A Multivariate Model for Predicting Respiratory Status in Patients with Chronic Obstructive Pulmonary Disease

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OBJECTIVE: To develop and validate a multivariate model for predicting respiratory status in patients with advanced chronic obstructive pulmonary disease (COPD).

DESIGN: Prospective, double-blind study of peak flow monitoring.

SETTING: Albuquerque Veterans Affairs Medical Center.

PATIENTS: Male veterans with an irreversible component of airflow obstruction on baseline pulmonary function tests.

MEASUREMENTS: This study was conducted between January 1995 and May 1996. At entry, subjects were instructed in the use of the modified Medical Research Council Dyspnea Scale and a mini-Wright peak flow meter equipped with electronic storage. For the next 6 months, they recorded their dyspnea scores once daily and peak expiratory flow rates twice daily, before and after the use of bronchodilators. Patients were blinded to their peak expiratory flow rates, and medical care was provided in the customary manner. Readings were aggregated into 7-day sampling intervals, and interval means were calculated for dyspnea score and peak expiratory flow rate parameters. Intervals from all subjects were then pooled and randomized to separate groups for model development (training set) and validation (test set). In the training set, logistic regression was used to identify variables that predicted future respiratory status. The dependent variable was the log odds that the subject would attain his highest level of dyspnea in the next 7 days. The final model was used to stratify the test set into "high-risk" and "low-risk" categories. The analysis was repeated for 3-day intervals.

MAIN RESULTS: Of the 40 patients considered eligible for study, 8 declined to participate, 4 could not master the technique of peak flow monitoring, and 6 had no fluctuations in their dyspnea level. The remaining 22 subjects form the basis of this report. Fourteen (64%) of the latter completed the 6-month protocol. Data from the 8 who were dropped or died were included up to the point of withdrawal. For 7-day forecasts, mean dyspnea score and mean daily prebronchodilator peak expiratory flow rate were identified as predictor variables. The adjusted odds ratio (OR) for mean dyspnea score was 2.71 (95% confidence interval [CI] 1.79, 4.12) per unit. For mean prebronchodilator peak expiratory flow rate, it was 1.05 (95% CI 1.01, 1.09) per percentage predicted. For 3-day forecasts, the model was composed of mean dyspnea score and mean daily bronchodilator response. The ORs for these

terms were 2.66 (95% CI 2.06, 3.44) per unit and 0.980 (95% CI 0.962, 0.998) per percentage of improvement over baseline, respectively. For a given level of dyspnea, higher prebronchodilator peak expiratory flow rate and lower bronchodilator response were poor prognostic findings. When the models were applied to the test sets, "high-risk" intervals were 4 times more likely to be followed by maximal symptoms than "low-risk" intervals.

CONCLUSIONS: Dyspnea scores and certain peak expiratory flow rate parameters are independent predictors of respiratory status in patients with COPD. However, our results suggest that monitoring is of little benefit except in patients with the most advanced form of this disease, and its contribution to their management is modest at best.

KEY WORDS: lung disease, obstructive; spirometry; peak expiratory flow rate (PEFR); ambulatory monitoring; self-care. J GEN INTERN MED 1998;13:462-468.

Home monitoring of peak expiratory flow rate (PEFR) has been recommended for the outpatient management of asthma.¹⁻⁴ Treatment programs based on these measurements have been shown to reduce symptoms,⁵ the number of attacks,⁶ days lost from work,^{5,6} medication requirements,⁵⁻⁷ airflow variability,^{8,9} the response to histamine challenge,⁸ and physician consultations and emergency department admissions.⁶ Despite these successes, the role of peak flow monitoring in management of chronic obstructive pulmonary disease (COPD) is unknown. Few studies have examined the significance of a falling PEFR or whether monitoring provides information that cannot be obtained by other means.

We performed a prospective, double-blind study of peak flow monitoring in patients with advanced COPD. The purpose of this study was to develop and validate a multivariate model based on symptom scores and PEFR that would predict the patient's future respiratory status.

