Diurnal variation in spirometry parameters of patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis

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Abstract. Diurnal variation in pulmonary function is a key physiological phenomenon, with potential clinical significance in chronic obstructive pulmonary disease (COPD). The reduced diurnal fluctuation of forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV_1) in patients with COPD may be attributed to airway inflammation, autonomic dysregulation and impaired lung compliance, with potential influence from altered cortisol rhythms. These fluctuations are clinically significant as they highlight the importance of optimizing bronchodilator timing and interpreting spirometry results within a diurnal context. The present systematic review and meta-analysis examined the diurnal fluctuations in FVC and FEV_1) among healthy individuals and patients with COPD. A total of 8 studies, including 595 for FVC (or 725 for FEV_1) healthy individuals and 172 patients with COPD, were analyzed. In healthy adults, the mean diurnal FVC difference was 1.92 (P<0.01), with morning values significantly higher than nighttime values. Patients with COPD also exhibited a morning increase in FVC values, but with a smaller, non-significant difference of 1.04 (P=0.06). The mean difference in diurnal FVC variation between the two groups was 1.46 (P<0.01), indicating a significantly greater variation in healthy individuals. For FEV_1, healthy individuals exhibited a mean diurnal difference of 4.94 (P<0.01), whereas patients with COPD showed a smaller but significant difference of 0.82 (P<0.01). However, the between-group difference in diurnal FEV_1 variation was 3.07 (P=0.17), which was not statistically significant. Heterogeneity was moderate to high (I^2=57-59%), suggesting variability across the included studies. The reduced diurnal fluctuation of FVC and FEV_1 in patients with COPD may be attributed to airway inflammation, autonomic dysregulation and impaired lung compliance, with potential influence from altered cortisol rhythms. These findings underscore the importance of personalized treatment approaches, optimizing bronchodilator timing and considering diurnal patterns in spirometry interpretation for improved COPD management. Future research should explore longitudinal home spirometry to refine therapeutic strategies.

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Introduction

Diurnal variation, which is defined as the fluctuation of physiological parameters over a 24-h cycle, is a fundamental aspect of human physiology and has important implications in various medical fields, particularly in respiratory medicine. In the context of pulmonary function testing, diurnal variation is prominently observed in key metrics, such as forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1) and peak expiratory flow (PEF) (1,2). These parameters are essential for assessing lung function, diagnosing respiratory conditions, and monitoring disease progression. Understanding the diurnal patterns of these metrics in both healthy individuals and patients with chronic obstructive pulmonary disease (COPD) is critical for optimizing clinical assessments and therapeutic strategies such as optimizing the dose and timing of bronchodilator therapy (for example,

administering long-acting bronchodilators in the morning for better symptom control), and tailoring spirometry interpretation based on time-of-day fluctuations (3-8).

In healthy individuals, the diurnal variation of FVC, FEV_1, and PEF typically follows a predictable and consistent pattern (9,10). Studies have shown that these parameters are often at their highest in the morning, staying rather stable throughout the day to reach lower values in the early evening before declining further overnight. This fluctuation is primarily influenced by circadian rhythms, which govern various physiological processes, including hormonal release, airway dynamics and lung volume changes due to postural effects and physical activity (10,11). For instance, increased airway resistance is commonly observed at night, likely due to elevated vagal tone and increased bronchial reactivity during sleep. As the day progresses and physical activity increases, improvements in lung volumes and reduced airway resistance contribute to enhanced pulmonary function (8).

Conversely, the diurnal variation of pulmonary function parameters in patients with COPD is often more complex and less predictable. COPD, which is characterized by chronic inflammation, airway remodeling and mucus hypersecretion, can notably alter the normal diurnal patterns compared with those observed in healthy individuals (12,13). While some patients with COPD may exhibit a diurnal variation similar to that of healthy individuals, a number of patients experience more pronounced fluctuations in lung function. Factors such as increased airway resistance, compromised lung compliance and the presence of comorbidities, including cardiovascular disease, obstructive sleep apnea and metabolic syndrome, can exacerbate these diurnal variations. For instance, patients with COPD may experience heightened symptoms, such as dyspnea and wheezing, during periods of increased bronchial reactivity, which are often associated with environmental triggers, such as allergens, pollution or changes in weather (11-14).

Several studies have documented the diurnal variation of FVC, FEV_1 and PEF in both healthy individuals and patients with COPD, revealing important insights into how these populations respond differently to time-of-day effects (7,8-16). In healthy individuals, the predictable rise in lung function throughout the day aligns with physiological expectations related to increased activity and diminished airway resistance. However, in patients with COPD, the diurnal pattern may be disrupted, reflecting the underlying pathophysiology of the disease (12,13). This disruption can lead to marked declines in lung function during specific times of the day, particularly in the morning, which may exacerbate the management challenges faced by healthcare providers (14).

The diurnal variation of FVC, FEV_1 and PEF represents a critical aspect of pulmonary physiology that warrants thorough investigation (10). The differences observed between healthy individuals and patients with COPD highlight the complex interplay of biological rhythms, disease mechanisms and environmental influences on lung function (11). The present meta-analysis aims to provide a detailed examination of these diurnal variations, ultimately contributing to enhanced understanding and management of respiratory health in diverse populations. It is anticipated that the insights gained will not only enrich the comprehension of lung function dynamics but also pave the way for improved clinical practices that address the unique needs of patients with COPD and other respiratory disorders.

