

# Seasonal Effects on Hospitalizations Due to Mood and Psychotic Disorders: A Nationwide 31-Year Register Study

Soili Törmälehto 1, Tanja Svirskis<sup>2</sup>, Timo Partonen 3, Erkki Isometsä 5, Sami Pirkola 4, Marianna Virtanen 1,5, Reijo Sund 6

<sup>1</sup>School of Educational Sciences and Psychology, University of Eastern Finland, Joensuu, Finland; <sup>2</sup>Department of Psychiatry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; <sup>3</sup>Department of Public Health and Welfare, Finnish Institute for Health and Welfare, Helsinki, Finland; <sup>4</sup>Faculty of Social Sciences, University of Tampere and Pirkanmaa Hospital District, Tampere, Finland; <sup>5</sup>Division of Insurance Medicine, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; <sup>6</sup>Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

Correspondence: Soili Törmälehto, School of Educational Sciences and Psychology C/O Institute of Clinical Medicine, University of Eastern Finland, P.O. Box 1627, Kuopio, Fl-70211, Finland, Email soili.tormalehto@uef.fi

**Purpose:** To examine seasonal patterns of hospital admissions due to mood and psychotic disorders and to investigate whether the admission rates show variation according to the seasonal daylength (photoperiods).

**Patients and Methods:** A retrospective nationwide register-based cohort of all psychiatric admissions (N=978,079) during 1987–2017 in Finland was utilized. The smoothed time-series of adjusted ratio of observed and expected (O/E) daily counts were estimated to examine seasonal variation. The mean O/E with 95% confidence intervals (CI) was used to study the admission rates by photoperiods. The calendar days were classified into the 71-day photoperiods based on the daylength (long/summer, short/winter, equal/spring, equal/fall) and the pace of change in daylength (slowly/rapidly increasing/decreasing daylength).

**Results:** Manic episodes peaked in summer during the long (mean O/E=1.10, 95% CI=1.06–1.13) and slowly decreasing (1.09, 1.06–1.13) photoperiods and had a nadir in winter during the slowly increasing (0.93, 0.89–0.98) photoperiod. Admissions for unipolar depressive (UPD) episodes peaked in autumn and in spring at the end of the rapidly decreasing (1.03, 1.02–1.04) and increasing (1.03, 1.01–1.04) photoperiod, and dropped in summer during the long and slowly decreasing (0.95, 0.94–0.96) photoperiods. Bipolar depressive (BPD) and mixed episodes signaled excess admissions in autumn and in spring. Admissions for schizophrenia were higher than expected from summer to early-autumn, during the long and slowly decreasing photoperiods (1.02, 1.02–1.03), and lower than expected in other seasons, especially in mid-spring during the rapidly increasing photoperiod (0.98, 0.98–0.99).

**Conclusion:** The study indicates the seasonality and photoperiodicity of mental disorders, especially for manic episodes. The seasonal pattern is similar between schizophrenia and manic episodes, and between UPD, BPD, and mixed episodes.

**Keywords:** seasonal variation, photoperiod, hospital admission, mood disorders, bipolar disorder, schizophrenia

#### Introduction

Exposure to artificial light in the evening and at night triggers phase delays of the circadian rhythms, contributing to mental health symptoms and changes in the timing and duration of nocturnal melatonin secretion, in turn, trigger seasonal changes in behavior.<sup>1,2</sup> Circadian rhythms are generated and controlled by circadian clocks present in nearly all tissues of the body, although the main clock is located in the hypothalamic suprachiasmatic nucleus and is primarily synchronized by ambient light–dark cycles detected by the eyes. Triggers of mental symptoms and behavior change over the seasons, as being driven by changes in the duration of photoperiod as well as usage of artificial lighting. Seasonal mood changes in patients with depression or bipolar disorder have been explained by changes in natural light–dark cycles and circadian phase shifts,<sup>3</sup> leading to a state of misalignment.<sup>4</sup> Coinciding with the state of circadian misalignment there are circadian clock-related changes in the metabolism of key neurotransmitters, ie, dopamine, serotonin and noradrenaline, and the

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ratio of their hypersensitized to hyposensitized receptors that may result in the onset or deepening of an episode or a relapse. 5 Abnormalities in circadian rhythms not only disturb the sleep-wakefulness cycle but may also contribute to chronic diseases from cardiometabolic diseases to mood disorders.<sup>6</sup>

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), both onsets of symptoms and relapses of depressive and bipolar disorders may exhibit a seasonal pattern, which has been acknowledged as a specifier of major depressive disorder and major depressive episodes of bipolar disorder in the diagnostic criteria. In addition to depression and bipolar disorder, schizophrenia and other psychotic disorders have been associated with abnormal circadian rhythms and seasonality.8

The existing literature on the seasonality of mental disorders is accumulating. Previous studies based on health service utilization have shown that hospital admissions of manic episodes of bipolar disorder mostly peak in spring or summer season with some exceptions. 9-16 A study from the southern hemisphere also observed a sudden turning point upwards in mania admissions parallel with the photoperiod change; in other words, when the day started to lengthen.<sup>14</sup> Depressive episodes of bipolar disorder have been shown to peak in early-winter or spring. 9,10,15,16 Only a few studies have explored the seasonality of mixed episodes of bipolar disorder, suggesting either early-spring, late-spring, summer, or winter peaks. 9,10,15 The minority of studies showed no associations between bipolar disorder related admissions and seasonality. Recently, it has been suggested that not only the seasonal daylength but the pace of change in daylength (rapid or slow) may play a critical role in symptoms of bipolar disorder. 17,18

Patient admission studies on unipolar depressive disorder have inconclusively suggested either winter seasonality or more admissions outside winter (in spring or late-autumn) or no seasonal pattern. 16,19,20 Admission rates of unipolar depressive disorder have been shown to be lower than expected in summer. 16,20

