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Circadian preference and mental health outcomes in youth: A systematic review and meta-analysis

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ABSTRACT

Youth is a vulnerable developmental period associated with an increased preference for eveningness and risk for developing psychopathology. Growing evidence suggests a link between eveningness and poorer mental health outcomes, but the findings in the current literature are inconsistent, and a comprehensive synthesis of evidence in this area remains lacking. This meta-analysis aimed to 1) synthesise the existing evidence on the association between circadian preference and mental health outcomes in youths and 2) explore potential sleep-related factors that may moderate the relationship between circadian preference and mental health outcomes. A systematic search of five electronic databases resulted in 81 observational studies included in the review. Eveningness was found to be significantly associated with general mental health ($r = 0.20$), mood-related disturbances ($r = 0.17$), and anxiety problems ($r = 0.13$). The qualitative review also identified that eveningness was associated with greater risks for psychotic symptoms and maladaptive eating behaviours. These findings highlighted the need to consider circadian preference in the clinical management of youth mental health problems. Further research is needed to examine the efficacy of a circadian-focused intervention in the context of youth mental health.

1. Introduction

Youth and adolescence are vulnerable developmental periods with substantial changes and challenges that may lead to the emergence of mental health problems [1]. One of the marked changes in sleep patterns is a shift in circadian preference towards eveningness with later bedtime and rise time [2]. This evening tendency has been linked to an increased risk of developing mental illnesses, especially mood symptoms [3,4]. Some evidence from longitudinal studies suggests a possible causal relationship, where eveningness was identified as a potential risk factor for developing mental health problems in youths [5]. Nonetheless, some studies found no association between evening preference and psychopathologies [6,7]. Given that youth is a sensitive period with susceptibility to mental health problems, there is a need for a comprehensive synthesis of the existing evidence to clarify whether circadian factors are implicated in the risk of youth psychopathologies.

There have been a few narrative reviews on the association between circadian preference and psychopathologies [4,8–15]. However, a comprehensive synthesis of the empirical evidence remained very limited, especially in the youth population. Au and Recee systematically reviewed and analysed 36 studies from 1976 to 2016, reporting a significant association between eveningness and depressive symptoms ($r = -0.20$) [16]. More recently, Norbury updated the literature up to 2021 and found similar findings on the association between eveningness and depressive symptomatology ($r = -0.21$) [17]. However, both meta-analyses included studies with a wide age range across several developmental stages (aged 13 to 55) that were not explicitly focused on the youth population. In addition, both studies focused exclusively on depressive symptoms and only included self-report questionnaires as measures of circadian preference. The relationship between circadian preference and other psychopathologies remained unclear and there is also a need to look into the findings based on the objective measures of circadian preference.

Previous research has suggested that individuals with eveningness are more susceptible to sleep disturbances, such as poorer sleep quality and greater sleep loss during weekdays, due to the misalignment between their circadian preference and the society's demands for early

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Abbreviations

BAD	bipolar affective disorders
CBCL	child behaviour checklist
COVID	Coronavirus disease
DLMO	dim-light melatonin onset
HAMD	Hamilton depression rating scale
ICC	intra-class correlation
ISI	insomnia severity index
MEQ	morningness-eveningness questionnaire
MESC	morningness-eveningness scale for children
NOS	Newcastle-Ottawa scale
OR	odd ratios
PRISMA	preferred reporting items for systematic review and meta-analysis
PSQI	Pittsburgh sleep quality index
SDQ	strengths and difficulties questionnaire
SMD	standardised mean difference
UHR	ultra-high risk

wake time (e.g., early school start time) [18]. These sleep problems could potentially moderate the relationship between eveningness and mental health outcomes. One recent study has demonstrated that evening-type adolescents with comorbid insomnia had significantly higher odds of having depression and suicidality than those with eveningness only or insomnia only [19]. Although there has been some research suggesting that several sleep-related factors, such as insomnia, poor sleep quality, and a lack of sleep, potentially impact the association between circadian preference and mental health outcomes in youths [20,21], a systematic synthesis on these potential moderating factors has been lacking.

Considering youth is a crucial period often associated with changes in circadian preference and the emergence of mental health problems, the current study aimed to systematically synthesise the existing evidence on the association between circadian preference and a broad spectrum of mental health outcomes with a particular focus on youths. It was hypothesised that evening preference would be significantly associated with mental health problems in youths. Secondly, it was hypothesised that multiple sleep factors, specifically insomnia symptoms, sleep quality, and sleep duration, would moderate the link between circadian preference and mental health outcomes.

2. Methods

The current review followed the guideline set forth by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [22] and was registered with the International Prospective Register of Systematic Reviews (CRD42020170048).

2.1. Search strategy

Articles were searched from five major electronic databases: PubMed, Web of Science, PsycINFO, Scopus, and EMBASE. Potential articles were searched from the database's inception to June 2021 using the following search terms: ("chrono*" OR "circadian" OR "eveningness" OR "morningness" OR "owl" OR "lark" OR "diurnal preference") AND ("psycho*" OR "mental disorder" OR "psychiatric disorders" OR "mood" OR "affective" OR "depress*" OR "anxi*") AND ("teen" OR "youth" OR "adolescen*" OR "young adult"). The initial search was limited to the studies conducted in human subjects. Two authors (FTWC and TKH) independently completed the article selection process in two phases. First, all titles and abstracts were reviewed, and those not meeting the inclusion criteria were excluded. Next, the full text of the remaining articles was assessed for eligibility for inclusion in the current review. To enhance the scope of the review, a manual search based on the reference list of the published papers was also conducted to identify other potentially relevant articles. Disagreements between the two authors were resolved by consulting and discussing with a third author (SXL).

2.2. Selection criteria

Articles were eligible for this review if they met the following criteria: 1) naturalistic observational studies (i.e., cross-sectional, case-control, cohort) published in a peer-reviewed journal, 2) written in English, and 3) conducted in the youth population with the sample mean age between 12 and 24 years old or in a secondary school (high school) sample if age was not reported. This age range was chosen to broadly cover the developmental period from young adolescence and the early phase of young adulthood. The lower bound of this chosen age range was based on the median age of puberty onset at 12 years old, whereas the upper bound was based on the United Nations' definition of youths (up to the age of 24). This wider age range would allow for studying circadian issues in relation to youth mental health from a wider developmental context. Exclusion criteria included grey literature, such as book chapters, commentaries, conference proceedings, clinical guidelines, editorials, meeting statements, unpublished manuscripts, and reports. As the current review was not aimed to examine the cohort effect under the impact of the Coronavirus pandemic, the studies that specifically investigated the association of circadian preference and mental health outcomes in the context of COVID-19 were excluded.

2.3. Exposure measures

The exposure was the circadian preference. A broad definition of *circadian preference* was adopted in the current review, including an individual's circadian typologies measured using self-report scales, chronotype based on wake and sleep timing, and the endogenous circadian phase reflected by circadian biomarkers. Therefore, the following exposure measures were included: 1) circadian typologies quantitatively measured by a validated scale [23], 2) the midpoint of sleep (defined as the clock time between sleep onset and offset) measured by self-report scales or ecological measurements, such as sleep diary and actigraphy, and 3) circadian rhythm physiological markers, such as actigraphy parameters (i.e., acrophase) and the endogenous melatonin biomarker derived from dim-light melatonin onset (DLMO).

2.4. Outcome measures

The current review focused on mental health outcomes defined by the following: validated self-report, clinician-rated scales, or the presence of psychiatric disorders according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases.

2.5. Data extraction

Data were extracted into Microsoft Excel and were checked to ensure accuracy. Relevant data obtained from each study included the article's metadata (i.e., authors, year, region of data collected), study design, sample composition, sample demographics (i.e., sex ratio and mean age), circadian preference measures, mental health outcome measures, statistical methodology, and key findings on the association between circadian preference and outcome measures. The authors were contacted if the relevant data of the eligible articles were missing or ambiguous.

2.6. Risk of bias assessment

Two raters independently appraised all reviewed articles using a modified Newcastle-Ottawa scale (NOS) to assess the quality of observational studies [24]. The NOS has been used extensively for assessing the risk of bias in meta-analysis in previous research [25]. Each article was assessed and scored based on the following three areas: *Selection* (e.g., recruitment strategy, sample size, sample representativeness), *Comparability* (i.e., the comparability of cohorts based on study design), and *Exposure/Outcome* (e.g., ascertainment of exposure or outcomes and the appropriateness of selected statistical test). Each article could receive a score ranging from 0 to 9, where a higher score represented a lower risk of bias. Articles with less than five points were considered to have a high risk of bias [25]. The two raters had a good inter-rater agreement (ICC = 0.86, 95% CI [0.35, 0.97]). The discrepancy in the scores between the two raters was resolved through discussions, with the final agreed score assigned to each study.

