Seasonality of depressive symptoms in women but not in men: a cross-sectional study in the UK Biobank cohort

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Running title: Seasonality of depressive symptoms

Abstract

Background: We examined whether seasonal variations in depressive symptoms occurred independently of demographic and lifestyle factors, and were related to change in day length and/or outdoor temperature.

Methods*:* In a cross-sectional analysis of >150,000 participants of the UK Biobank cohort, we used the cosinor method to assess evidence of seasonality of a total depressive symptoms score and of low mood, anhedonia, tenseness and tiredness scores in women and men. Associations of depressive symptoms with day length and mean outdoor temperature were then examined.

Results: Seasonality of total depressive symptom scores, anhedonia and tiredness scores was observed in women but not men, with peaks in winter. In women, increased day length was associated with reduced low mood and anhedonia scores, independent of demographic and lifestyle factors. For women, longer day length was associated with increased tiredness. Associations with day length were not independent of the average outdoor temperature preceding assessment.

Limitations: This was a cross-sectional investigation – longitudinal studies of within-subject seasonal variation in mood are necessary. Outcome measures relied on self-report and measured only a subset of depressive symptoms.

Conclusion: This large, population-based study provides evidence of seasonal variation in depressive symptoms in women. Shorter days were associated with increased feelings of low mood and anhedonia in women. Clinicians should be aware of these population-level sex differences in seasonal

mood variations in order to aid recognition and treatment of depression and subclinical depressive symptoms.

Keywords: depression; depressive symptoms; seasonal; anhedonia; photoperiod

Introduction

Seasonal differences in mood and depressive symptoms have often been reported in both the general population and in individuals with mood disorders. At the subclinical level, evidence of greater depressive symptoms, including depressed mood and fatigue, has been reported in winter compared to summer months at temperate latitudes such as Northern Europe, North America and East Asia (Baek et al., 2016; Basnet et al., 2016; Friborg et al., 2012; Kerr et al., 2013; Mersch et al., 2004).

A seasonal subtype of major depressive disorder (previously referred to as *Seasonal Affective Disorder*) may affect up to 3% of the population, and is characterised by reliable onset of depressive episodes in a particular season, usually winter (Levitt et al., 2000; Pjrek et al., 2016). Even among depressed patients not diagnosed with a seasonal subtype, peaks in depressive symptoms and new episodes are more common during winter (Cobb et al., 2014; Patten et al., 2017). New prescriptions of antidepressants also peak in the winter months (Gardarsdottir et al., 2010).

It has been suggested that seasonal variation in mood may be driven by changes in photoperiod (day length) (Walton et al., 2011). Reduced day length and later sunrise in winter is thought to lead to a phase shift in sleep-wake circadian rhythms, associated with disruptions in mood, as well as sleep, immune function, metabolic function, cognition and many other health outcomes (Friborg et al., 2012; Hopstock et al., 2013; LeGates et al., 2014; Meyer et al., 2016). Consistent with a photoperiod hypothesis, light therapy has been shown to be effective in reducing depressive symptoms (Penders et al., 2016).

Despite this assumption of the importance of day length in influencing circadian rhythm-based physiology and psychology, most studies to date have not accounted for the contribution of day length, nor for seasonal variations in other environmental factors such as temperature (O'Hare et al., 2016), and the reliability of conclusions concerning seasonality of mood has often been questioned (Murray, 2017). A number of studies have found no or very weak evidence for seasonal fluctuations

in mood or rates of depression (Traffanstedt et al., 2016; Winthorst et al., 2014), and, of studies that do report seasonal variation, many employ subjective and poorly validated measures such as the Seasonal Pattern Assessment Questionnaire (Magnusson, 1996). In patients diagnosed with a seasonal form of major depressive disorder, only a small minority reliably and persistently show a seasonal pattern (Cobb et al., 2014). The majority of studies simply report cross-sectional differences in outcomes between summer and winter months, or quadratic curves across months (Patten et al., 2017). These fall short of providing evidence of true seasonality as they do not demonstrate the periodicity which is expected if mood symptoms vary in line with regular annual patterns.

These issues can be largely overcome by use of a multivariable cosinor method (Barnett and Dobson, 2010; Cornelissen, 2014). Cosinor-based rhythmometry is able to detect and demonstrate periodicity across time periods, yielding parameter estimates for the amplitude and phase of seasonal variation and giving more robust support for seasonal variation than simple differences between months. Although this method is commonly used with time series data, it can also be applied to cross-sectional survey data (Barnett and Dobson, 2010; Down et al., 2011). Inclusion of lifestyle and environmental variables including day length in multivariable models can also demonstrate whether seasonal change in depressive symptoms tracks change in day length and/or temperature, independently of confounders.

This is an important issue for affective disorders research because evidence of a clear seasonal pattern of depressive symptoms at the population level should be conveyed to clinicians to aid the detection and appropriate treatment of these symptoms (O'Hare et al., 2016). Such evidence may also indicate the utility of screening patients for seasonal patterns in temperate countries (Murray, 2003). In this study, within a very large population cohort, we aimed to assess whether self-reported depressive symptoms show evidence of seasonality and association with environmental variables including day length and temperature, and whether these associations are independent of demographic and lifestyle factors.

Methods

Participants and ethical approval

From 2006-2010, 502,655 participants aged 37-73 years were recruited to the UK Biobank cohort. Participants attended one of 22 assessment centres across the UK and completed a range of lifestyle, demographic, health and mood questionnaires, cognitive assessments and physical measures (Sudlow et al., 2015). The 478,522 participants who completed a touchscreen questionnaire on their mood during the two weeks prior to assessment and who provided data on sociodemographic characteristics were included in this cross-sectional study. Sample sizes for specific analyses differed according to the number of participants with available data for all sociodemographic, lifestyle and environmental variables (sample sizes are reported in results tables, below). As the time of day of commencing the touchscreen assessment was available for only ~170,000 participants, sample sizes were reduced in analyses including this covariate compared to analyses not including this covariate. UK Biobank received ethical approval from the North West Multi-centre Research Ethics Committee (11/NW/03820). The current analyses were conducted under UK Biobank application number 26209 (PI Wyse).