Studies on seasonal variation in schizophrenia have mostly found that admission rates are higher than expected in summer, but spring and winter peaks have also been observed. 21-23 However, some studies have found no seasonal pattern in the schizophrenia admissions.<sup>21</sup>

In sum, although a growing body of research suggests a seasonal pattern in mood disorders and schizophrenia, the results are still inconclusive. As the etiology of mental disorders is multifactorial, it is unlikely that the amplitude of seasonal effect would be large. Therefore, to detect small effects, large sample sizes are essential, but large nationwide studies are still rare. In addition, there are only a few studies reporting seasonality of more than one mental disorder in the same study. Analyzing the patterns of different disorders in the same study allows for a comparison of the magnitude of seasonality between different disorders. Furthermore, there is a lack of studies from high-latitude countries with extreme seasonal variation in daylength. Here, Nordic countries with public health care systems and comprehensive hospital admission registries provide an opportunity to large population-based health research,<sup>24</sup> where a far north location exposes the population to extreme and rapidly changing seasonal variations in light and darkness.

The aim of this study is to investigate seasonality of hospital admissions due to psychotic and mood disorders using a nationwide register-based cohort data from a high-latitude country, Finland. We hypothesized that a photoperiod, in other words, both the daylength and the pace of change in daylength, is associated with the rate of hospital admissions.

#### **Materials and Methods**

# Hospital Admission Register

We used the daily-based hospital admission data which allowed us to examine the seasonal rates of hospital admissions. The data on hospital admissions were derived from the Finnish Care Register for Health Care and its precursor Finnish Hospital Discharge Register maintained by the Finnish Institute for Health and Welfare. The database contains information on all hospital admissions and discharges in Finland since 1969. It includes data, for example, on the admission and discharge dates and diagnoses as well as individual level data on the patient (eg, personal identity code, date of birth and sex). The completeness and accuracy of data in the register has been evaluated to be good.<sup>25</sup> Permission to use the data was provided by the register maintainers. The diagnoses in the database are coded according to the International

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Classification of Diseases (ICD) by the World Health Organization. <sup>26</sup> In Finland, the 10th edition (ICD-10) has been used since 1996, the 9th edition (ICD-9) between 1987 and 1996, and the 8th edition (ICD-8) between 1969 and 1987.

# Design and Sample

The flowchart yielding the final study episodes is presented in Figure 1. The study described psychiatric admissions between 1987 and 2017 due to psychotic and mood disorders (schizophrenia; psychotic disorders; manic, depressive, and mixed episodes of bipolar disorder; unipolar depressive disorder). To identify the relevant study population, the following procedure was followed. First, all psychiatric inpatient hospital admissions since the beginning of 1970 until the end of 2017 were identified. Admissions without personal identity code were excluded (2%, mainly from the period before 1972) because they were unlinkable to create episodes. Next, the primary and all the subsidiary diagnoses (ICD codes in Table 1) linked with admission were remapped in a hierarchical manner as 1) neurodegenerative disorders; 2) schizophrenia; 3) other nonaffective psychotic disorders, such as persistent delusional disorders and acute psychotic disorders; 4) manic episodes of bipolar disorder; 5) mixed episodes of bipolar disorder; 6) other episodes of bipolar disorder; 7) depressive episodes of bipolar disorder; 8) unipolar depressive disorder; and 9) other mental or behavioral disorders. Nested, transfer and readmission (interval between the discharge and readmission shorter than 14 days) hospitalizations were considered as a single episode and were merged to find out the initial admission date of the episode. Hierarchy was applied to categorize the person into a single diagnostic group per episode with more severe mental disorders placed higher in the hierarchy. Thereafter, the episodes with the admission date before 1987 were excluded because ICD-8 and ICD-9 diagnoses may not be fully comparable. The diagnosis at the highest level of the hierarchy was chosen as the primary diagnosis of the episode. Patient's unipolar depression episodes were considered as bipolar depressive episodes if the patient had any episode of unipolar manic or bipolar disorder earlier during the study period. Patients who had been hospitalized due to neurodegenerative disorder were excluded from the first episode of the diagnosis. In addition, the episodes during which the patient was younger than 13 years at the year of admission were excluded because young people aged under 13 are treated in child psychiatric units and the diagnostic criteria differ between children and adolescents or adults.

# Seasons and Seasonal Photoperiods

To study the association of the seasonal daylight exposure with the number of daily hospital admissions, the calendar days were classified according to the photoperiods. The 71-day photoperiods were based on the astronomical seasons, in other words, the summer and winter solstices (June 21 and December 21 or 22) and the vernal and autumnal equinoxes (March 20 or 21 and September 22 or 23), daylength and the pace of change in daylength (Supplemental Table 1). The data on the astronomical seasons, daylength, and rate of change in daylength were derived from the University Almanac Office.<sup>27</sup> Photoperiods based on the daylength were classified as follows: a spring (the vernal equinox  $\pm 35$  days), a long (the summer solstice  $\pm 35$  days), a fall (the autumnal equinox  $\pm 35$  days), or a short (the winter solstice  $\pm 35$  days) photoperiod. The daylength during long and short photoperiods is approximately 18 and 6 hours, respectively. The daylength during spring and fall is equal in length (12 hours), but the direction of change in daylength is opposite. Photoperiods based on the pace of daylength change were classified as follows: a slowly increasing (the winter solstice +70 days), a rapidly increasing (from the end of the previous photoperiod +70 days), a slowly decreasing (the summer solstice +70 days), a rapidly decreasing (from the end of the previous photoperiod +70 days) photoperiod. Additionally, both rapidly increasing and rapidly decreasing photoperiods were split into a beginning (39 days) or a tail end (40 days) of the rapidly increasing or rapidly decreasing photoperiod.