2.7. Data synthesis and statistical analysis

Data synthesis was conducted in Microsoft Excel after data extraction. Effect sizes were expressed as zero-order Pearson's correlation coefficients between exposure and outcome measures. Pearson's r was directly extracted or calculated from statistical information reported using the respective conversion formula. For the studies comparing continuous data between two or more groups (e.g., morning-type vs neither-type vs evening-type), a standardised mean difference (SMD) was calculated between the two most extreme groups (i.e., morning-type vs evening-type) [26]. For the studies reporting the likelihood of mental health outcomes (i.e., dichotomised data), odds ratios (OR) were used to calculate their respective effect sizes. The SMD and OR effect sizes were converted to Pearson's r to facilitate the interpretation and comparison between studies. Fisher's r-to-z transformation was used when pooling the Pearson's r effect sizes and reconverted to Pearson's r for presentation. Correlational data was prioritised if the study presented multiple effect sizes (e.g., when both correlations and between-group differences were provided). For the convenience of interpretation, the direction of effect size was set that a positive effect reflects that circadian preference toward eveningness increases the likelihood of psychopathology and a negative effect reflects that circadian preference toward morningness increases the possibility of psychopathology. For the studies that provided multiple measures of the same constructs (e.g., Hasler et al., 2010 [27] adopted both the Beck's depression inventory [BDI] and Hamilton rating scale for depression [HAMD] as the measures of depressive symptoms), the effect size of different measures of the same construct was averaged before pooling in the analyses. For the studies that reported results separately for males and females (e.g., Borisenkov et al., 2015 [28]), the effect sizes were combined into one effect size.

A meta-analysis was performed if at least three studies were available for the outcome measure. All the analyses were completed on R 3.5.2, primarily using the "dmetar" and "metafor" packages [29–31]. As considerable heterogeneity was anticipated across the studies, a random-effect model with Hartung-Knapp adjustment was used to estimate the pooled effect sizes. Tau-squared was estimated using a restricted maximum-likelihood estimator. Heterogeneity was indicated using Cochrane's Q and I-squared statistics. Publication bias was assessed by visually examining the contour-enhanced funnel plots and with Egger's test [32]. Statistical significance was set to a p-value of 0.05 for all tests.

Sensitivity analysis was conducted if there was a high heterogeneity and at least three studies were available. Influential cases and outliers were removed from the analyses based on interpreting Baujat plots [33]. Subgroup analyses or meta-regression were conducted on exposure and outcome measures, timeframe of the outcome scales, sample age group, sex ratio, composition, and study design to account for potential heterogeneity due to methodological diversity. Finally, a meta-regression was used to examine potential moderators (i.e., insomnia severity, sleep quality, and sleep duration) between circadian preference and mental health outcomes. A minimum of three effect sizes were needed to perform a meta-regression.

3. Results

The PRISMA diagram for searches, article selection, and inclusion is presented in Fig. 1. The searches yielded 16,565 citations, of which 8,217 were duplicates. Eight additional articles were identified from the reference list of the published articles. A total of 8,037 articles were excluded following an initial screening of titles and abstracts, and 238 articles were further excluded after a full-text review, resulting in 81 eligible articles included in the final review. The review identified five major groups of outcomes after data extraction, namely 1) general mental health (n = 16), defined as outcomes measuring global psychopathological symptoms (e.g., measured by symptom checklist 90), childhood behavioural problems (e.g., measured by strengths and difficulties questionnaire), or overall mental wellbeing (e.g., measured by general health questionnaire), 2) mood-related disturbances, including depressive symptoms and mania (n = 56), 3) anxiety problems (n = 28), 4) psychosis (n = 3), and 5) eating disorder-related behaviours (n = 2). The total sample size included in the review was N = 86,965.

3.1. Characteristics of the included studies

A summary of the included studies is presented in Tables 1–5. Among the 81 articles, most of the studies had a cross-sectional design (n = 71), followed by a longitudinal design (n = 9), and only one study adopted a case-control study design. Only cross-sectional associations between circadian preference and mental health outcomes at baseline could be extracted and included in the meta-analysis from four longitudinal studies [34–37] due to the lack of bivariate analysis on longitudinal data. Nonetheless, the prospective results for the longitudinal studies were summarised qualitatively. Nine studies [34,38–46] did not provide the mean age and were included based on the source of recruitment (secondary schools). Of those studies that provided data on age, the mean age was 19.0 ± 3.1, where 38% of the studies (n = 27) had a sample mean age between 12 and 18, whilst the remaining studies had samples aged 18 or above (63%, n = 45). University students (n = 42) made up most of the samples' composition, followed by secondary school students (n = 23) and participants recruited from the community outside of the school setting (n = 8). Six studies involved psychiatric patients recruited from outpatient clinics or mental health centres, one involving adolescents recruited from medical speciality clinics [47], and one involving young enlisted military personnel [48].

3.2. Risk of bias assessment

The summary of the risk of bias assessment is presented in supplementary data Table S1. Most of the included studies (n = 67, 82.7%) were considered to have a low risk of bias. The assessment revealed that the most frequent source of bias was the respondents' selection and sample size justifications. Authors most frequently failed to mention how participants were reached and provide justifications on the population and the number of participants needed. Studies were not excluded due to having a high risk of bias. Subgroup analysis showed no significant differences in the results of the meta-analyses between low- and high-risk studies.

3.3. Publication bias

A visual inspection of the contour-enhanced funnel plots and Eggers' test statistics indicated no evidence of publication bias for any of the meta-analysed outcomes (general mental health: y = 0.81, p = .558; mood-related disturbances: y = 0.99, p = .062; anxiety problems: y =

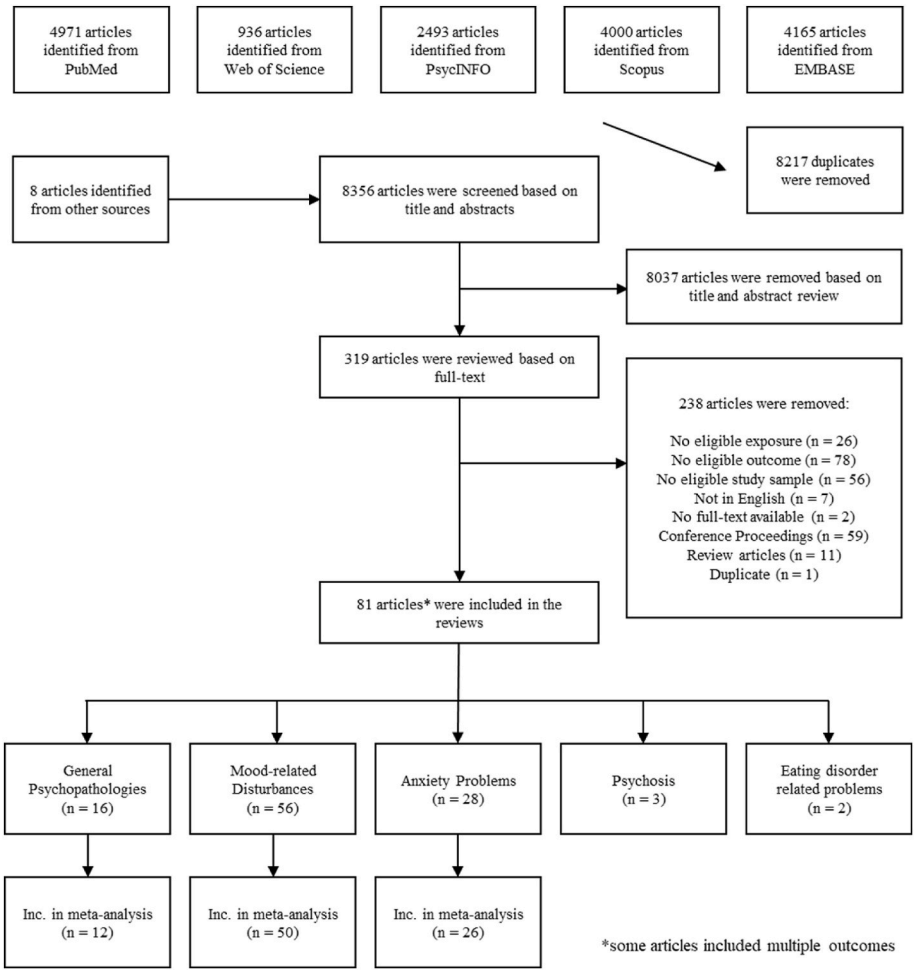

Fig. 1. Flowchart of literature searches and study selections.

0.68, $p = .486$). The three funnel plots are available as supplementary data in Fig. S1.

3.4. Circadian preference and general mental health

Sixteen studies examined the relationship between circadian preference and general mental health (see Table 1) [38,40,47,49–61], of which 12 studies were included in the meta-analysis. Considerable heterogeneity (Q = 143.00, $p < .001$; $I^2 = 92.3\%$) was found and two studies [49,52] were identified as influential cases which were subsequently excluded from analysis (Supplementary Table S2), resulting in an overall pooled effect of r = 0.20, 95% CI [0.15, 0.26], $p < .001$ with a prediction interval of 0.04–0.36. Subgroup analyses in terms of circadian and outcome measures and sample age showed no significant differences (Supplementary Table S3). Similarly, meta-regression showed no significant moderating effect of sex ($\beta = 0.001$, $p = .844$).