Mood, health and lifestyle variables

The principal outcome measure consisted of scores reflecting the frequency of depressive symptoms over the two weeks prior to the assessment. During a computerised touchscreen assessment, participants were asked to indicate how often over the previous two weeks they had experienced a) low mood (*"Over the past two weeks, how often have you felt down, depressed or hopeless?"*); b) anhedonia (*"Over the past two weeks, how often have you had little interest or pleasure in doing*

things?"); c) tenseness (*"Over the past two weeks, how often have you felt tense, fidgety or restless?"*) and d) tiredness (*Over the past two weeks, how often have you felt tired or had little energy?"*). Participants responded "*not at all*", "*several days*", "*more than half the days*", or "*nearly every day*" to these items. For the current analyses, these responses were coded from 0-3, respectively (that is, 0 = "*not at all*" and 3 = "*nearly every day*"). Items a), b) and d) are derived directly from the Patient Health Questionnaire-9 (PHQ-9), a depression screening instrument (Spitzer et al., 2000), and item c) is a modified version of a further PHQ-9 item ("Over the last two weeks, how often have you been bothered by moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual?"). For participants who responded to all four questions, a total depressive symptom score from 0-12 was calculated from the sum of the scores on each question. In secondary analyses, scores on each individual question were examined as separate outcomes.

Townsend deprivation scores (Townsend, 1987) were derived based on postcode of residence, with negative scores reflecting relatively greater affluence and positive scores reflecting greater deprivation. Smoking status (never smoked, previous smoker, current smoker) and frequency of alcohol intake (never; special occasions only; 1-3 times a month; 1-2 times a week; 3-4 times a week; daily/almost daily) were derived from the touchscreen lifestyle questionnaire. For both smoking and alcohol variables, 'never' was used as the reference category. Participants were asked to report their level and duration of physical activity in a typical day/week by answering physical activity questions derived from the International Physical Activity Questionnaire (Craig et al., 2003). An estimate of metabolic equivalent hours/week (MET.hours/week) of physical activity was derived by applying weights of 2.5, 4 and 8 to self-reported duration of light, moderate and vigorous physical activity, respectively, and then summing these measures. Time of day refers to the time at which participants commenced the touchscreen assessment: start times before 12pm were coded as 'morning', 12pm-5pm as 'afternoon', and after 5pm as 'evening'.

Season of completing the touchscreen assessment was included in some analyses. Following the UK Meteorological Office (Met Office) definitions of meteorological seasons (http://www.metoffice.gov.uk/), assessments taking place in March, April or May were coded as 'spring', June-August as 'summer', September-November as 'autumn' and December-February as 'winter'.

Environmental variables

Day length in hours of daylight on the day of attending the assessment centre was derived from the latitude and longitude of participants' postcode of residence at 1km^2 resolution using open source Geographic Information Systems software, QGIS (http://qgis.osgeo.org). Vectorial algorithms in R (Corripio, 2014) were then used to derive the duration of daylight on the day of attendance of the Biobank assessment centre for each participant. Mean outdoor temperature values consisted of the average outdoor temperature (° Celsius) for the 3 weeks preceding Biobank assessment, calculated from data from the UK Meteorological Office weather station nearest to the assessment centre.

Statistical analysis

Analyses were stratified by gender due to previous findings of greater prevalence and greater seasonality of depressive symptoms in women (Suhail and Cochrane, 1998), and due to evidence of interactions between sex and sine and/or cosine terms for four out of the five outcome variables assessed (Table S1). Sine and cosine transformations of the month of attending the Biobank assessment were calculated using:

1) $\text{Cos}(2\pi(t_i\text{-}1)/12)$
2) $\text{Sin}(2\pi(t_i\text{-}1)/12)$

where t_i is an integer from 1 to 12 representing the month of assessment. For bimodal cosinor models the ((t_i-1)/12) term was multiplied by 2 (Barnett and Dobson, 2010).

To investigate seasonality of depressive symptom scores, negative binomial regression models were employed to account for overdispersion as means for all outcome variables were lower than their variances, and because symptom scores consisted of discrete, non-negative count data. For all models, likelihood ratio tests demonstrated that the overdispersion parameter was significantly greater than 1, indicating negative binomial regression was more appropriate than Poisson (Cameron and Trivedi, 1986). The base model for each outcome included a range of covariates, as described below. Based on the Akaike Information Criterion (AIC), NB2 (mean dispersion) negative binomial models were employed for the total depressive symptom score and low mood, anhedonia and tenseness scores, while for tiredness scores, NB1 (constant dispersion) models were employed (Cameron and Trivedi, 1986). The cosinor method assumes the seasonal pattern of the outcome is sinusoidal: we assessed whether this assumption was valid and therefore whether significant evidence of seasonality was present by testing whether inclusion of sine and cosine transformations of month of assessment (equations 1 and 2) resulted in improved model fit compared to models not including month or a month transformation. Covariates included in the models with and without sine/cosine terms were age, ethnicity (white or non-white), Townsend deprivation score, UK Biobank centre, time of day (morning, afternoon or evening) and day of the week (weekend or weekday) the touchscreen assessment was started, self-reported typical physical activity (MET.hours/week), smoking status, frequency of alcohol intake, and mean environmental temperature. These covariates were selected because all showed associations with outcome (depressive symptom score) variables, and all but smoking status and day of the week of assessment varied by month. Improved model fit, and therefore seasonality, was indicated by i) significance of one or both of the sine and cosine (cosinor) terms ($p < 0.05$) (this indicates the amplitude of the cosinor curve is significantly different from zero); ii) lower Akaike Information Criterion (AIC) for the model including the cosinor terms; and iii) significance of the Wald Chi-squared test of the joint significance of the cosinor terms (Barnett and Dobson, 2010).

