ORIGINAL STUDY

Depression, hormone therapy, and the menopausal transition among women aged 45 to 64 years using Canadian Longitudinal Study on aging baseline data

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Abstract

Objective: To investigate the association between menopausal status, hormone therapy (HT) use and the presence of depressive symptoms among middle-aged women in Canada.

Methods: Cross-sectional baseline data from 13,216 women aged 45 to 64 years from the Canadian Longitudinal Study on Aging (CLSA) was used. The association between menopausal status (pre- vs postmenopausal) and self-reported symptoms of depression based on a score of 10 or more on the Center for Epidemiologic Studies Short Depression Scale-10 was assessed using logistic regression. Use and duration of use of HT, time since menopause, age at onset of menopause, and socioeconomic status and other contextual variables were explored for the association with depression.

Results: Overall, 18.4% of middle-aged women in the CLSA data were identified as depressed using the Center for Epidemiologic Studies Short Depression Scale-10. Based on the logistic regression models, women reporting premature menopause (before the age of 40 years) and postmenopausal women currently using HT had 1.45 (1.07-1.97) and 1.21 (1.02-1.44) greater odds of having depression. Chi-square analyses showed that women with depressive symptoms were more likely to have low education, low household incomes, live alone, be nulliparous, and have low social support.

Conclusions: Our findings highlight the association between depression and premature menopause among midlife women. Current HT use may be a proxy for more severe menopausal vasomotor symptoms, a known risk factor for depressive symptoms. Identification of risk factors, including social determinants of health, age at menopause, and menopausal symptoms can help guide clinicians when assessing mental health.

Key Words: Depression – Hormone replacement therapy – Menopause.

Video Summary: http://links.lww.com/MENO/A576.

Women experience a higher level of mental health morbidity as compared to men over the life course.[1] A particularly vulnerable time for women occurs during the menopausal transition, which is marked by drastic fluctuations in sex hormones.[2] This transition is often accompanied by the occurrence of significant life stressors and changes in personal, family, and professional responsibilities.[3,4] A growing body of literature has suggested

that, for some women, the perimenopause and the early postmenopausal years are associated with an increased risk of experiencing symptoms of depression and the development of an episode of major depressive disorder.[5] Depression can be a disabling condition and can lead to significant personal, economic, and societal costs. Although the physiological health consequences of menopause have been relatively well-characterized in the existing literature, the specific influence on mental well-being during this time is less clear.

As the baby boom generation reaches midlife, a large number of women are now postmenopausal in Canada. It is important for health care providers to understand the *window of vulnerability* for depressive symptoms among mid-life women.[6] In particular, the menopause transition, which occurs 2 to 3 years before the final menstrual period, and the early postmenopausal years have been associated with an increased risk for depressive symptoms as well as a twofold risk for major depressive disorder among women.[7-9] Endogenous estrogens are known to modulate systems that are critical for mood regulation[5,10] but the therapeutic benefit of hormone therapy (HT) has not been clearly elucidated among postmenopausal women for the treatment of depressive symptoms.[7] A large systematic review of 10 studies reported that vasomotor symptoms (VMS) increase the risk for depressive symptoms during the perimenopause.[11] The benefits of HT have been well-described for the treatment of VMS and for improving the quality of life among women. It is, however, unclear whether HT use is associated with a lower prevalence of depressive symptoms among postmenopausal women.

The main objective of this research was to investigate the association between menopausal status and self-reported depressive symptoms among middle-aged women in Canada. We explored the potential influences of the social determinants of health (education, income, social support) and health behaviors on current self-reported depressive symptoms. The characteristics of the menopausal transition and HT use were also examined to uncover potential associations.