Four studies could not be included in the meta-analysis due to insufficient data to derive a correlation coefficient [38,40,50,51]. Among these studies, two conducted in secondary school students reported that eveningness was associated with more behavioural and emotional problems [38,50], whilst one study conducted in university students demonstrated that eveningness was associated with more severe psychopathological symptoms and morningness was associated with better mental well-being [51]. Lastly, one study found no significant association between circadian preference and common psychiatric disorders in university students [40]. Fig. 2 shows the forest plot of the included studies after removing influential cases.

3.5. Circadian preference and mood-related disturbances

There were 56 studies that investigated the associations between circadian preference and mood-related disturbances (see Table 2) [5,7,19–21,27,28,34–37,41–46,48,54,62–98], of which 50 studies were included in the meta-analysis. The initial pooled effect had a high heterogeneity (Q = 847.00, $p < .001$; $I^2 = 93.4\%$) with four studies [45,79,85,93] identified as influential cases, which were removed from further analysis (Supplementary Table S2). The resulting overall pooled effect was r = 0.17, 95% CI [0.14, 0.20], $p < .001$, with a prediction interval of 0–0.34. Subgroup analysis revealed a significant between-group difference in outcome measures, Q = 37.09, $p < .001$. Mood-related outcomes, including both depressive symptoms (r = 0.18) and mania (r = 0.18), were associated with eveningness more strongly than seasonality-related affective problems (r = 0.08), suggesting a potential source of heterogeneity. Meanwhile, there were no significant differences in circadian measures, sample age and composition, and study design in subgroup analyses (Supplementary Table S4). Similarly, sex ratio did not significantly moderate the association between circadian preference and mood-related disturbances ($\beta = -0.001$, $p = .518$).

All but four cross-sectional studies included in the meta-analysis [27,62,72,77] showed significant associations between circadian preference and mood-related disturbances. However, longitudinal studies provided mixed results on the associations. Out of five longitudinal studies included in the review, three studies [5,79,96] showed that eveningness at baseline predicted greater depressive symptoms at follow-up ranging from six months to two years. In contrast, two longitudinal studies found an insignificant relationship between baseline eveningness and future

Table 1
Characteristics and main findings of included studies on general mental health.

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings[2]
Concepcion et al. (2014) [49]	N[#]	Chile	C–S	University	928	70.3	21.9 (3.4)	MEQ	GHQ-12	Past few weeks	ns
Gau et al. (2007) [38]	N	Taiwan	C–S	Secondary School	1332	48.80	NR	MESC	CBCL	Unspecified	+
Giannotti et al. (2002) [50]	N	Italy	C–S	Secondary School	6631	60.10	16.7 (1.7)	MESC	Composite[3]	Unspecified	+
Gulec et al. (2013) [51]	N	Turkey	C–S	University	220	67.70	20.25 (4.0)	MEQ	SF-36 + SCL-90-R	Past month + Lifetime	- SF-36; + SCL-90-R except phobic anxiety
Haregu et al. (2015) [52]	N[#]	Thailand	C–S	University	2970	66.9	20.4 (1.3)	MEQ	GHQ-12	Past few weeks	+
Hidalgo & Caumo (2002) [40]	N	Brazil	C–S	University	342	41.80	Range 18-35	MEQ	SRQ-20	Past month	ns
Hsu et al. (2012) [53]	Y	Taiwan	C–S	University	2919	51.5	19.4 (3.1)	MEQ	BSRS[4]	Past week	+ except phobic anxiety
Jankowski & Dmitrzak-Weglarz (2017) [54]	Y	Poland	C–S	University	338	51.0	22.2 (2.2)	CSM	GHQ-28	Past few weeks	+
Lange & Randler (2011) [55]	Y	Germany	C–S	Secondary School	300	50.0	13.62 (1.2)	CSM	SDQ	Past 6 months	+ total difficulties, conduct problems, hyperactivity; - pro-social behaviours
Li et al. (2018) [56]	Y	Hong Kong	C–S	Secondary School	4948	48.9	14.5 (1.8)	MEQ	SDQ	Past 6 months	+
Prat & Adan (2013) [57]	Y	Spain	C–S	University	507	66.5	21.4 (2.9)	CSM	GHQ-28	Past few weeks	+
Rose et al. (2015) [58]	Y	Peru	C–S	University	2538	61.2	21 (2.7)	MEQ	GHQ-12	Past few weeks	+
Schneider et al. (2011) [59]	Y	Brazil	C–S	University	372	66.7	21.6 (3.1)	MEQ	SRQ-20	Past month	+
Simon et al. (2020) [47]	Y	USA	C–S	Outpatients (Obese Clinic)	26	63.6	16.4 (1.1)	MESC	SDQ	Past 6 months	+
Tokur-Kesgin, (2021) [60]	Y	Turkey	C–S	Secondary School	1083	54.7	16.2 (0.9)	MEQ	GHQ-12	Past few weeks	+
Vardar et al. (2008) [61]	Y	Turkey	C–S	University	142	53.5	19.9 (1.3)	MEQ	SCL-90-R[3]	Lifetime	+

Abbreviations: BSRS = brief symptom rating scale; CBCL = child behaviour checklist; C–S = cross-sectional; CSM = composite scale for morningness; ET = evening type; GHQ = general health questionnaire; L = longitudinal; MEQ = morningness-eveningness questionnaire; MESC = morningness-eveningness scale for children; MT = morning type; NR = not reported; NT = neither type; SCL-90-R = symptoms checklist-revised; SDQ = strengths and difficulties questionnaire; SF-36 = short form health survey; SRQ = self-reporting questionnaire.

Notes:

[1] Age is presented as mean (standard deviation) unless otherwise specified.

[2] "+" denotes a significant positive association between eveningness and outcome measures; "-" denotes a significant negative association between eveningness and outcome measures; "ns" denotes no significant associations between circadian measures and mental health outcomes.

[3] The authors combined the total score of Rutter anxiety and Kandel and Davies depressed mood scales as a composite score of emotional problems.

[4] The global severity index (GSI) was used in the meta-analysis.

[#] Study was excluded from meta-analysis after influential case analysis.

depressive symptoms or diagnosis of depression [41,64]. Lastly, one study identified a different pattern of the associations between circadian preference and mood-related disturbances, where morningness was found to be significantly associated with depressive symptoms even after controlling for potential confounding variables [82]. A forest plot summarising the effect sizes after removing influential cases is presented in Fig. 3.

Six studies [43,44,84,88,90,96] were not included in the meta-analysis due to insufficient data. Two of these studies [43,84] showed a cross-sectional association between self-reported eveningness and a higher level of depressive symptoms. In contrast, one study conducted in young patients with ultra-high risk of psychosis found no significant association between circadian preference measured by the morningness-eveningness questionnaire (MEQ) and self-reported depressive symptoms [90]. A potential gender difference was reported in two studies [28,44], in which significant associations between eveningness and mood-related disturbances were found only in females but not in males. Lastly, Robillard et al. (2014) [88] found that participants with a higher level of depressive symptoms (HAMD $\geq$ 8) had an earlier acrophase than their counterparts with a lower level of depressive symptoms (HAMD < 8), suggesting earlier but not delayed circadian preference was associated with depressive symptoms.

3.6. Circadian preference and anxiety problems

There were 28 studies that examined the associations between circadian preference and anxiety problems (see Table 3) [7,19,35–37,43,62,63,65,66,68,69,71,79,80,84,89,92,94,99–105], of which 26 studies were included in the meta-analysis. The pooled effect size suggested that eveningness was significantly associated with more anxiety problems. The initial pooled effect had a high heterogeneity ($Q = 209.7$, $p < .001$; $I^2 = 88.1\%$). As a result, three studies [89,105,106] identified as influential cases were removed from subsequent analysis (Supplementary Table S2). The overall pooled effect was $r = 0.13$, 95% CI [0.09, 0.18], $p < .001$, with a prediction interval of −0.05 to 0.31. There were no significant differences in subgroup analyses on outcome measures,

Table 2
Characteristics and main findings of the included studies on mood-related disturbances.