The Wald test is equivalent to the Likelihood Ratio Test but can be used with robust standard errors (Armstrong and Sloan, 1989). In resulting cosinor models for which the above criteria were met, amplitude (A) was calculated by:

$$A = \sqrt{\beta^2 + \gamma^2}$$

where β is the cosine negative binomial regression coefficient and γ is the sine negative binomial regression coefficient. Acrophase (ϕ; peak of cosinor model) in months was calculated from:

$$\varphi = 12 * \frac{\tan^{-1}(\gamma / \beta)}{2\pi} + 1$$

Focussing on outcome variables displaying evidence of seasonality, we then examined whether associations with day length existed and whether these were independent of a range of demographic and lifestyle variables (age, ethnicity, Townsend deprivation score, UK Biobank centre, typical physical activity, smoking status, alcohol intake) as well as mean outdoor temperature and time/day of assessment in a series of successive models. These analyses were intended to investigate whether seasonal patterns might be driven by seasonal changes in day length. Analyses were conducted using Stata 14 (StataCorp).

Results

Characteristics of participants

Demographic characteristics are displayed in Table 1, both for the full sample included in any analyses, and for participants with data available for all outcomes and covariates ("subsample"). Participants in the subsample with data for all variables were numerically slightly older and more

deprived and consisted of a slightly higher proportion of ethnic minorities, while their physical activity estimates were slightly higher than the full sample. Formal comparisons of characteristics between samples were not conducted due to overlapping samples, but numerical differences were very small in magnitude, and in general, characteristics were very similar between both samples.

Tests of seasonality using cosinor models

Plots of mean symptom scores and cosinor models are shown for women in Figure 1 and for men in Figure 2. In women, comparison of model fit with and without cosinor terms indicated seasonality of the total depressive symptom score, as well as the anhedonia and tiredness subscores (Table 2). Cosinor terms were significant for low mood scores, but did not significantly improve model fit (p=0.067). The acrophase for the total depressive symptom score occurred in January, while anhedonia and tiredness subscores peaked in February (Table 2 and Figure 1). For tiredness, despite significance of the cosine parameters for a unimodal model (period of 12 months), plots of mean tiredness scores (Figure 1) suggested the scores may be characterised by a bimodal model. This was confirmed by findings of improved model fit for tiredness scores in women when including bimodal sine and cosine terms compared to unimodal terms. Bimodal parameters were not significant for any other outcome measures in women or men.

No evidence of seasonality of the total depressive symptom score, or any individual symptom score was observed for men (Table 2 and Figure 2).

Associations with day length

We then examined whether associations with day length were independent of a range of demographic and lifestyle variables and mean outdoor temperature (Table 3). For women, longer day length was associated with reduced reporting of low mood and anhedonia in women, independent of demographic and lifestyle variables (Models 1-2). These associations with day length were however attenuated in models further adjusting for mean outdoor temperature in the 3 weeks preceding assessment and for time and day of assessment (Models 3-4). Consistent with a contribution of

outdoor temperature to the seasonality of feelings of anhedonia, greater outdoor temperature was significantly associated with reduced anhedonia independently of demographic and lifestyle variables, day length and time/day of assessment (Table 4).

In women, longer day length was associated with increased recent feelings of tiredness after adjusting for demographic and lifestyle variables and mean temperature. The same pattern was observed in men, despite the lack of evidence of seasonality from cosinor models. In women and men, these associations did not, however, survive adjustment for time and day of assessment - as sample sizes were substantially reduced for Model 4 compared to Models 1-3, reduced power may have been a factor here. The apparent bimodal pattern of tiredness scores in women, and the variability in tiredness scores evident in Figure 1E are indicative of a complex relationship between reporting of tiredness and season and day length. Presence of a bimodal pattern of tiredness scores across months might suggest the influence of day length differs by season - tests of an interaction effect and analyses stratified by season are presented in supplementary material (Table S2). Independent of lifestyle, demographic, and temperature covariates, increased day length was associated with reduced reporting of tiredness in autumn, but with *increased* tiredness in winter (Table S2). These results should however be interpreted with caution due to the substantially reduced sample size after stratifying by season.

Effects of self-reported diagnosis of mood disorder

Chi square analysis found that for both women and men, the distribution of participants with self-reported mood disorder (depression or bipolar disorder) did not differ according to season (women: $\chi^2 = 5.55$, $p = 0.136$; men: $\chi^2 = 4.77$, $p = 0.190$; Table S3), suggesting it is unlikely that findings were driven by seasonal differences in the proportion of participants with self-reported existing diagnoses of mood disorder who attended for assessment. Results were also compared after excluding from analyses any participants who self-reported diagnoses of mood disorder, as well as participants

reporting anxiety, panic attacks, 'nervous breakdown', schizophrenia or self-harm/suicide attempt. Associations between low mood scores and day length were attenuated in women to non-significance, but all other associations were unchanged (Table S4 and Table S5).

Discussion

In this study we report evidence of seasonality of depressive symptoms in women but not men within a large sample of middle-aged adults in the UK. Among women, total depressive symptom score and anhedonia peaked in the winter months. Longer day length was associated with reduced reporting of low mood and anhedonia and with increased reporting of tiredness in women, independent of demographic and lifestyle confounders of age, ethnicity, deprivation, UK Biobank centre, typical physical activity, smoking status and alcohol intake. The association of tiredness with day length was also independent of mean outdoor temperature, but the remaining associations did not survive correction for temperature and time/day of assessment, suggesting that environmental factors other than day length may contribute to seasonal fluctuations in mood. Cosinor analysis did not reveal a seasonal pattern of depressive symptoms in men, but men showed similar associations of anhedonia and tiredness scores with day length to women.

These findings of seasonality of depressive symptoms are consistent with a large body of literature reporting lower mood and increased occurrence of depression in winter months (Basnet et al., 2016; Cobb et al., 2014; Patten et al., 2017). However, our study extends previous findings by reporting evidence of periodicity in the seasonal pattern of depressive symptom changes using the cosinor method (Cornelissen, 2014), and by directly examining associations of depressive symptoms with day length and environmental temperature.

Findings of seasonality of mood in women but not men are consistent with previous studies reporting a higher prevalence of depression with seasonal pattern among women (Kerr et al., 2013; Rosen et

al., 1990) and with findings of a winter peak in hospital admissions for depression in women but not men (Suhail and Cochrane, 1998). Support for greater influence of season on depressive symptoms in women has also been reported longitudinally (Harmatz et al., 2000). However, some other studies did not find evidence of sex differences in seasonal depression (Patten et al., 2017; Pjrek et al., 2016).

