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Mental health indices may fully mediate the relationship between morningness-eveningness and disease control among adult asthma patients

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Abstract

The aim of this study was to assess the association between morningness-eveningness and disease control with consideration of mental state as a mediator and the control of confounding factors among adult asthma patients. This is a cross-sectional study, which included a non-random sample of $N = 66$ patients from an outpatient unit with a confirmed asthma diagnosis, who gave an informed consent and completed a set of questionnaires: a survey comprising questions about sociodemographic and clinical characteristics, the Asthma Control Test (ACT), the Composite Scale of Morningness (CSM), and the General Health Questionnaire (GHQ-28). Mediation models were created separately for each GHQ-28 dimension (somatic symptoms, anxiety/insomnia, social dysfunction and depressive symptoms), for a total score and for four GHQ-28 dimensions together, considered as mediators. Low morning affect was related to poor disease symptom control among patients with asthma. The effect was fully mediated by non-psychotic mental health indices. Evening-time preference was associated with a rise in asthma control, and mediated by somatic symptoms and anxiety/insomnia, when controlled for morning affect. The current study underlines the significance of assessment of both individual morningness-eveningness preference and mental health in the management of asthma symptoms.

Keywords chronotype, morning affect, depression, anxiety, disease control

Introduction

Asthma is one of the most common chronic respiratory diseases, characterized by episodic cough, wheezing and breathlessness[1]. The main mechanisms involved in its pathophysiology include bronchial hyperreactivity and inflammation[2]. A contribution of psychological factors in terms of disease risk, course, prognosis and comorbidities has been well-recognized. Apart from

somatic comorbidities, an increased incidence of depression, anxiety, sleep disorders and hampered quality of life have been reported among asthma patients[3–5]. Also, personal dispositions towards poor mental health, asthma incidence and poor symptom control appear to be common and include high neuroticism, the type A behaviour pattern, high risk propensity, high impulsivity, and low empathy and type D personality[6–9]. Thus, recognition of the risk factors for psychological burden may be significant in the process of the diagnosis of and therapy for asthma.

The chronotype can be characterized as a biologically determined personal disposition towards a certain pattern of circadian functioning. It can be described in terms of daily fluctuations of mood, mental capacity, and physical activity beyond a mere sleep-wake pattern[10–12]. The term is usually considered as synonymous with morningness-eveningness, i.e. a preference for certain times of the day for sleep and activity, although some experts in the field make a distinction between chronotype and morningness-eveningness[13, 14]. Also, recent studies have revealed that morningness-eveningness may comprise more than one dimension[15]. For example, a division has been made between the cognitive-behavioural component (time of day preference) and arousal factor (morning affect)[16, 17]. Eveningness has been repeatedly reported as a risk factor for both somatic and mental disorders, e.g. depression, suicidality, type II diabetes or obesity[19–22]. In the case of asthma, the late type was found to be linked to the increased prevalence of the disease, severity of wheezing, nocturnal symptoms and comorbid allergic diseases in both adolescents and adults[22–24]. The clinical importance of chronobiological factors for asthma management has been emphasized in the context of the circadian variability of lung function and eosinophil sputum concentration [25–28]. However, no studies investigating the link between chronotype and asthma control has been published so far.

The aim of this study was to assess whether morningness-eveningness is associated with disease control, with consideration of mental state as a mediator, independently of selected confounding factors.

The following hypotheses were stated:

- 1) Morningness-eveningness may be linked to asthma control, i.e. evening preference and low morning affect may predispose an individual to poor asthma control.
- 2) The effect of morningness-eveningness on asthma control may be mediated by general mental health indices, i.e. depressive symptoms, anxiety and insomnia, social dysfunction and non-specific complaints of somatic symptoms.

Materials and methods

Study design and sample

This was a single-center, cross-sectional study. It was conducted from 13th July 2017 to 30th November 2019 on a non-random sample of patients of the Lung Disease Outpatient Clinic at [blinded for the purposes of the review]. The inclusion criteria were a confirmed diagnosis of asthma and informed consent for participation in the study. The asthma diagnosis was verified in accordance with the Global Initiative for Asthma practice guidelines[29]. The exclusion criteria comprised of lack of informed consent, diagnosis of major neurocognitive disorder, diagnosis of cancer, serious and unstable heart disease, a severe psychological trauma within the six months preceding the study, and serious mental illness (e.g. schizophrenia or bipolar affective disorder or other psychotic disorder).