METHODS

Setting and study population

The Canadian Longitudinal Study on Aging (CLSA) is one of the largest and most comprehensive research platforms in the world, examining health and aging in community-dwelling participants between the ages of 45 and 85 years at the time of recruitment from the 10 provinces. People were excluded from the CLSA if they lived on federal First Nations reserves, were full-time members of the Canadian Armed Forces, lived in institutions, were unable to respond in English or French, or were cognitively impaired. Enrollment and baseline data collection from 51,338 participants across Canada were completed from 2010 to 2015. There were 21,241 participants recruited into the Tracking Cohort that provided information through telephone interviews and 30,097 participants recruited into the Comprehensive Cohort who completed in-depth physical assessments and provided blood and urine samples in addition to completing
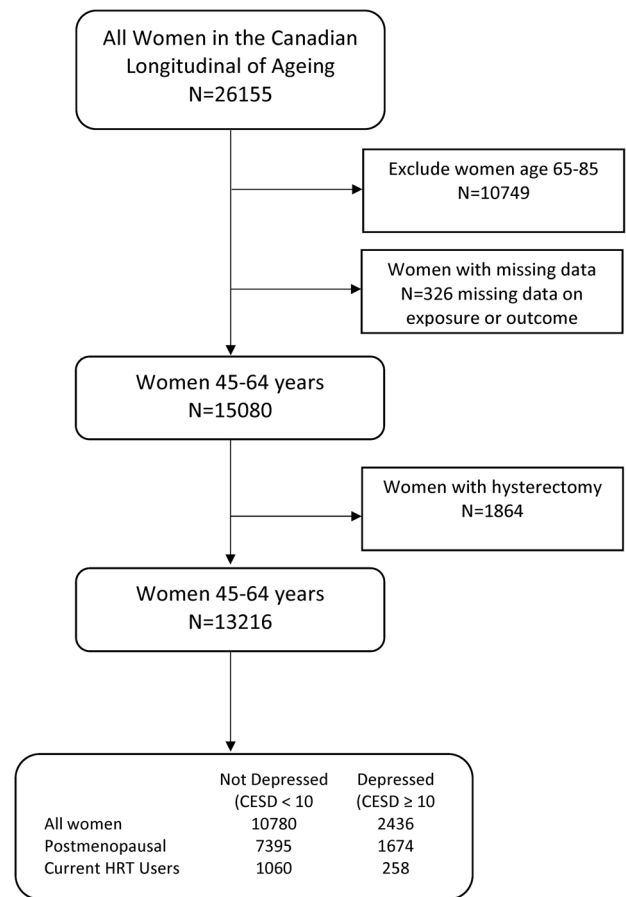
FIG. 1. Flowchart of women included in this analysis from the Canadian Longitudinal Study on Aging (CLSA) Comprehensive Cohort.

questionnaires in person. The CLSA study design has been previously described in detail elsewhere.[12] Baseline data from the Tracking Cohort (Dataset version 3.1) and Comprehensive Cohort (Dataset version 2.0) of the CLSA were accessed for this research project. Before accessing and analyzing the data, ethics approval was received from the Hamilton Integrated Research Ethics Board (Protocol Number: 0204). For these analyses, cross-sectional baseline data were used. Women aged 65 and older ($n = 10,749$) and those missing data on the exposure or the outcome ($n = 326$) were excluded. We also excluded participants who had undergone a hysterectomy at baseline ($n = 1,864$) due to lack of complete detailed information about the procedure. Women were not asked whether they had ovarian conservation or removal, rendering the age at true menopause difficult to ascertain. The analyses included 13,216 female CLSA participants (Fig. 1).

Depression Status

The primary outcome of this study was depression status measured using the Center for Epidemiologic Studies Short Depression Scale (CESD-10), which contains 10 questions about items such as feelings of depression, loneliness, hopefulness for the future, and restless sleep. Four possible

response options were provided to the participants for each question (all of the time, occasionally, some of the time, rarely or never) and the total score may range from 0 to 30. A total score of 10 or more is considered depressed.[13,14] This self-report scale has high sensitivity (0.89) to estimate current depression with a cut-off score of 10 points, and has demonstrated both convergent and divergent validity.[13,14]

Menopausal status

Self-reported menopausal status is commonly used in population-based studies. Women who reported having their menstrual periods stopped for at least 1 year without restarting, or who were over the age of 60 years were considered postmenopausal. All other women were considered premenopausal. Postmenopausal women were asked at what age menopause occurred. Based on this information, postmenopausal women were categorized as premature onset (<40 years), early onset (40-45 years), normal onset (46-55 years), and late onset (≥56 years) age at menopause. The validity of self-reported age at menopause has found to be acceptable but shown to decrease with increasing number of years since menopause.[15,16] Although the option was not read to the participants, some women reported to have had a hysterectomy. These participants were excluded from the analyses.

Hormone therapy use

Women were asked if they have ever used HT. Women reporting HT use were asked at what age they started HT, if estrogen, progesterone, or both were used, and how long HT was used.