Although sex differences in seasonality of mood and other outcomes have been relatively under-investigated, some evidence of increased sensitivity of brain electrophysiological responses (P300 event-related potential) to seasonal change in women compared to men has been reported (Kosmidis et al., 1998). Greater endocrine (cortisol) and inflammatory stress responses in women have been linked to increased prevalence of depression (Bale and Epperson, 2015; Kuehner, 2003) and women are more susceptible to depressed mood when inflammation is induced (Moieni et al., 2015). It is plausible that this heightened reactivity to stress in women extends to a more generalised vulnerability to external environmental factors, including change in day length and/or temperature.

Evidence of peaks in feelings of anhedonia in winter months and negative associations of anhedonia and low mood with day length are consistent with predictions (Friborg et al., 2012). Recent feelings of tiredness however were positively associated with day length across the year. Evidence of a possible bimodal pattern of tiredness scores across the year along with an interaction of season with day length indicate that the relationship between season and reporting of tiredness is not straightforward. A possibility is that the tiredness question posed to participants ("*Over the past two weeks, how often have you felt tired or had little energy?"*) is subject to bias where participants respond positively to this question based both on feelings of fatigue as a depressive symptom, but also on general non-pathological tiredness due to external factors such as physical activity levels, work and social factors. Consistent with this, tiredness scores were markedly higher than the other depressive symptom scores in men and women. If this assumption is correct, the overall positive association between day length and tiredness scores across all seasons, and in winter in stratified analyses, could simply reflect greater feelings of tiredness due to external causes which increase alongside increasing daylight, e.g.,

longer waking hours, earlier waking time, greater physical/social activity (O'Connell et al., 2014). In women, the total depressive symptom score and the low mood, anhedonia and tiredness scores were associated with day length independent of demographic and lifestyle confounders (LeGates et al., 2014; Meyer et al., 2016). For each of these outcomes apart from tiredness, associations with day length did not however survive correction for mean outdoor temperature during the 3 weeks preceding the Biobank assessment. Temperature was a significant predictor of low mood and anhedonia scores in women independent of day length and the other demographic/lifestyle confounders. Together these findings suggest that temperature may have a greater influence on seasonal variation in mood than day length, although it remains possible that shared variance between both day length and temperature contributes to fluctuations in depressive symptoms. Consistent with the role of temperature, an earlier study found that colder temperatures within summer were associated with increased prescriptions of antidepressant medication in Sweden (Hartig and Catalano, 2013). Of note, however, a small number of studies have reported no association between depressive symptoms and day length and/or temperature (Huibers et al., 2010; Kerr et al., 2013; O'Hare et al., 2016). One possibility is that effects of environmental variables on mood may be moderated by time spent outdoors and, in particular, time spent in natural light (Keller et al., 2005). Previous findings of a protective effect against depressive symptoms of natural light exposure which coincides with the natural day/light cycle (Dumont and Beaulieu, 2007; Harb et al., 2014) suggest that such factors will be important considerations for future studies aiming to clarify the factors driving seasonal variation in mood.

Previous evidence suggests that latitude may be a further important modifier of seasonal effects on mood. Both within and between countries, higher northern hemisphere latitude is associated with greater seasonal differences in health and mood (Kurata et al., 2016; Rosen et al., 1990), thought to be due to greater seasonal differences in day length and meteorological factors at higher latitudes. The location of the assessment centre was included as a covariate in the current analyses, but direct comparison of effects at higher and lower latitudes within the UK Biobank cohort were made difficult

by the fact that the recruitment time period differed by centre, and sample sizes were substantially smaller at higher latitudes. Such direct comparisons would be informative in future studies.

A limitation of the current study is its cross-sectional nature. The possibility remains that participants recruited to complete the UK Biobank baseline assessment during different months differed due to factors unrelated to seasonality. A follow-up web-based questionnaire which included depressive symptom questions was issued to many UK Biobank participants in 2016-2017. However, as data collection did not span a full year, it would not be possible to gain a clear picture of longitudinal change in mood using this data. Importantly, several studies employing a longitudinal approach have revealed findings similar to the current study, with winter peaks in depressive symptoms (McCarthy et al., 2002; Murray et al., 2001), and seasonal effects in depressive symptoms in women but not men (Harmatz et al., 2000).

A further limitation is that depressive symptom scores were based on subjective responses to retrospective questions about feelings over the previous 2 weeks. Responses may therefore have been subject to recall bias. Questions were derived from the PHQ-9 which has shown very good validity in detecting depression (Martin et al., 2006). Item c) (tenseness) in the current analyses did not, however, ask about recent slowing of movement/speech in addition to restlessness/tenseness, unlike the corresponding PHQ-9 item, and so compounds the issue that only a subset of depressive symptoms were assessed. Furthermore, the combination of the four recent depressive symptom questions used by UK Biobank has not previously been validated as a screening tool. Two of the included items (low mood and anhedonia) are, however, thought to reflect core depressive symptoms and form the PHQ-2, which has also demonstrated very good sensitivity and specificity in screening for depression (Kroenke et al., 2003). As lifestyle measures were based on self-report, and deprivation was based on postcode area, these measures may be subject to bias and some residual confounding may be present.

Measures of physical activity and alcohol intake were based on questions about the typical frequency of these activities, rather than recent trends, meaning that seasonal fluctuation in these lifestyle covariates was not fully taken into account. In addition to questions about typical levels of physical activity, UK Biobank participants also answered questions about the frequency of certain activities (e.g., “DIY”, “stair climbing”, “other exercises”) in the previous 4 weeks, but these questions did not include level or duration of activity and so were not sufficiently detailed to derive a metric of recent activity in metabolic equivalent hours. Recent alcohol intake questions referred only to the last 24 hours. Recent work, however, has demonstrated seasonal variation of the measure of typical physical activity used here (Wyse et al., manuscript in preparation), suggesting these variables based on typical behaviours do in fact capture some seasonal fluctuation.

