

# Association between higher morning preference and better health-related quality of life in asthma



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**Background:** Circadian preference for eveningness has been linked to a higher risk of asthma and allergies, but its association with health-related quality of life (HRQL) in asthma has not been studied yet.

**Objective:** We aimed to investigate the associations between individual circadian preference and HRQL in asthma.

**Methods:** Among 691 adult asthma patients from Canada, India, New Zealand, and the United Kingdom, a digital questionnaire was administered to capture demographic information, social and psychologic attributes, comorbidities, and medication adherence. Circadian preference and HRQL were assessed by the reduced version of the morningness–eveningness questionnaire (rMEQ) and the short form of the chronic respiratory questionnaire, respectively. We analyzed the association between chronotype and HRQL using mixed-effect linear regression models.

**Results:** Of all participants, 59% were female with a mean (standard deviation) age of 49 (17) years. Median (interquartile range) rMEQ total score was 17 (14–19). Mean (standard deviation) dyspnea, fatigue, emotional function, and mastery scores were 5.94 (1.2), 4.38 (1.3), 5.05 (1.3), and 1.96 (1.1),

respectively. In regression analysis, a higher rMEQ total score (higher morningness) was associated with less fatigue ( $\beta = 0.06$ ; 95% confidence interval, 0.04 to 0.09) and better emotional function ( $\beta = 0.03$ ; 95% confidence interval, 0.004 to 0.06), and these associations were mediated by less anxiety, depression, and alcohol abuse, and better sleep quality.

**Conclusion:** Morning orientation is associated with better HRQL in patients with asthma. The results suggest that working with patients to promote schedules and habits related to morningness may be beneficial. (J Allergy Clin Immunol Global 2025;4:100456.)

**Key words:** Anxiety, alcohol, chronotype, depression, morningness, SF-CRQ, sleep

Asthma is a chronic inflammatory disease of the airways. While several well-known physical, social, and environmental factors can cause asthma or exacerbate asthma symptoms, disrupted circadian rhythmicity as a determinant of asthma has garnered significant attention these days. Asthma symptoms and exacerbations have been known to follow circadian rhythmicity long ago,<sup>1</sup> and an increasing body of evidence has emerged recently describing the cellular and immunologic pathways of circadian rhythmicity of asthma and allergic diseases.<sup>2–5</sup> Several recent studies have also shown that disruption of circadian rhythmicity may also lead to asthma and other allergic diseases.<sup>2,3,6–13</sup> Exposure to artificial light at night, night shift work, and circadian preference (chronotype) toward eveningness are known to cause circadian phase delay, which ultimately reduces the rhythm amplitude to near zero,<sup>11,14–16</sup> finally leading to disruption of the circadian rhythm. Studies have shown that evening chronotype people and those exposed to night shift work have a higher prevalence of asthma and allergic diseases.<sup>7,9,12,13,17</sup>

Several studies demonstrated links between chronotype and the prevalence of asthma, but reports investigating associations between circadian preference and asthma-related outcomes such as asthma control and health-related quality of life (HRQL) are few. In clinical studies, HRQL is considered one of the most important considerations with a comprehensive understanding of disease outcomes and patient well-being.<sup>18,19</sup> Past reports have investigated the associations between chronotype and HRQL in several chronic diseases;<sup>20–27</sup> however, none of the studies was related to HRQL in asthma or allergic diseases. Although disease severity and symptom control are important determinants of HRQL, a recent study investigated the relationship

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**Abbreviations used**

CI: Confidence interval
HRQL: Health-related QoL
QoL: Quality of life
IQR: Interquartile range
MARS: Medication Adherence Rating Scale
rMEQ: Reduced version of morningness–eveningness questionnaire
SD: Standard deviation
SF-CRQ: Short form of chronic respiratory disease questionnaire

between morningness–eveningness and asthma control in a small group of asthma patients and found that a higher morning preference was associated with poorer asthma control and nonpsychotic mental health conditions fully mediated the association.<sup>28</sup> It should be noted that morning-preference individuals often experience better sleep quality<sup>29–31</sup> and healthier lifestyle patterns,<sup>32,33</sup> which may potentially enhance asthma management.<sup>34,35</sup> Furthermore, asthma symptoms often worsen in the early morning and at night,<sup>12,13</sup> and the symptom perception and control could be dependent on chronotype. Therefore, it could be hypothesized that asthma HRQL may also be influenced by chronotype; nevertheless, despite indirect evidence of chronotypes influencing asthma control, direct evidence data about chronotype and asthma HRQL including potential mediators are lacking.

Therefore, in this study, we aimed to examine the association between chronotype and HRQL in asthma and whether this association is influenced by the presence of other modifiable factors such as anxiety, depression, sleep deprivation, and alcohol abuse.