Sociodemographic and lifestyle variables

We explored sociodemographic factors previously reported to be associated with depression: highest attained education level (less than secondary, secondary, some postsecondary, postsecondary), household income (CAD$: <20,000; 20,000-49,000; 50,000-99,000; 100,000-149,000; ≥150,000), marital status (single, married/common law, widowed/divorced/ separated), and parity (0 biological children, ≥1 biological children). Lifestyle factors and health-related variables included body mass index (BMI; underweight <18.5 kg/m^2; normal weight 18.5-24.9 kg/m^2; overweight 25.0-29.9 kg/m^2; obese ≥30.0 kg/m^2); smoking status (never, former, current) and alcohol consumption (regular, occasional, infrequent); and perceived mental health and perceived general health (both categorized as poor/fair and good/very good/excellent). Social support was measured to capture whether an individual was receiving affectionate social interaction, emotional and informational support, positive social interaction, tangible social support, and whether or not they received caregiving. A social participation score was calculated based on frequency of involvement in social activities and then categorized by age-specific quintiles.

Statistical analyses

Descriptive statistics, expressed as frequencies and percentages, were calculated using chi square analyses across the different categories of depression status and menopausal status. The median and interquartile range of the CESD-10 score for each group of women was also calculated. Multivariable analyses were calculated using logistic regression (based on the presence or absence of self-reported depression on the CESD-10) and adjusted odds ratios (aORs) are presented. Age, education, and income were included in the model as a priori variables and lifestyle factors (smoking and alcohol consumption), health-related variables (BMI, perceived general health, and mental health), social support, and social participation variables were added one by one in the model to see the effect changes. Odds ratios (OR) were calculated along with the 95% confidence interval (95% CI). All hypotheses tests were two-sided and P values less than 0.05 were considered significant. The main analysis was done for women ages 45 to 64 years; however, we also performed the same analysis, stratified by age 45 to 54 and 55 to 64 years to see if any differences emerged. The stratification was completed as the literature suggests that the most vulnerable time for depressive symptoms exists during the menopause transition. All analyses were performed using sampling weights with appropriate methods for complex survey design methods. Descriptive analysis was done with sampling weights and association was measured using probability weights. Complex survey design methods were employed here to calculated estimates adjusted with strata for calculating appropriate CIs. All analyses were conducted using Stata version 14.2 software (StataCorp. 2015. *Stata Statistical Software: Release 14*.StataCorp LP, College Station, TX) and SAS 9.4 software (SAS Institute Inc 2013, SAS/ACCESS 9.4, Cary, NC).

Sensitivity analyses

Data regarding a history of physician diagnosed clinical depression and the current use of medication to treat depression were available in the Comprehensive Cohort (approximately 40% of participants), but not the Tracking Cohort. A sensitivity analyses was conducted to compare the odds of current depression based on the CESD-10 in the Comprehensive Cohort with and without these variables included.

RESULTS

Participant characteristics

The sociodemographic and lifestyle variables for middle-aged women, stratified by self-reported depression (estimated using CESD-10), are presented in Table 1. Using the CESD-10 score, 18.1% of the middle-aged women were identified as depressed with a median score of 12.1 (interquartile range 10.3-15.4). When stratified by age group 45 to 54 years (an estimate for the mean age of perimenopause and early menopause) versus 55 to 64 years, there was no difference in proportion who were categorized as depressed. Sociodemographic and lifestyle characteristics were different between depressed and nondepressed participants. Women who were not identified as depressed based on the CESD-10 had a higher level of education (76.8% vs 73.4%, completed at

TABLE 1. *Demographic, lifestyle, medical, and social support status by Center for Epidemiologic Studies Short Depression Scale-10 depressive symptoms (N = 13,216)*