In summary, we provide evidence that feelings of depressive symptoms (particularly anhedonia) are more common during winter months for women, consistent with previous research. Further, environmental factors including day length and outdoor temperature are important predictors of depressive symptoms, although future studies should also consider the role of time spent outdoors, time spent in natural light, and latitude. These findings have important implications for the provision of healthcare around the world. Subclinical depressive symptoms are associated with increased risk of developing major depression and with reduced wellbeing, but are often under-recognised and untreated (Horwath et al., 1994; O’Hare et al., 2016). Clinicians should be more aware of these differences in the experience of depressive symptoms between women and men across the seasons in order to facilitate their recognition and appropriate treatment (Patten et al., 2017). Use of screening tools for seasonal patterns of depressive symptoms may be of use in identifying patients who may need additional support at certain times of year (Vigod and Levitt, 2011).

Contributors

CAW, DJS and LML contributed to the design of the study. CAW derived cosinor and environmental variables. CACM derived physical activity variables. LML conducted data analysis and drafted the manuscript. DFM advised on analyses and DJS and CAW assisted in manuscript preparation. All authors contributed to editing of the manuscript, and have approved the final version of the manuscript.

Role of funding source

This research was conducted using the UK Biobank resource, under application 26209 (PI Wyse). UK Biobank was established by the Wellcome Trust, Medical Research Council, Department of Health, Scottish Government and Northwest Regional Development Agency. UK Biobank has also had funding from the Welsh Assembly Government and the British Heart Foundation. Data collection was funded by UK Biobank. LML is supported by an NHSGGC Partnership Award awarded to DJS. CAW was funded by a Lord Kelvin Adam Smith Fellowship from the University of Glasgow and a Starting Investigator Research Grant (13/SIRG/2130) provided to AMC from Science Foundation Ireland. BC is supported by a fellowship from the Scottish Executive Chief Scientist Office (ref. DTF/14/03) and by funding from The Dr Mortimer and Theresa Sackler Foundation. JW is supported by the JMAS Sim Fellowship for depression research from the Royal College of Physicians of Edinburgh (173558). DJS is supported by an Independent Investigator Award from the Brain and Behaviour Research Foundation (21930) and a Lister Prize Fellowship (173096). AF is supported by an MRC Doctoral Training Programme Studentship at the University of Glasgow (MR/K501335/1). The funders had no role in the design or analysis of this study, decision to publish, or preparation of the manuscript.

Acknowledgements

The authors are grateful to the participants of the UK Biobank.

Conflict of interest

All authors declare no conflict of interest. JPP is a member of UK Biobank advisory committee; this had no bearing on the study.

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Tables

Table 1. Demographic characteristics for participants included in any analyses ('Full sample'; n=478,522), and participants with data for all included covariates ('Subsample'; n=150,922).

		Full sample		Subsample	
Variable		**Female (n=260,457; 54.43%)**	**Male (n=218,065; 45.57%)**	**Female (n=81,594; 54.06%)**	**Male (n=69,328; 45.94%)**
Age (years), *M* (SD)		56.32 (7.99)	56.78 (8.17)	56.50 (8.04)	57.15 (8.21)
Ethnicity, N (%)					
	White	247,095 (94.87)	206,966 (94.91)	75,503 (92.53)	64,456 (92.97)
	Mixed	1,757 (0.67)	1,037 (0.48)	709 (0.87)	384 (0.55)
	Asian	4,090 (1.57)	4,711 (2.16)	1,958 (2.40)	2,243 (3.24)
	Black	4,262 (1.64)	3,038 (1.39)	2,123 (2.60)	1,418 (2.05)
	Chinese	903 (0.35)	547 (0.25)	339 (0.42)	187 (0.27)
	Other	2,350 (0.90)	1,766 (0.81)	962 (1.18)	640 (0.92)
Townsend deprivation score, *M* (SD)		-1.36 (3.02)	-1.30 (3.13)	-1.21 (2.87)	-1.20 (2.94)
Physical activity (MET.hours/week), *M* (SD)		40.00 (53.44)	49.38 (71.71)	43.03 (54.85)	50.54 (69.80)
Smoking, N (%)					
	Never	154,525 (59.33)	106,548 (48.86)	48,697 (59.68)	34,399 (49.62)
	Previous	81,826 (31.42)	83,843 (38.45)	26,002 (31.87)	26,895 (38.79)
	Current	23,244 (8.92)	26,936 (12.35)	6,895 (8.45)	8,034 (11.59)
	Data missing	862 (0.33)	738 (0.34)	0 (0)	0 (0)
Alcohol intake, N (%)					
	Never	24,372 (9.36)	13,543 (6.21)	7,899 (9.68)	4,350 (6.27)
	Special occasions only	38,864 (14.92)	15,771 (7.23)	12,436 (15.24)	5,189 (7.48)
	1-3 times a month	33,919 (13.02)	19,340 (8.87)	10,759 (13.19)	6,304 (9.09)
	1-2 times a week	67,170 (25.79)	56,304 (25.82)	20,476 (25.09)	17,568 (25.34)
	3-4 times a week	53,727 (20.63)	57,251 (26.25)	16,661 (20.42)	17,784 (25.65)
	Daily/almost daily	42,237 (16.22)	55,693 (25.54)	13,363 (16.38)	18,133 (26.16)

	Data missing	168 (0.06)	163 (0.07)	0 (0)	0 (0)
Self-reported mood disorder, N (%)					
	Depression	18,227 (7.00)	9,496 (4.35)	5,444 (6.67)	2,795 (4.03)
	Bipolar disorder	766 (0.29)	586 (0.27)	248 (0.30)	201 (0.29)
Total depressive symptom score, *M* (SD)		1.73 (2.15)	1.46 (2.04)	1.74 (2.19)	1.48 (2.07)
Low mood score, *M* (SD)		0.35 (0.65)	0.27 (0.59)	0.34 (0.65)	0.27 (0.60)
Anhedonia score, *M* (SD)		0.29 (0.63)	0.29 (0.63)	0.29 (0.63)	0.29 (0.62)
Tenseness score, *M* (SD)		0.35 (0.64)	0.31 (0.61)	0.34 (0.64)	0.30 (0.61)
Tiredness score, *M* (SD)		0.80 (0.87)	0.64 (0.81)	0.77 (0.84)	0.62 (0.79)