Admission rates were examined by seasons in which December, January, and February were considered as the winter season, March, April, and May as the spring season, June, July, and August as the summer season, and September, October, and November as the autumn season. The categorization into seasons was technical and was applied only after analyses to clarify the verbal interpretation of the visualized results.

# Statistical Analysis

As the number of daily admissions may fluctuate significantly for reasons other than seasonality, the study considered the adjusted ratio of observed and expected daily counts. First, to find out the daily and annual activity of admissions, the

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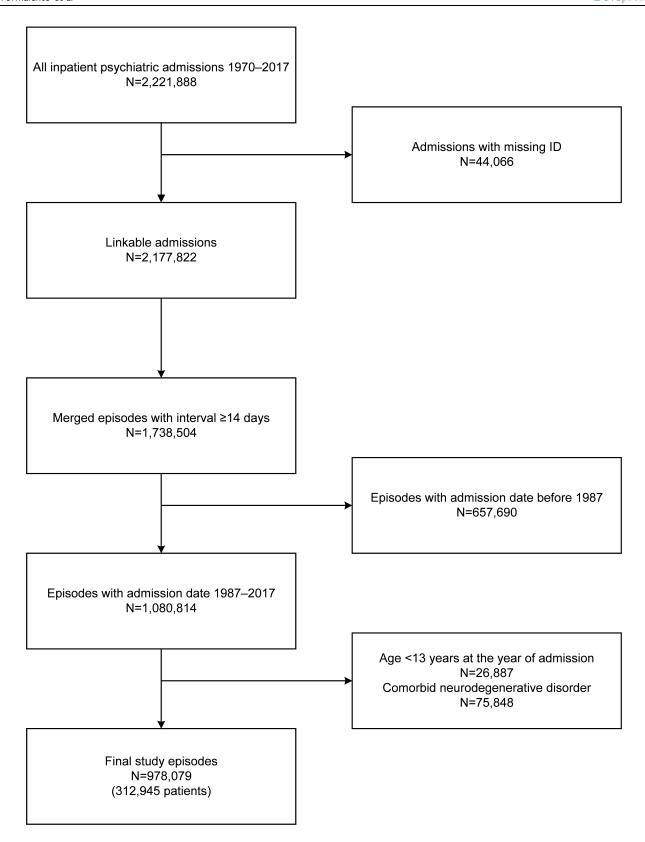


Figure I Flowchart yielding the final study episodes.

daily and annual counts of all psychiatric inpatient admissions between 1 January 1987 and 31 December 2017 were specified based on the admission date of the episode. The daily counts of all admissions were then standardized into an index by dividing them by the annual daily averages. The index reflects the activity of psychiatric inpatient hospital

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Table I Diagnosis Groups Based on ICD-10 and ICD-9 Codes and Hierarchy Used in the Study

Hierarchy Level <sup>a</sup>	Diagnosis	ICD-10 <sup>b</sup>	ICD-9 <sup>b</sup>
1	Neurodegenerative disorders	F00-F09, G30-G32	290, 293–294, 310, 331, 4378A
2	Schizophrenia	F20, F25	295
3	Other non-affective psychotic disorders	F21-F24, F28-F29	297–298
4	Manic episodes of bipolar disorder	F30, F31.0-F31.2	2962
5	Mixed episodes of bipolar disorder	F31.6, F38.00	2964
6	Other episodes of bipolar disorder	F31.7–F31.9	2967
7	Depressive episodes of bipolar disorder	F31.3–F31.5	2963
8	Unipolar depressive disorder	F32–F33, F38.10	2961, 2968
9	Other mental and behavioral disorders	Other F00–F99	Other 290–319

Notes: <sup>a</sup>The diagnosis at the highest hierarchy level was chosen as the primary diagnosis of the episode (the primary and all the subsidiary diagnoses were remapped in a hierarchical manner); <sup>b</sup>In Finland, ICD-10 has been used since 1996 and ICD-9 since 1987 and until 1996.

admissions within a year and enables us to adjust the administrative fluctuation in admissions, such as weekend or holiday season effects. Next, the daily counts of each diagnosis were specified annually. The daily numbers of specific diagnosis were considered as the observed counts. Expected counts were derived by multiplying the annual daily averages of specific diagnosis by the annual daily indices of all psychiatric admissions. Next the ratio of observed and expected (O/E) daily counts was calculated, reflecting the adjusted risk of admission on a specific calendar day due to a specific diagnosis. As the measure is adjusted for administrative fluctuation in daily admissions, it presumably describes the seasonal variation in the incidences more accurately than the unadjusted measure. Finally, the daily O/E values during the study period of 1987 to 2017 were aggregated by calculating a weighted arithmetic mean of O/E for each calendar day from 1 to 366 and for each diagnosis group. The daily O/E was assigned a weight that considered the share of the diagnosis-related admissions relative to all psychiatric admissions in a particular year. Examples of O/E calculation and weighing are presented in Supplementary Tables 2 and 3.

To study the admission rates by seasons, the O/E or the standardized score (Z-score) of O/E was plotted against the calendar days, and the method of locally estimated scatterplot smoothing (LOESS) was applied to fit the curve. An identical smoothing parameter (0.1) was selected for all diagnostic groups to allow for comparison. As a sensitivity analysis, smoothing parameters 0.02 and 0.2 were applied. Hospital admissions were inspected both as the O/E values and Z-scores. The Z-score was utilized to describe the number of standard deviations by which the O/E value deviates from the mean O/E value. The Z-score was used to standardize the distributions of each diagnosis group and to enable the comparison of diagnosis groups with different mean O/E values and different standard deviations.