| | 45-64 Years (N = 13,216) | | | | | | |
| | Not depressed | | | Depressed | | | |
	n	%	W%	n	%	W%	P
All women	10,780	81.6	81.9	2,436	18.4	18.1	
CESD-10 score, median (IQR)		3 (2-6)	3.0 (1.2-5.4)		13 (11-16)	12.1 (10.3-15.4)	
Education level							
Less than secondary	306	2.8	3.6	135	5.6	5.1	0.004
Secondary	1,128	10.5	12.4	297	12.2	14.3	
Some postsecondary	716	6.7	7.2	191	7.9	7.2	
Postsecondary	8,614	80.0	76.8	1,809	74.4	73.4	
Household income							
<$20,000	324	3.0	2.9	278	11.4	9.2	<0.001
$20,000-$49,999	1,722	16.0	15.0	594	24.4	23.6	
$50,000-$99,999	3,660	34.0	34.1	778	31.9	34.1	
$100,000-$149,999	2,415	22.4	23.7	370	15.2	17.1	
≥$150,000	2,130	19.8	20.1	247	10.1	10.5	
Do not know/Refuse	529	4.9	4.2	169	6.9	5.4	
Marital status							
Single, never married, never lived with partner	1,058	9.8	8.5	378	15.5	13.5	<0.001
Married, living common law	7,788	72.3	78.2	1,416	58.1	65.9	
Widowed, divorced, separated	1,929	17.9	13.3	642	26.4	20.6	
Parity							
Nulliparous	1,710	15.9	13.3	494	20.3	19.1	<0.001
Parous	9,070	84.1	86.7	1,942	79.7	80.9	
Body mass index							
Underweight (<18.5 kg/m^2)	106	1.0	1.0	34	1.4	1.9	<0.001
Normal weight (18.5-24.9 kg/m^2)	4,460	41.6	45.0	830	34.3	38.8	
Overweight (25.0-29.9 kg/m^2)	3,462	32.3	31.2	727	30.1	29.8	
Obese (≥30.0 kg/m^2)	2,693	25.1	22.8	828	34.2	29.5	
Smoking status							
Current smoker	1,056	9.8	10.2	440	18.1	18.3	<0.001
Former smoker	4,887	45.4	39.5	945	38.8	32.9	
Never smoker	4,822	44.8	50.2	1,048	43.1	48.8	
Alcohol use in past 12 mo							
Regular drinker	7,880	73.1	73.8	1,479	60.7	63.5	<0.001
Occasional drinker	1,650	15.3	15.3	498	20.5	19.2	
Infrequent drinker	1,244	11.6	10.9	458	18.8	17.2	
Affectionate social interaction							
Low	803	7.5	5.4	590	24.2	20.9	<0.001
Moderate	1,425	13.2	12.9	473	19.4	18.9	
High	8,552	79.3	81.6	1,373	56.4	60.1	
Emotional and informational support							
Low	828	7.7	7.4	628	25.8	24.3	<0.001
Moderate	2,699	25.0	23.6	766	31.4	29.0	
High	7,253	67.3	69.0	1,042	42.8	46.7	
Positive social interaction							
Low	1,000	9.3	7.9	746	30.6	27.9	<0.001
Moderate	2,693	25.0	24.1	775	31.8	29.0	
High	7,087	65.7	68.0	915	37.6	43.1	
Tangible social support							
Low	1,327	12.3	10.4	744	30.5	27.9	<0.001
Moderate	2,440	22.6	23.1	623	25.6	25.9	
High	7,013	65.1	66.5	1,069	43.9	46.2	
Caregiving							
Provided	5,635	52.4	56.0	1,263	51.9	56.0	
Not provided	5,126	47.6	44.0	1,169	48.1	44.0	0.98
Perceived mental health							
Good, very good or excellent	10,539	97.8	97.9	1,847	76.0	77.1	<0.001
Poor or fair	239	2.2	2.1	584	24.0	22.9	
Perceived general health							
Good, very good or excellent	10,182	94.5	93.9	1,822	74.8	73.6	<0.001
Poor or fair	594	5.5	6.1	613	25.2	26.4	
Social participation							
Moderate to high	8,902	83.1	80.2	1,656	68.2	65.8	<0.001
Low	1,811	16.9	19.8	771	31.8	34.2	

CESD-10, Center for Epidemiologic Studies Short Depression Scale; IQR, interquartile range.

least some postsecondary), higher income (20.1% vs 10.5%, had more than $150,000 yearly household income), were married or common law (78.2% vs 65.9%), had multiple children (86.7% vs 80.9%), were former or never smokers (90.2% vs 81.7%), were normal or over weight (73.9% vs 64.4%), had higher levels of social support (affectionate

TABLE 2. *Menopausal status and hormone therapy use by Center for Epidemiologic Studies Short Depression Scale-10 depressive symptoms and for women aged 45 to 64 years*