Materials and methods

Search strategy. A systematic search was conducted in three main databases [Pubmed (https://pubmed.ncbi.nlm.nih.gov/), Cochrane Library (https://www.cochranelibrary.com/) and Google Scholar (https://scholar.google.com)], with a time limit between 1980 and 2024. The search was limited to studies published from 1980 onwards to focus on spirometric measurements using standardized modern techniques and guidelines, which were not consistently applied in earlier literature. Gray literature was also included in the search. The references of the included studies were manually and individually searched to identify additional relevant studies.

Regarding the search strategy, both free-text terms and Medical Subject Headings terms were used. Boolean operators and special filters were applied to maximize search efficiency. Special filters included restriction to English-language studies, human subjects and studies involving adult populations. The complete search string used was as follows: ('Diurnal' OR 'during the day' OR 'all day' OR '24 h' OR 'daily' OR 'every day') AND ('measurement' OR 'assessment' OR 'score' OR 'evaluation' OR 'quantification' OR 'estimation' OR 'gauge' OR 'calculation') AND ('FVC' OR 'forced vital capacity') AND ('FEV_1' OR 'forced expiratory volume in 1 sec') AND 'spirometry' AND ('healthy adults' OR 'health' OR 'normal') AND ('COPD' OR 'chronic' OR 'bronchitis' OR 'emphysema' OR 'airflow limitation disorder' OR 'chronic lung disease' OR 'pulmonary obstructive disease').

Inclusion and exclusion criteria. The present review and meta-analysis included studies with populations consisting of either healthy individuals or patients diagnosed with COPD, irrespective of age, disease severity, therapeutic regimen or sex. The diagnosis of COPD was established based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (https://goldcopd.org/). The primary outcome of interest was the diurnal fluctuation of various spirometric parameters, including FVC and FEV_1. Spirometric measurements were conducted both in the morning and at nighttime, and the results were compared.

The present study encompassed observational studies, randomized controlled trials (RCTs), quasi-randomized trials, pre-post studies and historical control studies. Letters to the editor, editorials, comments, case reports and case series were excluded. Additionally, studies involving healthy individuals exposed to occupational hazards, patients with overlapping syndromes such as obstructive sleep apnea, morbidly obese individuals, patients with neuromuscular diseases and smokers were excluded. Non-human studies were also not considered.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) process. The present study was conducted according to the PRISMA guidelines (17). The current systematic review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO ID no. CRD420250654168).