**METHODS****Study design and population**

We performed this secondary analysis of data from a cross-sectional, anonymized, observational, survey conducted in Canada, India, New Zealand, and the United Kingdom. Details of the study participants, design, inclusion and exclusion criteria, and methodologies have been described previously.<sup>36,37</sup> In brief, adult ( $\geq 18$  years of age) asthma patients were recruited from existing cohorts, institutional or clinic-based registries, or general practice records and through advertisements. Asthma was diagnosed at the clinic following appropriate clinical methodologies such as lung function and bronchoprovocation tests. Asthma diagnosis was based on appropriate guidelines and clinical methods. Ethics approval was obtained from the Health Research Ethics Board of Alberta (HREBA-CHC-20-0056), the Health Research Ethics Board of the University of Alberta (Pro00105432) (Canada), and the Clinical Research Ethics Committee of Allergy and Asthma Research Centre (CREC-AARC/0027-20) (India). Because anonymized surveys are outside the purview of an ethical review as per Health and Disability Ethics Committee guidelines, ethics approval was not required for New Zealand and the UK sites. However, the questionnaire contained a brief description of the study, and participants had the option to provide digital consent on agreeing to the terms of participation. The study was conducted according to the Declaration of Helsinki and reported according to the STROBE (Strengthening the Reporting of

Observational Studies in Epidemiology) guidelines for observational studies.<sup>38</sup>

**Instruments**

We designed an anonymous digital survey using the REDCap (Research Electronic Data Capture) platform,<sup>39</sup> and the survey questionnaire was shared with patients via a URL by the study centers through text messages or emails as described previously in detail.<sup>36,37</sup> In brief, all responses were voluntary and unsupervised to ensure responses could not be linked to the medical records of the participants. All questions were self-explanatory and self-administered. We obtained demographic information such as age, sex, ethnicity, educational qualification, employment status, marital status, family size, and regular physical activity through a questionnaire as described previously.<sup>36,37</sup>

We used the reduced version of the morningness–eveningness questionnaire (rMEQ) to assess the chronotype of the participants.<sup>40</sup> While the original English version of the rMEQ instrument was used in all participating centers, a previously validated Bengali version of the instrument<sup>41</sup> was also used for a subset of participants in India. The rMEQ is a 5-item questionnaire about preferred sleep and activity timing and has a composite score ranging between 4 and 25, with a lower score indicating eveningness and a higher score indicating morningness. While we primarily used the actual rMEQ scores in analyses, we also stratified participants by chronotype by standard cutoff scores (morning type,  $>17$ ; intermediate type, scores between 12 and 17; and evening type,  $<12$ )<sup>40,41</sup> for secondary analyses. We used the 4-item (Short Form-4a) Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaires to assess anxiety, depression, and sleep disturbances, and the 7-item questionnaire (Short Form-7a) for alcohol abuse.<sup>36</sup> Compliance was determined by the Medication Adherence Rating Scale (MARS) (0 = worse compliance, 10 = better compliance),<sup>42</sup> and comorbidity was assessed by the Elixhauser comorbidity index ( $-19$  = less likely in-hospital death, 89 = more likely in-hospital death).<sup>43</sup> We evaluated the HRQL of the participants using the short form of the chronic respiratory questionnaire (SF-CRQ), which is composed of 4 domains, fatigue, emotional function, dyspnea, and mastery, with each domain score ranging between 1 (worse quality of life [QoL]) and 7 (better QoL).<sup>36,37</sup>

**Statistical analysis**

The sample size was fixed by the main objective of the previous study.<sup>36</sup> Because the study was planned as multicenter, no clustering by site was considered. Descriptive statistics are presented as mean (standard deviation [SD]), median (interquartile range [IQR]), or frequency (%) for continuous, count, and categorical variables, respectively. We first assessed the relationships between circadian typology (rMEQ total score and chronotype) and HRQL domain scores by Spearman rank-order correlations (for rMEQ total score), and by 1-way ANOVA tests (for chronotype). We also tested the associations between the primary independent variable (rMEQ total score), all available covariates (sex, age, ethnicity, educational qualification, employment status, family size, marital status, regular physical activity, Elixhauser comorbidity index, and MARS score), and HRQL domain scores by *t* test, ANOVA, and Spearman correlation as appropriate.

We constructed mixed-effect linear regression models to assess the relationships between the rMEQ total score and HRQL domain scores. To understand the relationships among the variables, we first constructed a directed acyclic graph, based on which we tested sex, age, ethnicity, educational qualification, employment status, family size, marital status, regular physical activity, Elixhauser comorbidity index, and MARS score as fixed factors and country as a random factor in the models. The goodness of fit of the models was determined by the Akaike information criterion,<sup>44</sup> and based on that, only sex, age, ethnicity, marital status, regular physical activity, and Elixhauser comorbidity index were retained in the final models as confounders. We also checked for multicollinearity among the confounders by determining the variance inflation factor.

