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PHOTOPERIOD DURING MATERNAL PREGNANCY AND LIFETIME DEPRESSION IN OFFSPRING

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Abstract

Experimental studies indicate that perinatal light exposure has enduring effects on affective behaviors in rodents; however, insufficient research has explored this hypothesis in humans. We examined photoperiod (i.e., day length) metrics during maternal pregnancy in relation to lifetime depression in the longitudinal Nurses' Health Study (NHS) and NHS II. 160,723 participants reported birth date and birth state (used to derive daily photoperiod based on published mathematical equations), and clinician-diagnosed depression and antidepressant use throughout adulthood. Logistic regression was used to estimate odds ratios (OR) (and 95% confidence intervals [CI]) for depression (defined as clinician diagnosis and antidepressant use) across quintiles of two exposures during maternal pregnancy: 1) total photoperiod (total number of daylight hours) and 2) differences between minimum/maximum photoperiod; each trimester of pregnancy was examined separately. Total photoperiod during maternal pregnancy was not

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associated with depression overall or by trimester of pregnancy. However, larger differences between minimum/maximum photoperiod during maternal pregnancy were related to lower odds of depression (multivariable [MV]-adjusted OR: 0.86, 95% CI: 0.83, 0.90 comparing extreme quintiles of exposure; p-trend<0.0001); this association appeared specific to the second trimester of pregnancy (MV-adjusted p-trends=0.03, <0.0001, and 0.3 across the three trimesters, respectively). In addition, birth at higher latitude (where larger differences in minimum/maximum photoperiod exist) was associated with a significant reduction in the lifetime risk of depression. These findings are consistent with an emerging hypothesis in which perinatal light exposure may influence risk of depression, and they might be understood through the conceptual framework of adaptive developmental plasticity.

Keywords

Photoperiod; light; pregnancy; depression; cohort; epidemiology

INTRODUCTION

Early-life factors, particularly during sensitive periods of brain development, influence the risk of neurodevelopmental disorders (Andersen, 2015; Bale et al., 2010). Historically, epidemiologic studies have identified birth season as an early-life factor with a modest association to psychiatric disorders, including depression (Disanto et al., 2012; Foster and Roenneberg, 2008; Joiner et al., 2002; Pfaff et al., 2006; Torrey et al., 1997; Torrey et al., 1996); however, mechanisms underlying a potential association have remained elusive (Schnittker, 2018). Meanwhile, research in rodents has uncovered a link between perinatal day length (i.e., photoperiod) and subsequent risk of depressive phenotypes (Ciarleglio et al., 2011), leading to an emerging hypothesis that early-life photoperiod may be an important predictor of depression and other psychiatric disorders.

In mice and hamsters, perinatal exposure to short, winter-like photoperiods produced more depressive- and anxiety-like behaviors than exposure to long, summer-like photoperiods (Green et al., 2015; Pyter and Nelson, 2006). Intriguingly, in mice, these effects were accompanied by changes in serotonin signaling in the brain, which represents a key element in the neurobiology of depression (Charney, 1998). Moreover, both signaling and behavioral effects were dependent on the melatonin 1 (MT1) receptor (Ciarleglio et al., 2011; Green et al., 2015), where the agonist melatonin is a hormonal regulator and primary molecular marker of the circadian system; melatonin secretion is entrained to the environmental light-dark cycle and acutely suppressed by light (Arendt, 2005). Maternal melatonin is known to freely cross the placenta during gestation (Tamura et al., 2008), in turn regulating the establishment of the fetal circadian system (Goldman, 2003) and development of the fetal adrenal gland and glucocorticoid signaling (Torres-Farfan et al., 2011; Torres-Farfan et al., 2004), which are thought to play an important role in the programming of emotional behaviors (Ikeda et al., 2013). More recently, in mice, changes in photoperiod during the perinatal period have been shown to have enduring effects on serotonin signaling into adulthood (Siemann and McMahon, unpublished data). Taken together, accumulating evidence suggests that perinatal photoperiod may act through melatonin signaling to

influence serotonergic pathways related to emotional behaviors, with implications for long-term risk of affective disorders.

