

**Burden of Chronic Obstructive
Pulmonary Disease (COPD)
Exacerbations and Implications
in Patients With COPD**

Objectives

- **Discuss the burden of COPD**
- **Review incidence and implications of COPD exacerbations**
- **Consider the current guidelines for COPD management**

COPD Is a Major Public Health Problem

- 16.3 million office visits each year due to COPD¹
- 672,000 hospitalizations each year for COPD²
 - 21% mortality rate at one year after being hospitalized for an exacerbation³
- COPD is currently the 4th-leading cause of death in the United States⁴
- On average, more people die every day from COPD than diabetes or breast cancer⁵
 - 341 per day from COPD
 - 198 per day from diabetes
 - 113 per day from breast cancer

1. National Institutes of Health, National Heart, Lung & Blood Institute. *Morbidity and Mortality: 2009 chart book on cardiovascular, lung and blood diseases*. www.nhlbi.nih.gov/resources/docs/cht-book.htm. Accessed June 2, 2010.
2. American Lung Association. *Trends in chronic bronchitis and emphysema: morbidity and mortality*. February 2010. www.lungusa.org. Accessed June 2, 2010.
3. McGhan R, et al. *Chest*. 2007;132:1748-1755.
4. Global Initiative for Chronic Obstructive Lung Disease. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease – Updated 2009*. www.goldcopd.org. Accessed June 2, 2010.
5. National Center for Health Statistics. *Deaths: Final data for 2006*. http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_14.pdf. Updated April 17, 2009. Accessed June 2, 2010.

The Majority of Healthcare Costs for Managing COPD Are Associated With Exacerbations

- Total costs for COPD were estimated to be \$49.9 billion in 2007¹
 - \$29.5 billion in direct costs
- 50%-75% of all COPD costs are for services associated with exacerbations²

1. American Lung Association. *Trends in chronic bronchitis and emphysema: morbidity and mortality*. February 2010. www.lungusa.org. Accessed June 2, 2010. www.nhlbi.nih.gov/resources/docs/cht-book.htm. Accessed April 1, 2010.

2. American Thoracic Society/European Respiratory Society. *Standards for the diagnosis and management of patients with COPD [Internet]*. Version 1.2. www.thoracic.org/go/copd. Accessed June 2, 2010.

What Is the Incidence of COPD Exacerbations?

Exacerbation Definition

- The definition of a COPD exacerbation is an acute change in a patient's baseline dyspnea, cough, and/or sputum beyond day-to-day variability sufficient to warrant a change in therapy

Evaluation of Incidence of Symptom- and Healthcare-Defined Exacerbations

Objective:

- To investigate the incidence of COPD exacerbations in primary care

Study Design:

- Prospective, 12-month observational study in primary care setting with patients who have a diagnosis of COPD
- Patients recorded information on symptoms, quality of life and use of healthcare services in daily diaries:
 - Symptom-defined exacerbations: Patients recorded an increase in major and minor symptoms. Exacerbation defined as a symptom score of at least 2 for 2 consecutive days, with no score for at least 2 of these symptoms in the preceding 5 days
 - Healthcare-defined exacerbations: Defined as the need to take antibiotics and/or oral corticosteroids (OCS) for chest problems
- Overall, 201 patients completed at least 1 diary card during the study and 127 completed diary cards covering $\geq 80\%$ of the year
- Mean baseline FEV₁ was 50% of predicted