We also performed several sensitivity analyses. First, we tested the associations between chronotype (evening type, intermediate type, and morning type, where evening type was the reference category) and HRQL domain scores using the same regression approach described above. Second, we performed exploratory mediation analyses to test the roles of anxiety, depression, sleep disturbances, and alcohol abuse in the associations between rMEQ total score and HRQL domain scores. Third, we stratified associations between rMEQ total score and HRQL domain scores by sex, comorbidities (less vs more risk), and compliance (less vs more compliant). Comorbidity and compliance scores were dichotomized using their median values (eg, less and more risk if Elixhauser comorbidity scores are  $\leq 0$  and  $>0$ ). Finally, we performed meta-analyses to determine if there was any heterogeneity in the associations between rMEQ total score and HRQL domain scores across participating countries. All analyses were conducted using a complete case approach in Stata v18.0 (StataCorp, College Station, Tex). Meta-analysis was performed in RevMan v5.4 (Cochrane Collaboration, London, United Kingdom).

## RESULTS

Of 691 participants, 400 (59%) were female, and the mean (SD) age was 49 (17) years. Sixty-eight percent of the participants were White, 77% had attained education above high school, and 64% were actively employed. The median (IQR) Elixhauser comorbidity index and MARS score were 0 (0-3) and 4 (2-7), respectively. The median (IQR) rMEQ total score was 17 (14-19). The median (IQR) values of anxiety, depression, sleep disturbance, and alcohol abuse were 6 (4-9), 5 (4-9), 10 (8-12), and 7 (7-10), respectively. The domains of SF-CRQ scores for fatigue, emotional function, dyspnea, and mastery had a mean (SD) of 4.4 (1.3), 5.1 (1.3), 5.9 (1.2), and 2.0 (1.1), respectively (Table I). The amount of missing data was very small, and except for the Elixhauser comorbidity score (8%), missingness was less than 5% (see Table E1 in the Online Repository available at [www.jaci-global.org](http://www.jaci-global.org)).

In multivariable analyses adjusted for potential confounders, we found that rMEQ total score was positively associated with fatigue (regression coefficient [ $\beta$ ] = 0.03; 95% confidence interval [CI], 0.01 to 0.06) and emotional function ( $\beta$  = 0.06; 95% CI, 0.04 to 0.09), which means that a higher morningness was associated with less fatigue and better emotional function. However, rMEQ total score was not significantly associated with dyspnea ( $\beta$  = 0.002; 95% CI, -0.02 to 0.03) and mastery ( $\beta$  = 0.01; -0.02 to 0.03) (Fig 1). In the sensitivity analysis, we found that