In humans, recent epidemiologic studies of birth season and depression have produced less consistent evidence of an association compared to older studies (Park et al., 2016; Schnittker, 2018; Talarowska et al., 2018), and the vast majority of studies have ignored the potential influence of birth latitude (Disanto et al., 2012; Foster and Roenneberg, 2008; Joiner et al., 2002; Pfaff et al., 2006; Torrey et al., 1997; Torrey et al., 1996). Indeed, there has been a specific call to evaluate the combined effects of birth season and birth latitude in relation to psychiatric disorders in large epidemiologic studies (Erren et al., 2012). Thus, in the present study, we examined photoperiod during maternal pregnancy (combining information on birth date and birth latitude) in relation to lifetime depression in the participant-offspring, utilizing existing information on >160,000 women in the Nurses' Health Studies.

METHODS AND MATERIALS

Study population

The Nurses' Health Study (NHS) was established in 1976, when 121,701 U.S. female nurses, aged 30–55 years, returned a mailed questionnaire with information on demographics, health, lifestyle, and medication use (Colditz, 1995). In 1989, the NHS II was initiated among a younger generation of 116,430 female nurses, aged 25–42 years, using a similar questionnaire to obtain information about participants (Rich-Edwards et al., 1994b). These cohorts were established at Harvard, and their purpose is to evaluate risk factors for chronic conditions in women. Biennial questionnaires were used to update this information in both cohorts since their inception, and the response rate was ⩾90% at each questionnaire cycle. The Institutional Review Board of Brigham and Women's Hospital approved both studies, and informed consent was implied by participants' return of the cohort questionnaires.

Ascertainment of perinatal photoperiod

Participants reported their date of birth on the initial questionnaire in each cohort, and they subsequently reported their state of birth on the 1992 questionnaire in NHS and the 1993 questionnaire in NHS II. Based on this information, we estimated the day length (i.e., photoperiod) during the presumed maternal pregnancy period (i.e., beginning 280 days prior to the participant's birth date, as this represents the average length of human pregnancy) using mathematical equations published by the National Oceanic and Atmospheric Administration (Earth System Research Laboratory). We used the longitudinal coordinates of the center of population density for a participant's birth state to represent the location of the participant during gestation. With these assumptions, we created two main exposures of interest: total photoperiod during maternal pregnancy (a proxy for total duration of light exposure, in hours, of the participant's mother during pregnancy), which was calculated by summing the lengths of all 280 days across the pregnancy; and extreme differences in photoperiod during maternal pregnancy (a proxy for variation in light exposure during

pregnancy), which was calculated by subtracting the longest and shortest day lengths during gestation.

Ascertainment of depression

In NHS, women reported regular use of antidepressant medication for the first time in 1996, and their history of clinician-diagnosed depression in 2000; this information was updated on each subsequent biennial questionnaire. In NHS II, data collection was similar for these variables: antidepressant use was first assessed in 1997, and history of clinician-diagnosed depression was assessed in 2001, with updated information obtained on each follow-up questionnaire. Consistent with previous studies in NHS (Chocano-Bedoya et al., 2014; Lucas et al., 2014), we utilized this information to define depression in two ways: a strict definition (primary outcome) included women who reported clinician-diagnosed depression *and* regular use of antidepressant medication, and a broader definition (secondary outcome) included women who reported either clinician-diagnosed depression or regular use of antidepressant medication. Based on these definitions, the primary outcome should maximize specificity of the case definition and may reduce potential bias in risk estimates, whereas the secondary outcome should have greater sensitivity and detect a higher number of cases (e.g., as described in Lucas et al. (2011b)).

Ascertainment of suicide

We obtained most information on participant deaths from relatives and postal authorities, as well as by a search of the National Death Index for non-responders after each questionnaire cycle; these methods have been shown to identify approximately 98% of participant deaths in NHS (Rich-Edwards et al., 1994a). Study physicians who were unaware of exposure status reviewed death certificates to determine each participant's cause of death. Suicide was defined as all cases of suicide and self-inflicted injury or harm, as described by International Classification of Disease codes E950-E959 (United States Department of Health, 1965).

Ascertainment of covariates

Participants reported information on race, hair color (as a proxy for skin tone), and early-life socioeconomic indicators (mother's smoking status during pregnancy, parents' home ownership at time of participant birth, participant birth weight and history of being breastfed, and each parent's occupation during the participant's childhood) on biennial questionnaires.

Population for analysis

For these analyses, we focused on 224,974 women (116,911 in NHS and 108,063 in NHS II) who were born full term. We excluded 20,912 women (16,600 in NHS and 4,312 in NHS II) who never reported information on depression status, and an additional 43,325 women (22,003 in NHS and 21,322 in NHS II) who did not report their state of birth; this left 160,737 participants (78,308 in NHS and 82,429 in NHS II) for our analysis of photoperiod during maternal pregnancy and lifetime depression in the participant-offspring.