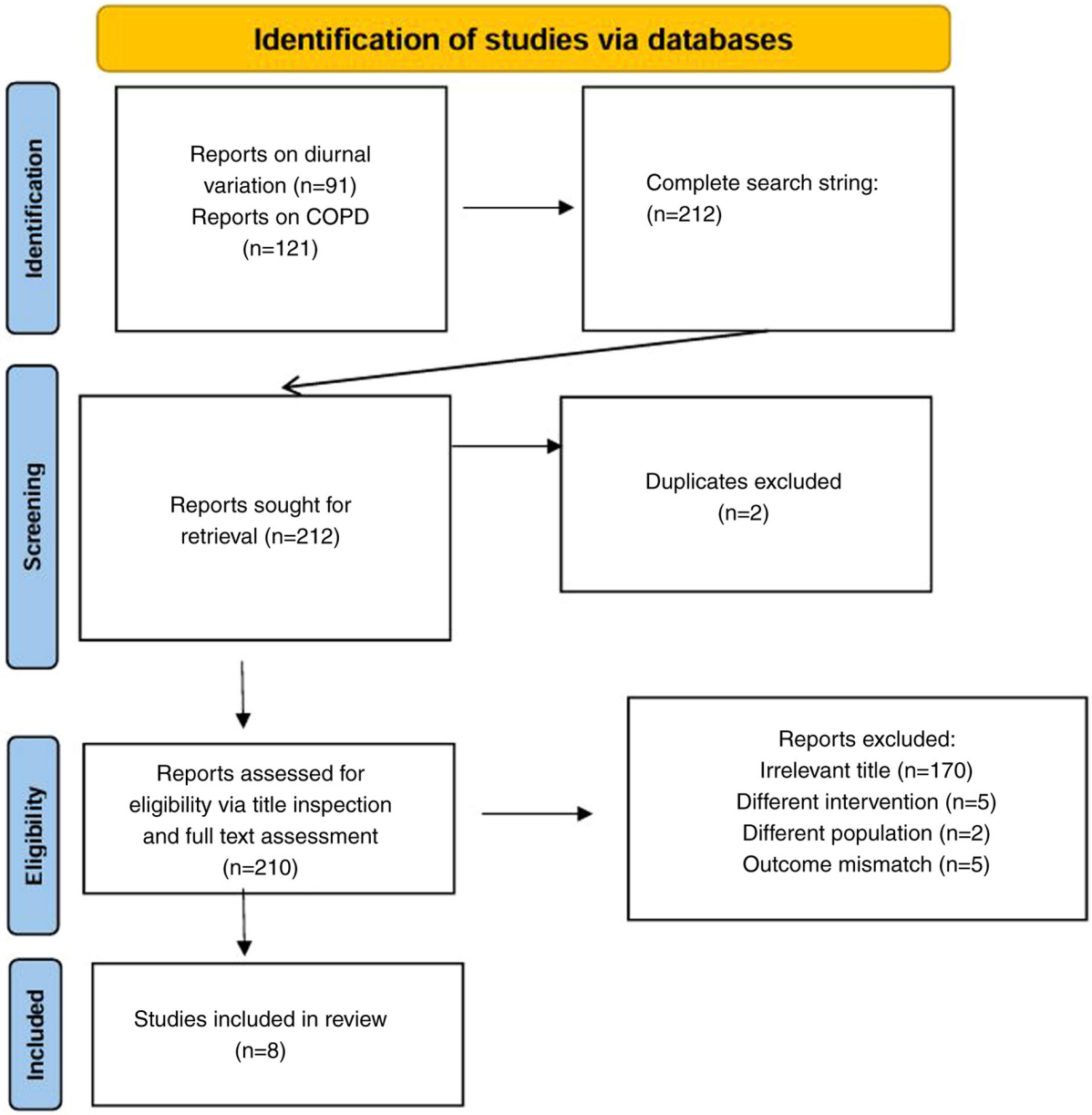

Figure 1. Flow diagram of the study selection process. COPD, chronic obstructive pulmonary disease.

The database search for spirometric diurnal variation in healthy subjects yielded 91 studies, while the search for COPD-related studies resulted in 121 studies. Combining both searches yielded a total of 212 studies. Following duplicate removal (n=2), 210 studies were screened based on their titles, with 170 studies excluded due to irrelevance. The remaining 40 studies underwent full-text evaluation, leading to the exclusion of 32 studies due to differences in intervention (such as timing or protocol of spirometric measurements that did not compare morning and nighttime values) (n=5), population (n=22) or outcome mismatch (n=5). Ultimately, eight studies met the inclusion criteria and were incorporated into the meta-analysis. The flow diagram illustrating the search strategy is presented in Fig. 1.

Data extraction. Data extraction was independently conducted by two authors (KD and VEG) using a data extraction sheet that contained all the following information about each included study: Study characteristics, author, year, location, sample size, population demographics, intervention details, outcome measures, results effect sizes and confidence intervals (CIs). Any possible discrepancies were resolved through constructive dialogue. The information included in the extraction sheets was computed in a local database in Microsoft Excel format allowing easy retrieval and analysis during the synthesis phase of the present study.

Quality assessment and risk of bias. To evaluate the quality of the included studies, the Newcastle-Ottawa Scale for non-randomized observational studies (18) was used, which assesses study quality based on three domains: Selection of study participants, comparability of groups and outcome assessment. This tool provides a structured approach to evaluating potential sources of bias and methodological rigor.

Table I. Basic characteristics of the included studies with a population or sub-population of healthy individuals.

First author, year	Population, n	Morning mean value (FVC/FEV_1), l	Morning SD value	Night mean value (FVC/FEV_1), l	Night SD value	Quality assessment	(Refs.)
Teramoto *et al*, 1999	120	4.50/4.00	0.12/0.01	4.40/3.85	0.12/0.01	NOS 6	(8)
Zhang *et al*, 2024	35	3.85/3.15	0.02/0.05	3.75/3.10	0.02/0.05	NOS 7	(9)
Zhang *et al*, 2022	36	3.83/3.14	0.79/0.70	3.77/3.10	0.90/0.80	NOS 7	(10)
Borsboom *et al*, 1999	404	4.30/3.29	0.10/0.01	4.10/3.20	0.10/0.01	NOS 6	(11)
Goyal *et al*, 2019	130	-/3.20	-/1.00	-/3.00	-/0.90	NOS 8	(14)

FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; SD, standard deviation; NOS, Newcastle-Ottawa Scale.

Table II. Basic characteristics of the included studies with a population or sub-population of patients with chronic obstructive pulmonary disease.

First author, year	Population, n	Morning mean value (FVC/FEV_1), l	Morning SD value	Night mean value (FVC/FEV_1), l	Night SD value	Quality assessment	(Refs.)
Fregonezi *et al*, 2012	7	2.50/1.24	1.00/0.62	1.99/0.96	1.00/0.50	NOS 8	(1)
Teramoto *et al*, 1999	30	1.90/1.34	0.60/0.30	1.60/1.10	0.30/0.05	CASP RCT high quality	(8)
Martin *et al*, 1992	14	2.66/1.18	0.21/0.13	2.31/1.21	0.19/0.14	CASP RCT high quality	(12)
Calverley *et al*, 2003	121	2.12/1.11	0.04/0.03	2.07/1.06	0.04/0.03	CASP RCT high quality	(13)

FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; SD, standard deviation; NOS, Newcastle-Ottawa Scale; CASP RCT, Critical Appraisal Skills Program for randomized controlled trials.

For RCTs, the Critical Appraisal Skills Program (CASP) checklist was applied (19), which systematically assesses key methodological aspects. The checklist examines whether the randomization process was adequately generated and concealed to prevent selection bias. It evaluates the extent to which blinding was implemented for participants, investigators and outcome assessors. The comparability of groups at baseline is assessed to ensure balanced characteristics between intervention and control groups. Follow-up duration and completeness are reviewed to determine whether attrition was accounted for appropriately. The checklist also considers whether outcomes were clearly defined, measured using valid methods and analyzed appropriately. Finally, the checklist assesses the applicability of results to the target population and the feasibility of the intervention in clinical practice.