**TABLE I.** Demographic characteristics of 691 participants

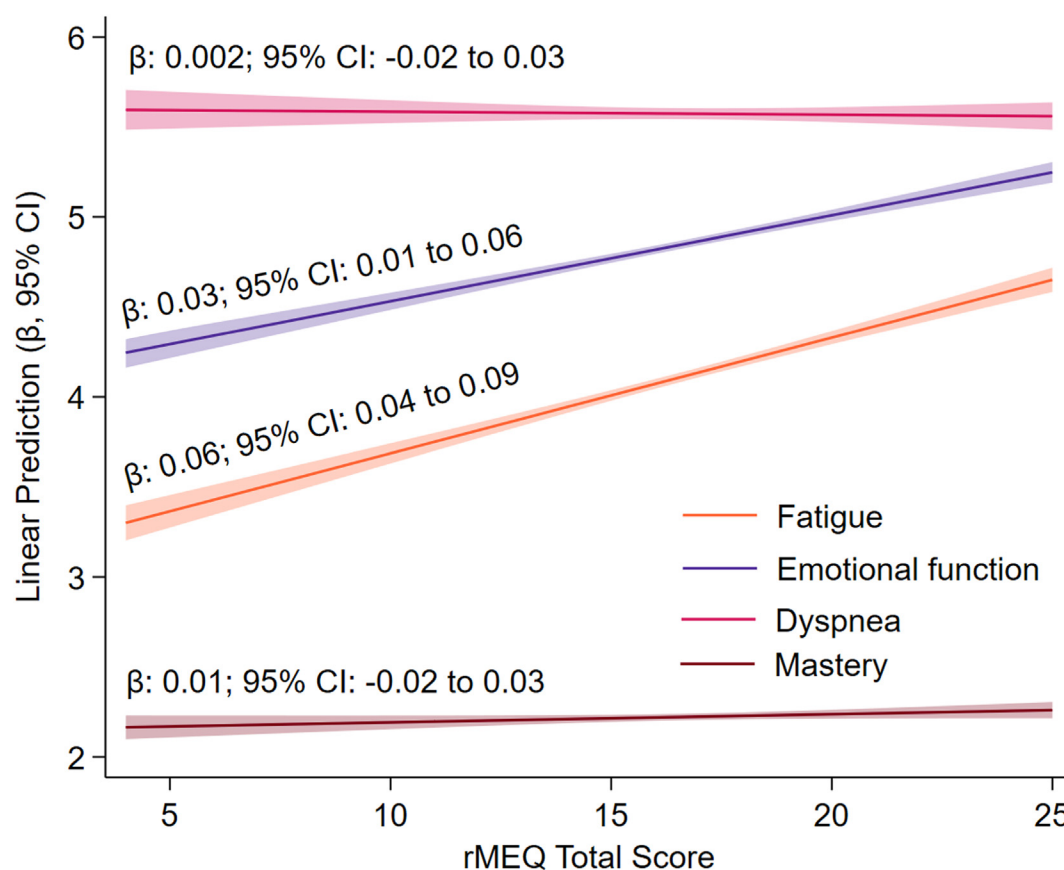
Characteristic	Value
Female sex	400 (59)
Age (years), mean (SD)	49 (17)
Ethnicity	
White	472 (68)
Asian	120 (17)
Other	99 (15)
Country	
Canada	103 (15)
India	105 (15)
New Zealand	448 (65)
United Kingdom	35 (5)
Educational qualification (beyond high school)	524 (77)
Employment status (employed)	442 (64)
Family size ( $>2$ members)	365 (53)
Marital status (married/with partner)	446 (64)
Regular physical activity	449 (65.0)
Elixhauser comorbidity index, median (IQR)*	0 (0-3)
Comorbidity (more risk)	211 (33.2)
MARS score, median (IQR)†	4 (2-7)
Compliance (more compliant)	280 (40.5)
Anxiety, median (IQR)‡	6 (4-9)
Depression, median (IQR)‡	5 (4-9)
Sleep disturbance, median (IQR)‡	10 (8-12)
Alcohol abuse, median (IQR)§	7 (7-10)
rMEQ total score, median (IQR)¶	17 (14-19)
SF-CRQ score, mean (SD)	
Dyspnea	5.9 (1.2)
Fatigue	4.4 (1.3)
Emotional	5.1 (1.3)
Mastery	2.0 (1.1)

Data are presented as frequencies (%), means with SDs, and medians with IQRs unless otherwise noted. Score ranges are as follows: \*19 (lesser risk of in-hospital death) to 89 (higher risk of in-hospital death); †0 (worse) to 10 (better); ‡4 (better) to 20 (worse); §7 (better) to 35 (worse); ¶4 (toward eveningness) to 25 (toward morningness); and ||1 (worse) to 7 (better).

compared to evening-type participants, substantially less fatigue was observed among morning-type individuals ( $\beta$  = 0.70; 95% CI, 0.42 to 0.99), followed by intermediate-type individuals ( $\beta$  = 0.31; 95% CI, 0.10 to 0.53) (Fig 2). We observed a similar trend for better emotional function but not for dyspnea or mastery.

In exploratory mediation analysis, we found that the association between higher morningness and less fatigue score was significantly mediated by less anxiety, depression, and sleep deprivation, and less alcohol abuse. These factors played a similar mediating role (except for anxiety) in the association between higher morningness and better emotional function among participants with asthma (see Table E2 in the Online Repository available at [www.jaci-global.org](http://www.jaci-global.org)). However, we did not observe any influence of these factors in associations between morningness and dyspnea and mastery scores.

In stratification analysis, we observed that higher morningness (higher rMEQ total score) was significantly associated with less fatigue both in female ( $\beta$  = 0.07, 95% CI, 0.04 to 0.10) and male ( $\beta$  = 0.06, 95% CI, 0.02 to 0.10) subjects, and the magnitudes of associations were similar. However, we observed a significant association between higher morningness and better emotional function only in male ( $\beta$  = 0.05; 95% CI, 0.01 to 0.09) but not in female ( $\beta$  = 0.02; 95% CI, -0.01 to 0.06) subjects (see Table E3 in the Online Repository available at [www.jaci-global.org](http://www.jaci-global.org)), although the differences were not statistically significant. We



**FIG 1.** Association between rMEQ total score and HRQL domain scores. Data shown as mixed-effect linear regression coefficient ( $\beta$ ) (lines) and 95% CI (shaded areas). Models were adjusted for sex, age, ethnicity, marital status, regular physical activity, and Elixhauser comorbidity index as fixed factors and country as random factor.

observed that higher morningness was associated with less fatigue ( $\beta = 0.07$ ; 95% CI, 0.04 to 0.10) and better emotional function ( $\beta = 0.04$ ; 95% CI, 0.01 to 0.07) among participants with less risk of comorbidities compared to those with a higher risk of comorbidities; however, the estimates did not differ significantly across the groups. Higher morningness was associated with less fatigue ( $\beta = 0.07$ ; 95% CI, 0.04 to 0.10) and better emotional function ( $\beta = 0.04$ ; 95% CI, 0.01 to 0.07) among participants who were less compliant with medication than those with more compliance, but there was no significant difference between the groupwise estimates.