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings[2]
Alvaro et al. (2014) [7]	Y	Australia	C–S	Secondary School	318	48.4%	14.96 (1.3)	MESC	RCADS	Unspecified	+
Aoun et al. (2019) [62]	Y	Lebanon	C–S	University	400	65.8	20.39 (1.8)	MEQ	HADS-D	Past week	ns
Aydin et al. 2021 [63]	Y	Turkey	C–S	University	493	48.3	21.7 (2.3)	MEQ	DASS-D	Past week	+
Bai et al. (2021) [64]	Y	USA	L	Secondary School	411	50.6	15.5	MSFsc (self-reported)	CESD	Past week	ns (at 1-year follow-up)
Bakotic et al. (2017) [20]	Y	Croatia	C–S	University	1052	62.4	20.82 (1.7)	CSM	DMS	Past two weeks	+
Borisenkov et al. (2015) [28]	Y	Russia	C–S	Secondary School	3435	55.8%	14.8 (2.6)	MSFsc (MCTQ)	SPAQ	Unspecified	+ in females; ns in males
Carciofo (2020) [65]	Y	China	C–S	University	625	69.8	19.78 (1.5)	MESSi	DASS-D	Past week	+
Cellini et al. (2020) [66]	Y	Italy	C–S	University	82	53.7	23.89 (2.5)	MEQ	BDI	Past two weeks	ns
Chan et al. (2020) [19]	Y	Hong Kong	C–S	Secondary School	1667	43.5	14.8 (1.6)	MEQ	HADS-D	Past week	+
Chelminski et al. (1999) [67]	Y	USA	C–S	University	1617	64.4	Median: 19	MEQ	BDI + GDS + CESD	Past two weeks/Past week/Past week	+
Chung et al. (2020) [68]	Y	Korea	C–S	Secondary School	765	39.1	15.07 (1.4)	MESC	CDI	Past two weeks	+
Danielsson et al. (2019) [69]	Y	Sweden	C–S	Community	669	55.4	21.8 (3.1)	MEQ	HADS-D	Past week	+
de Souza & Hidalgo (2014) [70]	Y	Brazil	C–S	Community	351	70.4	14.7 (1.81)	MST (MCTQ)	BDI	Past two weeks	+
Fares et al. (2015) [71]	Y	Australia	C–C	Outpatients	67C + 194P_{Dep} + 101P_{BPD}	55.2C + 40.7P_{Dep} + 72.3P_{BPD}	23.53 (3.6) C + 19.26 (4.9) P_{Dep} +21.08 (3.8) P_{BPD}	MEQ	DSM-IV Diagnosis	Past two weeks	+ depression patients + bipolar patients
Grierson et al. (2016) [72]	Y	Australia	C–S	Outpatients	63	69.8	19.27 (2.69)	Actigraphy	HAMD + YMRS	Past week/ Past 2 days	+ mania; ns depression
Haraden et al. (2017) [5]	Y	USA	L	Community	255	56.5	15.3 (2.31)	MESC	CDI	Past two weeks	+ (at one-year follow-up)
Haraden et al. (2019) [37]	Y	USA	L (C–S)*	Community	282	57.0	13.59 (2.3)	MESC	CDI	Past two weeks	+
Hasler et al. (2010) [27]	Y	USA	C–S	Community	208	67.0	19.23	MEQ	BDI + HAMD	Past two weeks	+ measured by BDI; ns measured by HAMD
Haynie et al. (2018) [34]	Y	USA	L (C–S)*	Secondary School	2057	55.4	NR	MSFsc (self-reported)	MDS	Past month	+
Hirata et al. (2007) [73]	Y	Brazil	C–S	University	161	52.2	22.1 (2.1)	MEQ	BDI	Past two weeks	+
Inomata et al. (2014) [74]	Y	Japan	C–S	University	102	46.1	21.7 (3)	MEQ	CESD	Past week	+

(*continued on next page*)

Table 2 (*continued*)

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings[2]
Jankowski & Dmitrzak-Weglarz (2017) [54]	Y	Poland	C–S	University	338	51.0	22.2 (2.2)	CSM	CESD + SPAQ	Past week/ Unspecified	+ depressive symptoms; ns global seasonality
Jankowski (2016) [75]	Y	Poland	C–S	University	947	67.9	21.7 (2)	CSM	CESD	Past week	+
Kang et al. (2020) [35]	Y	China	C–S	University	944	63.2	19.1 (0.9)	MEQ	BDI	Past two weeks	+
Karan et al. (2021) [41]	Y	USA	L	Secondary School	144	NR	Range: 14-17	MST_{acti}	CESD	Past week	ns
Kasof (2001) [76]	Y	USA	C–S	University	151	62.3	22.7 (4.9)	CSM	BDI	Past two weeks	+
Keller et al. (2017) [77]	Y	Germany	C–S	Outpatients + Community	19 + 19	68.0 + 63.0	16.51 (1.68) + 16.06 (1.68)	MST_{act}	BDI	Past two weeks	ns
Koo et al. (2021) [78]	Y	Korea	C–S	Secondary School	8565	47.9	16.77 (0.85)	MESC	BDI	Past two weeks	+
Lau et al. (2013) [79]	N[#]	Hong Kong	L	University	1628	67.6	20.9 (2.66)	CSM	DASS-D	Past week	+ (at 6 months follow-up)
Lee et al. (2016) [80]	Y	Korea	C–S	University	1094	13.4	22.8 (1.9)	MEQ	HADS-D	Past week	+
Lester (2015) [81]	Y	USA	C–S	University	194	72.1	21.6 (1.4)	MEQ	BDI	Past two weeks	+
Li et al. (2020) [56]	Y	China	C–S	University	1135	61.9	18.8 (1.2)	MEQ	PHQ-9	Past two weeks	+
Mercacci & Rocchetti (1998) [42]	Y	Italy	C–S	University	232	52.2	Range: 20-26	MEQ	BDI	Past two weeks	+
Mokros et al. (2017) [82]	Y	Poland	C–S	University	140	NR	22.34 (1.37)	CQ	BDI + HCL-32	Past two weeks/ Unspecified	- depressive symptoms; ns hypomania
Natale et al. (2005) [83]	Y	Italy, Spain	C–S	University	1715	70.1	22.39 (3.92)	MEQ	SPAQ	Unspecified	+
Nguyen et al. (2019) [43]	N	USA	C–S	University	528	64.01	NR	MEQ/MSF	BDI	Past two weeks	+
Orchard et al. (2020) [36]	Y	UK	L (C–S)*	Community	4759	53.0	15	MSF (self-report)	ICD-10 Diagnosis	Unspecified	ns
Pabst et al. (2009) [84]	N	USA	C–S	Community	264	100.00	14.90 (2.20)	MESC	CDI	Past two weeks	+
Park et al. (2018) [85]	N[#]	Korea	C–S	University	5632	50.8	19.3	CSM	PHQ-9	Past two weeks	+
Przepiorka et al. (2021) [86]	Y	Poland	C–S	University	398	71.1	20.37 (2.29)	CSM	CESD	Past week	+
Randler et al. (2012) [87]	Y	Germany	C–S	University	277	100.0	22.25 (2.47)	CSM	PHQ-9	Past two weeks	+
Robillard et al. (2014) [88]	N	Australia	C–S	Outpatients	47	78.70	16.5 (2.00)	Acrophase (Actigraphy)	HAMD	Past week	–
Sheaves et al. (2016) [89]	Y	UK	C–S	University	1403	55.6	Median: 21 (IQR: 20–23)	MSFsc (MCTQ)	DASS-D + MDQ	Past week	+
Shetty et al. (2021) [90]	N	Australia	C–S	Outpatients	81	17.74	17.74 (3.11)	MEQ	MADRS	Unspecified	ns

(*continued on next page*)

Table 2 (*continued*)

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings[2]
Short et al. (2013) [91]	Y	Australia	C–S	Secondary School	385	40.0	15.6 (0.95)	CSM	CESD	Past week	+
Silva et al. (2020a) [92]	Y	Brazil	C–S	University	804	67.8	21.37 (2.88)	MEQ	CESD	Past week	ns
Takeuchi et al. (2002) [44]	N	Japan	C–S	Secondary School	1339	48.46	Range: 12-15	MEQ	Sleep and Mood Evaluation Questionnaire	Unspecified	+ in females; ns in males
Tonetti et al. (2012) [93]	N[#]	Italy	C–S	Community	1539	57.2	13.75 (2.12)	MEQ	SPAQ	Unspecified	+
Tonon et al. (2020) [48]	Y	Brazil	C–S	Military	236	0.0	18 (0)	MEQ	BDI	Past two weeks	+
Tosuntas et al. (2020) [94]	Y	Turkey	C–S	Secondary School	493	47.0	16.56 (0.5)	MEQ	SDS	Past week	+
Üzer & Yücens (2020) [95]	Y	Turkey	C–S	University	339	53.7	22.18 (1.79)	MEQ	BDI	Past two weeks	+
Van den Berg et al. (2018) [96]	N	Netherlands	L	University	742	74.50	21.4 (2.90)	MEQ	QIDS-SR	Past week	+
Wang et al. (2017) [45]	N[#]	China	C–S	Secondary School	8998	50.7	NR	MESC	CESD	Past week	+
Weiss et al. (2020) [21]	Y	USA	C–S	University	806	71.6	19	MSF (self-report)	BDI	Past two weeks	+
Yang et al. (2020) [46]	Y	USA + Taiwan	C–S	Secondary School	128 (US) + 548 (TW)	50.8 (US) + 51.6 (TW)	NR	MESC	CESD	Past week	+
Zhou et al. (2021) [97]	Y	China	C–S	University	4531	29.8	19.2 (1.77)	MEQ	DASS	Past week	+

Abbreviations: BDI = Beck depression inventory; C = control; C–C = case-control; CDI = children's depression inventory; CESD = centre for epidemiological studies - depression scale; CQ = chronotype questionnaire; C–S = cross-sectional; CSM = composite scale for morningness; DASS = depression anxiety and stress scale; DMS = depressive mood scale; ET = evening type; GDS = geriatric depression scale; HADS = hospital anxiety and depression scale; HAMD = Hamilton depression rating scale; HCL-32 = hypomania checklist; L = longitudinal; MADRS = Montgomery-Åsberg depression rating scale; MCTQ = Munich chronotype questionnaire; MDS = modified depression scale; MEQ = morningness-eveningness questionnaire; MESC = morningness-eveningness scale for children; MESSi = morningness-eveningness stability scale improved; MT = morning type; MSF = midpoint of sleep during free day; MSFsc = midpoint of sleep corrected for sleep debt; MST = midpoint of sleep; MST_{act} = midpoint of sleep derived from actigraphy; NR = not reported; NT = neither type; P = patients; PHQ-9 = patient health questionnaire; QIDS-SR = quick inventory of depressive symptomatology; RCADS = revised child anxiety depression scale; SDS = short depression scale; SPAQ = seasonal pattern assessment questionnaire; TW = Taiwan; US = United State of America; YMSR = Young mania rating scale.