The overall quality score of each study, based on the aforementioned assessment tools, is presented in Tables I and II. Based on the Newcastle-Ottawa Scale, the observational studies were rated as moderate-to-high quality (scores ranging from 6 to 8). The RCTs were evaluated using the CASP checklist and were rated as high quality.

Population, Intervention, Comparison and Outcome (PICO) framework. The present study followed the PICO framework (20) to structure the research question. The population includes healthy individuals and patients diagnosed with COPD according to the GOLD criteria. The intervention

involves measuring FVC and FEV_1 at two different time points, in the morning and at nighttime. The comparators include both healthy individuals and patients with COPD, allowing for intra-group and inter-group comparisons. The outcome focuses on identifying potential differences in the measured spirometric parameters between the different time points and populations.

Statistical analysis. Meta-analysis was conducted using the Meta-Mar platform (version 2.1; https://www.meta-mar.com). Mean diurnal differences in FVC and FEV_1 levels were measured in both groups (healthy individuals and patients with COPD) using the random-effects model. A heterogeneity assessment was also conducted using the I^2 statistics to quantify any possible total variation due to heterogeneity. I^2 values were interpreted as follows: 0-25% (low heterogeneity), 26-50% (moderate heterogeneity), 51-75% (substantial heterogeneity) and >75% (considerable heterogeneity). Lastly, the interpretation of the results included not only the mean differences of the aforementioned spirometric values in the two groups but also the possible clinical significance of the observed differences. Publication bias was assessed using Egger's test for funnel plot asymmetry. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Overview of the included studies. The present meta-analysis synthesized data from eight different studies (1,8-14) that measured the diurnal variation of FVC and/or FEV_1 using healthy individuals or patients with COPD as the target population. Subgroup analyses comparing the FVC and FEV_1 spirometric measurements between healthy adults and patients with COPD were conducted. Healthy adults were defined as subgroup 1 and patients with COPD were defined as subgroup 2. In total, 595 for FVC (or 725 for FEV_1) healthy adults and 172 patients with COPD were analyzed.

Description of the included studies. The basic characteristics of the included studies with a population or sub-population of healthy individuals are presented in Table I, while those of patients with COPD are presented in Table II.

Among the studies examining healthy individuals, Teramoto *et al* (8) evaluated diurnal variation in both healthy elderly subjects and patients with respiratory conditions including COPD, performing spirometric measurements at multiple time points across the day. Their findings demonstrated that diurnal fluctuations in FVC and FEV_1 were more pronounced in healthy subjects. Zhang *et al* (10) and Zhang *et al* (9) conducted studies using electronic portable spirometers for home-based, multi-day monitoring in healthy non-smoking adults. Both studies reported consistent circadian patterns, with peak spirometric values observed in the morning and progressive declines during the night. Borsboom *et al* (11) investigated diurnal lung function in two Dutch cohorts, emphasizing the impact of the time of measurement on longitudinal lung function analysis and supporting the concept of marked morning-to-evening variability in healthy individuals. Goyal *et al* (14) investigated the circadian variability of airway caliber in healthy young male adults by assessing spirometric indices, including FEV_1 and mid-expiratory flow rates, across seven time points from early morning (5:00 a.m.) to late evening (23:00 p.m.). Using Cosinor rhythm analysis, they demonstrated marked temporal variability in spirometric values, with peak values generally occurring during daytime and troughs at night. Although only 31% of subjects exhibited statistically significant circadian rhythms in FEV_1, variability patterns suggested marked inter-individual differences (chronophenotypes).

The COPD-related studies included that by Fregonezi *et al* (1), who measured both pulmonary function and respiratory muscle strength across time intervals in patients with stable COPD. The study found that diurnal variation existed in both FVC and respiratory muscle strength parameters (such as maximal inspiratory and expiratory pressures), although the magnitude of change was smaller compared with that in healthy individuals. Teramoto *et al* (8) also examined patients with COPD in the same dataset as aforementioned and confirmed the reduced amplitude of spirometric fluctuations in these patients. Martin and Pak (12) observed slight improvements in nighttime FEV_1 and symptom scores in patients receiving overnight theophylline, possibly reflecting a pharmacological effect compared with baseline morning values. Lastly, Calverley *et al* (13) found that tiotropium bromide improved overall airflow in patients with COPD; however, it did not significantly alter the diurnal variation in FVC or FEV_1, suggesting that bronchodilator therapy alone may not restore normal circadian lung function patterns.

Forest plots. In Fig. 2, the mean differences in diurnal FVC between healthy individuals and patients with COPD were synthesized and analyzed using a random-effects model. The goal was to compare the observed mean differences between the two subgroups.