Majority of COPD Patients Experience Exacerbations

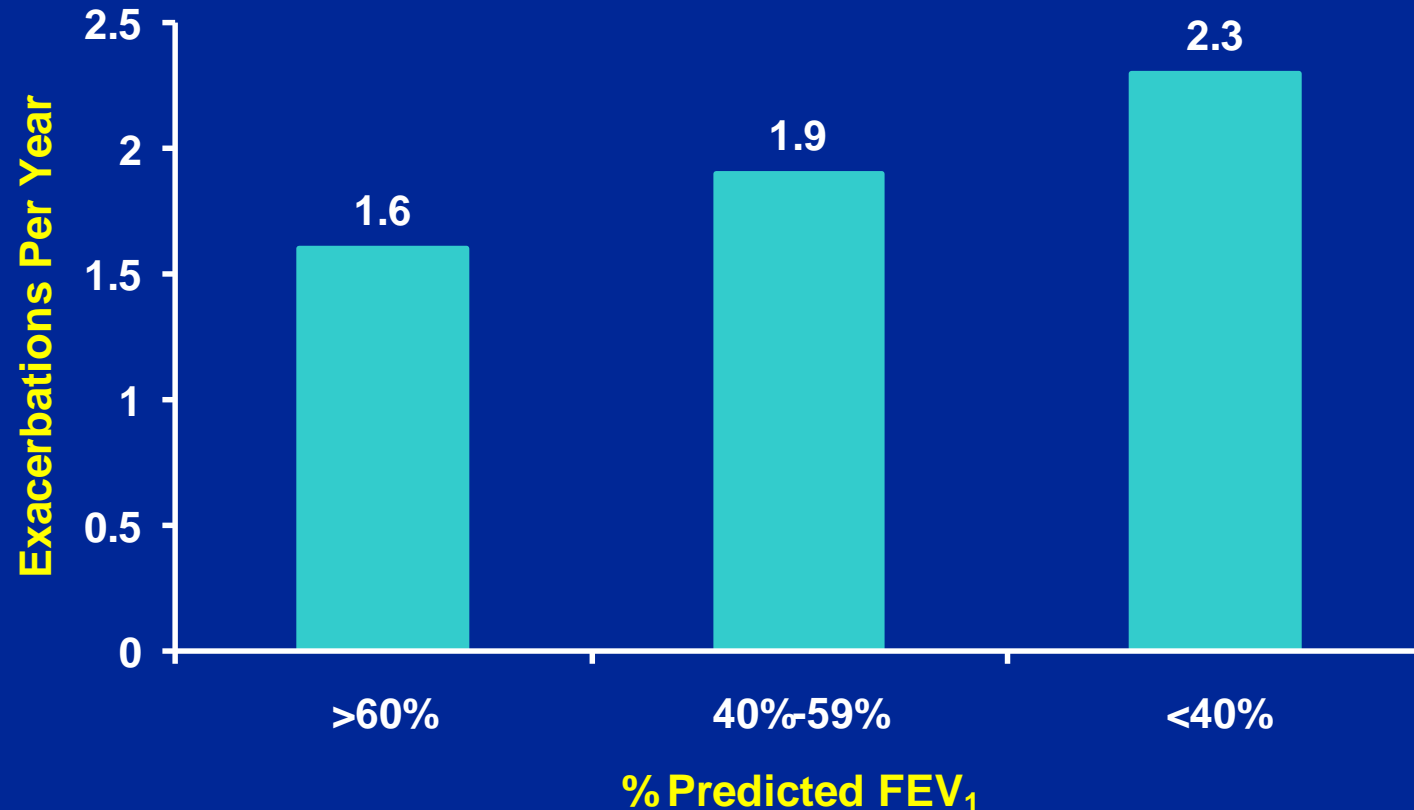
- In a 12-month study, 77% of patients had at least one exacerbation*

	Type of exacerbation dependent on definition	
	Symptom-defined	Healthcare-defined
Total number of exacerbations experienced	296	351
Mean yearly rate of exacerbations	2.3	2.8
Patients experiencing 0 exacerbations, n (%)	29 (23)	29 (23)
Patients experiencing 1-2 exacerbations, n (%)	56 (44)	41 (32)
Patients experiencing 3 or more exacerbations, n (%)	42 (33)	57 (45)

*Based on 127 of 201 subjects who completed diary cards covering >80% of the year.

O'Reilly J, et al. *Prim Care Respir J*. 2006;15:346-353.

Exacerbation Frequency Increases With Disease Severity



Results based on a cross-sectional observational study of ambulatory COPD patients in Spain. General practitioners (N=201) between October 1994 and May 1995 completed a questionnaire on COPD characteristics of 1001 patients.

Exacerbation was defined as an increase in dyspnea, sputum volume, and/or sputum purulence.

Miravittles M, et al. *Respir Med.* 1999;93:173-179.

What Are the Implications of Exacerbations in Patients With COPD?