In total, 80 sets of questionnaires were handed out personally by the researchers [initials blinded for the purposes of the review] to the patients upon their routine visit to the outpatient clinic.

After signing the informed consent form, the participants underwent a structured interview performed by the researcher and were asked to complete a set of self-reported questionnaires, with a possibility of asking for assistance from the researcher at any point. $N = 14$ patients did not return the form. The clinical and demographic data including sex, age, night shift work (i.e. between 10PM and 6AM), history of asthma and comorbidities were collected on the basis of the interview. Upon completion of the questionnaires and interview, the patients were once again verified regarding the exclusion/inclusion criteria by the researcher. The final sample comprised $N = 66$ patients.

Questionnaires

The chosen questionnaires were all recognized and sufficient in terms of validity and reliability for use in clinical practice, psychological diagnosis and scientific research.

Asthma control was evaluated with the *Asthma Control Test* (ACT), developed by Nathan et al.[30]. The questionnaire consists of five items concerning the self-rating of control, incidence of shortness of breath, disruption of daytime activity and sleep due to symptoms, and the need for the use of rescue medications. The total score ranges from 0 to 25 – the lower the score, the better the asthma control. The internal consistency of the original questionnaire was 0.84. In the original validation research, the ACT score was correlated with asthmatic patients' lung function and distinguished between groups of different types of asthma control according to the specialists' assessment [30]. The ACT is made available by GlaxoSmithKline at www.asthmacontroltest.com

Mornigness-eveningness was assessed with the *Composite Scale of Morningness* (CSM), created by Smith et al. [31] and adapted to Polish by Jankowski[17]. It comprises 13 items representing two facets: Time of Day Preference (or Clock Timing, seven items, scores range from 7 to 31) and Morning Affect (MA, six items, scores range from 6 to 24). A higher score indicates morningness. Cronbach's alpha for the Polish version of the CSM was 0.84. High CSM scores (i.e. morning preferences) were associated with earlier midsleep on free days (a chronotype indicator derived from the Munich Chronotype Questionnaire) [16, 17, 31].

The *General Health Questionnaire, 28-item version* (GHQ-28) was utilized to measure mental health issues in four areas, i.e. somatic symptoms (A), anxiety/insomnia (B), social dysfunction (C), and depressive symptoms (D). The test was developed by Goldberg and adapted to Polish by Makowska and Merecz [32, 33]. Each scale consists of seven items, with answers recorded on a four-point Likert-like scale representing the frequency of the named symptoms. Scores for each item ranged from 1 to 4, and those in each scale ranged from 7 to 28. Cronbach's alphas for the scales range from 0.77 to 0.86. In the Polish validation study, patients from a psychiatric outpatient clinic and a psychiatric outpatient ward scored higher in all four scales compared to a non-psychiatric sample [32].

The *Functional Comorbidity Index* (FCI) was used to assess and quantify the comorbidities of the patients. The scale was originally developed by Groll et al. for the purposes of prediction of functional outcome in chronic diseases. An increase in the score indicates an increase in the number of comorbidities, which is associated with a worsening of functional outcome, i.e. health-related quality of life. In the original validation study, the FCI score was correlated with general physical function [34].

Ethical considerations

This research was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Bioethical Committee of the Medical University of Lodz (RNN/237/17/KE, issued 11th July 2017). The ethical matters of the study concern mainly the

selection and use of self-reported questionnaires and the interpretation of their results; these are discussed in a more detailed manner in the literature[35, 36].