Statistical analysis

We used birth year- and multivariable (MV)-adjusted logistic regression models to estimate odds ratios (OR) and corresponding 95% confidence intervals (CI) for lifetime depression (defined according to both the stricter and broader definitions described above) across quintiles of total photoperiod and extreme differences in minimum/maximum photoperiod during maternal pregnancy; these exposures were also examined by trimester of maternal pregnancy. For each exposure, we evaluated tests of trend using midpoints of the corresponding quintiles. These models were run for each cohort separately and then for both cohorts combined by pooling. Using a similar approach, we examined associations of total photoperiod and extreme differences in minimum/maximum photoperiod during maternal pregnancy with risk of suicide, as this outcome likely reflects participants with the most severe depression. Because suicide is a rare outcome, we combined data from NHS and NHS II to maximize power.

Initial models were adjusted for birth year in five-year categories: ⩽1925, 1926–1930, 1931–1935, 1936–1940, and ⩾1941 in NHS, and ⩽1945, 1946–1950, 1951–1955, and ⩾1956 in NHS II. To reduce variation in exposure variables due to factors that might affect perinatal light exposure or gestational development, we additionally controlled for the following variables in MV models: race (white, black, other), hair color (dark brown, light brown, black, blond, red, missing), mother's smoking status during pregnancy (yes, no, missing), parents' home ownership at time of participant birth (yes, no, missing), participant birth weight (<5.5, 5.5–6.9, 7–8.4, 8.5+ pounds, missing), the participant's history of being breastfed (yes, no, missing), and both mother's and father's occupations during the participant's childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing). Within each cohort, these characteristics were similar across quintiles of total photoperiod during maternal pregnancy (Table 1) and quintiles of extreme differences in minimum/maximum photoperiod during maternal pregnancy (data not shown). In analyses by trimester of maternal pregnancy, we additionally adjusted models for the corresponding photoperiod exposure during previous trimesters of pregnancy. Indicator variables were used to represent missing data in regression models.

In additional analyses, we examined birth latitude (categorized into northern, middle, and southern latitudes, which is consistent with previous studies in these cohorts (Hernan et al., 1999; Khalili et al., 2012)) and birth season (categorized into four seasons centered on dates of the winter solstice, spring equinox, summer solstice, and autumn equinox) in relation to lifetime depression. An alternative definition of birth season (categorized into four seasons bounded by dates of the winter/summer solstices and spring/autumn equinoxes) was also considered. Because birth latitude and birth season were used to derive our main exposures of interest, we evaluated their relative contribution to total perinatal photoperiod and extreme differences in minimum/maximum photoperiod during maternal pregnancy by regressing birth latitude and birth season on these exposure variables, and calculating R^2 values to estimate the amount of variation explained by birth latitude and birth season.

Statistical tests were two sided and were considered statistically significant at $p<0.05$. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Total photoperiod during maternal pregnancy had a borderline significant association with odds of lifetime depression (defined as clinician-diagnosed depression and antidepressant medication use during follow up) in MV models in NHS (p=0.04; Table 2). However, qualitatively, this trend was not convincing, and individual estimates across quintiles of exposure were not statistically significant (e.g., MV-adjusted OR=0.97, 95% CI=0.91, 1.03 comparing extreme quintiles). In NHS II, total photoperiod during maternal pregnancy was also unrelated to depression in a MV-adjusted model (p-trend=0.26), and odds of depression were similar comparing women in extreme quintiles of this exposure (MV-adjusted OR=1.02, 95% CI=0.96, 1.07). Accordingly, results from the combined cohorts were null (MV-adjusted OR=0.99, 95% CI=0.95, 1.03; p-trend=0.58), as were results by trimester of maternal pregnancy (p-trends=0.18, 0.51, and 0.09 for the three trimesters, respectively; Table 3).