	45-64 Years ($n = 13,216$)						
	Not depressed			Depressed			
	n	%	W%	n	%	W%	P
All women	10,780	81.6	81.9	2,436	18.4	18.1	
Menopausal status							0.580
Premenopausal	3,385	31.4	36.8	762	31.3	35.8	
Postmenopausal	7,395	68.6	63.2	1,674	68.7	64.2	
Current HT use							
Yes	1,060	90.1	89.9	258	89.4	89.1	0.423
No	9,662	9.9	10.1	2,165	10.7	10.9	
Menopausal status by HT use							
Premenopausal + current HT	189	1.8	2.0	52	2.2	1.7	0.505
Premenopausal + no HT	3,190	29.8	34.9	708	29.2	34.2	
Postmenopausal + current HT	871	8.1	8.1	206	8.5	9.2	0.280
Postmenopausal + no HT	6,472	60.4	55.0	1,457	60.1	54.9	
Postmenopausal women only	7,268	81.5	81.6	1,646	18.5	18.4	
Age at menopause							
Years, mean (SD)	49.6 (5.0)		49.2 (5.2)	48.6 (5.9)		48.2 (6.3)	
Years since menopause[a]							
<5 Years postmenopausal	2,241	30.8	34.3	480	29.2	32.4	0.027
5-9 Years postmenopausal	2,530	34.8	33.4	511	31.0	29.8	
≥10 Years postmenopausal	2,497	34.4	32.3	655	39.8	37.8	
Onset of menopause[b]							
Premature menopause (<40 y)	276	3.8	4.4	126	7.8	9.2	<0.001
Early menopause (40-45)	982	13.5	14.5	250	15.2	14.4	
Normal menopause (46-55 y)	5,518	75.9	75.2	1,186	72.1	71.6	
Late-onset menopause (≥56 y)	492	6.8	5.9	84	5.1	4.8	
Current HT users only	1,060	80.4	80.7	258	19.6	19.3	
Duration of current HT use[c]							
<5 y	629	59.3	61.3	150	58.1	55.6	0.314
5-9 y	228	21.5	20.5	50	19.4	20.1	
≥10 y	203	19.2	18.2	58	22.5	24.3	

CESD-10, Center for Epidemiologic Studies Short Depression Scale; HT, hormone therapy.
[a]P value for less than 5 years versus 10+ years (0.0479), 5 to 9 years versus 10+ years (0.009).
[b]P value between normal versus premature (<0.001), normal versus early (0.710), and normal versus late (0.376).
[c]P value between duration of current HT user 10 years or older versus younger than 5 years (0.119) and 10 years or older versus 5 to 9 years (0.3401).

social interaction: 81.6% vs 60.1%; emotional and informational support: 69.0% vs 46.7%; positive social interaction: 68.0% vs 43.1%; tangible social support: 66.5% vs 46.2%); and rated their mental and general health as good, very good, or excellent (mental health: 97.9% vs 77.1%; general health: 93.9% vs 73.6%) compared to women who met the CESD-10 criteria for depression.

Menopausal transition and HT use

The majority of women were postmenopausal and never users of HT. The average age of menopause was approximately 49 years (not depressed: 49.2 years; depressed: 48.2 years) (Table 2). There were 1,318 women currently using HT. Among women who were current HT users, the majority of women were using HT for less than 5 years, and started HT use either the same year or after menopause.

Depression status and covariates

The association of current depression status (as estimated using the CESD-10) and covariates adjusted for age, education, income, and marital status are presented in Table 3. Women who reported current smoking, regular alcohol use, obesity, and self-reported ''fair'' or ''poor'' general health had a higher risk of current depression based on the CESD-10.

Moderate to high social interaction, emotional and informational support, positive social interaction, tangible social support, and social participation reduced the risk of current depression among women.