METHODS

Subjects

The Albuquerque Veterans Affairs (VA) Medical Center is a 400-bed, acute-care facility serving veterans in New Mexico and west Texas. Names of potential subjects were gathered from the logs of the emergency department and urgent care clinic, as well as pharmacy printouts of prescriptions for albuterol, records of patients on home oxygen, and appointments to the chest clinic. Patients

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were included in this study if they met standard criteria for the diagnosis of COPD¹⁰ and their pulmonary function tests showed an irreversible component of airflow obstruction. Airflow obstruction was considered to have an irreversible component if the forced expiratory volume in 1 second (FEV₁) was less than 70% predicted and the ratio of FEV₁ to vital capacity (VC) was less than 70%, before and after bronchodilators. Patients were excluded from the study if:

1. the onset of symptoms was before the age of 40;
2. they had nasal polyposis, aspirin sensitivity, or multiple allergies;
3. they did not have the physical or mental capacity to measure PEFR at home;
4. they had other medical problems for which dyspnea was a common complaint;
5. they were immunosuppressed or taking immunosuppressive drugs other than corticosteroids; or
6. they had alternative sources of medical care.

Equipment

Peak flow rates were measured on a hand-held, mini-Wright device with electronic storage (VMX Mini-Log, Clement Clark, Columbus, Ohio). The displays were disabled so that patients and their physicians were blinded to all values.

Study Protocol

Prospective subjects entered a run-in period to ensure that they were clinically stable. They were followed until: (1) there were no episodes of respiratory distress requiring an emergency department visit or hospital admission; (2) there was no adjustment of maintenance medications or institution of new bronchodilator treatment; and (3) there were no intercurrent illnesses requiring antibiotic therapy for at least 2 weeks. At the conclusion of this period, a history was taken and they were given a physical examination and underwent formal pulmonary function testing. Spirometry was performed on a Jaeger pneumoscope (Jaeger, Wuerzburg, Germany). Equipment and procedures in our laboratory conform to standards set by the American Thoracic Society.¹¹ All subjects were trained in the use of the peak flow meter and the modified Medical Research Council dyspnea scale.¹² This scale is a 5-point rating system based on physical activities that precipitate breathlessness. Scores range from 0 to 4. Instruction continued until subjects could generate reproducible measurements under the supervision of a research technician. Subjective criteria were used to determine the end of the run-in phase. For the next 6 months, patients recorded PEFR at 8:00 AM and 4:00 PM daily, before and after bronchodilators. Dyspnea scores were recorded at 4:00 PM daily.

The bronchodilator was albuterol or metaproterenol administered by metered dose inhaler with a spacer. Post-bronchodilator PEFR was measured 20 minutes after the second of two doses but before the administration of other inhaled medications.

Subjects were appointed to the research technician at monthly intervals. At these visits, dyspnea logs were collected and peak flow readings were downloaded into a microcomputer. During the monitoring period, patients were followed by their own physicians, and medical care was provided in the customary manner. At no time did the investigators provide care or advice to any patient. This study protocol was approved by the institutional committee on human research. Informed consent was obtained from all subjects.

Calculated Parameters

We converted FEV₁ and VC to percentage predicted according to the methods of Crapo et al.¹³ We converted PEFR to percentage predicted by dividing observed values by predicted values. Predicted PEFR was obtained from the following expression¹⁴:

$$\log_e(\text{PEFR}) = 0.544 \log_e(\text{Age}) - 0.0151(\text{Age}) - 74.7/\text{Height} + 5.48,$$

where PEFR is expressed in liters per minute, age in years, and height in centimeters.

Bronchodilator response was expressed in two ways. The percentage increase over the pretreatment value (%CHANGE) was given by the expression:

$$\frac{100 \times \left(\frac{\text{Postbronchodilator measurement} - \text{Prebronchodilator measurement}}{\text{Prebronchodilator measurement}} \right)}{\text{Prebronchodilator measurement}}$$

The percentage of the expiratory defect corrected by bronchodilators¹⁵ (%CORRECTED) was derived from the expression:

$$\frac{100 \times \left(\frac{\text{Postbronchodilator measurement} - \text{Prebronchodilator measurement}}{\text{Prebronchodilator measurement}} \right)}{(\text{Predicted value} - \text{Prebronchodilator measurement})}$$

Daily variability of PEFR was expressed as the amplitude-to-mean ratio, the ratio of the amplitude to the highest value, and the ratio of the amplitude to the predicted PEFR.¹⁶ Amplitude refers to the absolute difference between the morning PEFR and evening PEFR. Variability was derived separately for prebronchodilator and post-bronchodilator measurements. Compliance was defined as the ratio of readings obtained to the number specified by the protocol, exclusive of those missed owing to circumstances beyond the patient's control.