In contrast, we found that a greater difference between minimum and maximum photoperiod during maternal pregnancy was significantly associated with lower lifetime depression risk (defined as clinician-diagnosed depression and antidepressant medication use during follow up) in NHS, NHS II, and the cohorts combined (all p-trends<0.001) (Table 2). Women in NHS with the largest differences in minimum/maximum photoperiod during maternal pregnancy had 12% lower odds of depression (MV-adjusted OR=0.88, 95% CI=0.83, 0.94) compared to women with the smallest differences. Similarly, women in NHS II had 15% lower odds of depression comparing largest vs. smallest differences in photoperiod during maternal pregnancy (MV-adjusted OR=0.85, 95% CI=0.81, 0.89). Finally, in models combining both cohorts, there was a 13% reduction in odds of depression comparing women in extreme groups of differences in photoperiod during maternal pregnancy (MV-adjusted OR=0.87, 95% CI=0.84, 0.91). In combined cohort analyses considering trimester of maternal pregnancy, an association was observed for the first trimester (MV-adjusted OR=0.96, 95% CI 0.92, 1.00 comparing largest vs. smallest differences in photoperiod during this trimester; p-trend=0.02), but a much stronger association was observed for the second trimester (MV-adjusted OR=0.77, 95% CI=0.72, 0.82 comparing extreme quintiles of minimum/maximum differences during the trimester; p-trend<0.001); there was no association for this exposure during the third trimester of pregnancy (OR=0.93, 95% CI=0.81, 1.06 comparing the smallest vs. largest differences in photoperiod; p-trend=0.45; Table 3).

We found no significant associations of total photoperiod and differences in minimum/maximum photoperiod during maternal pregnancy with suicide in the combined cohort analysis (MV-adjusted p-trend=0.78 and 0.44, respectively) (Supplemental Table 1). Comparing extreme tertiles of minimum/maximum differences in photoperiod during maternal pregnancy, the MV-adjusted OR for suicide was 0.86 (95% CI=0.55, 1.36).

In additional analyses (results not shown in tables), we observed that women born in northern latitudes had 7% lower odds of lifetime depression (defined as clinician-diagnosed depression and antidepressant medication use during follow up) compared to women born in middle latitudes (MV-adjusted OR=0.93, 95% CI=0.90, 0.95), whereas women in the

southern latitudes had 15% greater odds of depression compared to the same reference group (MV-adjusted OR=1.15, 95% CI=1.11, 1.20). Birth latitude explained most of the variation in minimum/maximum differences in photoperiod during maternal pregnancy (R^2=0.61), which is consistent with the observation that lower (southern) birth latitude is associated with higher odds of depression. There was no association between birth season and lifetime depression in this study regardless of the definition used to define season; for example, the odds of depression were similar comparing women born in winter vs. summer when seasons were centered on the winter/summer solstices and spring/autumn equinoxes (MV-adjusted OR=1.01, 95% CI=0.97, 1.05). Birth season explained the majority of variation in total photoperiod during maternal pregnancy (R^2=0.79), which aligned with our finding of no association between total photoperiod and depression in these cohorts.

Results were similar using our secondary outcome of depression defined as *either* clinician-diagnosed depression *or* antidepressant medication use during follow-up, and when we adjusted models for birth year only.

DISCUSSION

In two large cohorts of adult women, we observed that larger amplitudes of photoperiod change during maternal pregnancy were related to lower odds of lifetime depression. Total photoperiod duration during maternal pregnancy was not independently associated with lifetime depression. The associations for amplitude of photoperiod change appeared to be driven by the presence of extreme differences in photoperiod during the second trimester of maternal pregnancy. The magnitude of these associations was modest, but could translate into larger effects at the population level, particularly given the relatively common occurrence of depression. Overall, these results are consistent with an emerging hypothesis that perinatal light exposure could modulate the risk of affective disorders in humans.

Previous studies have demonstrated that perinatal light exposure may have implications for depression. In rodents, long (summer-like) daily photoperiods during the perinatal period can reduce depressive-like behavior (Green et al., 2015; Pyter and Nelson, 2006), and photoperiodic changes during the perinatal period can influence serotonergic pathways in an enduring fashion (Siemann and McMahon, unpublished data). However, these studies expose rodents to simulated and discrete photoperiods during a much shorter gestational period averaging 21 days compared to our study, which evaluated participants subject to natural and slowly-changing photoperiods across nine months of human gestation. In humans, epidemiologic studies have evaluated birth season (a proxy for light exposure) in relation to depression, with older studies indicating that individuals whose mother's pregnancy spanned summer months (i.e., longer photoperiods) may be at modestly lower risk of depression in adulthood (Disanto et al., 2012; Joiner et al., 2002; Pfaff et al., 2006; Torrey et al., 1996). Yet, two recent studies have yielded equivocal results (Park et al., 2016; Talarowska et al., 2018), and another recent study using data from the National Health and Nutrition Examination Survey (NHANES) found no association between birth season and depression among birth cohorts after 1930 (Schnittker, 2018). Interestingly, the NHANES study also reported that participants born at higher latitudes had significantly less depression compared with those born at lower latitudes, although these results were not discussed in

detail and there were no joint effects of birth season and birth latitude identified for depression. Thus, our results were generally similar to those of the NHANES study, and extend prior work by identifying an association between extreme changes in photoperiod during maternal pregnancy and lifetime depression.