Menopausal transition, HT use, and depression status

After adjustment for age, education level, household income, marital status, BMI, smoking status, alcohol consumption, social support, perceived general health, and social participation, current users of HT had a higher odds for current self-reported depression on the CESD-10 (aOR: 1.21, 95% CI: 1.02-1.44) as did women who experienced premature menopause (aOR: 1.45, 95% CI: 1.07-1.97) (Fig. 2). Supplemental Digital Content 1, http://links.lww.com/MENO/A577 contains the unadjusted OR and aORs. The age-stratified analyses with participants aged 45 to 54 years and participants aged 55 to 64 years did not reveal any meaningful differences for the magnitude of the association of premature menopause or HT use with current self-reported depression on the CESD-10. For women aged 45 to 54 years and 55 to 64 years, respectively, the adjusted odds of depression based on the CESD-10 for HT use were 1.20 (95% CI: 0.91-1.56) and 1.24 (95% CI: 1.00-1.55) and for premature menopause the aORs were 1.19 (95% CI: 0.51-2.77) and 1.52 (1.08-2.14).

TABLE 3. *Risk factors for Center for Epidemiologic Studies Short Depression Scale-10 depressive symptoms for women aged 45 to 64 years (odds ratios)[a,b]*

Variable	Tracking and comprehensive Odds ratio (95% CI)	Comprehensive Odds ratio (95% CI)
History of clinical depression		2.87 (2.50-3.30)
Current medication for depression		3.11 (2.68-3.61)
Age at menopause 51.5 years	0.84 (0.74-0.95)	0.84 (0.71-0.99)
Current smoking	1.64 (1.43-1.88)	1.57 (1.30-1.91)
Regular alcohol use	1.35 (1.18-1.54)	1.30 (1.08-1.55)
BMI ≥ 30 kg/m^2	1.38 (1.24-1.53)	1.43 (1.25-1.64)
Affectionate social interaction		
Low	Reference	Reference
Moderate	0.48 (0.41-0.57)	0.49 (0.40-0.62)
High	0.25 (0.21-0.29)	0.26 (0.21-0.31)
Emotional and informational support		
Low	Reference	Reference
Moderate	0.42 (0.36-0.48)	0.43 (0.36-0.52)
High	0.22 (0.19-0.25)	0.20 (0.16-0.23)
Positive social interaction		
Low	Reference	Reference
Moderate	0.43 (0.37-0.49)	0.45 (0.38-0.54)
High	0.20 (0.18-0.23)	0.19 (0.16-0.23)
Tangible social support		
Low	Reference	Reference
Moderate	0.51 (0.44-0.58)	0.50 (0.41-0.60)
High	0.32 (0.29-0.37)	0.32 (0.27-0.37)
Perceived general health "poor/fair"	4.31 (3.76-4.95)	4.17 (3.42-5.08)
Moderate/high social participation	0.53 (0.47-0.59)	0.51 (0.43-0.59)

BMI, body mass index; CESD-10, Center for Epidemiologic Studies Depression Scale; CI, confidence interval.
[a]All data adjusted for age, education, income, and marital status.
[b]Data presented for menopausal women only.

Sensitivity analyses

In the Comprehensive Cohort, a history of physician diagnosed clinical depression and the current use of medication to treat depression were associated with a 1.77 (95% CI: 1.44-2.14) and a 1.88 (95% CI: 1.52-2.32) greater odds of current depression based on the CESD-10 in the adjusted model (Supplemental Digital Content 2, http://links.lww.com/MENO/A578). Including a history of depression and use of medication to treat depression had a minimal impact on the magnitude of the association between any of the other variables with depression.

DISCUSSION

Overall, 18.1% of middle-aged women in the CLSA data were identified as "depressed," as estimated by a score of 10 or more on the CESD-10. A premature menopause and current use of HT were identified as risk factors for current self-reported depression after adjustment for other important variables. We did not observe any association with duration of current HT use with current symptoms of depression. Several positive social determinants of health and health behaviors were observed as protective (eg, education level, household income, nonsmoking status, social support, and social participation).

The estimated prevalence of depressive symptoms in our sample of women (18.1%) is lower than previously reported in American, Polish, and Chinese Cohorts around the time of the menopausal transition, with rates ranging from 25% to 36%.[17-19] Nevertheless, these findings from our large representative sample suggest that a large number of Canadian women are at risk. Previously identified prognostic factors for poor mental health were also demonstrated in our sample, including low social support, lower income, obesity, and cigarette smoking. Some of these factors may help health care providers to identify which patients are at the highest risk, and may be modifiable, such as cigarette smoking and obesity. In the United Kingdom, the government has recently appointed a "Minister for Loneliness" as poor social support has been identified as a significant public health challenge (https://www.gov.uk/government/news/pm-launches-governments-first-loneliness-strategy). Health care providers have begun "social prescribing," which will potentially lessen the isolation commonly seen in older adults. Perhaps a similar program in Canada would help to improve mental health given that we found such profound differences on all of our social support and interaction items (Table 1).