MET = metabolic equivalent of task; M = mean; SD = standard deviation

Table 2. Cosinor parameters and model comparison for a) women and b) men

Outcome	Multivariate negative binomial regression estimates						ΔAIC	Wald test		Acrophase (month)	Amplitude
	Sine coefficient (robust SE)	Sine IRR	p	Cosine coefficient (robust SE)	Cosine IRR	p		χ^2	p		
a) Women											
Total depressive symptom score (n=82,325)	0.025 (0.010)	1.025	**0.014**	0.097 (0.036)	1.102	**0.008**	-3.702	7.59	**0.023**	Jan	0.100
Low mood (n=88,008)	0.031 (0.014)	1.031	**0.033**	0.116 (0.053)	1.123	**0.027**	-1.352	5.40	0.067	Jan	0.120
Anhedonia (n=88,889)	0.045 (0.016)	1.046	**0.006**	0.141 (0.060)	1.151	**0.019**	-3.517	7.64	**0.022**	Feb	0.148
Tenseness (n=88,288)	0.012 (0.014)	1.012	0.417	0.086 (0.052)	1.090	0.102	0.910	3.06	0.216	NA	NA
Tiredness* (n=89,418)	0.023 (0.008)	1.023	**0.006**	0.061 (0.030)	1.063	**0.044**	-2.594	7.47	**0.024**	Feb	0.065
Tiredness: bimodal cosinor model* (n=89,418)	0.258 (0.078)	1.294	**0.001**	0.164 (0.049)	1.178	**0.001**	-3.201	11.24	**0.004**	March	0.306
b) Men											
Total depressive symptom score (n=70,072)	-0.008 (0.012)	0.992	0.530	-0.041 (0.044)	0.960	0.346	3.117	0.90	0.637	NA	NA
Low mood (n=74,211)	-0.021 (0.019)	0.979	0.269	-0.077 (0.068)	0.926	0.257	2.557	1.43	0.488	NA	NA
Anhedonia (n=74,481)	-0.020 (0.018)	0.980	0.264	-0.091 (0.065)	0.913	0.162	2.050	1.97	0.373	NA	NA
Tenseness (n=74,297)	-0.002 (0.017)	0.998	0.905	0.003 (0.060)	1.003	0.960	3.943	0.06	0.972	NA	NA
Tiredness*† (n=75,200)	0.006 (0.011)	1.006	0.601	-0.004 (0.039)	0.996	0.924	3.206	0.80	0.670	NA	NA

Negative binomial regression coefficients, robust standard error (SE) and incidence rate ratios (IRR) for sine and cosine transformations of the month of assessment, for a) women and b) men. Models for which coefficients are reported are adjusted for age, ethnicity, Townsend deprivation score, location of Biobank centre, time of day and day of week of the touchscreen assessment, physical activity (MET.hours/week), smoking status, frequency of alcohol intake, mean environmental temperature in 3 weeks preceding assessment, in addition to sine and cosine transformations of month. ΔAIC and Wald test values refer to the differences between this model and a model excluding sine and cosine terms but including all other covariates. Seasonality of outcome variables is inferred from i) significance ($p < 0.05$; indicated in **bold**) of the sine and/or cosine negative binomial regression coefficients and ii) improved model fit following addition of cosinor (cosine and sine) terms, indicated by reduced AIC and significance of the Wald test. For the bimodal cosinor model for tiredness scores in women, ΔAIC and Wald test values refer to the comparison of the model including bimodal cosinor terms with the model including unimodal cosinor terms.
* Alcohol intake excluded as a covariate due to collinearity. † Smoking status omitted due to collinearity.

Table 3. Associations between day length and recent depressive symptoms in a) women and b) men.

	Model 1 b(robust SE)	IRR	p	Model 2 b(robust SE)	IRR	p	Model 3 b(robust SE)	IRR	p	Model 4 b(robust SE)	IRR	p
a) Women												
Total depressive symptom score (n=81,594 - 239,540)	$4.3x10^{-4}$ (0.001)	1.001	0.606	$5.2x10^{-4}$ (0.001)	1.000	0.530	0.002 (0.001)	1.002	0.083	-0.001 (0.002)	0.999	0.597
Low mood (n=87,232 - 256,060)	-0.003 (0.001)	0.997	**0.024**	-0.003 (0.001)	0.997	**0.035**	0.001 (0.002)	1.001	0.518	-0.002 (0.003)	0.998	0.582
Anhedonia (n=88,099 - 259,249)	-0.005 (0.001)	0.995	**0.001**	-0.004 (0.001)	0.996	**0.002**	0.002 (0.002)	1.002	0.320	0.001 (0.004)	1.001	0.857
Tenseness (n=87,506 - 257,438)	*$2.9x10^{-4}$ (0.001)*	*1.000*	*0.805*	*$3.2x10^{-4}$ (0.001)*	*1.000*	*0.788*	*$7.3x10^{-4}$ (0.002)*	*1.001*	*0.715*	*-0.005 (0.003)*	*0.995*	*0.160*
Tiredness (n=88,557 - 261,129)	0.003* (0.001)	1.003	**<0.001**	0.004† (0.001)	1.004	**<0.001**	0.004† (0.001)	1.004	**<0.001**	0.002 (0.002)	1.002	0.264
b) Men												
Total depressive symptom score (n= 69,328 - 203,313)	*0.002 (0.001)*	*1.002*	*0.100*	*0.002 (0.001)*	*1.002*	***0.023***	*$4.9x10^{-4}$*	*1.000*	*0.770*	*0.002 (0.003)*	*1.002*	*0.367*
Low mood (n=73,426 - 215,682)	*-0.003 (0.002)*	*0.997*	*0.059*	*-0.002 (0.002)*	*0.998*	*0.158*	*-0.005 (0.003)*	*0.995*	*0.079*	*$-2.0x10^{-4}$ (0.004)*	*0.999*	*0.963*
Anhedonia (n= 73,695 - 216,810)	*-0.004 (0.001)*	*0.996*	***0.003***	*-0.004 (0.001)*	*0.996*	***0.013***	*-0.001 (0.003)*	*0.999*	*0.643*	*0.002 (0.004)*	*1.002*	*0.602*
Tenseness (n=73,515 - 217,145)	*-0.001 (0.001)*	*0.999*	*0.304*	*-0.001 (0.001)*	*0.999*	*0.503*	*-0.001 (0.002)*	*0.999*	*0.540*	*$1.4x10^{-4}$ (0.004)*	*0.999*	*0.971*
Tiredness (n= 69,633 - 218,065)	*0.007 (0.001)*	*1.007*	***<0.001***	*0.009‡ (0.001)*	*1.009*	***<0.001***	*0.004‡ (0.001)*	*1.004*	***0.011***	*0.004‡ (0.002)*	*1.004*	*0.098*