To study the admission rates by photoperiods, the mean O/E with 95% confidence interval were specified for each photoperiod. First, it was screened, whether there was a difference in admission rates between short versus long photoperiod, or spring versus fall photoperiod, or slowly versus rapidly increasing photoperiod, or slowly versus rapidly decreasing photoperiod concerning each diagnosis group. It was also dissected whether there was a difference in admission rates between the beginning versus the tail end of the rapidly increasing or rapidly decreasing photoperiods. Data preprocessing was carried out in SAS 9.4 and R 3.6.1, and statistical analyses in SAS 9.4.

#### Results

# Sample Characteristics

The cohort included in total 312,945 patients, of which 51% were male. The mean age was 40 years (SD, standard deviation 18 years) at the admission date of the first episode during the years considered in the study (1987–2017). One third of the total number of episodes were the first, 16% were the second, and 10% were the third episode of the same patient during the study years.

There were 978,079 episodes, of which 42% stemmed from schizophrenia and other non-affective psychotic disorders, 32% from mood disorders (bipolar disorder and unipolar depressive disorder), and 26% from other mental and behavioral disorders (Table 2).

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**Diagnosis** Episodes N (%) Patients n (%) Schizophrenia 290,263 (29.7) 53,870 (13.1) Other non-affective psychotic disorders 118,297 (12.1) 66,728 (16.2) 13,231 (3.2) Manic episodes of bipolar disorder 28,358 (2.9) Mixed episodes of bipolar disorder 8,821 (0.9) 5,031 (1.2) Other episodes of bipolar disorder 17,191 (1.8) 8,766 (2.1) 11,936 (2.9) Depressive episodes of bipolar disorder 28,984 (3.0)

Table 2 Number of Inpatient Psychiatric Episodes and Patients According to Diagnosis (ICD-10 or ICD-9) During the Years 1987-2017 in Finland

Notes: <sup>a</sup>Number of patients does not add up to the number of patients (312,945) presented in the flowchart (Figure 1), because the same person may have distinct episodes with a different diagnosis.

229,403 (23.5)

256,762 (26.3)

978.079 (100.0)

119,569 (29.1)

132,398 (32.2)

411,529a (100.0)

# Admission Rates by Season

Total

Unipolar depressive disorder

Other mental and behavioral disorders

Hospital admissions by season presented as the smoothed time series of adjusted ratio of annual daily counts are shown in Figures 2 (Z-score) and 3 (O/E) and Supplementary Figures 1 and 2. Admission rates for manic episodes were higher than expected in late spring and in summer (circa +0.7 SD above the mean O/E) and lower than expected at other times, reaching nadirs in late winter (circa -0.7 SD below the mean O/E) and in late autumn (-0.3 SD). Inflection points, where the curve started to increase, occurred in early February and mid-November, whereas the shift from deficit to excess admissions and vice versa occurred at the turn of April-May and in mid-September.

Admissions due to mixed episodes of bipolar disorder indicated an excess in autumn (+0.3 SD) and in spring (+0.2 SD) and a deficit in winter (-0.3 SD) and in summer (-0.2 SD). Other episodes of bipolar disorder indicated an increase in early winter (+0.5 SD) and a decrease in mid-summer (-0.5 SD). Admission rates for depressive episodes of bipolar disorder were higher than expected in autumn (+0.4 SD) and spring (+0.25 SD) and lower than expected in winter (-0.4 SD) and in summer (-0.3 SD). The shifts from deficit to excess admissions occurred in March and at the turn of August-September, and from excess to deficit in May and November.

For unipolar depressive disorder, the admission rate peaked in autumn (+0.7 SD), had a secondary peak in spring (+0.4 SD), and a minor increase in late winter (+0.25 SD), and had a nadir in summer (-1.2 SD). A secondary dip was observed in early winter, but the admission rate remained at the expected level. Inflection points, where the curve started to increase, occurred in July, in December and in March, whereas the shift from excess to deficit admissions and vice versa occurred in late May and in September. The general trend in admission rates for unipolar depressive disorder contrasted manic episodes but was similar to bipolar depressive episodes and mixed episodes of bipolar disorder.

Admission rates for schizophrenia were higher than expected in summer (+0.7 SD) and early autumn (+0.5 SD) and lower than expected in other seasons, reaching nadirs in mid-spring (-0.7 SD) and in late autumn (-0.5 SD). Inflection points, where the curve started to increase, occurred in late April and mid-November, whereas the shift from deficit to excess admissions and vice versa occurred in late May and in the beginning of October. The general trend in admission rates for schizophrenia was similar to manic episodes. Other non-affective psychotic disorders had excess admissions in early winter (+0.8 SD) and in mid-summer (+0.25 SD).

# Admission Rates by Photoperiod

Mean admission rates related to photoperiods are presented in Table 3. Manic episodes peaked during the long (mean admission rate=1.10, 95% confidence interval=1.06-1.13) and the slowly decreasing (1.09, 1.06-1.13) photoperiods. The admission rate was lower than expected during other photoperiods except the fall photoperiod, reaching the nadir during the slowly increasing photoperiod (0.93, 0.89–0.98).