The association between rMEQ total score and fatigue score was significantly heterogeneous ( $I^2 = 70\%$ ;  $P$  value for heterogeneity = .02) across participating countries (Fig 3, A). While the association was the highest in Canada ( $\beta = 0.08$ ; 95% CI, 0.02 to 0.15) followed by New Zealand ( $\beta = 0.07$ ; 95% CI, 0.04 to 0.10), it tended toward the reverse among Indian participants ( $\beta = -0.06$ , 95% CI,  $-0.14$  to 0.02). Intriguingly, we did not observe any heterogeneity in the associations between rMEQ total score and other HRQL domain scores (Fig 3, B-D).

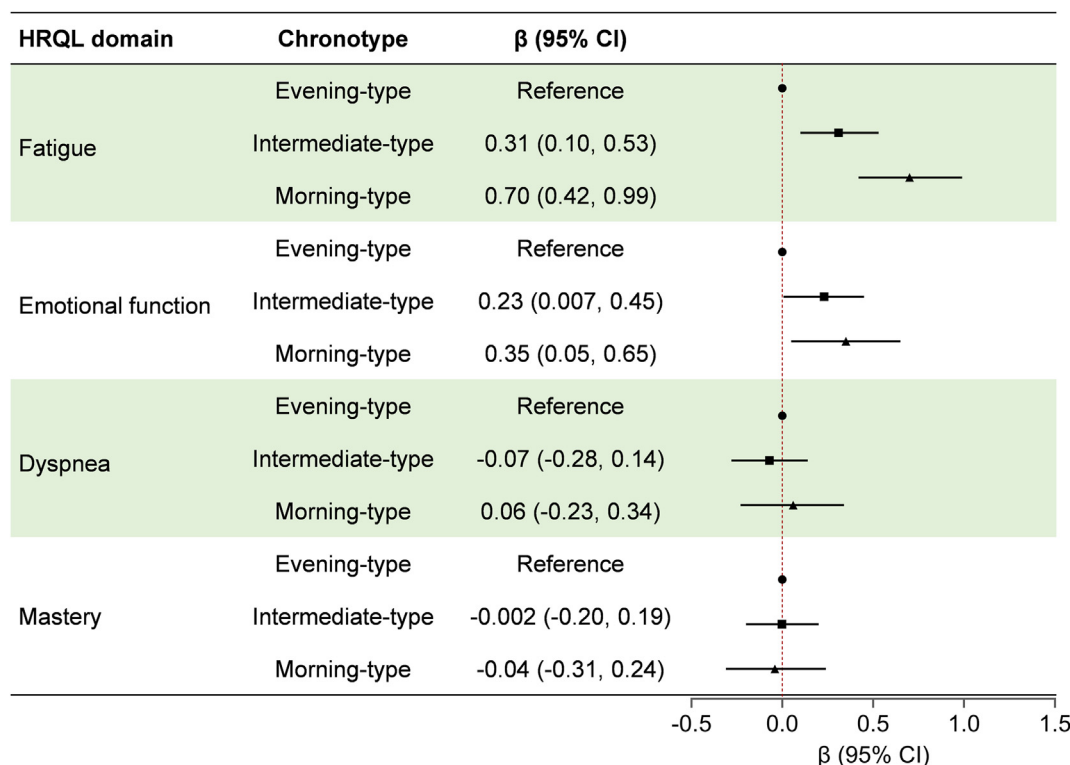
## DISCUSSION

In this multicenter study, we found that higher morningness was associated with less fatigue and better emotional function in

asthma and that this association did not differ much across participating countries. This association was more significant among male participants, participants with less risk of comorbidities, and those with less compliance with medication. We also observed that the associations between higher morningness, and less fatigue and better emotional function were mediated by less anxiety, depression, sleep disturbances, and alcohol abuse.