Several studies, including those by Teramoto *et al* (8), Zhang *et al* (9), Zhang *et al* (10) and Borsboom *et al* (11), reported higher FVC values in healthy adults during the morning compared with those at nighttime. In subgroup 1 (healthy individuals), a statistically significant mean difference in diurnal FVC (morning FVC-nighttime FVC) of 1.92 (CI, -1.45, 5.30; $P<0.01$) was observed. However, the CI was relatively large, including zero. Although the P-value indicated statistical significance ($P<0.01$), the wide confidence interval includes zero, suggesting uncertainty about the direction or magnitude of the effect. Therefore, the result should be interpreted with caution. The heterogeneity, assessed using the I^2 statistic, was 58%, indicating substantial variability among the studies. Sources of heterogeneity included differences in study location (for example, Japan, Netherlands and Brazil), participant characteristics (for example, the mean age ranged from 19 to 70 years and there were male-only vs. mixed-gender cohorts), timing of spirometric measurements (certain studies used two while others used seven time points) and types of devices (such as portable electronic spirometers vs. standard clinical spirometers).

In subgroup 2 (patients with COPD), Fregonezi *et al* (1), Teramoto *et al* (8) and Martin and Pak (12) reported higher morning FVC values compared with those at nighttime. By contrast, Calverley *et al* (13) observed the opposite effect, with lower FVC values in the morning than at night. Although the

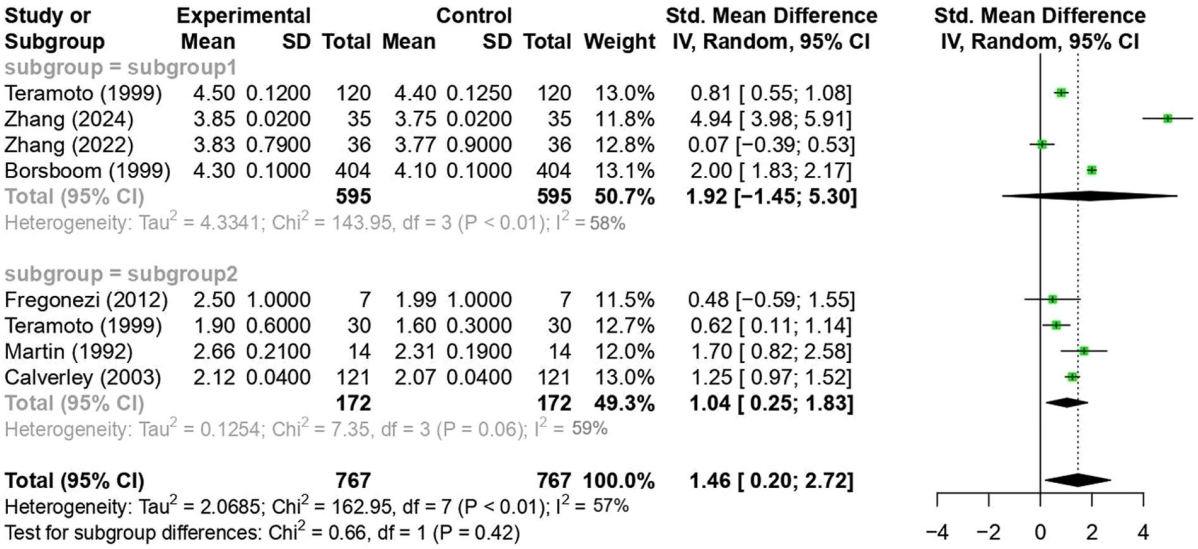

Figure 2. Forest plot of diurnal variations in forced vital capacity among healthy individuals and patients with chronic obstructive pulmonary disease. CI, confidence interval; Std., standard deviation; IV, inverse variance; df, degrees of freedom.

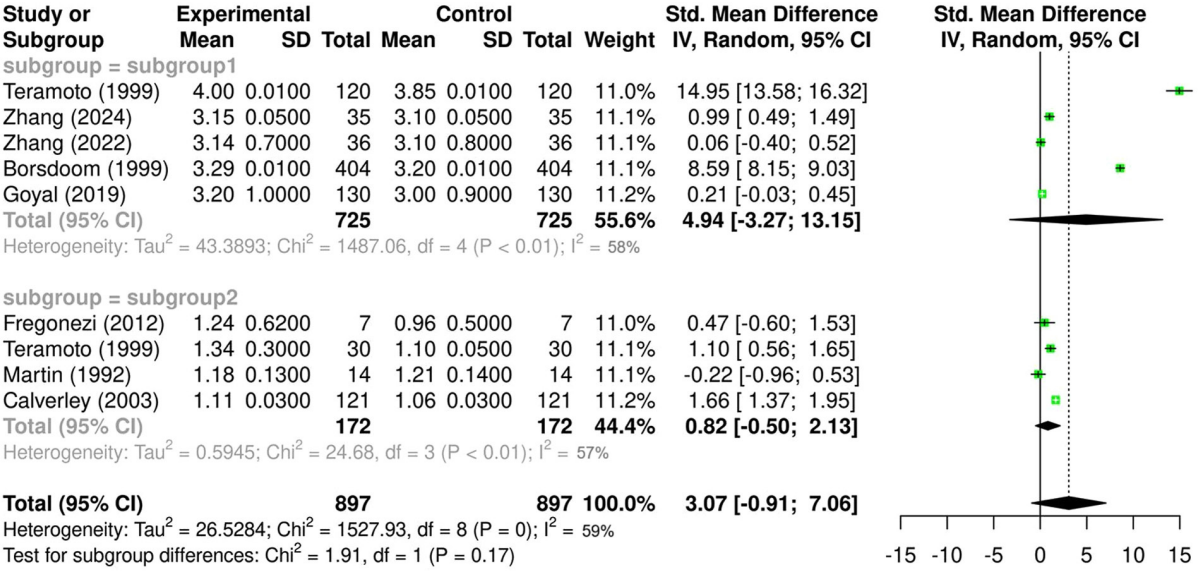

Figure 3. Forest plot of diurnal variations in forced expiratory volume in 1 sec among healthy individuals and patients with chronic obstructive pulmonary disease. CI, confidence interval; Std., standard deviation; IV, inverse variance; df, degrees of freedom.