Biologically, there is growing literature to support the notion that prenatal programming can impact psychiatric disorders, which may occur through modulation of the HPA axis with downstream effects on the circadian and limbic systems (Kim et al., 2015). In our study, we found that extreme changes in photoperiod during maternal pregnancy were associated with lifetime depression risk, potentially suggesting a role for early entrainment of the circadian and limbic systems in lowering the risk of mood disorders in adulthood. These results were strongest when we considered light exposure during the second trimester of maternal pregnancy, a critical period of neuronal generation, migration, and organization (Muraki and Tanigaki, 2015; Rakic, 1978). Of particular relevance, the MT1 receptor is necessary for photoperiodic programming of serotonergic neurons and anxiety- and depressive-like phenotypes in rodents (Green et al., 2015), and is widely expressed in the SCN and other brain regions during the second trimester of pregnancy (Thomas et al., 2002). Therefore, as reported in prior studies, environmental exposures during the second trimester of maternal pregnancy may be especially influential for psychiatric disorders in offspring during adulthood (Jakob and Beckmann, 1986; Kovelman and Scheibel, 1984; Mednick et al., 1988; Otake and Schull, 1984; Torrey et al., 1975).

A potential explanation for our finding that greater variation, but not total length, of gestational photoperiod is related to lower depression risk may be based in the conceptual framework of adaptive developmental plasticity, which suggests that early-life input during fetal development can influence the development of adult phenotypes that confer a fitness advantage in the adult environment (Nettle and Bateson, 2015). Although this explanation is speculative at this point, our results could relate to this framework as follows: 1) a fetus receives maternal signals that indicate greater amplitudes of photoperiodic change occurring in the outside environment (input); 2) the fetus responds to a highly dynamic photoperiodic environment by developing more robust circadian and/or limbic systems (adult phenotypes); and 3) these more robust systems reduce an individual’s overall risk of lifetime depression (fitness advantage).

Limitations of this study should be mentioned. First, a key limitation is likely exposure misclassification because we did not collect information on behavioral factors (e.g., time spent outdoors) that influence maternal light exposure during pregnancy. Our method of exposure calculation relied on the assumption that participants’ mothers were exposed to sunlight from sunrise to sunset. However, this assumption is likely to have caused non-differential exposure misclassification, and therefore likely only biased our results toward the null. Second, we identified an association of extreme differences in daily photoperiod (which was determined largely by birth latitude in these cohorts) and lifetime depression, but almost all participants (91%) continued living in their birth latitude at age 15, and most participants (77%) remained in the same latitude at age 30; therefore, it is possible that non-light related factors associated with their birth latitude, even later in life, might explain the observed association. However, if this were the case, we might have expected to observe

comparable associations across all trimesters of maternal pregnancy instead of finding specificity involving the second trimester. In the case of other environmental factors (e.g., temperature), we did not have readily available data to incorporate this information in our analyses, and we cannot rule out the possibility that our observed associations might be attributable to such factors. Future studies should explore this possibility. Third, there is the potential for outcome misclassification. Our primary analyses used an outcome definition based on both depression diagnosis and treatment, which maximized the specificity of the outcome; however, we may have underestimated lifetime prevalence of depression because clinicians tend to under diagnose and undertreat depression, and participants may erroneously report their depression or antidepressant medication status. Still, outcome misclassification was likely non-differential with respect to exposure, and numerous studies conducted in these cohorts have identified important associations with depression using our outcome definitions (Chang et al., 2016a; Chang et al., 2016b; Lucas et al., 2011a; Lucas et al., 2011b; Pan et al., 2010; Trudel-Fitzgerald et al., 2016).