We observed that a higher rMEQ total score was associated with less fatigue and better emotional function domains of the HRQL instrument. Similarly, when tested against chronotype, we observed a gradient of improvement in fatigue and emotional function—that is, compared to evening-type individuals, fatigue and emotional function scores were higher among intermediate-type individuals with the highest degree of improvement in morning-type individuals. Although the relationship between chronotype and QoL in asthma remains to be disentangled, its relation with QoL in other chronic diseases such as Parkinson disease,<sup>26</sup> Alzheimer disease,<sup>45</sup> diabetes,<sup>33</sup> inflammatory bowel disease,<sup>25</sup> and cardiovascular conditions<sup>46,47</sup> is well established. A significant link between eveningness and chronic disease directs to circadian misalignment as a result of desynchrony between their endogenous biological clocks and the timing of social activities such as food and sleep timing, work, and physical activity.<sup>47</sup> A dysregulated food and sleep timing due to delayed chronotype may lead to poor symptom control and ultimately a





**FIG 2.** Association between chronotype and HRQL domain scores. Data shown as mixed-effect linear regression coefficient ( $\beta$ ) (markers) and 95% CI (error bars). Models were adjusted for sex, age, ethnicity, marital status, regular physical activity, and Elixhauser comorbidity index as fixed factors and country as random factor.

poor QoL.<sup>4,33</sup> Overexposure to artificial light at night, particularly blue-white light emitting from electronic devices such as mobile phones, television, or computer screens, is also an additive risk factor for circadian misalignment among evening-type individuals. A recent meta-analysis demonstrated that higher eveningness, outdoor exposure to light at night, and night shift work are associated with a higher risk of asthma and other allergic diseases.<sup>11</sup> Although eveningness is not the same as night shift work, one recent study among rotating shift workers showed that night shift was associated with disruption of multiple immune response pathways, many of which share common links with asthma.<sup>48</sup> Paganelli et al in 2018 summarized that almost all immunologic functions have circadian variations that might influence susceptibility to infections, and that this phenomenon could also be modulated by sleep quality and quantity as well as shift work employment, thus disrupting the circadian rhythms.<sup>49</sup> Thus, the possibility of an aggravated asthma symptom as a result of higher eveningness or associated activities may significantly influence QoL. Nevertheless, we could not assess asthma control in this study; therefore, a direct link between poor asthma control and QoL in relation to chronotype could not be established.

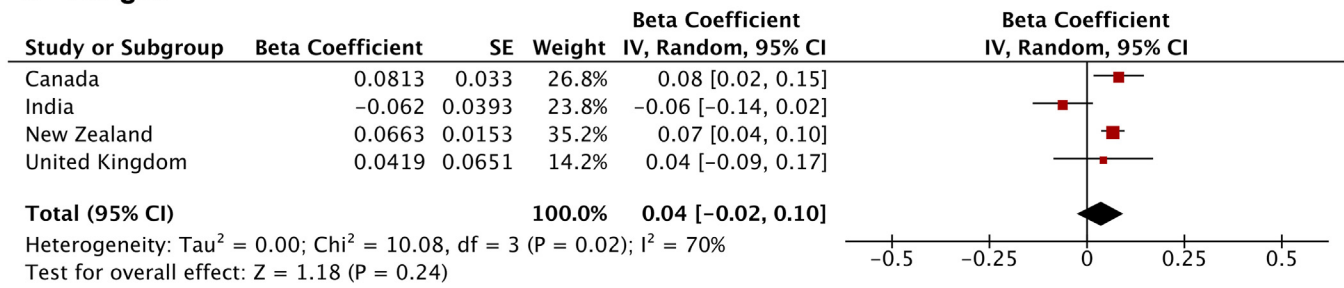
We observed that the relationships between higher morningness and less fatigue and better emotional function were mediated by better anxiety and depression, less sleep disturbance, and less alcohol abuse. Previous data have shown that chronotype for morningness was associated with lower anxiety, depression, and better sleep quality.<sup>50-55</sup> Some recent studies have demonstrated that individuals with higher evening preferences, particularly young adults, are likely to be more addicted to alcohol.<sup>56-58</sup> It is

noteworthy that all these 4 factors have a significant impact on chronic diseases such as asthma. There is substantial evidence showing that anxiety, depression, and poor sleep quality significantly influence asthma symptoms and QoL.<sup>59-65</sup> Therefore, mental health, behavioral function, and addiction can significantly influence the link between circadian preference and HRQL in asthma. However, apart from indirect evidence, studies with direct links among these variables are scarce, and more epidemiologic studies are required to expand our understanding of this interaction.