Statistical analysis

Statistical analysis was conducted in JASP 0.14.1 (University of Amsterdam, Netherlands). Each binominal variable was presented as prevalence in the sample – in both an absolute (number of observations, N) and relative way (percentage, %). Each continuous variable was characterized as mean, with standard deviation stratified for patients' sex. Intergroup comparisons for categorical variables were performed with a Chi² test or Fisher's exact test. The latter was done in case of an expected value of less than five in any of the 2×2 contingency cells. For continuous variables, the distribution was assessed with the Shapiro-Wilk W test and the analysis of the Q-Q plots of the residuals. The homogeneity of variance between the groups was verified with Levene's test. Intergroup comparisons of continuous variables were performed with the analysis of variance. The Welch test was used in cases of non-homogenic variances between the groups. The association between two continuous variables was initially checked with the Pearson correlation coefficient. Mediation models were created separately for each GHQ-28 dimension, for a total score and for four GHQ-28 dimensions together, considered as mediators. Asthma control, i.e. an ACT score, was considered as an outcome in each model. CSM Clock Timing and MA scales were considered as predictors together as they form a theoretical whole, i.e. they identify morningness-eveningness. Each model was calculated in two forms: unadjusted and adjusted for patients' sex, age, night shift work, and somatic comorbidity (FCI score). A post-hoc analysis was performed to verify the statistical power with G*Power 3.1 software. Bootstrapping, with sampling set at $n = 1000$, was performed to empower the results and account for possible non-parametric distribution. The confidence intervals were computed using the bias-corrected percentile method as suggested by Biesanz et al.[37]. Statistical significance was defined as $p < 0.05$ or a confidence interval not encompassing 0.

Results

Group characteristics and comparison between men and women

In the studied sample, men had a higher mean age than women (Table 1). Also, men exhibited higher CSM MA scores than women. There was a statistically significant difference in average FCI score. Differences were also seen between men and women in the case of GHQ-28: total score, somatic symptoms, social dysfunction and depressive symptoms. It should be noted that all of the effects of sex differences mentioned were small (below 0.1).

A larger prevalence of obesity could be seen among women than men. No other difference regarding the prevalence of selected comorbid diseases was statistically significant. A greater proportion of men declared they worked night shifts than women, but the difference was on the verge of statistical significance (respectively, 25% vs 7%, $p = 0.063$).

Detailed descriptive statistics and sex comparisons are shown in Table 1 and the Supplementary Table.

Initial analysis – correlations

There was a moderate and positive correlation between the CSM MA and ACT scores (Table 2). Also, both the ACT and MA scores correlated with each of the GHQ-28 dimensions and the total score. Those statistically significant correlations provide a rationale for considering the mental health

indices (GHQ-28 dimensions) as mediators between morningness-eveningness and asthma control. A detailed matrix of the correlation coefficients is presented in Table 2.

Mediation analysis

In total, a rise in CSM MA score predicted a rise in ACT score. An indirect and statistically significant effect of MA on ACT was seen in all six models, i.e. considering each of the GHQ-28 dimensions separately, altogether and the total score as mediators. In each model, the direct effect of MA became insignificant after inclusion of a given mediator (or mediators). Thus, all of those mediations may be considered as full. Also, in mediation analyses the indirect effects of the CSM Clock Timing score on the ACT score via GHQ-28 Somatic symptoms and Anxiety/insomnia scores were revealed in single-mediator models – a fall in the Clock Timing score predicted a rise in the ACT score.

In a model combining the scores of four GHQ-28 scales as mediators, only the mediating effect of Somatic symptoms kept its statistical significance.

Tables 3 and 4 show the summary of the parameters of the mediation analysis models. No significant differences regarding the presented mediating effects could be seen in comparison to the non-adjusted models.

Discussion

The association between morning affect and asthma control

The role of morningness-eveningness in asthma has been postulated previously, with evening type being the risk factor for the development of asthma and its comorbidities; yet the link between morningness-eveningness and asthma control has not been investigated[22–24]. In the current study, it was found that the effect of morningness-eveningness on asthma control may be fully exerted via mental health.

Low morning affect predicted poor symptom control among adult patients with asthma. The effect was seen in mediation with the GHQ-28 total score and its dimensions considered separately, i.e. somatic symptoms, anxiety/insomnia, social dysfunction and depressive symptoms. Such an effect can be considered as expected in the light of previous evidence, since morningness has been associated with pro-health trait variants, including emotional stability (low neuroticism), high conscientiousness, low procrastination, high self-control, high self-efficacy, a future time perspective, and the ability to delay gratification [42–45]. In the case of asthma management, a particular significance of neuroticism, conscientiousness, self-control and self-efficacy has been reported[46–48].