The admission rate of mixed episodes of bipolar disorder was higher than expected from the spring to the rapidly increasing photoperiod as well as from the fall to the rapidly decreasing photoperiod and lower than expected from the

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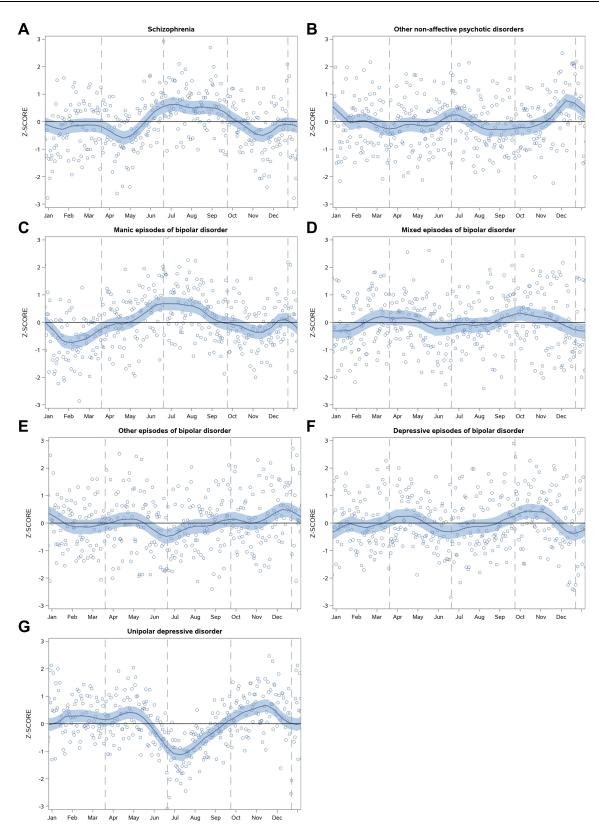


Figure 2 The smoothed time series of adjusted ratio of observed and expected daily counts of hospital admissions (presented as standard Z-score) for schizophrenia (A), other non-affective psychotic disorders (B), manic episodes of bipolar disorder (C), mixed episodes of bipolar disorder (D), other episodes of bipolar disorder (E), depressive episodes of bipolar disorder (F), and unipolar depressive disorder (G) during the years 1987–2017 in Finland.

Notes: The circles represent a weighted arithmetic mean of O/E (observed/expected) values presented as standard Z-score during the study period. The shaded area represents the 95% confidence interval for the fitted curve. Vertical dashed lines from left to right represent vernal equinox, summer solstice, autumnal equinox, and winter solstice, respectively. Smoothing parameter 0.1.

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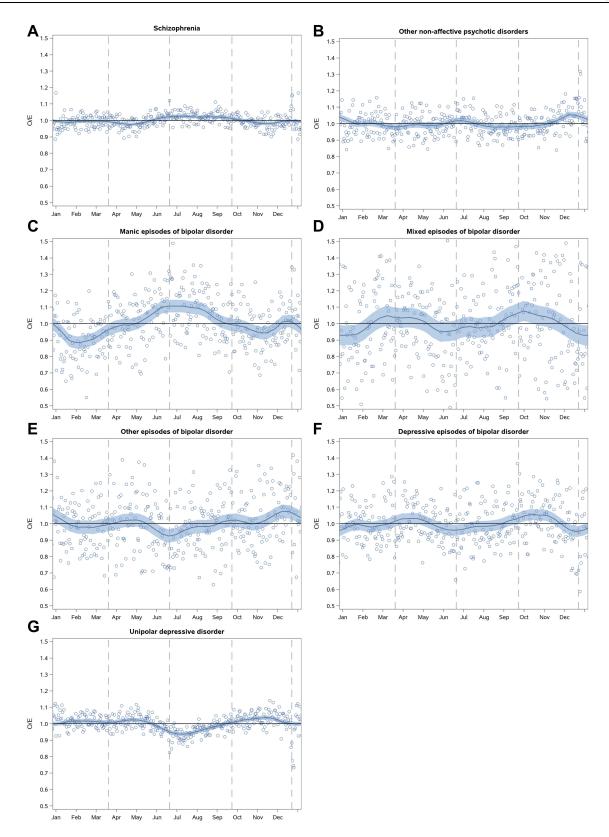


Figure 3 The smoothed time series of adjusted ratio of observed and expected daily counts of hospital admissions for schizophrenia (A), other non-affective psychotic disorders (B), manic episodes of bipolar disorder (C), mixed episodes of bipolar disorder (D), other episodes of bipolar disorder (E), depressive episodes of bipolar disorder (F), and unipolar depressive disorder (G) during the years 1987–2017 in Finland.

Notes: The circles represent a weighted arithmetic mean of O/E (observed/expected) values during the study period. The shaded area represents the 95% confidence interval for the fitted curve. Vertical dashed lines from left to right represent vernal equinox, summer solstice, autumnal equinox, and winter solstice, respectively. Smoothing parameter 0.1.

**Table 3** Mean Observed/Expected Count of Admissions During the Years 1987–2017 in Finland by Diagnosis Groups and Photoperiods and Upper and Lower Limits of 95% Confidence Intervals (CI)