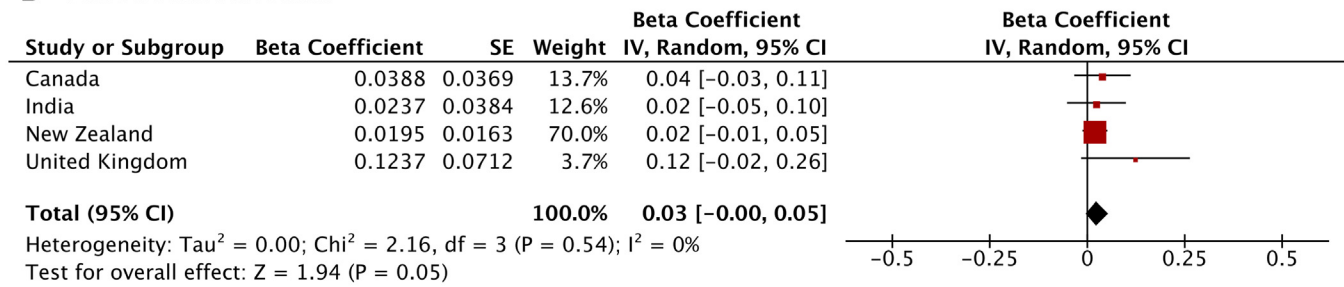
Recent studies assessing sex differences in asthma HRQL showed a poorer HRQL among female asthma patients.<sup>66-68</sup> Although we observed significantly poorer HRQL domain scores in female compared to male participants, a similar association between chronotype and fatigue in male and female participants was obtained, as was a slightly lower (but not statistically significant) association between morningness and emotional function in female participants. It is important to note here that chronotype also varies between sexes, with female subjects being more morning oriented than their male counterparts.<sup>69-71</sup> Therefore, it can be assumed that a shift toward morningness would have a greater impact on HRQL in male compared to female subjects. Nevertheless, there could be several other residual confounders such as social or behavioral attributes that might have influenced the associations between chronotype and asthma HRQL across sexes, which needs further exploration.

We observed significant associations between higher morningness, and less fatigue and better emotional function among participants with less comorbidity risk. It is already known that

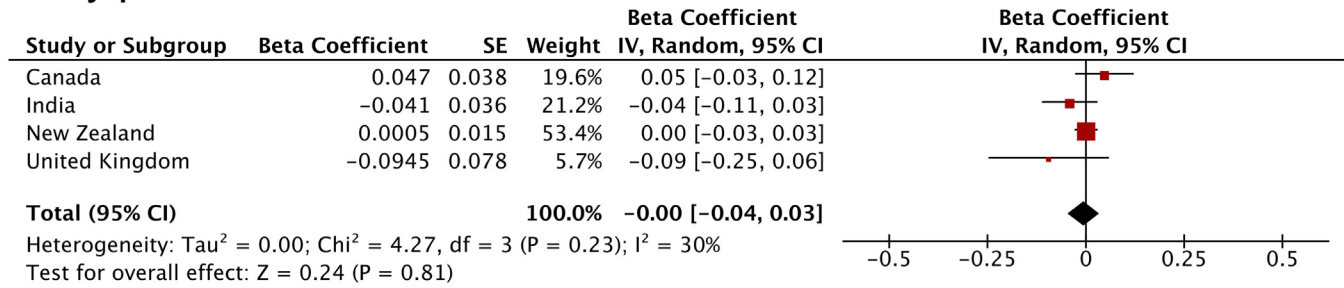
A Fatigue



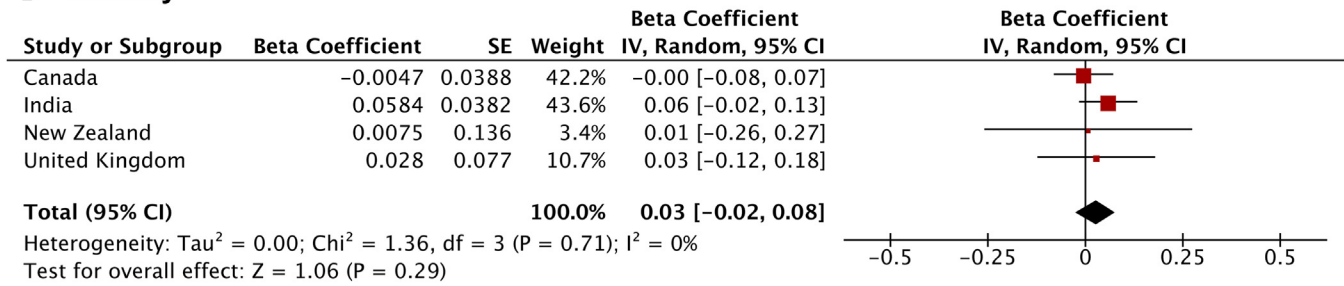
B Emotional function



C Dyspnea



D Mastery



**FIG 3.** Meta-analysis of association between rMEQ total score and HRQL domain scores by country. Models were adjusted for sex, age, ethnicity, marital status, regular physical activity, and Elixhauser comorbidity index as fixed factors.  $I^2$  indicates variation in estimated effect attributable to heterogeneity.