A recent meta-analysis investigated the association between age at menopause and risk for depression among postmenopausal women with naturally occurring menopause.[20] Among the 14 included studies, an inverse association with depression in postmenopausal women was shown for increasing age at menopause. For example, those women who experienced premature menopause (before age of 40 years) experienced a 50% increased risk for depression as compared to women with longer reproductive years. Similarly, a study using the Korean National Health and Nutrition Examination Survey (KNHANES V) reported that those women who experienced an earlier menopause (before the age of 45) experienced a 65% increased risk for depression as compared to women with longer reproductive years.[21] As such, longer exposure to endogenous estrogens (having a normal or late onset of menopause, either naturally or surgically) can be protective against the occurrence of depression in later life. Considering these findings, it is of utmost importance to identify those women who experience premature menopause (from any cause), and who may be at a higher risk for depression (such as those women with previous depressive episodes). These women may benefit from psychiatric support and intervention and/or estrogen-based therapies, as clinically appropriate. The perimenopause and the early postmenopausal years represent a vulnerable time for the development of depressive symptoms as related to the dramatic shifts in endogenous estrogen levels[22] and we therefore expected to find a greater proportion of self-reported depression among women closer to the mean age of the menopause transition (45-54 years) compared to women aged 55 to 64 years. This expected result was not observed, but may be in part attributable to our study measuring current symptoms of depression rather than incident depression.

The finding that current HT use was associated with an increased risk for depressive symptoms is interesting and
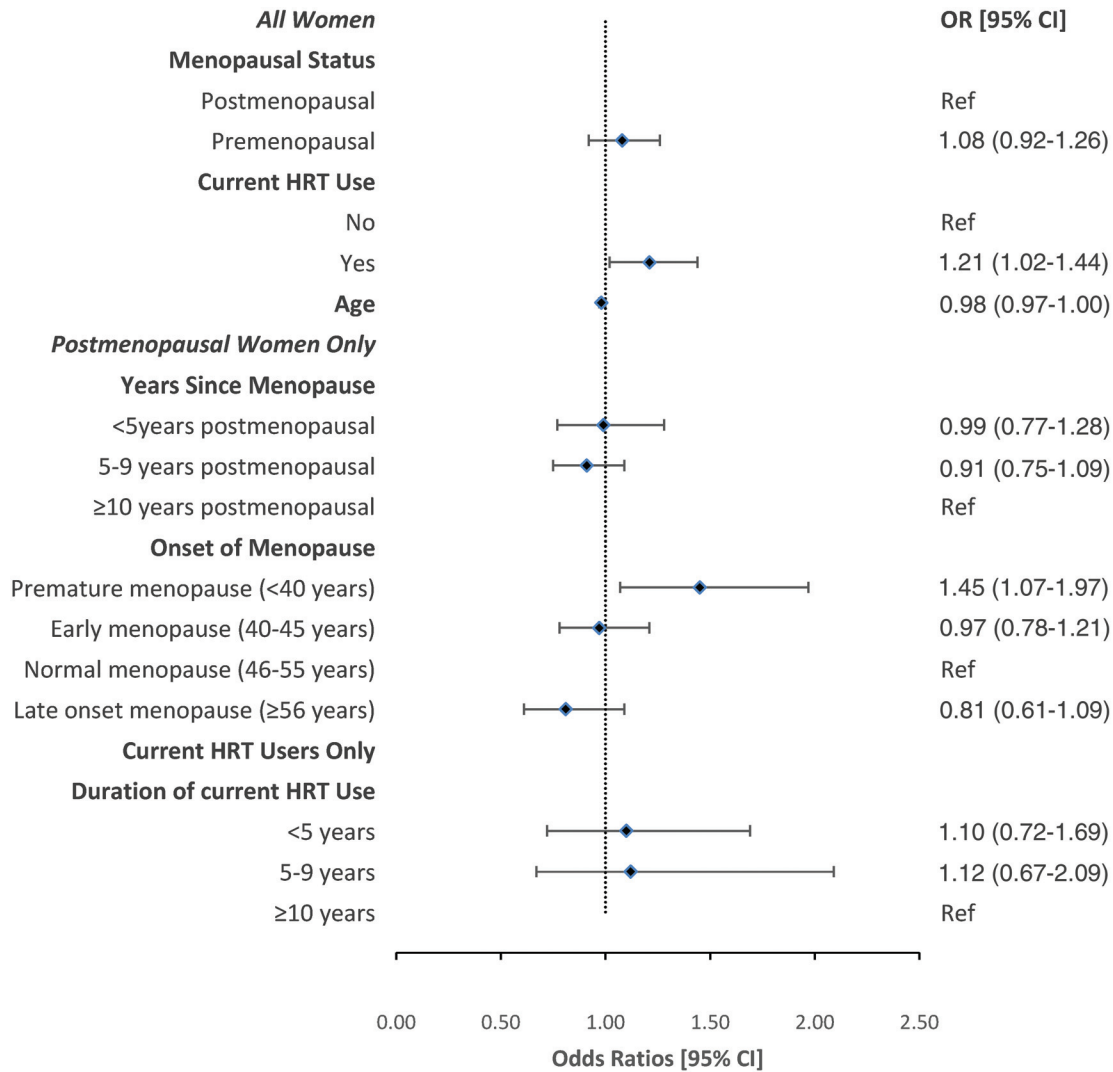
FIG. 2. Association of menopausal status, hormone therapy use, and odds of having current depressive symptoms for women aged 45 to 64 years (*n* = 13,216, weighted analysis). Adjusted for age, education level, household income, marital status, body mass index, smoking status, alcohol consumption in past 12 months, social support (affectionate social interaction, emotional and informational support, positive social interaction, tangible social support), and social participation.