The association between Clock Timing and asthma control

In the case of Clock Timing, evening preference predicted good asthma control, but only when controlled for morning affect and when mediated by somatic symptoms and anxiety/insomnia in single-mediator models. These results appear to be in line with the observation that evening orientation was found to predict less depressive/somatic affect and general depressiveness when controlled for morning affect[56, 57]. This suggests that evening-oriented persons who do not experience unpleasant emotions and physical symptoms during the transition from sleep to wakefulness may present less emotion-related difficulties and, in the case of asthma, better symptom control. Such an idea has been postulated previously, with regards to the possible role of present-

oriented time perspective and emotional intelligence, both linked to eveningness and less pronounced psychological distress[42, 58–61]. Yet ours is the first study investigating such a relationship among patients with asthma, and the confirmation of such surprising results warrants further research on the topic.[62]

The association between asthma control and mental health

The current study is in line with previous research findings that asthma control is linked to mental health, since the severity of somatic complaints, anxiety and insomnia, social dysfunction and the severity of depressive symptoms were found to be correlated with asthma control. Vieria et al. reported that the severity of depression and anxiety is higher among patients with uncontrolled asthma than with controlled asthma [38]. Similarly to the present study, Liu et al. found a negative correlation between asthma control and self-reported measures of depression and anxiety [39]. The effect of uncontrolled asthma on depression and poor health-related quality of life in general was further confirmed in a prospective study among patients with adult-onset asthma[40].

Explanation of the results in the light of previous evidence

The possible role of morningness in asthma control can be discussed in terms of biological factors associated with the pathophysiology of asthma. Low morning affect, via poor mental health, might be related to worse pulmonary function, increased inflammation and diminished surge of cortisol blood concentration in the morning - and thus poor asthma control[49, 50]. The circadian variability of the listed biological mechanisms has been studied already and suggested to be endogenous; thus, this is probably also linked to morningness-eveningness[51]. The forced expiratory volume in the first second (FEV1 – a spirometric measure of lung performance and disease monitoring in asthma) was reported to be the lowest in the early morning among patients with mild to moderate asthma [52]. Kelly et al. found higher levels of lymphocytes, a greater proportion of CD4+ T and increased *ex vivo* proinflammatory cytokine secretion in bronchoalveolar lavage material at 4:00 h compared to 16:00 h among patients with mild atopic asthma[53]. Further support for the role of morning affect in asthma symptoms is that, for the early types, the morning surge in cortisol concentration is higher than in late types, which may directly correspond to improved lung function and decreased inflammation[54, 55].

Despite a congruent reporting on diminished pulmonary function and increased inflammation in the morning hours among patients with asthma, none of the aforementioned studies included morningness-eveningness as a confounding factor. It should be also noted that in the current study, a model incorporating all four dimensions of GHQ-28 as mediators between morningness-eveningness and asthma control yielded a statistically significant effect only on the somatic symptoms scale. It may be hypothesized that low morning affect reveals a tendency to react with increased complaints of somatic symptoms and, secondarily, depressive mood, anxiety and impaired daily functioning. In turn, all of those symptoms may contribute to poor asthma control.

It should be noted that the research mentioned considered morningness-eveningness as a unidimensional construct. In the light of present research, it may be hypothesized that the arousal aspect, namely morning affect, may be of greater significance for health-related behaviours and well-being than the cognitive-behavioural aspect of Clock Timing.

Practical implications and future directions

The current results provide a rationale for the inclusion of the assessment of morningness-eveningness as part of an examination of a patient suffering from asthma. This may be particularly important in cases of poor symptom control, as it may warrant specific therapeutic schema. The

improvement of treatment to foster disease control has been previously found to reduce the severity of depression and anxiety among patients with asthma[50]. A question arises as to whether non-pharmacological interventions related to circadian preference may also play a part in asthma management. So far, both designed psychoeducation on circadian rhythms and interventions resulting in the earlier circadian endogenous phase (morningness) have been found to improve social, emotional, behavioural, cognitive and physical health among adolescents. The topic requires further research with a particular focus on patients suffering from asthma[62].