Photoperiod <sup>a</sup>	N	Mean (95% CI) <sup>b</sup>
Schizophrenia		
Slowly increasing	71	0.99 (0.98–1.01)
Spring		0.99 (0.98–1.00)
Rapidly increasing		0.98 (0.98–0.99)
Start of rapidly increasing	39	1.00 (0.99–1.01)
End of rapidly increasing	40	0.97 (0.96–0.98)
Long		1.02 (1.01-1.03)
Slowly decreasing		1.02 (1.02-1.03)
Fall	71	1.01 (1.00-1.02)
Rapidly decreasing	71	1.00 (1.00-1.01)
Start of rapidly decreasing	39	1.02 (1.01-1.03)
End of rapidly decreasing	40	0.99 (0.99-1.00)
Short	71	0.99 (0.98-1.00)
Other non-affective psychotic disorders		
Slowly increasing	71	1.01 (0.99–1.03)
Spring	71	0.99 (0.97-1.00)
Rapidly increasing	71	0.98 (0.97-1.00)
Start of rapidly increasing	39	0.98 (0.96-1.00)
End of rapidly increasing	40	0.99 (0.97-1.02)
Long	71	1.01 (0.99-1.02)
Slowly decreasing	71	1.00 (0.98-1.02)
Fall	71	0.98 (0.97-1.00)
Rapidly decreasing	71	0.98 (0.97–0.99)
Start of rapidly decreasing	39	0.98 (0.96–1.00)
End of rapidly decreasing	40	0.99 (0.97–1.00)
Short	71	1.03 (1.01–1.05)
Manic episodes of bipolar disorder		
Slowly increasing	71	0.93 (0.89-0.98)
Spring	71	0.95 (0.92-0.98)
Rapidly increasing	71	0.97 (0.94–1.00)
Start of rapidly increasing	39	0.95 (0.92-0.99)
End of rapidly increasing	40	0.98 (0.94–1.03)
Long	71	1.10 (1.06–1.13)
Slowly decreasing	71	1.09 (1.06–1.13)
Fall	71	1.00 (0.97–1.03)
Rapidly decreasing	71	0.98 (0.95-1.01)
Start of rapidly decreasing	39	1.00 (0.96-1.04)
End of rapidly decreasing	40	0.97 (0.92-1.01)
Short	71	0.97 (0.93-1.01)
Mixed episodes of bipolar disorder		
Slowly increasing	71	0.98 (0.92-1.03)
Spring	71	1.04 (0.99-1.09)
Rapidly increasing		1.02 (0.98-1.07)
Start of rapidly increasing		1.05 (0.99–1.12)
End of rapidly increasing	40	1.03 (0.96–1.09)
Long		0.96 (0.91-1.02)
Slowly decreasing		1.00 (0.95–1.04)
Fall	71	1.04 (0.99–1.10)
Rapidly decreasing	71	1.05 (1.00–1.11)

(Continued)

Table 3 (Continued).

Photoperiod <sup>a</sup>		Mean (95% CI) <sup>b</sup>
Start of rapidly decreasing		1.04 (0.97–1.10)
End of rapidly decreasing		1.04 (0.96–1.12)
Short		0.95 (0.90–1.01)
Other episodes of bipolar disorder		
Slowly increasing		1.00 (0.96–1.03)
Spring		1.00 (0.96–1.04)
Rapidly increasing		1.00 (0.97–1.04)
Start of rapidly increasing		0.99 (0.94-1.04)
End of rapidly increasing		1.01 (0.95-1.07)
Long		0.96 (0.93-0.99)
Slowly decreasing		0.96 (0.93-1.00)
, G Fall		1.00 (0.97-1.04)
Rapidly decreasing		1.01 (0.97-1.04)
Start of rapidly decreasing	39	1.02 (0.97-1.07)
End of rapidly decreasing	40	0.98 (0.94-1.03)
Short	71	1.04 (1.01-1.08)
Depressive episodes of bipolar disorder		
Slowly increasing		0.97 (0.94-1.00)
Spring	71	1.02 (0.99-1.05)
Rapidly increasing	71	1.03 (1.00-1.05)
Start of rapidly increasing	39	0.99 (0.95-1.03)
End of rapidly increasing	40	1.04 (1.01-1.08)
Long	71	0.97 (0.94–1.00)
Slowly decreasing		0.98 (0.95-1.01)
Fall	71	1.03 (1.01-1.06)
Rapidly decreasing	71	1.05 (1.02–1.08)
Start of rapidly decreasing		1.02 (0.98–1.06)
End of rapidly decreasing	40	1.05 (1.01-1.09)
Short		0.98 (0.95-1.02)
Unipolar depressive disorder		
Slowly increasing	71	1.01 (0.99–1.02)
Spring	71	1.01 (1.01-1.02)
Rapidly increasing		1.02 (1.01-1.02)
Start of rapidly increasing	39	1.01 (1.00–1.02)
End of rapidly increasing	40	1.03 (1.01–1.04)
Long		0.96 (0.95–0.97)
Slowly decreasing		0.95 (0.94–0.96)
Fall		1.01 (1.00–1.02)
Rapidly decreasing		1.02 (1.01–1.02)
Start of rapidly decreasing		1.00 (0.99–1.01)
End of rapidly decreasing		1.03 (1.02–1.04)
Short		1.01 (1.00–1.03)

**Notes:** <sup>a</sup>Photoperiods (daylength and pace of change) are described in <u>Supplemental Table 1</u>; <sup>b</sup>The mean O/E with 95% CI for each photoperiod to study the admission rates by photoperiods.

short to the slowly increasing photoperiod as well as during the long photoperiod. The admission rate related to other episodes of bipolar disorder was higher than expected during the short photoperiod (1.04, 1.01–1.08), and lower than expected from the long (0.96, 0.93–0.99) to the slowly decreasing photoperiod.

The admission rate related to depressive episodes of bipolar disorder was higher than expected during the spring photoperiod as well as from the fall (1.03, 1.01–1.06) to the rapidly decreasing photoperiod (1.05, 1.02–1.08). The

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admission rate was lower than expected from the short to the slowly increasing photoperiod as well as from the long to the slowly decreasing photoperiod.

The admission rate related to unipolar depressive episodes was lower than expected from the long (0.96, 0.95–0.97) to the slowly decreasing (0.95, 0.94–0.96) photoperiod and higher than expected during any other photoperiod. Admissions reached the highest level during the tail ends of the rapidly increasing (1.03, 1.01–1.04) and the rapidly decreasing (1.03, 1.02-1.04) photoperiods.

The admission rate related to schizophrenia was higher than expected from the long (1.02, 1.01–1.03) and the slowly decreasing (1.02, 1.02–1.03) photoperiods to the start of the rapidly decreasing (1.02, 1.01–1.03) photoperiod. The admission rate was lower than expected from the tail end of the rapidly decreasing photoperiod to the rapidly increasing photoperiod (0.98, 0.98–0.99).

Admissions due to other non-affective psychotic disorders were higher than expected from the short (1.03, 1.01–1.05) to the slowly increasing photoperiod as well as during the long photoperiod. The admission rate was lower than expected during other photoperiods except the slowly decreasing photoperiod.