In this study, extreme differences in daily photoperiod, but not total photoperiod, during maternal pregnancy were related to risk of lifetime depression in the participant-offspring. This association was particularly strong during the second trimester of maternal pregnancy. Our results could add support to an emerging hypothesis that perinatal photoperiod may influence depression risk, and they might be understood through the conceptual framework of adaptive developmental plasticity. Clearly, more studies are needed to evaluate the combined effects of birth season and birth latitude in relation to depression. If replicated, however, these results could translate into safe and inexpensive light-related interventions for mothers and babies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Near-birth characteristics of participants in Nurses' Health Study and Nurses' Health Study II across quintiles of total photoperiod during maternal pregnancy (n=160,737) [a]

QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY (BY COHORT)										
	Nurses' Health Study (n=78,308)					Nurses' Health Study II (n=82,429)				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Birth year, %										
<1925	13	13	13	14	14	--	--	--	--	--
1925–1929	20	21	21	20	20	--	--	--	--	--
1930–1934	21	21	21	21	21	--	--	--	--	--
1935–1939	22	21	20	20	20	--	--	--	--	--
1940–1944	24	24	25	25	25	--	--	--	--	--
1945–1949	--	--	--	--	--	16	14	15	14	13
1950–1954	--	--	--	--	--	33	33	33	32	33
1955–1959	--	--	--	--	--	33	33	33	34	33
⩾1960	--	--	--	--	--	18	20	19	20	21
Race, %										
White	98	97	98	97	98	98	97	97	97	98
Black	1	2	1	2	1	1	2	2	2	1
Other	1	1	1	1	1	1	1	1	1	1
Hair color, %										
Dark brown	43	43	43	42	43	39	39	39	38	39
Light brown	38	38	38	38	39	39	38	39	39	39
Blond	11	11	11	12	11	16	16	16	16	16
Black	4	4	4	4	3	2	3	2	3	2
Red	4	4	4	4	4	4	4	4	4	4
Parents owned a home, %	44	43	44	44	44	55	55	54	55	55
Mother's occupation, %										
Professional/executive	9	9	9	9	9	12	12	11	12	12

QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY (BY COHORT)										
	Nurses' Health Study (n=78,308)					Nurses' Health Study II (n=82,429)				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Sales/clerical	12	12	11	12	12	10	10	10	10	9
Craftsman/service	11	10	11	10	11	4	4	4	4	4
Laborer/farmer/military	1	1	1	1	1	4	5	5	4	5
Stay at home	67	68	68	68	67	70	69	70	70	70
Father's occupation, %										
Professional/executive	28	28	28	28	28	29	29	29	29	28
Sales/clerical	37	36	36	36	36	10	10	10	10	10
Craftsman/service	22	22	22	22	23	36	36	35	35	36
Laborer/farmer/military	12	13	13	13	12	24	24	25	25	25
Stay at home	1	1	1	1	1	1	1	1	1	1
Mother smoked during pregnancy, %	12	12	12	12	12	28	27	28	27	27
Birth weight, in pounds, %										
<5.5	7	7	7	7	7	4	4	4	4	4
5.5 to 6.9	33	32	31	31	31	29	30	29	30	30
7.0 to 8.4	46	47	48	47	48	52	52	52	52	51
⩾8.5	14	14	14	15	14	15	14	15	14	15
History of being breast fed, %	64	65	66	65	63	33	35	34	35	33

[a]Percentages are of non-missing values.

Table 2.

Multivariable-adjusted odds ratios of lifetime depression [a] among participants in Nurses' Health Study and Nurses' Health Study II across quintiles of total photoperiod and extreme differences in photoperiod during maternal pregnancy

QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY						
Nurses' Health Study (n=78,308)						
Median values	Quintile 1 (3,209 hours)	Quintile 2 (3,295 hours)	Quintile 3 (3,419 hours)	Quintile 4 (3,542 hours)	Quintile 5 (3,630 hours)	p-trend
Cases of depression (%)	2,064 (13.18%)	2,090 (13.34%)	2,050 (13.09%)	1,954 (12.48%)	2,012 (12.85%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.02 (0.96, 1.09)	1.00 (0.93, 1.07)	0.94 (0.88, 1.01)	0.97 (0.91, 1.03)	0.04
Nurses' Health Study II (n=82,429)						
Median values	Quintile 1 (3,214 hours)	Quintile 2 (3,298 hours)	Quintile 3 (3,418 hours)	Quintile 4 (3,537 hours)	Quintile 5 (3,625 hours)	p-trend
Cases of depression (%)	3,565 (21.63%)	3,565 (21.62%)	3,620 (21.96%)	3,662 (22.21%)	3,598 (21.82%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.01 (0.96, 1.07)	1.03 (0.97, 1.08)	1.05 (0.99, 1.10)	1.02 (0.96, 1.07)	0.26
Combined cohorts (n=160,737)						
Median values	Quintile 1 (3,211 hours)	Quintile 2 (3,297 hours)	Quintile 3 (3,419 hours)	Quintile 4 (3,540 hours)	Quintile 5 (3,628 hours)	p-trend
Cases of depression (%)	5,607 (17.44%)	5,677 (17.66%)	5,682 (17.68%)	5,698 (17.72%)	5,516 (17.16%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.01 (0.97, 1.05)	1.01 (0.97, 1.05)	1.01 (0.97, 1.05)	0.99 (0.95, 1.03)	0.58
QUINTILES OF EXTREME DIFFERENCES IN PHOTOPERIOD DURING MATERNAL PREGNANCY						
Nurses' Health Study (n=78,308)						
Median values	Quintile 1 (4.97 hours)	Quintile 2 (5.57 hours)	Quintile 3 (5.78 hours)	Quintile 4 (5.98 hours)	Quintile 5 (6.20 hours)	p-trend
Cases of depression (%)	2,111 (13.48%)	2,116 (13.51%)	2,066 (13.15%)	1,958 (12.49%)	1,919 (12.30%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	0.96 (0.90, 1.03)	0.92 (0.86, 0.98)	0.88 (0.82, 0.94)	0.88 (0.83, 0.94)	<0.001
Nurses' Health Study II (n=82,429)						
Median values	Quintile 1 (4.55 hours)	Quintile 2 (5.35 hours)	Quintile 3 (5.77 hours)	Quintile 4 (5.95 hours)	Quintile 5 (6.20 hours)	p-trend
Cases of depression (%)	3,913 (23.74%)	3,722 (22.57%)	3,473 (21.05%)	3,352 (20.35%)	3,550 (21.54%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	0.92 (0.87, 0.97)	0.86 (0.82, 0.91)	0.80 (0.76, 0.84)	0.85 (0.81, 0.89)	<0.001
Combined cohorts (n=160,737)						
Median values	Quintile 1 (4.70 hours)	Quintile 2 (5.45 hours)	Quintile 3 (5.78 hours)	Quintile 4 (5.97 hours)	Quintile 5 (6.20 hours)	p-trend
Cases of depression (%)	6,283 (19.56%)	5,848 (18.18%)	5,623 (17.51%)	5,112 (15.87%)	5,314 (16.55%)	

	QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY					
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	0.94 (0.91, 0.98)	0.90 (0.86, 0.93)	0.82 (0.79, 0.86)	0.87 (0.84, 0.91)	<0.001

Abbreviations: CI=confidence interval; OR=odds ratio

[a]Defined as cases with clinician-diagnosed depression and antidepressant medication use during follow up.

[b]Models are adjusted for birth year (⩽1925, 1926–1930, 1931–1935, 1936–1940, ⩾1941 in NHS, and ⩽1945, 1946–1950, 1951–1955, ⩾1956 in NHS II), race (white, black, other), hair color (dark brown, light brown, black, blond, red, missing), parent's home ownership at birth (yes, no, missing), mother's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), father's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), mother's smoking status during pregnancy (yes, no, missing), birth weight (<5.5, 5.5–6.9, 7–8.4, 8.5+ pounds, missing), and breastfeeding (yes, no, missing).

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Table 3.

Multivariable-adjusted odds ratios of lifetime depression [a], by trimester, among participants in Nurses' Health Study and Nurses' Health Study II combined across quintiles of total photoperiod and extreme differences in photoperiod during maternal pregnancy (n=160,737)

QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY						
First trimester						
	Quintile 1 (909 hours)	Quintile 2 (995 hours)	Quintile 3 (1,127 hours)	Quintile 4 (1,264 hours)	Quintile 5 (1,357 hours)	p-trend
Cases of depression (%)	5,461 (16.99%)	5,679 (17.67%)	5,731 (17.83%)	5,755 (17.90%)	5,554 (17.28%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.05 (1.01, 1.09)	1.06 (1.02, 1.11)	1.07 (1.02, 1.11)	1.02 (0.98, 1.07)	0.18
Second trimester						
	Quintile 1 (911 hours)	Quintile 2 (1,007 hours)	Quintile 3 (1,140 hours)	Quintile 4 (1,269 hours)	Quintile 5 (1,357 hours)	
Cases of depression (%)	5,601 (17.42%)	5,667 (17.63%)	5,681 (17.67%)	5,709 (17.76%)	5,522 (17.18%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.09 (1.04, 1.15)	1.14 (1.08, 1.20)	1.09 (1.04, 1.14)	0.98 (0.94, 1.02)	0.51
Third trimester						
	Quintile 1 (921 hours)	Quintile 2 (1,018 hours)	Quintile 3 (1,158 hours)	Quintile 4 (1,288 hours)	Quintile 5 (1,372 hours)	
Cases of depression (%)	5,540 (17.23%)	5,756 (17.91%)	5,717 (17.78%)	5,694 (17.71%)	5,473 (17.02%)	
Multivariable-adjusted OR, 95% CI [b]	1.00 (ref)	1.12 (1.01, 1.23)	1.17 (1.02, 1.34)	1.21 (1.03, 1.43)	1.19 (0.99, 1.44)	0.09
QUINTILES OF EXTREME DIFFERENCES IN PHOTOPERIOD DURING MATERNAL PREGNANCY						
First trimester						
	Quintile 1 (1.30 hours)	Quintile 2 (2.05 hours)	Quintile 3 (2.78 hours)	Quintile 4 (3.48 hours)	Quintile 5 (3.92 hours)	p-trend
Cases of depression (%)	5,729 (17.82%)	5,731 (17.83%)	5,646 (17.56%)	5,609 (17.45%)	5,465 (17.00%)	
Multivariable-adjusted OR, 95% CI [c]	1.00 (ref)	1.00 (0.96, 1.04)	0.98 (0.94, 1.02)	0.98 (0.94, 1.02)	0.96 (0.92, 1.00)	0.02
Second trimester						
	Quintile 1 (1.30 hours)	Quintile 2 (2.08 hours)	Quintile 3 (2.82 hours)	Quintile 4 (3.50 hours)	Quintile 5 (3.92 hours)	
Cases of depression (%)	5,687 (17.69%)	5,796 (18.03%)	5,727 (17.82%)	5,614 (17.46%)	5,356 (16.66%)	
Multivariable-adjusted OR, 95% CI [c]	1.00 (ref)	1.00 (0.95, 1.04)	0.92 (0.87, 0.97)	0.84 (0.80, 0.89)	0.77 (0.72, 0.82)	<0.001
Third trimester						
	Quintile 1 (1.32 hours)	Quintile 2 (2.07 hours)	Quintile 3 (2.80 hours)	Quintile 4 (3.52 hours)	Quintile 5 (3.95 hours)	
Cases of depression (%)	5,731 (17.83%)	5,684 (17.68%)	5,665 (17.62%)	5,637 (17.54%)	5,463 (16.99%)	

	QUINTILES OF TOTAL PHOTOPERIOD DURING MATERNAL PREGNANCY					
Multivariable-adjusted OR, 95% CI [c]	1.00 (ref)	0.97 (0.91, 1.03)	0.96 (0.88, 1.05)	0.96 (0.85, 1.07)	0.93 (0.81, 1.06)	0.45

Abbreviations: CI=confidence interval; OR=odds ratio

[a]Defined as cases with clinician-diagnosed depression and antidepressant medication use during follow up.

[b]Models are adjusted for birth year (⩽1925, 1926–1930, 1931–1935, 1936–1940, ⩾1941 in NHS, and ⩽1945, 1946–1950, 1951–1955, ⩾1956 in NHS II), race (white, black, other), hair color (dark brown, light brown, black, blond, red, missing), parent's home ownership at birth (yes, no, missing), mother's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), father's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), mother's smoking status during pregnancy (yes, no, missing), birth weight (<5.5, 5.5–6.9, 7–8.4, 8.5+ pounds, missing), breastfeeding (yes, no, missing), and total perinatal photoperiod during previous trimesters (in quintiles).

[c]Models are adjusted for birth year (⩽1925, 1926–1930, 1931–1935, 1936–1940, ⩾1941 in NHS, and ⩽1945, 1946–1950, 1951–1955, ⩾1956 in NHS II), race (white, black, other), hair color (dark brown, light brown, black, blond, red, missing), parent's home ownership at birth (yes, no, missing), mother's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), father's occupation in childhood (professional/executive, sales/clerical, craftsman/service, laborer/farmer/military, stay at home parent, missing), mother's smoking status during pregnancy (yes, no, missing), birth weight (<5.5, 5.5–6.9, 7–8.4, 8.5+ pounds, missing), breastfeeding (yes, no, missing), and extreme differences in perinatal photoperiod during previous trimesters (in quintiles).