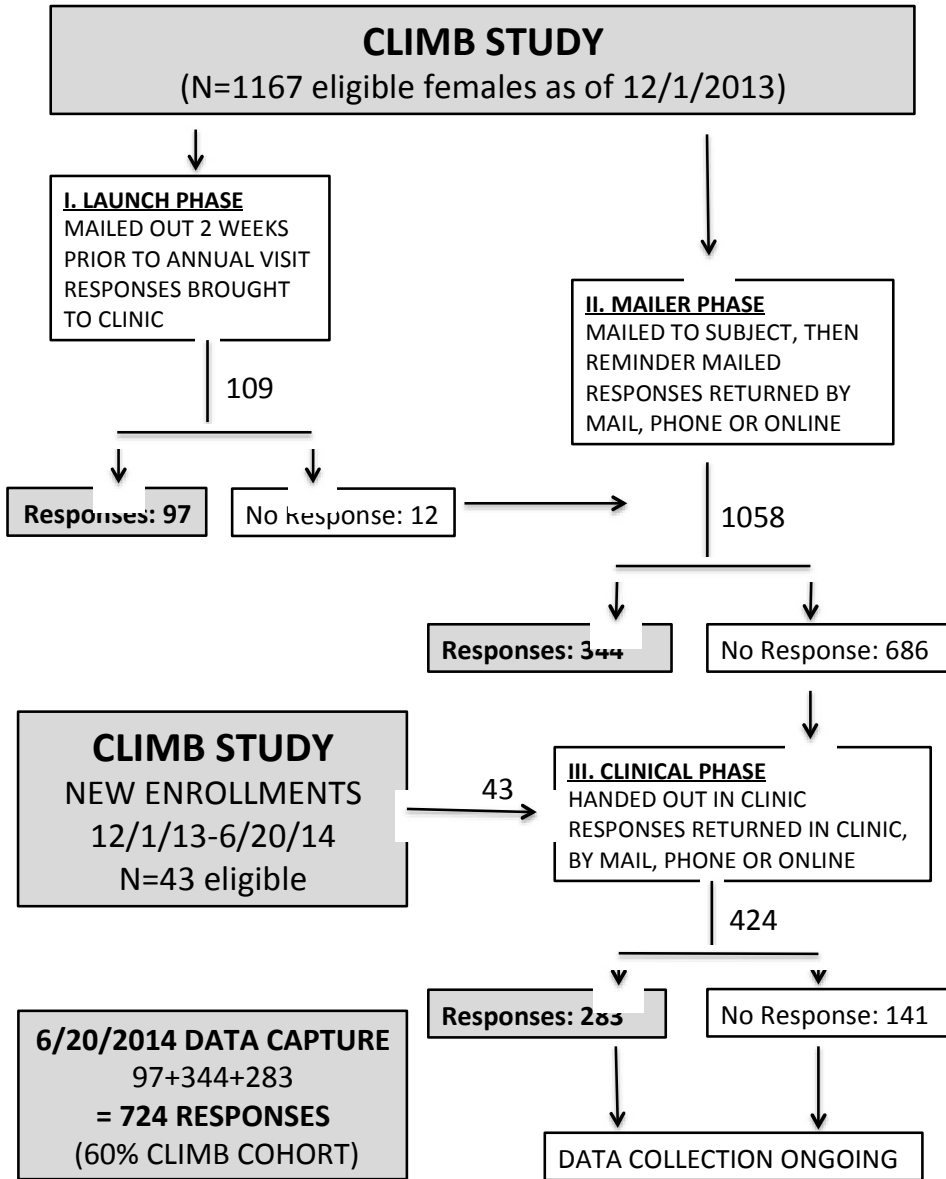
Supplementary Table 4. Effect of Menopause on Patient-Reported Outcome Measures in a subset of 70 women followed prospectively through their menopausal transition.

	Analysis 1: Inflection point analysis* (n=70)	Range
SF-36: Physical functioning	-0.23 (0.32)	<u>(13.1, 56.8)</u>
SF-36: Role physical	-0.53 (0.17)	<u>(26.0, 55.6)</u>
SF-36: Bodily pain	-0.073 (0.80)	<u>(18.0, 60.4)</u>
SF-36: General health	-0.59 (0.017)	<u>(19.1, 63.8)</u>
SF-36: Vitality	-0.048 (0.87)	<u>(20.7, 68.7)</u>
SF-36: Social functioning	-0.43 (0.11)	<u>(12.6, 57.3)</u>
SF-36: Role emotional	0.026 (0.94)	<u>(25.4, 55.7)</u>
SF-36: Mental health	-0.26 (0.36)	<u>(15.1, 64.0)</u>
SF-36: Physical composite score	-0.39 (0.15)	<u>(13.7, 67.6)</u>
SF-36: Mental composite score	-0.070 (0.80)	<u>(16.5, 65.6)</u>
MFIS	-0.96 (0.025)	<u>(0, 84)</u>
CES-D	0.063 (0.78)	<u>(20, 71)</u>

*Estimated change in slope after menopause (p-value). Inflection point model included only random intercept and slope due to problems with estimation in model including random intercept, slope and change in slope.

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Supplementary Figure 1. Reproductive Survey Completion Rates.



Supplementary Figure 2. Distribution of Age at Natural Menopause in a large clinical cohort of women with MS.

Legend: Kaplan-Meier curve depicting time to menopause in 668 subjects. Median age at last menstrual period is 51.5 years. A subset of postmenopausal subjects (n=56) did not provide a date for final menstrual period and thus did not contribute to this analysis.