## Discussion

This large nationwide study from a high-latitude Nordic country provided new evidence of the association between seasonality and mental disorders. The study adds knowledge on the seasonal admission rates and their association with photoperiods. The distinct seasonal pattern was observed especially for manic episodes, but also for unipolar depressive episodes and schizophrenia. Although the effect sizes were relatively small, the findings do indicate that seasonal effects may play a role in hospital admissions due to mental disorders. In addition, we found some similarities in admissions between manic episodes and schizophrenia, as well as in admissions between unipolar and bipolar depressive episodes and mixed episodes of bipolar disorder.

Our results of seasonality in mania agree with the previous nationwide register-studies from Austria, Denmark, and the Czech Republic, showing that hospital admissions due to manic episodes are at their highest during summer or summer-autumn seasons 11,15,16 when the daylight hours are at maximum. Interestingly, we could not replicate the previously observed manic episodes coinciding with the increasing daylength in spring. 9,10,12-14 Instead, we found a nadir in admissions in winter when the daylength was slowly lengthening. After that, the admission rates started to rise which indicated a manifestation of manic episodes with the rapidly increasing daylength, even though the final shift from a deficit to excess admissions occurred later in May. Sleep loss due to the disturbed sleep-wake cycle or behavioral activities can trigger symptoms of hypomania or mania in vulnerable persons, 28 and as exposure to light might have a similar effect in some patients with seasonal forms of bipolar disorder.<sup>29</sup> this may explain the increase in manic episode admissions during spring/summer season. Conversely, the admissions started to decline when the daylength was rapidly shortening, followed by the shift from a peak to deficit admissions in September and a secondary drop in late autumn. A study from Poland has also reported a drop in manic episode admissions in late autumn.<sup>10</sup>

In line with the previous findings, <sup>16,20</sup> but opposite to the manic episode admissions, the unipolar depressive disorder admissions dropped in the summer season, followed by a rise during the period when the daylength was at its most extreme but then slowly shortening. Major seasonal peaks for unipolar depression were found in autumn and in spring. Consistently, the Czech study found two major rises in autumn and in spring. 16 The major peaks found for depressive episodes in our study occurred in periods in which the day and night are almost equal, but the daylength is either rapidly shortening or rapidly lengthening. Depressive symptoms of seasonal affective disorder are generally linked with light deprivation in autumn and winter seasons, but symptoms may exacerbate also in spring, as also observed in our study. It is known that light may induce pain, 31,32 which could partly explain the aggravation of depressive symptoms with increasing light exposure in spring, as well as the spring peaks of suicides.<sup>33</sup> Our results give support to the idea that ambient light has a bidirectional effect, both ameliorating or inducing depressive symptoms.<sup>34</sup>

It is noteworthy that depressive episodes of bipolar disorder indicated a similar seasonal pattern as unipolar depressive disorder with autumn and spring excess and drops in mid-summer and early winter. A higher rate of depressive episode admissions in spring has been reported earlier 10,16 as well as a lower rate in summer 10 and early winter. 16 We could not confirm the previous findings concerning early-winter 9,15 or summer 9 seasonality.

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Our results supported the previous studies mostly reporting summer seasonality of schizophrenia, although some have suggested spring or winter seasonality or no seasonal pattern. <sup>21–23</sup> On the other hand, previous studies have also reported higher rates of schizophrenia admissions associated with temperature increases.<sup>21</sup> Therefore, it has been suggested that not only daylight hours or abnormalities in circadian rhythms, but also higher temperature may trigger acute episodes of schizophrenia.<sup>21</sup>

Both manic episodes and schizophrenia presented excess admissions in the summer season coinciding with the extreme hours of daylight, and the admissions due to these diagnoses started to increase in spring when the daylength was rapidly lengthening. Unipolar depressive episodes showed autumn and spring seasonality during the periods in which the day and night were almost equal in length but the daylength was either rapidly shortening or lengthening. These admissions, contrary to manic episodes and schizophrenia, dropped in summer. Bipolar depressive episodes indicated similar autumn and spring seasonality to that of unipolar depressive episodes. One possible explanation for schizophrenia admission trend coupling with manic episodes could be a shared genetic basis for these disorders.<sup>35</sup> It may also hold for bipolar depressive episodes coupling with unipolar depressive episodes. Seasonal pattern similarities and differences between diagnostic groups may also be explained by the circadian phase shifts, which have been shown to be advanced in manic episodes but delayed in depressive and mixed episodes of bipolar disorder.<sup>3</sup> These disorders may also share similar symptoms (eg., acute psychotic episodes of schizophrenia and those of psychotic mania), or symptoms opposite by polarity (eg, mania and depression), 36 which may play a role in their seasonal trends. There are seasonal fluctuations in the longer-term activity level as well as the shorter-term dynamics of monoamine neurotransmitters in these disorders, 5,37 which might explain further the similarities and differences in the seasonal trends.

Our findings also imply that mixed episodes cluster with depressive episodes. The mixed episode is characterized as a condition in which symptoms of both polarities of bipolar disorder (mania or hypomania and depression) are present during most days. Mixed episodes have been suggested to cluster with depressive episodes because the predominant polarity of depression associates with the onset polarity, being either depressive or mixed, as well as with a higher number of mixed episodes. 38,39

Other episodes of bipolar disorder implied excess admissions in early winter coinciding with few hours of daylight, and fewer admissions in mid-summer. Also, other non-affective psychotic disorders peaked in early winter and associated with short daylength but had another increase in mid-summer.