study by Calverley *et al* (13) reported nighttime FVC values slightly higher than morning values, the overall effect size direction in the forest plot aligns due to standardized mean differences, which adjust for variation across studies. The overall mean difference in subgroup 2 was 1.04 (CI, 0.25, 1.83; P=0.06) with a large CI value excluding zero, which was not statistically significant but approached the threshold of 0.05. In subgroup 2 (patients with COPD), heterogeneity was 59%, indicating substantial variability. This could reflect differences in disease severity, bronchodilator use and measurement timing protocols among the studies.

Comparing the mean differences between the two subgroups, a difference of 1.46 (CI, 0.20, 2.72; P<0.01) was observed, indicating a statistically significant difference in diurnal FVC variation between healthy individuals and patients with COPD. This suggests that the diurnal variation in FVC among healthy individuals was 1.46 times greater than that observed in the COPD group. The overall heterogeneity was 57%, again indicating substantial variability.

In Fig. 3, the mean differences in diurnal FEV_1 in healthy individuals and patients with COPD were synthesized and analyzed, and the observed mean differences between the two subgroups were compared using the random-effects model.

While the analysis of diurnal FVC differences in Fig. 2 included a total of 595 healthy individuals (from four studies), the analysis of diurnal FEV_1 differences in Fig. 3 included 725 healthy individuals due to the inclusion of an additional eligible study (14), bringing the total to five studies in subgroup 1.

In subgroup 1, all included studies reported higher FEV_1 values in the morning than at night, in line with the

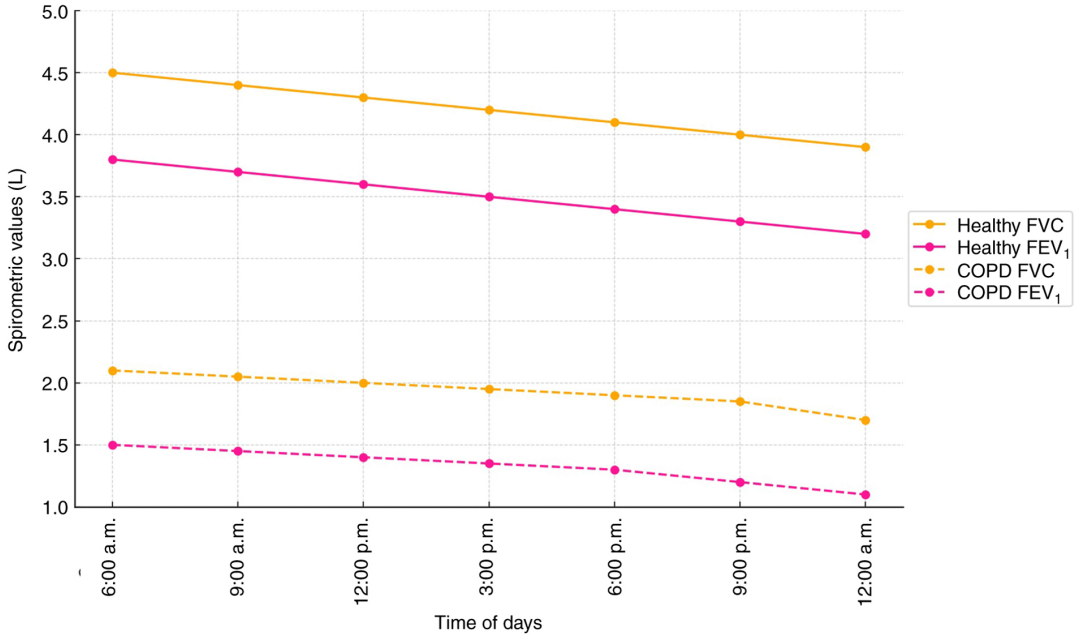

Figure 4. Diurnal variation of FVC and FEV_1 in healthy individuals and patients with COPD. FVC and FEV_1 values (in liters) were plotted from early morning (6:00 a.m.) to midnight (12:00 a.m.). Solid lines represent healthy individuals, while dashed lines represent patients with COPD (orange for FVC, pink for FEV_1). The mean values were derived from pooled data across the included studies to illustrate typical diurnal spirometric trends in both populations. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; COPD, chronic obstructive pulmonary disease.

aforementioned FVC measurements. The overall mean difference in this subgroup was 4.94 (CI, -3.27, 13.15; P<0.01), with a large CI that included zero, but demonstrated statistical significance. Despite reaching statistical significance, the wide confidence intervals that included zero suggest variability in the data and reduce confidence in the precision of the effect estimate. This result suggests that the mean difference in diurnal FEV_1 values in subgroup 1 was 4.94 times higher in the morning compared with that at nighttime. The heterogeneity was 58%, indicating a relatively high variability in the included studies, which can be attributed to the aforementioned factors.