Limitations

Certain limitations should be outlined concerning the current study's design and the implications of the interpretation of its results. The sample was small, non-randomly selected, and derived from a single center, which limits the generalizability of the findings. However, the sample represented a naturalistic, ambulatory, and homogenous group regarding the diagnosis. In addition, the number of observations was sufficient to meet the assumptions of the statistical methods employed, with an additional sensitivity analysis to improve the power of the results. Another possible limitation is the study's observational, single time-point character. Also, it did not include certain clinical variables, such as pulmonary function or pharmacological treatment. A study with a prospective, multicenter design, employing a larger number of asthma patients, might be of particular value in studying the predictive role of morningness-eveningness. Only self-reported assessment techniques were used. However, the questionnaires chosen for the study are widely-recognized and highly-valued tools used commonly in clinical practice and scientific research. It should be noted that in the present study, in the case of Clock Timing the mediating effect of mental health indices was investigated despite the lack of a total effect of Clock Timing on asthma control. Such an approach may be considered methodologically inappropriate, but Loeys et al. argue that it is acceptable as long as sensitivity analysis is carried out[63]. Here, each model underwent bootstrapping with $n = 1000$ sampling. Additionally, the differences observed between the sexes regarding the variables of interest may be considered a bias. However, the differences regarding morningness, General Health Questionnaire results and comorbidities in asthma were indicated in previous studies[1, 17, 32, 64]. Also, the mediation models constructed in this study were adjusted for both sex and age to minimize the effect of bias. It should be noted that all of the effects of sex differences were small (below 0.1)

Conclusions

- 1) Low morning affect predicted poor disease symptom control among patients with asthma. The effect was fully mediated by non-psychotic mental health indices, i.e. somatic symptoms, social dysfunction, anxiety and insomnia, and depressive symptoms. The strongest effect was observed for complaints of general somatic symptoms.
- 2) Evening-time preference was associated with a rise in asthma control and mediated by somatic symptoms and anxiety/insomnia when controlled for morning affect.
- 3) The current study underlines the significance of assessment of both individual morningness-eveningness preference and mental health in the management of asthma symptoms.

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The contribution of the first two authors is equivalent and accounts for 80% of the contribution to this research.

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Declaration of Interest statement

The authors have no conflict of interest to report

Data availability statement

The database used to support this study's findings may be obtained upon request to the corresponding author.

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Table 1. Comparison of the continuous variables of interest between men and women in the studied sample of adult asthma patients.

		Men (N = 24)		Women (N = 42)		F	P	η^2
		M	SD	M	SD			
Age		57.67	9.99	51.52	14.26	4.193*	0.045	0.051
CSM	Clock Timing	21.29	4.47	20.43	5.26	0.456	0.502	0.007
	MA	17.71	2.96	15.17	4.42	7.797*	0.007	0.090
FCI		1.42	0.58	2.02	1.20	5.393	0.023	0.078
GHQ-28	A	12.92	3.26	15.10	3.96	5.205	0.026	0.076
	B	13.67	3.98	14.93	4.83	1.169	0.284	0.018
	C	14.58	1.50	16.02	3.67	4.915*	0.031	0.051
	D	8.46	2.19	10.34	5.22	4.107*	0.047	0.043
	Total Score	49.63	9.38	56.39	14.96	3.980	0.050	0.059
ACT		17.75	5.82	16.67	5.15	0.615	0.436	0.010

CSM – Composite Scale of Morningness, MA – morning affect, FCI – Functional Comorbidity Index, GHQ-28 – General Health Questionnaire, 28-item version: A – somatic symptoms score, B – anxiety/insomnia score, C – social dysfunction score, D – depressive symptoms score, ACT – Asthma Control Test score, M – mean, SD – standard deviation, F – Fisher-Snedecor test statistics in the analysis of variance, * - the Welch test was performed to correct for non-homogeneity of variance between the groups, p -probability in the test, η^2 - size of effect.

Table 2. Matrix of Pearson's correlation coefficients of associations between the continuous variables of interest in the studied sample of adult asthma patients.

		Age	CSM Clock Timing	CSM MA	FCI	GHQ- 28 A	GHQ- 28 B	GHQ- 28 C	GHQ- 28 D	GHQ- 28 total
CSM	Clock Timing	0.118	—							
	MA	0.132	0.601†	—						
	FCI	0.195	0.078	-0.109	—					
GHQ-28	A	- 0.004	0.043	- 0.354**	0.275*	—				
	B	- 0.166	0.040	- 0.321**	0.154	0.696†	—			
	C	- 0.108	-0.082	-0.434†	0.473**	0.625†	0.609†	—		
	D	- 0.055	-0.089	- 0.328**	0.443**	0.571†	0.541†	0.722†	—	
	Total Score	- 0.100	-0.022	-0.416†	0.384**	0.850†	0.852†	0.850†	0.839†	—
	ACT	- 0.148	0.047	0.309*	0.320**	0.491†	0.359**	0.434†	0.361**	0.479†

CSM – Composite Scale of Morningness; MA – Morning Affect subscale; GHQ-28 – General Health Questionnaire, 28-item version: A – Somatic symptoms subscale, B – Anxiety/insomnia subscale, C – Social dysfunction subscale, D – Depressive symptoms subscale; ACT – Asthma Control Test; * $p < 0.05$, ** $p < 0.01$, † $p < 0.001$.