Negative binomial regression coefficients (b), robust standard error (SE) and incidence rate ratios (IRR) for associations between day length and depressive mood symptoms for a) women and b) men. *Italics* denote variables which did not show evidence of seasonality in Table1. Significant associations ($p<0.05$) are highlighted in **bold**. Sample size was largest for Model 1 and smallest for Model 4 due to inclusion of progressively more covariates for which data was missing for some participants. The range of n from Model 4 to Model 1 is displayed for each outcome.

Model 1 adjusted for age, ethnicity, Townsend deprivation score and location of UK Biobank centre.

Model 2 adjusted for the covariates in Model 1 in addition to physical activity (MET.hours/week), frequency of alcohol intake, and smoking status.

Model 3 adjusted for the covariates in Model 2 in addition to mean outdoor temperature.

Model 4 adjusted for the covariates in Model 3 in addition to the time of day (morning, afternoon, evening) and day of week (weekend/weekday) of touchscreen assessment. This was examined in a separate model from Model 3 due to limited availability of time of day data, resulting in reduced sample size for Model 4.

*Ethnicity covariate omitted due to collinearity. †Smoking status covariate omitted due to collinearity. ‡ Physical activity log(1+x) transformed.

Table 4. Associations between mean outdoor temperature in the 3 weeks preceding assessment and depressive symptom scores in women.

	Model 3			Model 4		
	b (robust SE)	IRR	*p*	b (robust SE)	IRR	*p*
Total depressive symptom score (n= 238,775; 81,594)	-0.002 (0.001)	0.998	0.093	$5.8x10^{-5}$ (0.001)	1.000	0.969
Low mood (n=255,086; 87,232)	-0.003 (0.001)	0.997	**0.020**	-0.002 (0.002)	0.998	0.251
Anhedonia (n=258,256; 88,099)	-0.006 (0.002)	0.994	**<0.001**	-0.005 (0.002)	0.995	**0.042**
Tenseness (n=256,462; 87,506)	$-3.5x10^{-4}$ (0.001)	0.999	0.798	0.003 (0.002)	1.003	0.204
Tiredness (n=260,289; 88,557)	$4.2x10^{-4}$ (0.001)	1.001	0.592	$9.8x10^{-4}$ (0.001)	1.001	0.422

Negative binomial regression coefficients (b), robust standard error (SE) and incidence rate ratios (IRR) for associations between mean outdoor temperature and depressive mood in women. See Table 3 for covariates included in Models 3 and 4. N refers to sample sizes for Model 3 and Model 4, respectively. Significant ($p < 0.05$) associations highlighted in **bold**.