Regarding subgroup 2, all included studies reported higher morning FEV_1 values except for the study by Martin and Pak (12). Nevertheless, the overall mean difference was 0.82 (CI, -0.5, 2.13; P<0.01), with a large CI that included zero, and demonstrated statistical significance. Based on this, it can be inferred that the mean FEV_1 in the morning in patients with COPD was 0.82 times higher than that at night.

The comparison of the mean differences between the two subgroups yielded a value of 3.07 (CI, -0.91, 7.06; P=0.17), indicating that the mean diurnal FEV_1 difference in subgroup 1 was 3.07 times greater than that in subgroup 2, although this result was not statistically significant. The overall heterogeneity was 59%, which can be attributed to the aforementioned factors.

Finally, Egger's test yielded a regression coefficient of -1.7 (P=0.17), indicating no statistically significant evidence of publication bias. A slight asymmetry in the funnel plot was observed (data not shown), possibly indicating underrepresentation of smaller studies (for example, those with sample sizes <30) that reported null or non-significant results. Fig. 4 graphically illustrates the pooled diurnal trends in FVC and FEV_1 values across time points from 6:00 a.m. to 12:00 a.m. Healthy individuals show a steeper decline in values over the day, while patients with COPD exhibit flatter curves, reflecting blunted diurnal variation. The steeper slope in the healthy group suggests greater diurnal variation, whereas the relatively flat trend in the COPD group indicates blunted respiratory fluctuations, likely due to airway inflammation, autonomic dysregulation and reduced lung compliance.

Discussion

The present study aimed to synthesize and critically assess the existing literature on diurnal variations in FVC and FEV_1 measurements in healthy adults and patients with COPD, with the goal of drawing conclusions that could be useful in daily clinical practice and guide therapeutic decisions and strategies.

The present findings indicated a statistically significant difference in mean diurnal FVC measurements in healthy adults, with morning values being 1.92 times higher than nighttime values. A similar trend was observed in patients with COPD, where morning FVC was 1.04 times higher than that at night; however, this result was not statistically significant. Additionally, the mean difference in diurnal FVC variations between healthy individuals and patients with COPD was 1.46 times higher in healthy adults, demonstrating statistical significance.

Similar results were observed for FEV_1. The mean FEV_1 values in healthy adults were 4.94 times higher in the morning than those at night. A similar pattern was noted in patients with COPD, although the difference was smaller (0.82 times). However, there was no statistically significant difference in the mean diurnal FEV_1 variations between healthy individuals and patients with COPD.

The results of the present meta-analysis indicate that mean diurnal differences in FVC and FEV_1 are significantly greater in healthy adults compared with individuals diagnosed with

COPD. This finding aligns with established knowledge on COPD pathophysiology, emphasizing the impaired lung function that characterizes the disease.

In healthy individuals, diurnal variations in FVC and FEV_1 are typically influenced by circadian rhythms, respiratory muscle activity and fluctuations in airway resistance (1,8,9,14,16). These fluctuations are generally mild and reflect the ability of the lungs to adapt to daily activities and environmental changes. By contrast, patients with COPD experience diminished pulmonary function due to structural airway changes and alveolar damage, which limit their ability to maintain optimal airflow and lung volumes throughout the day. In healthy adults, total airway resistance (Raw) typically ranges from 1.5-2.5 cmH_2O/l/sec, whereas in patients with moderate-to-severe COPD, Raw can exceed 5.0 cmH_2O/l/sec (1,14,16).

The reduced diurnal variability observed in patients with COPD may be attributed to several underlying mechanisms (2,3,6). Chronic airway inflammation and remodeling, along with the destruction of alveolar structures, contribute to fixed airflow limitations, notably affecting respiratory mechanics. As a result, diurnal fluctuations in FVC and FEV_1 are markedly diminished, reflecting a more static and compromised pulmonary function (21).

Patients with COPD often experience autonomic dysfunction, marked by increased sympathetic activity and reduced parasympathetic tone. Factors such as chronic hypoxemia, hypercapnia, systemic inflammation and the use of certain medications, such as long-acting β2-agonists (for example, salmeterol) and anticholinergics (for example, tiotropium) contribute to this imbalance. This dysregulation affects the airway smooth muscle tone and heart rate variability, leading to a blunted diurnal variation in respiratory function (22). Structural changes in the lungs, including emphysematous destruction and airway remodeling, lead to decreased lung compliance in patients with COPD. This rigidity also impairs the ability of the lungs to adapt to physiological changes throughout the day (23).

Cortisol, a glucocorticoid hormone regulated by the hypothalamic-pituitary-adrenal axis, exhibits a natural diurnal rhythm, peaking in the early morning and declining throughout the day. In patients with COPD, altered cortisol levels and adrenal gland sizes have been observed, which are closely associated with disease severity. Compared with healthy individuals, patients with COPD exhibit lower morning serum cortisol levels and smaller adrenal gland volumes, particularly in those with frequent exacerbations, reflecting impaired hypothalamic-pituitary-adrenal axis activity. These hormonal imbalances may contribute to the reduced diurnal variation in lung function observed in these patients (24,25).

The current findings have clinical relevance. The reduced diurnal variation in FVC and FEV_1 among patients with COPD may affect their ability to perform daily activities and could serve as an indicator of the disease exacerbation risk. Recognizing these patterns can help healthcare providers to develop personalized management strategies that account for lung function variability, potentially leading to improved patient outcomes through timely interventions.