Notes:

[1] Age is presented as mean (standard deviation) unless otherwise specified.

[2] "+" denotes a significant positive association between eveningness and outcome measures; "-" denotes a significant negative association between eveningness and outcome measures; "ns" denotes no significant associations between circadian measures and mental health outcomes.

[#] Study was excluded from meta-analysis after influential case analysis.

[*] Study was a prospective research design, but only cross-sectional results could be extracted for meta-analysis. Longitudinal results are presented in the table if available.

circadian measures, sample age, or sample composition (Supplementary Table S5). Similarly, sex ratio did not significantly moderate the association between circadian preference and anxiety problems ($\beta = -0.002$, $p = .108$).

Among the studies included in the review, three longitudinal studies investigated the prospective associations between circadian preference and anxiety problems. Among those, only Lau et al. (2013) [79] reported that an eveningness preference at baseline significantly predicted a higher level of anxiety symptoms after six months ($r = -0.15$, $p < .001$) in university students (mean age of 20.2). The other two studies conducted in samples with younger age (mean age 13–15) did not find a significant association between baseline eveningness and anxiety severity at 1-year and 4-year follow-ups [36,37].

Two studies [43,84] were not included in the meta-analysis due to insufficient data. One of the studies conducted exclusively in adolescent girls found that eveningness, as measured by the morningness-eveningness scale for children (MESC), was significantly associated with a higher level of trait anxiety [84]. The other study conducted in university students did not find a significant association between MEQ-measured circadian preference and trait anxiety [43]. A forest plot summarising the effect sizes after removing influential cases is presented in Fig. 4.

3.7. Circadian preference and psychosis

Three studies examined the associations between circadian

Table 3
Characteristics and main findings of the included studies on anxiety problems.

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings[2]
Alvaro et al. (2014) [7]	Y	Australia	C–S	Secondary School	318	48.4	14.96 (1.3)	MESC	RCADS-A	Unspecified	+ except generalised anxiety disorder
Aoun et al. (2019) [62]	Y	Lebanon	C–S	University	400	65.8	20.39 (1.8)	MEQ	HADS-A	Past week	ns
Aydin et al. (2021) [63]	Y	Turkey	C–S	University	493	48.3	21.7 (2.3)	MEQ	DASS-A	Past week	+
Azad-Marzabadi et al. (2017) [99]	Y	Iran	C–S	University	510	72.0	20.79 (2.0)	MEQ	SIAS + SAQ	Unspecified	+
Bettencourt et al. (2020) [100]	Y	Portugal	C–S	Secondary School	190	46.3	13.47 (0.7)	CSM	STAIc-S	Present	+ (only when measured in the morning)
Carciofo, (2020) [65]	Y	China	C–S	University	625	69.8	19.78 (1.4)	MESSi	DASS-A	Past week	+
Cellini et al. (2020) [66]	Y	Italy	C–S	University	82	53.7	23.89 (2.5)	rMEQ	STAI-T	Present	ns
Chan et al. (2020) [19]	Y	Hong Kong	C–S	Secondary School	1667	43.5	14.8 (1.6)	rMEQ	HADS-A	Past week	+
Chung et al. (2020) [68]	Y	Korea	C–S	Secondary School	765	39.1	15.07 (1.3)	MESC	RCMAS	Unspecified	ns
Danielsson et al. (2019) [69]	Y	Sweden	C–S	Community	669	55.4	21.8 (3.1)	rMEQ	HADS-A	Past week	ns
Diaz-Morales, (2016) [101]	Y	Spain	C–S	Secondary School	1406	50.9	13.95 (1.6)	MESC	STAI-T	Present	+
Evans & Norbury, (2021) [102]	Y	UK	C–S	University	191	88.5	19.56 (1.3)	rMEQ	STAI-T	Present	+
Fares et al. (2015) [71]	Y	Australia	C–C	Outpatients	67C + 52P	55.2C + 51.9P	23.53 (3.6) C + 19.7 (4.4) P	MEQ	DSM-IV Diagnosis	Unspecified	+
Haraden et al. (2019) [37]	Y	USA	L	Community	282	57.0	13.59 (2.3)	MESC	MASC	Unspecified	+ (cross-sectionally); ns (at 18-month follow-up)
Kang et al. (2020) [35]	Y	China	C–S	University	944	63.2	19.1 (0.9)	rMEQ	SAS	Past week	+
Lau et al. (2013) [79]	Y	Hong Kong	L	University	1628	67.6	20.9 (2.6)	CSM	DASS-A	Past week	+
Lee et al. (2016) [80]	Y	Korea	C–S	University	1094	13.4	22.8 (1.9)	MEQ	HADS-A	Past week	+
Lin & Gau (2013) [105]	N[#]	Taiwan	C–S	University	2731	52.4	19.4 (3.6)	CSM	ASRI-4	Unspecified	+
Nguyen et al. (2019) [43]	N	USA	C–S	University	528	64.01	NR	MEQ/MSF	STAI-T	Present	ns
Orchard et al. (2020) [36]	Y	UK	L (C–S)[*]	Community	4658C + 65P	53.0	15 (0)	MSF (self-report)	ICD-10 Diagnosis	Unspecified	ns
Pabst et al. (2009) [84]	N	USA	C–S	Community	264	100.00	14.90 (2.20)	MESC	STAIc-T	Present	+
Pace-Schott et al. (2015) [108]	Y	USA	C–S	University	109	0.0	20.8 (2.6)	MEQ	STAI-T	Present	+
Pereira-Morales et al. (2018) [103]	Y	Colombia	C–S	University	467	64.8	20.7 (2.3)	CSM	HADS-A	Past week	ns
Rodrigues et al. (2019) [104]	Y	Portugal	C–S	Secondary School	217	50.7	12.84 (0.7)	rMEQ	STAIc-T	Present	+
Sheaves et al. (2016) [89]	N[#]	UK	C–S	University	1403	55.6	Median: 21 (IQR: 20–23)	MSFsc (MCTQ)	DASS-A	Past week	ns
Silva et al. (2020a) [92]	Y	Brazil	C–S	University	804	67.8	21.37 (2.8)	MEQ	BAI	Past month	ns
Silva et al. (2020b) [106]	N[#]	Brazil	C–S	University	96	59.0	22.47 (3.8)	MEQ	STAI	Present	+
Tosuntas et al. (2020) [94]	Y	Turkey	C–S	Secondary School	493	47.0	16.56 (0.5)	rMEQ	STAI-T-SF	Present	+

Abbreviations: ASRI-4 = adult self-report inventory-4; BAI = Beck anxiety inventory; C = control; C–C = case-control; C–S = cross-sectional; CSM = composite scale for morningness; DASS = depression anxiety and stress scale; ET = evening type; HADS = hospital anxiety and depression scale; L = longitudinal; MASC = multidimensional anxiety scale for children; MCTQ = Munich chronotype questionnaire; MEQ = morningness-eveningness questionnaire; MESC = morningness-eveningness scale for children; MESSi = morningness-eveningness stability scale improved; MT = morning type; MSF = midpoint of sleep during free day; MSFsc = midpoint of sleep corrected for sleep debt; NR = not reported; NT = neither type; P = patients; RCADS-A = revised child anxiety depression scale; RCMAS = revised children's manifest anxiety scale; SAQ = social anxiety questionnaire; SAS = Zung self-rating anxiety scale; SIAS = social interaction anxiety scale; STAI(c)-S/T = state-

trait anxiety inventory (for children).

Notes:

[1] Age is presented as mean (standard deviation) unless otherwise specified.

[2] "+" denotes a significant positive association between eveningness and outcome measures; "-" denotes a significant negative association between eveningness and outcome measures; "ns" denotes no significant associations between circadian measures and mental health outcomes.

[#] Study was excluded from meta-analysis after influential case analysis.

[*] Study was a prospective research design, but only cross-sectional results could be extracted for meta-analysis. Longitudinal results are presented in the table if available.

Table 4
Characteristics and main findings of included studies on psychosis.