The main strength of the present study is the utilization of a nationwide register which covers the individual-level information on all hospital admissions in Finland dating back decades. The study exploited a 31-year period and, consequently, with 978,079 hospital episodes and 312,945 patients, this is the largest study on seasonality in mental disorders. The study also covers multiple diagnoses from psychotic disorders to mood disorders. Secondly, the geographical location of Finland in the far north and with extreme seasonal variation in daylength makes this study unique. The high latitude exposes the population to extreme variation and rapid changes in photoperiods: in the southern part of the country, the daylength is around 18 hours in mid-summer season, whereas in mid-winter the daylength is roughly 6 hours. In northern Finland, the contrast in daylength is even more intense. Finally, the study considered the administrative fluctuation in hospital admissions in order to filter the primary focus on seasonality. In other words, there is regular fluctuation in hospital admissions due to weekend or holiday season effects. Furthermore, the overall number of psychiatric hospital beds varied during the study period due to a notable deinstitutionalization process in Finland between 1987 and 2009, during which numerous psychiatric hospitals were closed. To rule out this period effect, we utilized the annually standardized counts to adjust the daily admissions, and the daily and photoperiodic results are shown as aggregates of a longer period, ie, of 31 years. This adjustment of daily fluctuations is important as it allows us to extract pure seasonal variation from the trends, but similar techniques have been used only rarely in earlier studies.

Our study has some limitations to be considered for interpreting the results. First, hospital admissions describe the incidence of severe episodes of mental disorders only, and therefore the results are not necessarily generalizable to the less severe or untreated episodes. In addition, the date of hospital admission is a proxy measure, as there is an interval between the onset of symptoms and hospitalization. However, the interval is probably shorter with manic or psychotic episodes which are more challenging to treat in an outpatient setting than, for example, depressive episodes without psychotic symptoms or selfdestructiveness. The median latency between symptom onset and hospitalization in mania has been suggested to be 2 weeks, ranging from 1 day to 16 weeks. 40 Consequently, the bias caused by a proxy measure may be less significant than expected.

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Second, the increased use of antidepressants and mood stabilizers may also dilute the seasonal effects. However, pharmacoepidemiologic studies have shown that the rate of hospital admissions in bipolar disorder remains substantial despite maintenance therapy, even though the mood stabilizers reduce the risk of hospitalization. <sup>41,42</sup> Third, there is also uncertainty related to the diagnoses of unipolar and bipolar depressive disorders, since persons diagnosed with unipolar depressive disorder may have had bipolar disorder. 43 However, unipolar depression episodes were considered as bipolar, if the patient had any episode of bipolar disorder earlier during the study period, and the seasonal pattern was mostly similar for both unipolar and bipolar depressive episodes. Also, other episodes of bipolar disorder are a heterogeneous group and the present study also included the bipolar episodes coded without a specifier of polarity, hence the conclusions should be drawn with caution in this diagnosis group. Fourth, the study applied astronomical seasons, in other words, the solstices and equinoxes, and not the real amount of solar radiation to which the individuals were exposed. There are other factors, such as clouds, snow cover and precipitation, that also influence light exposure. 44 However, because of the high latitude, there is considerable seasonal variation in daylength in Finland, and hence the study exploited a rational estimate of population-level light exposure. Finally, we acknowledged hierarchically the most severe diagnosis, and thus ignored the psychiatric comorbidities related to the episode which may have confounded the seasonal effect.

In addition to academic and scientific interest, seasonality should also be considered in the treatment of mood and psychotic disorders. First, screening for the seasonal variations in mood and behavior may help in identifying the individuals at high risk of season-bound course of illness. Second, the detection of a seasonal pattern may help in anticipating the clinical effort needed for intensifying their treatment. Climate change may also be reflected in the public mental health, as the winter season is expected to become darker due to a shorter duration of snow cover, increased cloudiness and precipitation and reduced solar radiation. 45,46 Furthermore, the thermal seasons will change due to an expected increase in air temperature. 47 To further study the seasonality of hospital admissions due to mental disorders, the individual-level exposure to solar radiation, together with air temperature and the secular trend in biometeorological variables, should be considered. Further research could focus on the development of a model using the photoperiod as a variable to predict hospitalization risk in clinical setting. Such models might deliver potential clinical benefits as a decision-making tool in practice.

#### Conclusion

We found seasonality in hospital admissions due to major mental disorders as well as significant associations of the photoperiod with admission rates. The seasonal pattern and associations with photoperiods were the most notable for manic episodes, but also for unipolar depressive episodes and schizophrenia. The results were principally consistent with the previous literature supporting higher rates of manic episode and schizophrenia admissions in summer and higher rates of depressive disorder admissions in autumn and spring. Our findings suggest that the seasonal pattern of manic episodes and schizophrenia are quite similar and that unipolar depressive disorder, depressive episodes of bipolar disorder and mixed episodes of bipolar disorder present similar seasonal patterns. These findings give supporting evidence for the hypothesis that individuals with mental disorders are sensitive to stimuli such as ambient light, or that ambient light may trigger an episode of a certain mental disorder.

#### **Abbreviations**

BPD, bipolar depressive; CI, confidence interval; DSM-5, the Diagnostic and Statistical Manual of Mental Disorders; ICD, the International Classification of Diseases; LOESS, locally estimated scatterplot smoothing; O/E, observed/ expected; SD, standard deviation; UPD, unipolar depressive.

# **Data Sharing Statement**

The data that support the findings of this study are available from the Finnish Institute of Health and Welfare, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Permission to the data used in this study can be applied from the Finnish Social and Health Data Permit Authority Findata.

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# **Ethics Approval and Informed Consent**

This study was conducted retrospectively from data obtained for research purposes. The pertinent institutional authority at the Finnish Institute of Health and Welfare (THL/1695/6.02.01/2019) and at Statistics Finland (TK-53-500-19) granted the permission to use the register data. These authorities also pseudonymized the data. Neither ethics committee approval nor informed consent are required for register-based studies in Finland. This study was performed in line with the principles of the Declaration of Helsinki or comparable ethical standards.

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