Monitoring diurnal patterns in lung function may be particularly important for patients with COPD, who may benefit from personalized treatment regimens (7,16). For instance, pharmacotherapeutic strategies, such as bronchodilator administration, may need to be adjusted based on the time of day to optimize efficacy and symptom control. Additionally, lifestyle modifications, including smoking cessation and pulmonary rehabilitation, play a crucial role in enhancing lung function and increasing diurnal variability (2-4,15).

Emerging evidence has highlighted the potential of longitudinal home spirometry as a tool for daily monitoring in chronic lung diseases, including COPD and fibrotic interstitial lung disease. Notably, the feasibility and reliability of portable electronic spirometers, which allow patients to perform self-assessments in their home environments over extended periods, has been demonstrated. These devices have been used successfully to detect early declines in lung function, guide therapeutic adjustments, and assess treatment efficacy in real time (2). For example, Moor *et al* (2) used home spirometry to detect progressive FVC decline in patients with fibrotic interstitial lung disease, which prompted timely therapeutic adjustments, including corticosteroid tapering or initiation of antifibrotic therapy. Lung function decline was assessed via consistent downward trends in daily FVC values, confirmed by clinical reassessment. Similar approaches could be applied to COPD populations to identify early exacerbation risk. However, broader implementation requires addressing challenges such as patient adherence, data integration with electronic health records and standardization of measurement protocols. Incorporating such digital tools into clinical practice may revolutionize disease monitoring by providing continuous, patient-specific data, ultimately facilitating personalized and timely interventions.

The clinical importance of recognizing diurnal variations in spirometry extends beyond academic interest, as it has direct implications for COPD management. Awareness of daily lung function fluctuations could influence the optimal timing of diagnostic spirometry to avoid underestimating disease severity during nighttime or early morning periods when pulmonary function is at its lowest level. Moreover, time-specific tailoring of bronchodilator therapy could improve symptom control by synchronizing drug administration with periods of greatest airflow limitation. Personalized scheduling of rehabilitation exercises and daily activities may also reduce dyspnea episodes and improve the quality of life. Importantly, longitudinal home spirometry monitoring could detect early signs of exacerbations by identifying deviations from the typical diurnal pattern of the patient, allowing pre-emptive interventions. Integrating diurnal variation assessment into routine COPD care protocols could thus enhance disease control, reduce healthcare use, and promote precision medicine approaches in respiratory care.

The present study exhibited moderate-to-high heterogeneity (I^2=57-59%) due to differences in study design, population characteristics and measurement techniques, which may limit generalizability. The included studies exhibited substantial heterogeneity in design, population characteristics and spirometry measurement methods, leading to moderate-to-high variability (I^2=57-59%). These differences included variation in participant age (ranging from young adults to elderly populations), measurement timing (two vs. seven daily time points) and spirometry equipment (portable vs. clinical devices), which may have influenced the observed heterogeneity. The sample

size was relatively small [595 for FVC (or 725 for FEV_1) healthy individuals and 172 patients with COPD], potentially limiting the generalizability of the findings. Additionally, the marked disparity in sample sizes between healthy individuals and patients with COPD (595/725 vs. 172) may have introduced bias into the pooled estimates and reduced the comparative statistical power between groups. Moreover, the exclusion of individuals with overlapping syndromes, smokers and those exposed to occupational hazards restricts the applicability of the results to broader populations with COPD. Furthermore, the fact that the included patients with COPD were not stratified according to their disease severity could affect the validity of the observed results. Stratification is vital for external validity, as clinicians often rely on disease staging to guide treatment (21). By not accounting for disease severity, the present meta-analysis limits its applicability to real-world patient populations. Future research should prioritize stratified analyses based on standardized classifications, such as the GOLD criteria, to enhance the precision, interpretability and clinical utility of the findings in COPD research. Most included studies did not provide FVC and FEV_1 values stratified by COPD severity (GOLD stage I-IV), preventing subgroup meta-analysis based on disease stage. Environmental and lifestyle factors such as air pollution, temperature, medication adherence and physical activity were not consistently accounted for across studies, potentially affecting lung function variability. Lastly, although not statistically significant, the potential for publication bias suggests that studies with small sample sizes and non-significant findings may be underrepresented in the literature.

In conclusion, the present meta-analysis revealed that diurnal variations in FVC and FEV_1 were greater in healthy individuals than those in patients with COPD. This may be attributed to the airway inflammation, autonomic dysregulation and reduced lung compliance observed in patients with COPD. Altered cortisol rhythms may further contribute to blunted fluctuations. These findings underscore the need for optimized spirometry timing and tailored treatment strategies to improve COPD management. Future research should focus on personalized therapy adjustments and home-based lung function monitoring to enhance patient outcomes.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KD and VEG conceptualized the study. KD, DK, TVK, AM, NT, AC, VEG and DAS made a substantial contribution to data interpretation and analysis and wrote and prepared the draft of the manuscript. KD and VEG analyzed the data and performed critical revisions. KD and VEG confirm the authenticity of all the raw data. All authors contributed to manuscript revision and read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

DAS is the Editor-in-Chief for the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tool Chat GPT was used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tool as necessary, taking full responsibility for the ultimate content of the present manuscript.

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