higher morningness is associated with a lesser risk of chronic diseases, including asthma,<sup>11-13,57,72</sup> and lower comorbidities are associated with better HRQL.<sup>73,74</sup> Intriguingly, we observed significant associations between higher morningness and less fatigue and better emotional function among participants who were less compliant with medication, but the associations tended to be null among those who were more compliant. Although more

compliance with medication leads to a better HRQL in asthma, we could not determine whether less compliant participants had a lesser disease severity or better asthma control, thus requiring less medication. Nevertheless, one possible explanation is that morning-oriented individuals are likely to have higher adherence to medication schedules,<sup>75</sup> engage more consistently in physical activity, and experience lower stress levels,<sup>76</sup> all of which could

enhance immune function and reduce inflammation—critical for asthma control. These factors collectively contribute to an improved HRQL. However, it might be possible that other unaccounted environmental variables, such as air pollution, noise pollution, and temperature, which might be at a nadir in the early morning hours, could lead to better asthma control and HRQL; however, we could not measure those, and there is limited evidence to date to effectively propose an indirect causal pathway between morning chronotype and better asthma HRQL through environmental parameters. Therefore, more empirical research on disease severity, symptom control, and dose/type of asthma medications, along with a robust undertaking of environmental parameters, would have been useful to justify this association.

Despite significant variations in rMEQ total score and HRQL domain scores among participating countries, the associations remained similar, leading to homogeneity in the associations between chronotype and HRQL domain scores, except for fatigue. The heterogeneity in fatigue could be due to the higher annual average temperature in India than in other countries, which might have an additional impact on fatigue levels among Indian participants.<sup>77</sup> In the case of other HRQL domains, this homogeneity is possibly because of the proportionately similar variations in rMEQ total score and HRQL domain scores across participating countries. Another plausible explanation could regard variations in other factors that might influence HRQL differently, such as environmental variables like temperature, sunlight exposure, and air pollution. These associations could also be linked to differences in cultural attitudes; further studies are warranted in this area.

The strengths of our study included its multicenter design, with participants from many different regions with substantial geographic, demographic, environmental, physiologic, behavioral, and cultural variations. To our knowledge, this is the first report investigating the role of chronotype in HRQL in asthma. In addition to our rigorous sensitivity analyses for the possible mediating roles of anxiety, depression, sleep quality, and alcohol abuse that might play crucial roles in the associations between chronotype asthma HRQL, the associations were homogeneous across the participating countries, indicating a generalizability of the study findings. Although social functioning and behavioral factors such as sleep quality and activity pattern are often considered indicators of QoL,<sup>78-80</sup> clinicians should also pay attention to individual chronotype as a possible determinant of HRQL in asthma that may be further influenced by other behavioral attributes such as anxiety, depression, sleep, and addictions. While it is too early to claim that shifting chronotype toward morningness may improve HRQL in asthma, it is already established that behavioral modification may help in improving symptom control and HRQL in asthma.<sup>34,81,82</sup> Our findings advocate a patient-centered strategy for asthma management, particularly focusing on a wide spectrum of psychologic, behavioral, and sociologic attributes, although more research is required to delineate the interactions among these factors.

Our study had some limitations. First, our study design was cross-sectional, so any causal relationship between chronotype and HRQL could not be established. There could also be an argument of reverse causality—that is, preferred morningness that is due to waking up with asthma symptoms in the morning. However, it must be remembered that disease conditions may influence sleep–wakefulness timing but not chronotype. Second, this was a self-reported survey, with possibilities of potential

recall and other biases. Third, we could not perform any objective assessment of the participants, such as lung function or asthma severity. Fourth, because the survey was conducted digitally, asthma patients without access to a digital device might have opted out of this study. Fifth, apart from medication adherence, we could not determine the type of medication or treatment, disease etiology, or symptom control. Sixth, we cannot rule out the involvement of residual confounding by other environmental factors such as weather or sunlight exposure, which might also play crucial roles in HRQL in asthma. Seventh, the mediators we tested in this study such as anxiety and depression were not clinically diagnosed; therefore, the possibility of over- or under-reporting conditions may not be omitted. Finally, this study was conducted in an adult population; thus, the reproducibility of the study findings may differ in the pediatric or adolescent population.

In summary, our study demonstrated that individual chronotype is an important determinant of HRQL in asthma. This association is also mediated by anxiety, depression, sleep disturbances, and alcohol abuse. Therefore, it is important to recognize behavioral aspects while assessing HRQL in chronic respiratory diseases, such as asthma. Our study also suggests that there is a need to explore other, less-recognized domains of HRQL through more epidemiologic research in chronic respiratory diseases.

## DISCLOSURE STATEMENT

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### Key messages

- Previous studies have demonstrated that a higher eveningness is associated with an increased risk of asthma; however, the role of morningness and eveningness on HRQL in asthma remains understudied.
- Our study demonstrated for the first time that compared to evening-type asthma patients, morning-type asthma patients had a better HRQL, and this was partially driven by improved anxiety, depression, alcohol abuse, and sleep quality.
- Shifting toward morningness might be beneficial for improving HRQL in asthma.

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