Table 3. Summary of the assessment of the effect of chronotype (assessed with the Composite Scale of Morningness) on asthma control (ACT) – direct and indirect (mediated by mental health indices) in the sample of adult asthma patients – part 1: consideration of each GHQ-28 dimension as a dimension in separate models. Presented as standardized estimates (from linear regression models), with 95% Confidence Intervals (CI), derived from bootstrapping. All models were adjusted for age, sex, night shift work and FCI score, i.e. comorbidities.

The effect of mornigness-eveningness on ACT score, without mediators							
<i>Total effects</i>				Estimate	95%CI		
Clock Timing		→		ACT	-0.139	-0.386	0.139
CSM MA		→		ACT	0.367*	0.062	0.672
The effect of mornigness-eveningness on ACT score, with mediation via GHQ-28 Somatic symptoms, R²=0.329							
<i>Direct effects</i>				Estimate	95%CI		
Clock Timing		→		ACT	-0.024	-0.245	0.256
CSM MA		→		ACT	0.201	-0.087	0.524
<i>Indirect effects</i>				Estimate	95%CI		
Clock Timing	→	GHQ-28 A	→	ACT	-0.115*	-0.303	-0.029
CSM MA	→	GHQ-28 A	→	ACT	0.165*	0.060	0.335
The effect of mornigness-eveningness on ACT score, with mediation via GHQ-28 Anxiety/insomnia, R²=0.279							
<i>Direct effects</i>				Estimate	95%CI		
Clock Timing		→		ACT	-0.063	-0.281	0.288
CSM MA		→		ACT	0.259	-0.081	0.598
<i>Indirect effects</i>				Estimate	95%CI		
Clock Timing	→	GHQ-28 B	→	ACT	-0.076*	-0.242	-0.009
CSM MA	→	GHQ-28 B	→	ACT	0.108*	0.020	0.249
The effect of mornigness-eveningness on ACT score, with mediation via GHQ-28 Social dysfunction, R²=0.288							
<i>Direct effects</i>				Estimate	95%CI		
Clock Timing		→		ACT	-0.086	-0.332	0.217
CSM MA		→		ACT	0.222	-0.120	0.556
<i>Indirect effects</i>				Estimate	95%CI		
Clock Timing	→	GHQ-28 C	→	ACT	-0.053	-0.268	0.027
CSM MA	→	GHQ-28 C	→	ACT	0.145*	0.014	0.334
The effect of mornigness-eveningness on ACT score, with mediation via GHQ-28 Depressive symptoms, R²=0.275							
<i>Direct effects</i>				Estimate	95%CI		
Clock Timing		→		ACT	-0.120	-0.360	0.183

CSM MA	→		ACT	0.286	-0.021	0.602
<i>Indirect effects</i>				Estimate	95%CI	
Clock Timing	→	GHQ-28 D	→ ACT	-0.019	-0.141	0.056
CSM MA	→	GHQ-28 D	→ ACT	0.081*	0.010	0.236

CSM – Composite Scale of Morningness; MA – Morning Affect subscale; GHQ-28 – General Health Questionnaire, 28-item version: A – Somatic symptoms subscale, B – Anxiety/insomnia subscale, C – Social dysfunction subscale, D – Depressive symptoms subscale; ACT – Asthma Control Test; * statistically significant effects, based on 95% Confidence Intervals.

Table 4. Summary of the assessment of the effect of mornigness-eveningness (assessed with the Composite Scale of Morningness) on asthma control (ACT) – direct and indirect (mediated by mental health indices) in the sample of adult asthma patients, part 2: GHQ-28 total score as mediator and consideration of all four GHQ-28 dimensions combined in one model. Presented as standardized estimates (from linear regression models), with 95% Confidence Intervals (CI), derived from bootstrapping. All models were adjusted for age, sex, night shift work and FCI score, i.e. comorbidities.