Analytical Methods

Dyspnea scores were reviewed for all subjects, and a patient maximum for the monitoring period was deter-

mined. Study days were then aggregated into 7-day sampling intervals, and weekly mean values were calculated for dyspnea score and all PEFr parameters. Intervals missing more than 2 days of readings were excluded from analysis. Data from all subjects were pooled, and a microcomputer random number generator was used to separate the intervals into two groups. The *training set* was used to derive the model, while the *test set* was used to validate the model.¹⁷

To identify predictors of future respiratory status, stepwise logistic regression was used on the training set (Stepwise logistic regression. In: Dixon WJ, ed. BMDP Statistical Software Manual, vol 2, 1992: 1105–44).¹⁸ The dependent variable was the log odds that the subject would attain his highest level of dyspnea in the next 7 days. The independent variables were mean values for dyspnea score and PEFr parameters from the current week. The candidate variables are defined in Table 1. Correlational analysis was used to screen for multicollinearity. Independent variables were incorporated in a stepwise fashion with an α of 0.10 to enter and 0.10 to remove. Step selections were based on the maximum likelihood method. The degree of improvement at each step was tested by improvement χ^2 analysis. The goodness-of-fit for the final model was evaluated by the Hosmer-Lemeshow Test.¹⁹

The logistic model was used to calculate the probability that the patient would reach his maximum level of

dyspnea within 7 days of each test interval. The test intervals were then categorized as either “low-risk” or “high-risk,” depending on whether the calculated probability exceeded a critical value. This value was chosen so that the model had a sensitivity of 80% in the training set. Differences in outcomes for the low-risk and high-risk intervals were tested by χ^2 analysis.

To improve the forecast, the analysis was repeated with study days grouped into 3-day intervals. The independent variables were 3-day mean values for dyspnea score and all PEFr parameters. The dependent variable was the log odds that the patient would reach his maximal level of dyspnea in the succeeding 3 days. This analysis was performed on intervals containing 2 or more days of readings.

All continuous variables are expressed as mean $\pm$ SD; *p* values $< .05$ were considered significant. Statistical analysis was performed on a microcomputer equipped with two commercial software packages (Systat and BMDP).

RESULTS

Seventy potential subjects were found by searching hospital databases. Of the 40 patients considered eligible for study, 8 declined to participate, and another 4 could not generate reproducible results during the run-in phase. Six other subjects were excluded from analysis because there was no fluctuation in their level of dyspnea during the study. This report is based on the remaining 22 male subjects. The mean age of this group was 65.6 ± 7.0 years. Eighty-two percent were white, and 18% were of Hispanic origin. All subjects were either current smokers ($n = 3$) or former smokers ($n = 19$). Cigarette consumption was heavy (mean number of pack-years = 74.0 ± 48.6). The average age at the onset of respiratory symptoms was 54.9 ± 8.3 years, and at the time of entry, symptoms were incapacitating. Physical activity was limited to 2.4 ± 3.3 blocks of level ambulation and 0.5 ± 0.9 flights of stairs. Seventy-three percent were on home oxygen, while 32% were on maintenance prednisone. Table 2 shows the FEV₁, VC, and PEFr values for the 22 subjects at entry.

Mean follow-up was 144 ± 49 days. Of the 22 subjects, 14 (64%) completed the 6-month protocol. Eight

Table 1. Candidate Variables for Stepwise Logistic Regression*

DYSPNEA: Interval mean dyspnea score [†]
AMPRE: Interval mean for 8:00 AM prebronchodilator PEFr
AMPOST: Interval mean for 8:00 AM postbronchodilator PEFr
PMPRE: Interval mean for 4:00 PM prebronchodilator PEFr
PMPOST: Interval mean for 4:00 PM postbronchodilator PEFr
MEANPRE: Interval mean for the daily average prebronchodilator PEFr
MEANPOST: Interval mean for the daily average postbronchodilator PEFr
MEAN%CHANGE: Interval mean for the daily average % CHANGE
MEAN%CORRECTED: Interval mean for the daily average % CORRECTED
AMP/MEAN (PRE): Interval mean for the prebronchodilator amplitude/mean ratio
AMP/HIGH (PRE): Interval mean for the prebronchodilator amplitude/daily maximum ratio
AMP/PRED (PRE): Interval mean for the prebronchodilator amplitude/predicted PEFr ratio
AMP/MEAN (POST): Interval mean for the postbronchodilator amplitude/mean ratio
AMP/HIGH (POST): Interval mean for the postbronchodilator amplitude/daily maximum ratio
AMP/PRED (POST): Interval mean for the postbronchodilator amplitude/predicted PEFr ratio

*All expiratory flow rates are expressed as percentage predicted.