Figures

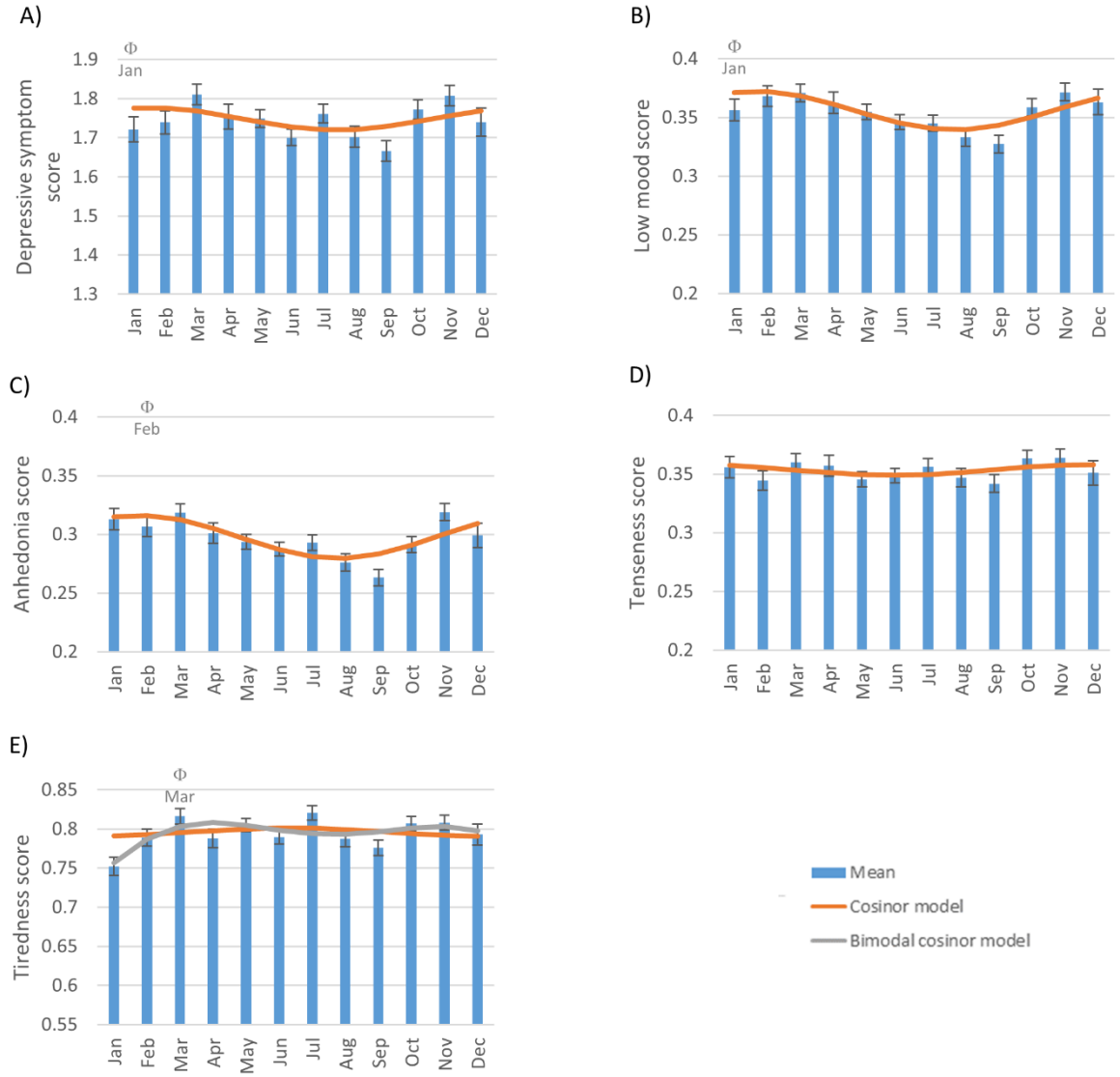

Figure 1. Mean (± robust SE) unadjusted depressive symptom scores in women, fitted with cosinor model to illustrate seasonal pattern. Means, SE and cosinor models are for the subsample of participants with data for all covariates. A) total depressive symptom score; B) low mood C) anhedonia; D) tenseness; E) tiredness. For tiredness (E), both unimodal and bimodal cosinor models are displayed, and the displayed acrophase is for the bimodal model. Acrophase is not displayed for tenseness (D) as evidence of seasonality was not revealed. SE = standard error; Φ= acrophase.

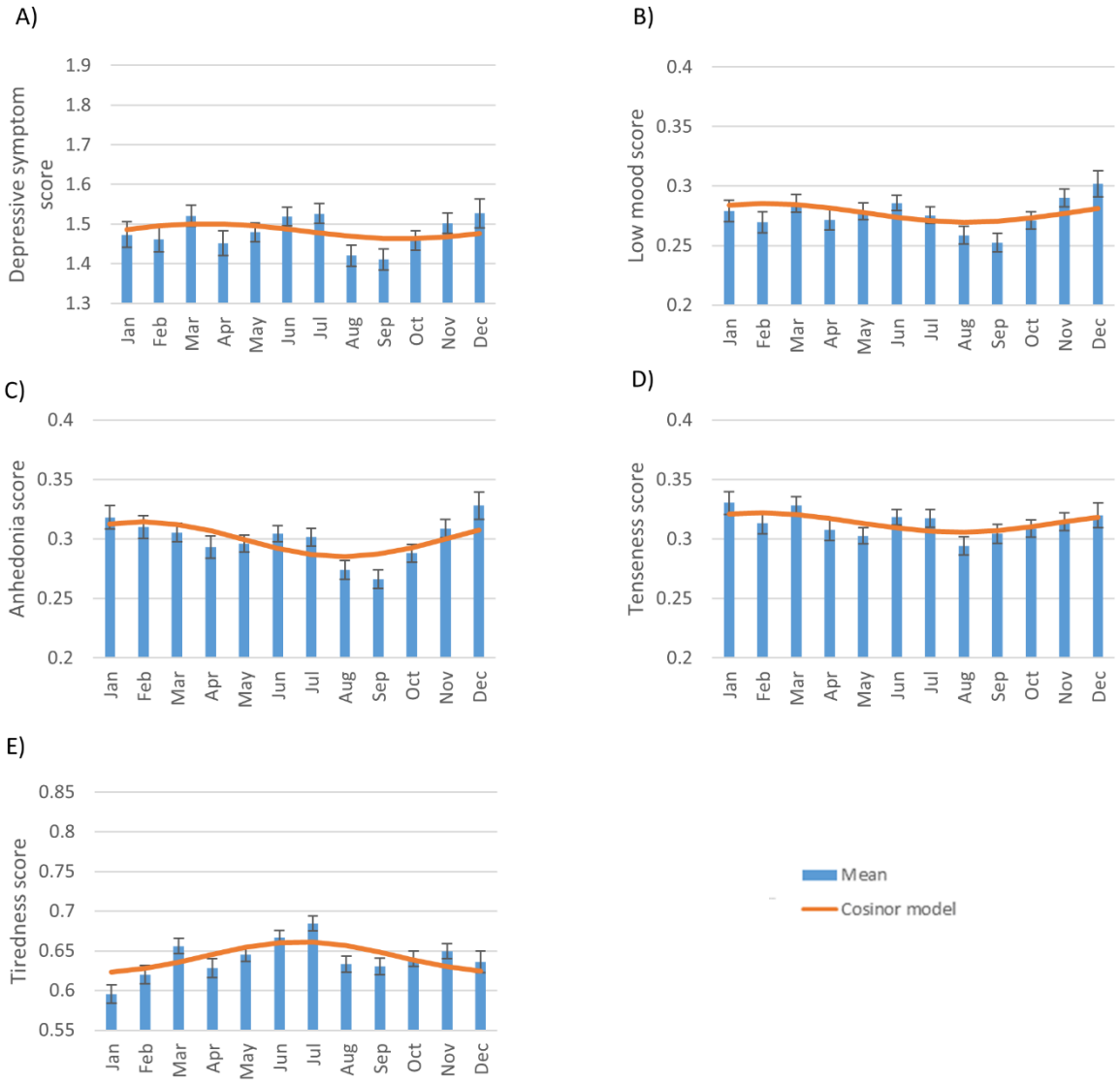

Figure 2. Mean (± robust SE) unadjusted depressive symptom scores in men, fitted with cosinor model to illustrate seasonal pattern. Means, SE and cosinor models are for the subsample of participants with data for all covariates. A) total depressive symptom score; B) low mood; C) anhedonia; D) tenseness; E) tiredness. SE = standard error.