The effect of mornigness-eveningness on ACT score, without mediators						
<i>Total effects</i>				Estimate	95%CI	
Clock Timing	→		ACT	-0.139	-0.386	0.139
CSM MA	→		ACT	0.367*	0.062	0.672
The effect of mornigness-eveningness on ACT score, with mediation via GHQ-28 total score, $R^2=0.316$						
<i>Direct effects</i>				Estimate	95%CI	
Clock Timing	→		ACT	-0.046	-0.255	0.280
CSM MA	→		ACT	0.187	-0.125	0.521
<i>Indirect effects</i>				Estimate	95%CI	
Clock Timing	→	GHQ-28	→ ACT	-0.094	-0.390	0.008
CSM MA	→	GHQ-28	→ ACT	0.179*	0.058	0.360
The effect of mornigness-eveningness on ACT score, with mediation via all four GHQ-28 scales scores, $R^2=0.336$						
<i>Direct effects</i>				Estimate	95%CI	
Clock Timing	→		ACT	-0.022	-0.263	0.297
CSM MA	→		ACT	0.169	-0.186	0.502
<i>Indirect effects</i>				Estimate	95%CI	
Clock Timing	→	GHQ-28 A	→ ACT	-0.097*	-0.301	-0.008
Clock Timing	→	GHQ-28 B	→ ACT	0.002	-0.090	0.112
Clock Timing	→	GHQ-28 C	→ ACT	-0.021	-0.214	0.028
Clock Timing	→	GHQ-28 D	→ ACT	-0.001	-0.098	0.064
CSM MA	→	GHQ-28 A	→ ACT	0.139*	0.006	0.382

CSM MA	→	GHQ-28 B	→	ACT	-0.002	-0.146	0.137
CSM MA	→	GHQ-28 C	→	ACT	0.056	-0.119	0.295
CSM MA	→	GHQ-28 D	→	ACT	0.004	-0.125	0.123

CSM – Composite Scale of Morningness: MA – Morning Affect subscale; GHQ-28 – General Health Questionnaire, 28-item version: A – Somatic symptoms subscale, B – Anxiety/insomnia subscale, C – Social dysfunction subscale, D – Depressive symptoms subscale; ACT – Asthma Control Test; * statistically significant effects, based on 95% Confidence Intervals.

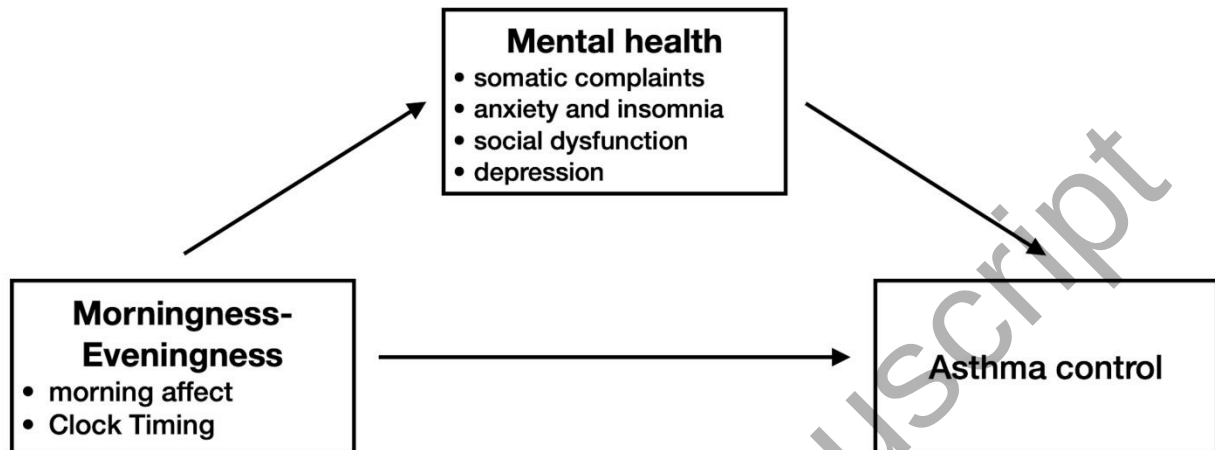


Figure 1. Hypothetical model of relationship between morningness-eveningness and asthma control. All paths adjusted for age, sex, night shift work and comorbidities.