[†]The term “interval” refers to either the 7-day or 3-day sampling interval.

Table 2. Baseline Spirometry for 22 Subjects with Advanced Chronic Obstructive Pulmonary Disease

Spirometric Measure	Before Bronchodilators	After Bronchodilators
FEV ₁ , L	1.02 ± 0.46	1.10 ± 0.50
FEV ₁ , % predicted	33.8 ± 14.3	36.3 ± 15.8
VC, L	2.78 ± 0.88	2.96 ± 0.91
VC, % predicted	61.0 ± 19.0	65.2 ± 19.9
FEV ₁ /VC ratio, %	37.1 ± 12.5	37.2 ± 12.5
PEFr, L/min	197 ± 82	216 ± 75
PEFr, % predicted	34.6 ± 14.2	38.0 ± 12.9

were dropped because of noncompliance (3 subjects), personal reasons (1 subject), or death (4 subjects). Data from the latter subjects were included up to the point of withdrawal. Most patients found monitoring to be simple and convenient. Although the patients were clinically unstable, compliance was surprisingly high ($87.5\% \pm 16.2\%$).

The group average for the lowest dyspnea score was 1.24 ± 0.83 (on a scale from 0 to 4). The average for the highest score was 3.33 ± 1.02 . Thirteen subjects reached a level of 4 at least once during the monitoring period. The majority of subjects had respiratory distress at rest when they were at their worst. Eleven (50%) developed respiratory decompensation that required treatment in the emergency department.

Seven-Day Forecasts

Monitoring was done for a total of 451 weeks. Of the 404 sampling intervals suitable for analysis, 192 were randomized to a training set for model development. The remaining 212 were used for model validation. In the training set, mean dyspnea scores were not highly correlated with peak flow rates, daily variability, or bronchodilator response. Table 3 shows a correlation matrix for some of the major variables considered for the model. In 40% of the training set, subjects reached their maximal level of dyspnea within 7 days. Stepwise logistic regression showed that mean dyspnea score was a major determinant of this outcome. Several parameters met criteria for inclusion as the next variable in the model. The strongest predictors (MEANPRE and MEAN%CHANGE) were equivalent in terms of the improvement χ^2 ($p < .001$) and the ratio of coefficient to standard error (2.7). High values for MEANPRE and low values for bronchodilator response were poor prognostic findings. Because MEANPRE required fewer measurements, the model composed of dyspnea score and MEANPRE was selected as the final model (Appendix A). The adjusted odds ratio for the mean dyspnea score was 2.71 (95% confidence interval [CI] 1.79, 4.12) per unit. For MEANPRE, it was 1.05 (95% CI 1.01, 1.09) per percentage predicted. Once entered, no other terms resulted in significant improvement in the model.

When the specified model was fitted to the test set, mean dyspnea score and MEANPRE were again identified as significant predictors. Both the direction and magni-

tude of the effect for these predictors were comparable to those obtained in the training set. The model was also used to stratify test cases into low-risk and high-risk subsets. A patient was much more likely to experience his worst dyspnea after high-risk intervals than after low-risk intervals (68.4% vs 16.3%; $p < .001$). The sensitivity and specificity of this model were 81% and 72%, respectively.

Three-Day Forecasts

We attempted to improve the preceding model by shortening the time interval to 3 days. Of 1,052 sampling intervals, 923 were suitable for analysis. We randomized 431 to the training set, while 492 were assigned to the test set. In the training set, correlational analysis produced essentially the same results as for the 7-day forecasts. In 28% of this set, maximum symptoms occurred within 3 days. Stepwise logistic regression showed that the 3-day mean dyspnea score and MEAN%CHANGE were predictive of this event (Appendix A). Both terms resulted in an improvement in the model ($p \leq .02$), and the two-variable model provided a good description of the data (Hosmer-Lemeshow $p = .767$). The adjusted odds ratios for mean dyspnea score and mean bronchodilator response were 2.66 (95% CI 2.06, 3.44) per unit and 0.980 (95% CI 0.962, 0.998) per percentage of improvement over baseline, respectively. This model was again used to assign the test intervals to low-risk and high-risk categories. The patient was much more likely to reach his highest level of dyspnea after high-risk intervals than after low-risk intervals (58.3% vs 15.1%; $p < .001$). The sensitivity of this model was 81%, while the specificity was 65%.

