



# Advancing Stage of Female Reproductive Life Associated with Bipolar Illness Exacerbation



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## ABSTRACT

**Introduction:** Perimenopause confers an increased risk of depression in the general population, yet bipolar disorder mood course remains unknown.

**Methods:** Clinic visits in 519 premenopausal, 116 perimenopausal including 13 women transitioning from peri- to postmenopause, and 133 postmenopausal women with bipolar disorder who received naturalistic treatment in the multisite STEP-Bipolar Disorder study over 19.8±15.5 months were analyzed for mood state.

**Results:** Advancing female reproductive stage was significantly associated with percent of visits decreasing in euthymia (29.3%, 27%, 25%, respectively, p<0.05) decreasing in syndromal mood elevation (5.3%, 4.1%, and 3.0%, respectively, p<0.001). Thirteen women transitioning from peri- to postmenopause had a significantly greater proportion of visits in syndromal depression (24.4%, p<0.001) compared to premenopausal, perimenopausal and postmenopausal women, while depression in the latter three groups (18.1%, 18.1%, and 19.3%, respectively) did not differ.

**Conclusions:** Advancing stage of female reproductive life was associated with bipolar illness exacerbation. Women transitioning from peri- to postmenopause had significantly greater depression than other female reproductive groups.

## BACKGROUND

Well designed prospective studies report that women from the population are at increased risk of depression during the menopausal transition or early post menopause. Small studies have looked at the risk of mood episodes during the menopausal years in women with bipolar disorder but did not report menstrual status.

This study reports on advancing stage of female reproductive life associated with bipolar illness exacerbation highlighting illness course in women transitioning from late peri- to early postmenopause.

## METHODS

**Subjects:** Consented reproductive age women (28-38 year olds, <60day menstrual cycle), late menopausal transition women (42-60yo, menstruated between 60-365days) and postmenopausal women (>42 yo, >365days since menstruation) with bipolar I, II, NOS or schizoaffective do were selected from prospectively collected systematic clinical data from the multi-site STEP-BD. 13 women transitioned from late to post menopause.

**Procedure:** Mood state at each clinic visit was categorized by DSM-IV criteria as major depression, mood elevation (hypomania or mania), symptomatic (>2 symptoms of depression or mood elevation but not meeting criteria) or euthymic (<2 pervasive mood symptoms).

**Analysis:** The three reproductive groups plus the 13 transition women were evaluated for differences in the proportion of clinic visits meeting DSM-IV criteria for major depressive episode, syndromal mood elevation, or euthymia by chi square analysis.