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings
Fares et al. (2015) [71]	N	Australia	C–C	Community/ Outpatients	67C + 82P	55.2C + 25.6P	23.53 (3.6) C + 22.04 (4.16) P	MEQ	DSM-IV Diagnosis	Unspecified	+
Sheaves et al. (2016) [89]	N	UK	C–S	University	1403	55.6	Median: 21 (IQR: 20–23)	MSFsc (MCTQ)	SPEQ	Unspecified	ns
Shetty et al. (2021) [90]	N	Australia	C–S	Outpatients	81	17.74	17.74 (3.11)	MEQ	CAARMS + SANS	Unspecified	ns positive psychotic symptoms; + negative psychotic symptoms

Abbreviations: CAARMS = comprehensive assessment of at-risk mental states; C–C = case-control; C–S = cross-sectional; L = longitudinal; MCTQ = Munich chronotype questionnaire; MEQ = morningness-eveningness questionnaire; MSFsc = midpoint of sleep corrected for sleep debt; SANS = scale for the assessment of negative symptoms; SPEQ = specific psychotic experiences questionnaire.

Notes:

[1] Age is presented as mean (standard deviation) unless otherwise specified.

Table 5
Characteristics and main findings of included studies on eating-related problems.

Authors	Meta	Region	Design	Setting	N	% Female	Age[1]	Circadian Measures	Outcomes Measures	Scale Time Frame	Main Findings
Kasof (2001) [76]	N	USA	C–S	University	151	62.3	22.7 (4.9)	CSM	EDI-2 + BULIT-R	Unspecified	+ measured by BULIT-R; ns measured by EDI-2
Schmidt & Randler (2010) [107]	N	Germany	C–S	Secondary School	284	100	14.1 (1.2)	CSM	EDI-2	Unspecified	+

Abbreviations: BULIT-R = bulimia test-revised; C–S = cross-sectional; CSM = composite scale of morningness; EDI = eating disorder inventory.

Notes:

[1] Age is presented as mean (standard deviation) unless otherwise specified.

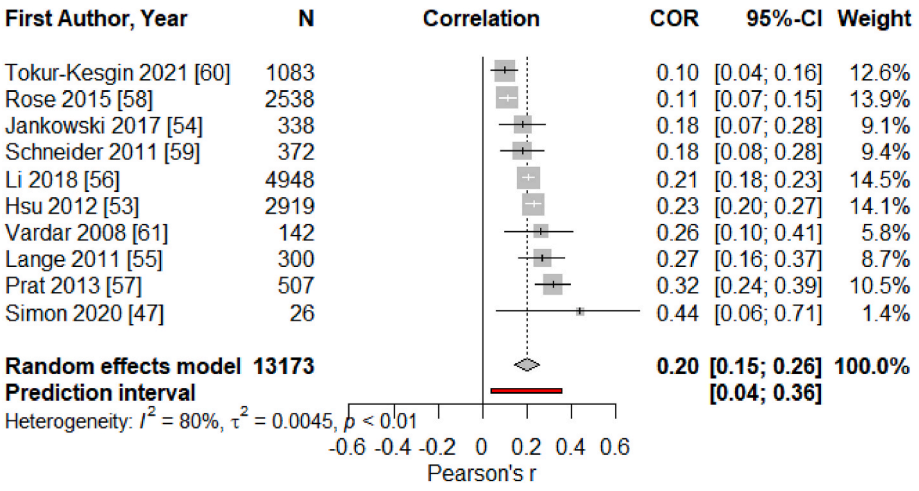

Fig. 2. Summary of studies included in general psychopathologies after removing influential cases.

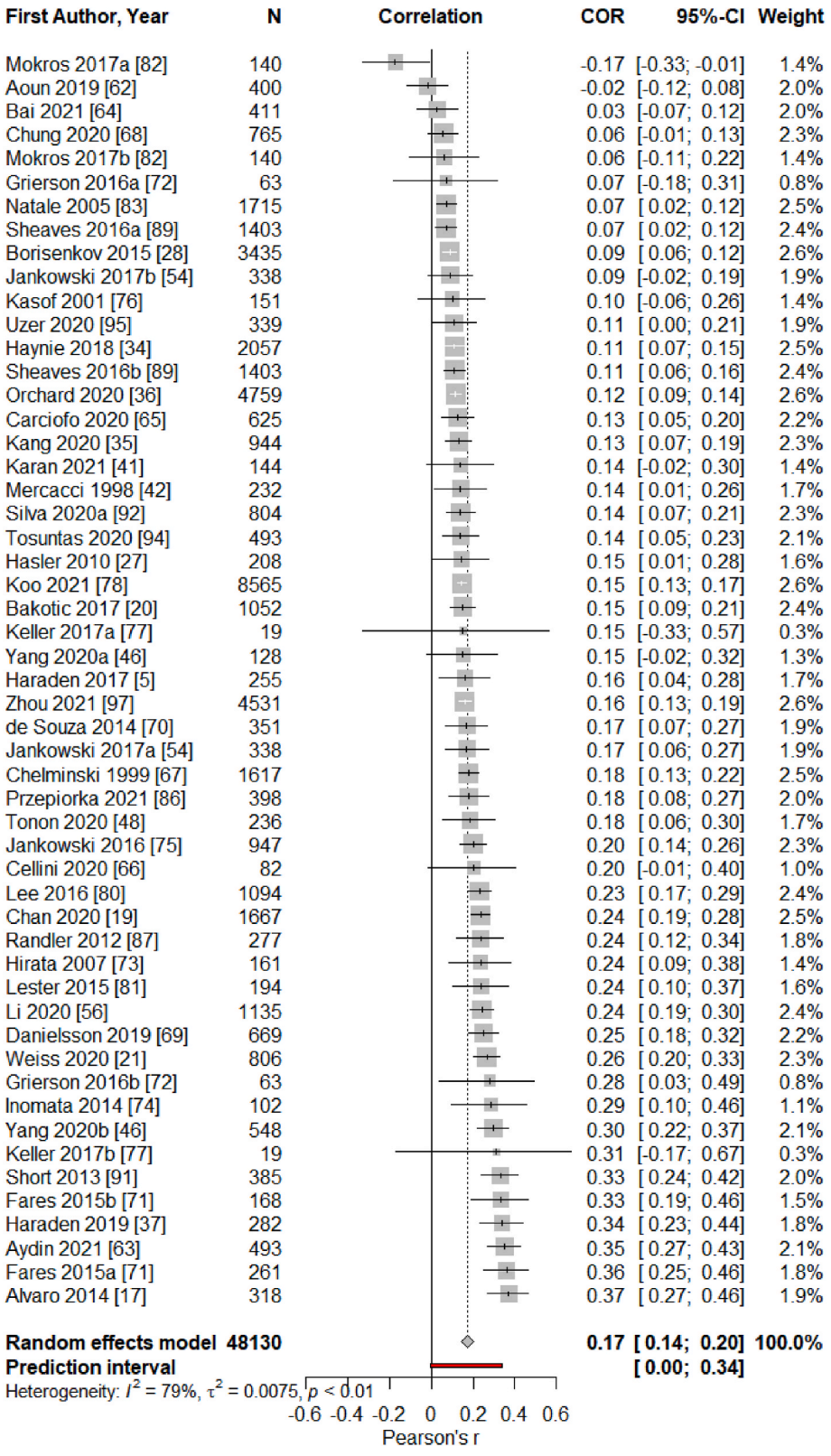

Fig. 3. Summary of studies included in mood-related disturbances after removing influential cases.

preference and psychosis (see Table 4), but a meta-analysis was not conducted because the correlation coefficient could not be extracted from one of these studies. Fares et al. (2005) [71] was the only study conducted in the clinical sample involving patients with diagnosed psychotic disorders. Compared to healthy controls, patients with psychotic disorders were more evening-oriented. On the other hand, two studies involving 1403 university students aged 20–23 and adolescents with ultra-high risk (UHR) for psychosis found that circadian preference was not associated with positive symptoms of psychosis [89,90]. In terms of negative symptoms of psychosis, one study reported that

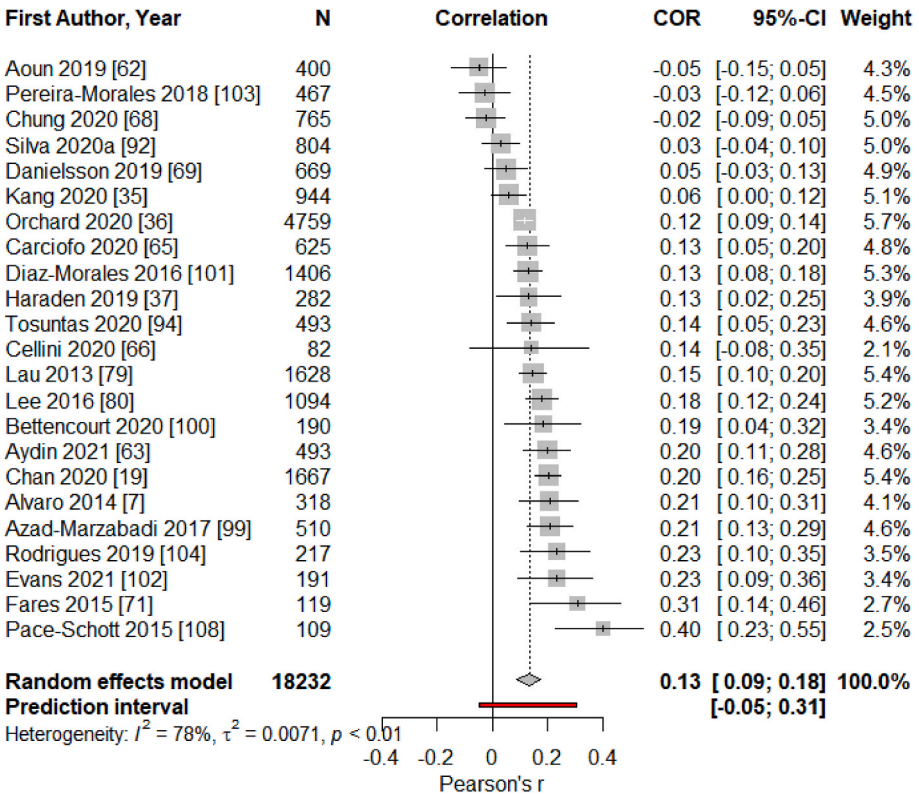

Fig. 4. Summary of studies included in anxiety problems after removing influential cases.