DISCUSSION

Peak flow monitoring is used to follow respiratory function in asthmatic patients.¹⁻⁴ When combined with individualized treatment plans, monitoring has been shown to improve symptoms, decrease resource consumption, and favorably affect the physiologic processes implicated in asthmatic attacks.⁵⁻⁹ We conducted a prospective, double-blind study to determine if PEFR monitoring could be of similar value in patients with advanced COPD. Stepwise logistic regression showed that higher symptom scores, higher MEANPRE, and lower bronchodilator re-

Table 3. Correlation Matrix for Selected Variables in the 7-Day Training Set

Variables	DYSPNEA	MEANPRE	MEANPOST	MEAN%CHANGE	MEAN%CORRECTED	AMP/MEAN (PRE)
DYSPNEA	1.0					
MEANPRE	-0.22	1.0				
MEANPOST	-0.24	0.96	1.0			
MEAN%CHANGE	0.02	-0.25	-0.05	1.0		
MEAN%CORRECTED	-0.13	0.27	0.48	0.59	1.0	
AMP/MEAN (PRE)	-0.06	-0.10	-0.10	0.22	-0.12	1.0
AMP/MEAN (POST)	0.19	-0.27	-0.27	0.25	-0.10	0.53

sponse were poor prognostic findings. When used to stratify independent samples, time intervals categorized as high risk were 4 times more likely to be followed by maximum dyspnea than those categorized as low-risk. Thus, dyspnea and certain peak flow parameters are independent determinants of future clinical status. No benefit was obtained when the forecasting interval was reduced from 7 to 3 days because the two strategies produced the same relative risk for high-risk patients.

Most of the predictive value of our models could be attributed to the mean dyspnea score. The contribution of peak flow measurements was modest. For example, for 7-day forecasts, the odds ratio associated with an increase in MEANPRE of 10% predicted is 1.6. For 3-day forecasts, an increase in bronchodilator response of 10% of baseline is associated with a ratio of 0.82. It is unclear if these changes are large enough to justify the use of monitoring in routine practice.

Our results were of interest, not because monitoring was validated for clinical use, but because it provided insight into the pathogenesis of respiratory decompensation. Changes in airway function could be demonstrated several days before the development of respiratory symptoms. This finding suggests that COPD exacerbation is a rather indolent process. We feel that the roles of bronchospasm, inflammation, or other mechanisms in the pathogenesis of decompensation should be reexamined in the light of this observation.

At first, it seems unreasonable to use a model that identifies high MEANPRE as a poor prognostic sign. However, it should be recalled that MEANPRE is an *adjusted* risk factor. That is, for a given level of dyspnea, higher PEFR is associated with an increased risk of decompensation. There are several possible explanations for this observation. One is that dyspneic patients with higher PEFR have greater sensitivity to airflow obstruction and are less tolerant of further deterioration. Another is that these patients have a process superimposed on airflow obstruction that has a poor prognosis, such as an increased ventilatory demand, gas exchange abnormalities, diminished lung compliance, or respiratory muscle fatigue. A third explanation is that high MEANPRE is a marker for excessive bronchodilator use. In this case, all readings might be considered "postbronchodilator," and little improvement would be expected from an intensified regimen. Our study was not designed to examine these hypotheses.

We considered three outcome variables for our prediction rule: peak expiratory flow rates, emergency department visits, and symptom scores. We chose the occurrence of the patient's maximal dyspnea score. For instance, if the highest score was a 3 in the 6-month follow-up period, we derived models to predict when these 3 scores would occur. There were several advantages to this approach. The number of end points was large because all of our patients reached a level that they considered their worst. This end point was also not affected by changes in the manner in which health care was delivered to our pa-

tients. While this study was in progress, an increasing number of patients were instructed in self-care, more advice was delivered by telephone, and more treatment was given in the primary care setting. We thought that these practice innovations would affect outcomes based on types of services used (such as emergency department visits) but have minimal effect on symptom-based end points. Finally, it is reasonable to assume that severe dyspnea adversely affects the patient's quality of life. The same is not true for asymptomatic declines in PEFR, which occur because COPD patients have blunted perceptions of respiratory loads.²⁰⁻²³ Forecasting was done over an interval of 3 to 7 days because this time frame provides an opportunity for abortive medications to take effect.

A model predicting a patient's worst status is the most versatile one because treatment can be tailored to the individual's needs. Some patients may not need an early intervention if their respiratory decompensation tends to be mild. Others require aggressive treatment at the first sign of deterioration because they have had life-threatening episodes. We considered a model that predicted the occurrence of an absolute level of dyspnea, such as a score of 4. We abandoned this approach because there was no consistent relation between dyspnea score and the need for treatment from patient to patient. Some of our subjects tolerated a score level of 4 without complaint, while others sought emergency treatment at much lower levels. The absence of a critical value suggests that there are other factors affecting the patient's perception that he needs medical care. These factors include his self-care skills, his psychological status, his access to services, and his tolerance of dyspnea.