complex. Although the models were adjusted for a range of covariates, we were unable to adjust for the presence of menopausal VMS as these data were not captured by the CLSA. VMS are the primary reason why HT is used in menopause and current use may be a proxy for more severe symptoms, a known risk factor for depressive symptoms. HT has been used to successfully treat depression in conjunction with antidepressant medications.[23] Further research should explore the relationship between HT use and ongoing depressive symptoms as women experience the menopausal transition. The burden associated with symptoms or diagnoses for depression at any stage of life is considerable and undeniable. The current description of the CLSA data is from the baseline visit and therefore cross-sectional in nature. Future analyses using the longitudinal data of these women may, however, capture the changes that may occur in older age (such as loss of a partner or social isolation) and that can impact the health and well-being of women before, during, and after the menopausal transition.

A key strength of this study is the use of the CLSA Cohort data, which captures information on the menopausal transition and self-reported depressive symptoms among a large group of midlife and older women in Canada. An important limitation to these data is that both the prior physician diagnosis of clinical depression and the current depressive symptoms, as measured using the CESD-10, are self-report data which may be subject to social desirability bias. Recall bias may have affected the reporting of these variables, and the timing of the menopausal transition and details of HT use. Another limitation is that certain populations were not included in the CLSA (women living on federal First Nations reserves; full-time members of the Canadian Armed Forces; those living in institutions; those who were unable to respond in English or French; and women who were cognitively impaired), and

these women are often vulnerable to mental distress, including depression. The CLSA also did not include women younger than 45 years of age; therefore, stratified analyses investigating the association of menopausal status and depression in women currently undergoing early menopause could not be evaluated. Previous studies have included a prior diagnosis of depression and the use of medication to treat depression as covariates in their models. This information was only available for Comprehensive Cohort participants (approximately 40% of participants) and therefore could not be included in our main analyses. Although both variables were associated with increased odds of being identified as depressed, as estimated using the CESD-10, they did not meaningfully alter the association between the other variables and depression when the analyses were limited to the Comprehensive Cohort. Therefore, it is unlikely that the exclusion of these variables had a meaningful impact in our main analyses.

CONCLUSIONS

Overall based on the CLSA Cohort, approximately 18% of women in Canada aged 45 to 64 had self-reported high levels of depressive symptoms measured using the CESD-10. Premature menopause (menopause occurring before 40 years) and current use of HT were both associated with an increased odds of having current depression after adjustment for other covariates. Other risk factors for depression included low education, low household income, living alone, being nulliparous, and low social support. Given that the menopausal transition is a vulnerable time for mental health, the identification of risk factors, including social determinants of health, age at menopause, and menopausal symptoms can help guide clinicians when assessing mental health.

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