eveningness, as measured by the MEQ, was weakly associated with negative symptoms after accounting for depressive symptoms (β = −0.15, p = .02) in UHR adolescents with a mean age of 17 [90].

3.8. Circadian preference and eating disorders related problems

Only two studies, one conducted exclusively in young adolescent girls with a mean age of 14 and one in a university sample with a mean age of 22, examined the associations between circadian preference and eating disorders or related problems (see Table 5). Both studies supported a link between eveningness and eating disorders related problems, such as a higher degree of body dissatisfaction and bulimic behaviours [76,107].

3.9. Potential sleep-related moderators in the relationship between circadian preference and mental health outcomes

Only three studies reported insomnia severity using the insomnia severity index (ISI) [7,19,68], twelve studies provided data on sleep quality as measured by the Pittsburgh sleep quality index (PSQI) [48,61,65,66,74,77,82,95,97,102,106,108], and 21 studies provided data on average sleep duration [7,19,34,36,45,47,56,59,61,65,66,68,70,74,77,91,92,100,103,105]. A series of meta-regression analyses were conducted on the overall pooled effect and separately on mood-related disturbances and anxiety problems. Meta-regressions were not performed separately on general mental health due to insufficient data to perform the analysis. Insomnia severity significantly moderated the association between circadian preference and mental health outcomes (β = −0.13, p = .027) in the overall model, suggesting that an increase in insomnia severity reduced the strength of the association between circadian preference and mental health outcomes. The moderating effects of sleep quality and duration were insignificant (all $ps > .05$). The summary of the meta-regression is in Table 6.

Table 6
Summary of meta-regression analysis on sleep-related moderators.

Moderators	No. ES	β	*se*	LCI	UCI	*P*
Overall						
Insomnia Severity	6	−0.13	0.03	−0.24	−0.03	**.027**
Sleep Quality	15	0.01	0.03	−0.06	0.06	.852
Sleep Duration	27	0.03	0.03	−0.03	0.08	.329
Mood-related Disturbances						
Sleep Quality	10	0.02	0.04	−0.06	0.10	.574
Sleep Duration	14	0.02	0.04	−0.07	0.10	.687
Anxiety Problems						
Sleep Quality	4	−0.07	0.05	−0.28	0.14	.282
Sleep Duration	9	0.06	0.03	−0.02	0.04	.110

Abbreviations: ES = effect size; LCI/UCI = lower/upper confidence intervals; *se* = standard error; β = estimate/regression coefficient.
Notes:
- Insomnia severity was measured by the insomnia severity index (ISI).
- Sleep quality was measured by the Pittsburgh sleep quality index (PSQI).

4. Discussion

The current study aimed to systematically synthesise the existing evidence on the association between circadian preference and mental health outcomes in youths. The results demonstrated that eveningness was significantly associated with general mental health (r = 0.20), mood-related disturbances (r = 0.17), and anxiety problems (r = 0.13). There was also evidence showing that eveningness was associated with the risk of psychosis and eating disorders and related problems. In addition, the current study showed that insomnia severity (β = −0.13, p = .027), but not sleep quality and duration, significantly moderated their associations.

4.1. Eveningness and psychopathologies

The findings showed a clear association of mood-related

disturbances with eveningness with a modest effect size (r = 0.17). The results were in accord with the two previous meta-analyses on the relationship between chronotype and depressive symptomatology, albeit the current results showed a slightly weaker effect. A previous meta-analysis of 36 studies on adolescents and adults (age range 13–55) found a significant association of eveningness with unipolar depression (|r| = 0.28) and bipolar disorders (|r| = 0.23) [16]. In another meta-analysis of 51 studies conducted by Norbury, similar results were reported for depressive symptomatology (|r| = 0.21) [17]. Notably, two studies included in this review have found contradictory findings. In a cross-sectional study, Mokros et al. (2017) [82] found that morningness was significantly associated with depressive symptoms. It is worth noting that this study used the Polish chronotype questionnaire, a much less widely used measure for circadian preference. The other study by Robillard et al. (2014) found that the acrophase, as derived from fitting actigraphy data on a cosinor model, was earlier in participants with a higher level of depressive symptoms than those with a lower level of depressive symptoms [88]. However, there remained concerns about whether actigraphy-estimated data could accurately reflect one's circadian preference because it has been suggested that human activities poorly fit a sinusoidal pattern [109].

Overall, the current findings supported that a preference for eveningness was associated with mood disturbances. Several biological and psychological factors could potentially explain such an association. Genetically, polymorphisms of several circadian-related genes significantly overlap with those related to affective disorders [39]. Genome-wide analysis of the UK Biobank data also found evidence that genetic reflection of eveningness was negatively correlated with mental well-being [110]. In particular, in a sample of university students (n = 528), individuals with a *PER3* polymorphism were found to be three times more likely to have an evening circadian typology associated with depression [111]. From a cognitive perspective, individuals with eveningness are more likely to have negative thoughts during a low mood episode, increased rumination, and disrupted reward functioning [112], which have been linked to the risk of depression. In particular, the role of altered reward processing and emotional regulation has received increased attention in the literature. Hasler et al. (2010) examined the association between eveningness, reward processing, and depression in a sample of young adults (mean age 19.2, range 17–33). They found that eveningness and depression were associated via multi-step indirect paths involving reward responsiveness, positive and negative affects [27]. Berdynaj and colleagues found that young adults with eveningness had higher accuracy in recognising sad facial expressions, greater recall of negative words, and reduced attention to happy faces [113]. In a functional magnetic resonance imaging study, Horne and Norbury found that individuals with eveningness showed greater amygdala response to fearful faces compared to happy faces and reduced functional connectivity between the amygdala and anterior cingulate cortex, an anatomical site related to emotional regulation. These neurophysiological findings further supported the possible role of aberrant emotional regulation underlying the association between circadian preference and depressive symptoms [114].

The results on mania were aligned with the current understanding of circadian dysfunction as the pathophysiology of bipolar affective disorders (BAD) [115]. Eveningness is highly prevalent in BAD, with previous research showing that up to one-fourth of BAD patients (24.5%) were considered as evening type [116]. In this regard, a discrete sub-phenotype of BAD associated with eveningness has been proposed [117]. It is worth noting that research on the role of circadian preference and BAD in the youth population is very limited to date, and the underlying mechanism has remained elusive. It is speculated that individuals with BAD might have greater melatonin suppression due to hypersensitivity to light [118]. This was supported by a recent study showing that offspring of BAD patients had a more blunted melatonin secretion as measured by DLMO assessment compared to offspring of healthy controls [119]. Nonetheless, further research is needed to unravel the association and mechanism of eveningness and bipolar disorders.

The current meta-analysis was the first to synthesise evidence on the association between circadian preference and anxiety problems. Similar to mood-related disturbances, eveningness had a significant association of small magnitude with anxiety problems. In particular, eveningness was seemingly more strongly associated with trait anxiety, which refers to a personality attribute with a tendency to anxiousness. Previous research has shown that individuals with eveningness were more prone to have a higher level of neuroticism, a personality trait that is highly correlated with trait anxiety [120]. As such, it is possible that neuroticism could moderate the association between eveningness and trait anxiety. This notion was also indirectly supported by one of the studies included in this review, in which there was a strong correlation between neuroticism and anxiety (r = 0.64), and both constructs were significantly correlated with eveningness [65]. Nevertheless, despite an overall significant finding on the association of eveningness with anxiety problems, the literature included in the review showed mixed findings. Twelve of the 28 studies, including two longitudinal studies, failed to find a significant relationship between circadian preference and anxiety problems. These mixed findings suggested a complicated mechanism underlying the link between circadian preference and anxiety. One possible reason could be related to the types of anxiety disorders. Whilst the majority of the included studies examined general anxiety symptoms, previous research identified individuals with evening type were more likely to meet the diagnosis of specific phobia and post-traumatic stress disorders rather than generalised anxiety disorder [121]. Another possible reason is related to the high comorbidity between anxiety and depression. The relationship between eveningness and anxiety could be driven by the shared affective components (e.g., low level of positive affect) between both disorders [37]. Taken together, the relationship between circadian preference and anxiety requires further investigation. Future research deploying a longitudinal design and controlling for depressive symptoms would be recommended to further explore the shared mechanisms linking circadian preference and anxiety problems.