Prediction models for relapse and the need for hospitalization after emergency department treatment of acute asthma have incorporated PEFR.^{24,25} Klaustermeyer et al. also showed that PEFR was helpful for predicting response to therapy in hospitalized adult asthmatics.²⁶ Taplin and Creer used PEFR in a probability equation to predict the occurrence of asthma in two children.²⁷ Determinations were based on two values: the base rate and the critical PEFR that most increased the predictability of the adverse event. The risk of an attack increased 3-fold over the base rate when the critical value was surpassed.

The most detailed study of a prediction model for asthma attacks in children was done by Harm et al.²⁸ These authors studied 25 children aged 6 to 16 years who monitored PEFR at 12-hour intervals and recorded symptoms in diaries over a 4-month period. The authors used Bayesian analysis to determine the posterior probability of an acute attack based on PEFR values in the preceding 12 hours. Two values were reported, the PEFR at which the posterior probability reached its highest value and the PEFR at which the change in prior to posterior probability was statistically significant. Although large increases in the probability of an attack were documented at critical levels of PEFR, the posterior probabilities did not exceed 40%.

Pinzone et al. developed individual logistic regression

models for asthma episodes in 10 children.²⁹ PEFR was incorporated into the model for 9 of the 10 subjects. Other important determinants were exercise and whether preceding attacks had occurred within 12 and 24 hours.

Unfortunately, most of the studies on asthma do not meet the current methodologic standards for clinical prediction rules.¹⁷ These standards include measures to reduce bias, testing of the prediction rule in an independent sample, and a parsimonious model that is biologically plausible. Our study addressed many of these issues. The displays on our meters were disabled so that patients and their physicians were blinded to the readings. This aspect of the protocol was critical because it eliminated expectation bias.³⁰ This bias tends to occur when the patient becomes aware that his PEFR is deteriorating. Because of heightened vigilance and anxiety, he is more likely to overstate his symptoms than if he had been unaware of the readings. In our study, there was no possibility that peak flow readings had an effect on dyspnea ratings, influenced patients to seek medical care, or prompted physicians to follow patients more closely. Finally, our models were relatively simple and validated on independent samples.

The purpose of this study was to develop a prediction rule for repeated adverse events experienced by a relatively small group of patients. Moreover, the study focused on unstable patients with the most advanced COPD. Its scope was too narrow to allow validation of the rules on other patient groups, particularly those with milder forms of the disease. It is also unclear if the same level of compliance or quality of the data can be achieved with monitoring less intense than that used in this study. Finally, forecasting respiratory status requires symptom scoring, four daily PEFR measurements, and complex mathematical calculations. Peak flow monitoring cannot be recommended as a part of routine care unless its feasibility is established for a broader spectrum of patients treated in conventional settings.

In conclusion, peak flow monitoring provides information about the respiratory status of patients with COPD that is not apparent from their level of dyspnea. However, our study suggests that monitoring is of little benefit except for patients with the most advanced forms of COPD. Moreover, its contribution to their management is modest at best and may not justify the inconvenience to patients.

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APPENDIX A

Logistic Models

For 7-day forecasts, the probability p of developing maximal dyspnea is given by the expression:

$$p = \frac{e^{\Sigma}}{1 + e^{\Sigma}}$$

where $\Sigma = -3.59 + 0.998 * (\text{DYS-PNEA}) + 0.048 * (\text{MEANPRE})$. DYS-PNEA and MEANPRE are the weekly averages for daily dyspnea score and mean prebronchodilator PEFR (expressed as percentage predicted). In the validation set, calculated probabilities exceeding 0.420 were considered "high risk."

For 3-day forecasts, the probability p of developing maximal dyspnea is given by the expression:

$$p = \frac{e^{\Sigma}}{1 + e^{\Sigma}}$$

where $\Sigma = -2.43 + 0.979 * (\text{DYS-PNEA}) - 0.020 * (\text{MEAN}\% \text{CHANGE})$. DYS-PNEA and MEAN%CHANGE are the 3-day averages for the daily dyspnea score and mean bronchodilator response (expressed as percentage improvement over baseline). In the validation set, calculated probabilities exceeding 0.300 were considered "high-risk."

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