## RESULTS

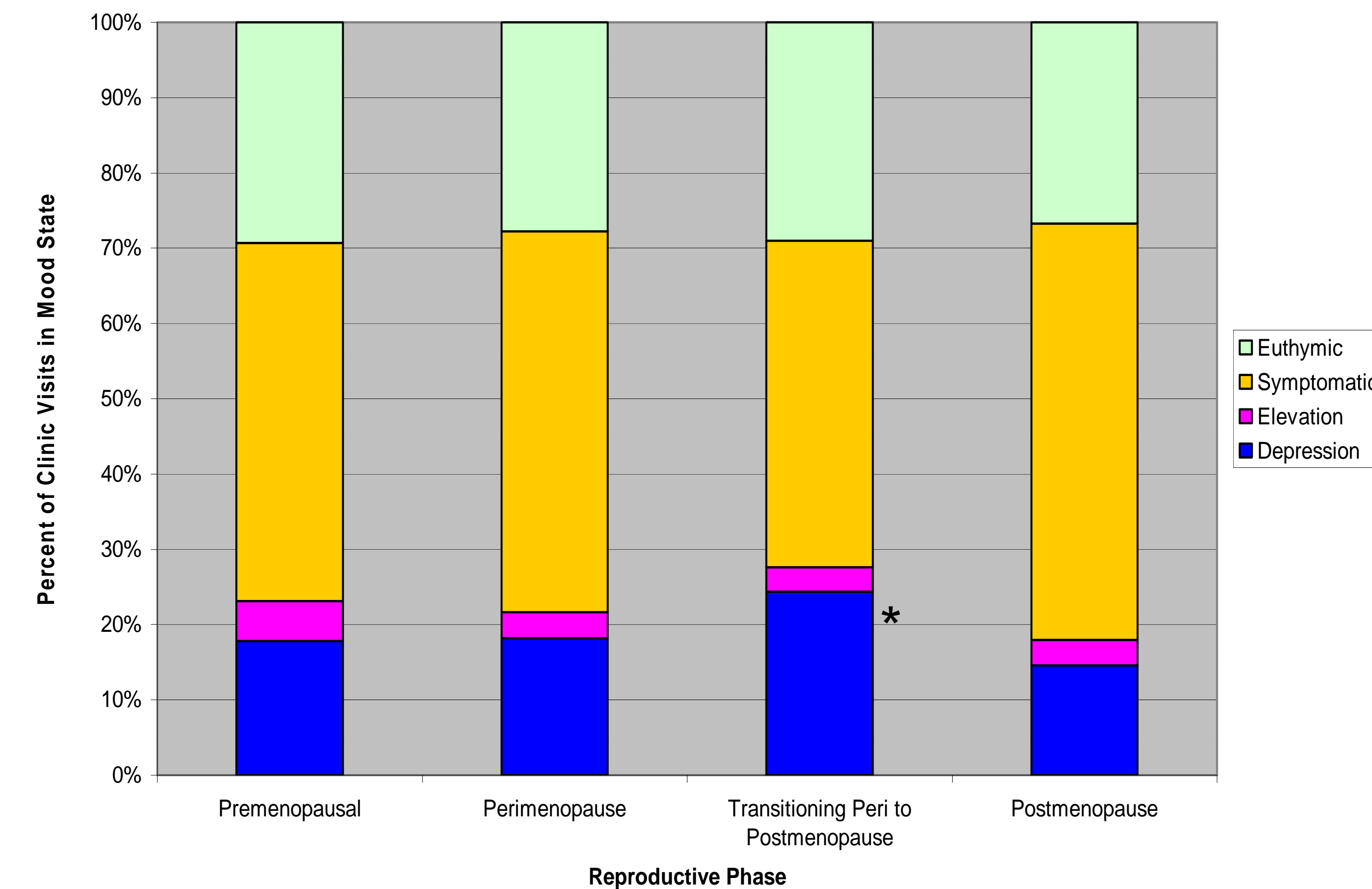
Table 1 Subject Characteristics

	Premenopause (n=519)	Perimenopause (n=116)	Postmenopause (n=133)	Combined (n=768)	P-value
	N (%)	N (%)	N (%)	N (%)	
<b>Number of Observations</b>	5989	2046	1925	9960	
<b>Race: Caucasian</b>	460 (89)	102 (88)	119 (89)	681 (89)	0.046
<b>Bipolar Diagnosis</b>					0.79
Bipolar I	317 (61)	67 (58)	87 (65)	471 (61)	
Bipolar II	166 (32)	42 (36)	37 (28)	245 (32)	
Bipolar NOS	31 (6)	5 (4)	8 (6)	44 (6)	
Schizoaffective Disorder	5 (1)	2 (2)	1 (1)	8 (1)	
<b>Rapid cycling</b>					0.059
Yes	160 (31)	39 (34)	35 (26)	234 (30)	
No	152 (29)	34 (29)	57 (43)	243 (32)	
<b>Current Substance Abuse</b>	14 (3)	3 (3)	1 (1)	18 (2)	0.32
<b>Anxiety Diagnosis</b>	201 (39)	44 (38)	30 (23)	275 (36)	0.002
<b>HT/OCP Use</b>	65 (13)	20 (17)	49 (37)	134 (17)	<.0001
	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>P-value</b>
<b>Months in Clinic</b>	17.29 (14.23)	28.65 (17.0)	22.15 (15.7)	19.84 (15.5)	<.0001
<b>Average # Visits/month</b>	0.86 (0.67)	0.72 (0.44)	0.78 (0.55)	0.82 (0.62)	0.056

Transitioning peri to post women had significantly greater depression (24.4±18%) than pooled women  $X^2(3, N = 9960) = 19.8, p < 0.0002$

## RESULTS

Proportion of Clinic Visits in Mood State by Reproductive Phase in Women with Bipolar Disorder



Advancing Reproductive Stage was associated with:  
**Mood elevation:** significant decline ( $X^2=19.5, df=2, p<0.0001$ ) seen by paired comparisons: pre vs peri ( $X^2=4.9, df=1, p<0.03$ ), peri vs post ( $X^2=2.4, df=1, p<0.06$ ); pre vs post ( $X^2=17.4, df=1, p<0.0001$ ).  
**Euthymia:** significant decline ( $X^2=7.6, df=2, p<0.02$ ).  
**Major depression:** no significant difference ( $X^2=1.6, df=2, p<0.4$ ).  
**Symptomatic:** significant increase ( $F(2, N=768) 3.0, p=0.05$ ).

## CONCLUSION

Advancing reproductive age was associated with worse illness course (more symptoms, less euthymia), less mood elevation, and no significant change in depression. However the 13 women who transitioned from peri to postmenopause had significantly greater depression than the other groups. Limitations of this study include missing age and menstrual cycle data, and lack of hormonal assessment. Future work will include analyzing if hormone therapy use, history of menstrual cycle and/or postpartum mood exacerbation are associated with risk of mood episodes.