The results showed that eveningness was significantly associated with the general mental health category (r = 0.20). It is worth noting that the definition of "general mental health" was labelled based on three main groups of outcome measures, namely symptoms checklists (e.g., symptom checklist 90 and brief symptom rating scale), behaviour checklists or questionnaires for children and adolescents (e.g., strengths and difficulties questionnaire [SDQ] and child behaviour checklist [CBCL]), and scales on general mental health (i.e., general health questionnaire and self-reporting questionnaire). While some items of these outcome measures may overlap with those of psychiatric disorders that have been independently reviewed (i.e., depression and anxiety), the overall construct should be best considered as the overall mental health instead of a particular disorder category. In addition, as the presentation of mental health problems in children and adolescents is often categorised into internalising and externalising behaviours, the studies using the typical child-related psychopathology measures, such as SDQ and CBCL, as the outcome measures, highlighted the clinical features of the unique population being studied. The findings on the general mental health category, regardless of the diverse yet relevant outcome measures included, highlighted the clinical implications of eveningness in youth psychopathology.

One notable finding from this review was that cross-sectional studies consistently found associations between eveningness and mental health outcomes. In contrast, the results from the longitudinal studies were mixed (five out of 10 longitudinal studies showed an insignificant relationship). One possible explanation is that cross-sectional studies capture the typical effect of eveningness in youths' daily life, where eveningness causes circadian misalignment due to a mismatch of the conventional social schedule (e.g., waking up early for school) and subsequently leads to mental health problems. The mixed findings from longitudinal studies may be due to some of the confounding variables,

such as a change in environment (e.g., from secondary school to university) and sleep behaviour (e.g., change in sleep duration or quality) over time, which could potentially influence the associations between eveningness and mental health outcomes. Although it appeared that cross-sectional studies had a stronger association compared to longitudinal studies, it is worth noting that subgroup analyses (see Supplementary Tables) showed there was no significant difference in the strength of associations between cross-sectional and longitudinal studies. The present review also postulated that variations in the timeframe for participants to report their symptoms in the outcome measures might have influenced the associations between circadian preference and mental health outcomes. The results from subgroup analyses showed that a shorter timeframe (e.g., within the past week), especially for mood-related disturbances and anxiety problems, were generally associated with stronger associations between eveningness and mental health outcomes, albeit that there were no significant differences amongst various timeframes. These findings might suggest a state-dependent link between circadian preference and mood disturbances. Nonetheless, the current results underscore the intricate relationship between eveningness and mental health outcomes in youths, and more longitudinal studies incorporating the measures of potential confounding factors on the association of circadian preference and mental health are warranted.

An alternative view on the discrepancies between cross-sectional and longitudinal studies was that circadian preference could be considered as a modifiable factor that could influence the trajectory of mental health in youths. There has been growing research, albeit with mixed findings, on the effects of circadian-focused interventions on mental health outcomes in youth [122,123]. For example, bright light therapy was found to improve sleep and advance bedtime and waketime as well as significantly improving depressive symptoms in adolescents with delayed sleep phase disorder [124]. Nonetheless, the effect of circadian-focused interventions on mental health outcomes in youths remained under-studied and more research is needed in this area.

Regarding the potential moderating factors in the association between circadian preference and mental health outcomes, our results showed that insomnia severity, as measured by the insomnia severity index, significantly moderated the correlation between circadian preference and mental health outcomes with a modest effect ($\beta = -0.14$). Insomnia and eveningness are common comorbidities in youths, and insomnia problems are often the presenting symptoms of delayed sleep phase disorder, which is considered the extreme end of eveningness [125]. The intricate relationship between these two conditions was demonstrated in previous research, where youths with evening tendency were found to be more likely to report insomnia symptoms which impose as a risk factor for mental health problems [19,56]. Moreover, one previous study showed that depressed patients with evening type had better mood outcomes when treated with antidepressants combined with cognitive behavioural therapy for insomnia compared to antidepressants alone, suggesting the need for additional sleep-focused treatment for this group [126]. Taken together, these findings highlighted the need for enhanced clinical attention to youths with eveningness for the risk of insomnia and psychopathology.

4.2. Limitations

The findings of this review need to be considered in light of several limitations. Firstly, methodological variations across studies led to considerable statistical heterogeneities in the meta-analysis. A similar problem of methodological heterogeneities was also apparent in the previous meta-analysis on the relationship between chronotype and depression [16]. Despite the high statistical heterogeneities, a lack of publication bias and a relatively homogeneous selection of articles (i.e., all observational studies with a mean age between 12 and 24) strengthened the findings, thus providing robust evidence for the association between eveningness and mental health outcomes in youths. Secondly, the current review was designed to include studies that utilised circadian biomarkers (e.g., endogenous melatonin or core body temperature) as exposure measures. However, our literature search yielded minimal studies utilising circadian biomarkers to measure circadian preference. Although measuring circadian biomarkers is considered as the most accurate approach to determining an individual's circadian timing, this method is labour- and time-intensive, requiring a laboratory environment to collect high-quality well-controlled samples [127]. Therefore, it is impractical for large-scale epidemiological studies to measure circadian biomarkers. Nonetheless, future research may consider utilising new, more user-friendly, and advanced technology to examine the link between circadian preference and mental health outcomes. For example, growing evidence has demonstrated good accuracy and compliance with home-based DLMO assessment [128]. Moreover, the results from meta-regression should be interpreted with caution because only a few studies involved the variables in quantifying the sleep-related factors.

Lastly, it was noted that there is a lack of research on the role of circadian rhythm in a range of neuropsychiatric and neurodevelopmental disorders commonly seen in children and adolescents, such as autism spectrum disorder, bipolar disorders, psychosis, and eating disorders. Research on these disorders in the existing literature was often limited, likely due to their relatively low prevalence and incidence rate, despite the onset and the presentation of these problems typically emerging during adolescence [129]. These disorders often lead to debilitating long-term impacts on young people [130]. Therefore, it is recommended that future research should additionally examine how circadian rhythm contributes to the aetiology and clinical course of these disorders.

4.3. Implications

The current review highlighted the need to address circadian preference in the assessment, management, and prevention of mental health problems in youths. Assessing one's circadian phase may inform case formulation and treatment planning as individuals with eveningness are likely at risk of poor sleep with impairment of daytime performance and functioning. From an intervention perspective, growing evidence has shown that an individual's circadian preference could be modified with chronobiotic medications (e.g., strategically timed melatonin) and circadian zeitgebers (e.g., light). Light therapies or melatonin supplement is relatively safe and inexpensive. There is a potential for using these approaches as an adjunctive intervention for psychiatric disorders. Previous research has shown the efficacy of light therapy in improving the clinical symptoms of mood disorders [131,132] and seasonal affective disorders [133]. A recent study further demonstrated that adjunctive bright light therapy enhanced treatment outcomes with faster remission for patients with unipolar depression and eveningness [134]. However, despite the promising results in the existing literature, there has been limited research on the use of bright light therapy in the youth population. More research is needed to examine whether circadian-focused intervention and prevention are effective in improving mental health outcomes in youths [135].

5. Conclusion

In summary, this is the first meta-analysis to consolidate the evidence of the relationship between circadian preference and mental health issues in youths. It was found that eveningness is associated with poorer mental health outcomes, including mood, anxiety, psychosis, and eating-related problems. Moderation analysis also found that insomnia severity, but not sleep quality and duration, moderates the association between circadian preference and mental health outcomes. Given the implications of circadian preference in youth mental health, there is a need for future research to explore the underlying mechanisms and to examine the effects of circadian-focused interventions in the clinical

management and prevention of youth psychopathology.

6. Practice points

- Eveningness is associated with poorer general mental health, mood-related disturbance, and anxiety problems.
- Insomnia severity may moderate the association between circadian preference and mental health outcomes.
- Circadian preference is a potentially modifiable factor that should be considered in the clinical management of youth mental health problems.

7. Research agenda

- There is a need for more research to examine the association of circadian preference with specific areas of child and adolescent psychopathology, such as psychosis and eating disorders.
- There is also a need for more research on circadian typology in the context of neurodevelopmental disorders, such as attention deficit hyperactivity disorder and autism spectrum disorder.
- Future research on the relationship between circadian preference and anxiety should also consider the potential confounding effect of depression.
- There is a need for more longitudinal investigations of the association between psychopathologies and circadian preference in youths. More focus should be placed on investigating the mechanisms underlying these two conditions over time.
- More research is needed to examine the efficacy of a circadian-focused intervention and prevention in youth mental health.

Declaration of competing interest

JWY Chan receives a personal fee for participating in an expert panel meeting of Eisai Co., Ltd. YK Wing receives personal fee from Eisai Co., Ltd. for providing consultation. Other authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

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