Evaluation of Link Between Exacerbations and Decline in Lung Function

Objective:

- Evaluate the relationship between the frequency of exacerbations and the decline in lung function

Study Design:

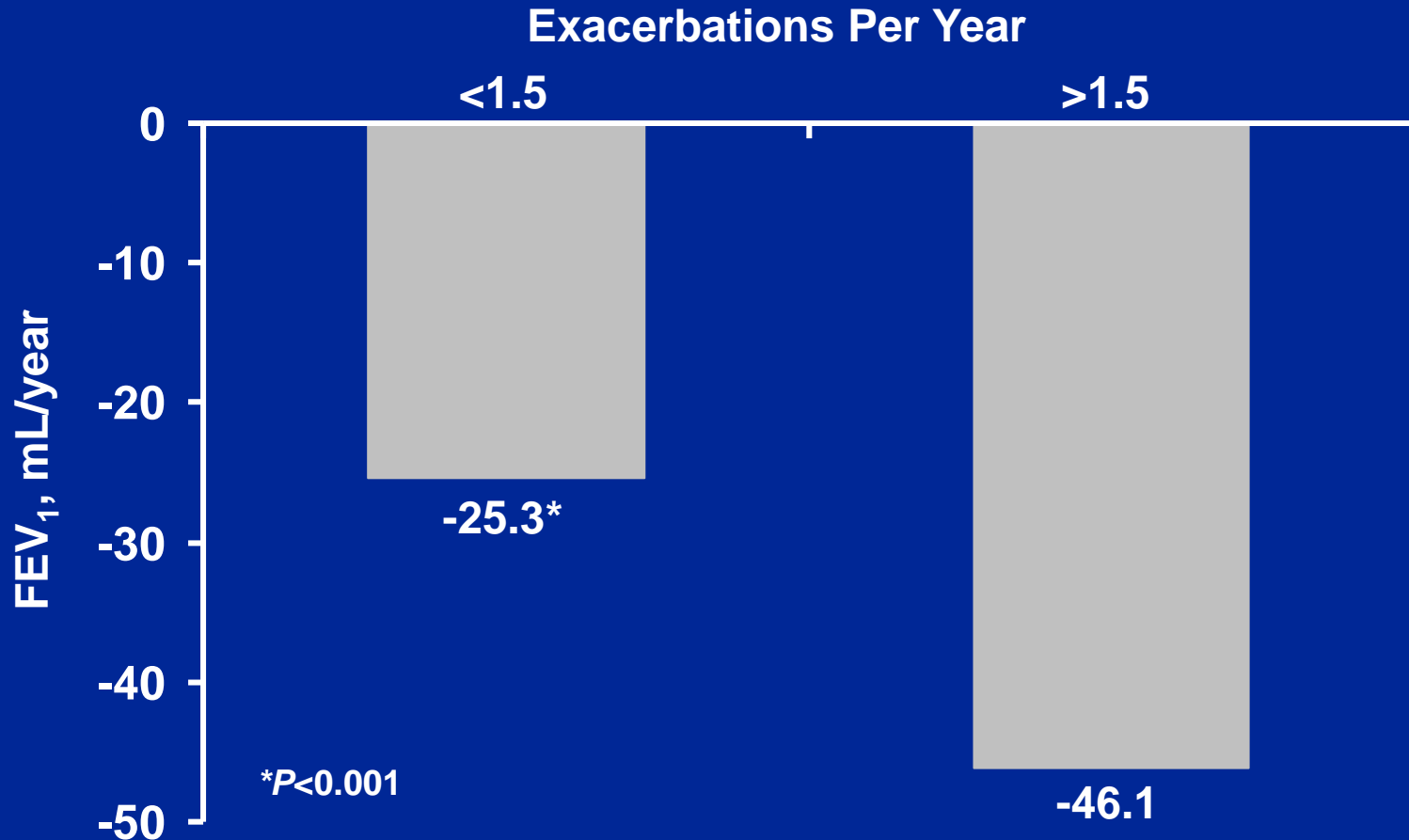
- Included patients with COPD attending outpatient clinics ($FEV_1 < 70\%$ of predicted)
- In diaries, 109 patients recorded daily PEF, increase in symptoms (above normal)
 - Daily FEV_1 was recorded in subset of patients (n=32)
- Exacerbations were diagnosed based on diary cards or patients contacting the investigator
 - Exacerbations were defined as the presence for ≥ 2 consecutive days of increase in any 2 “major” symptoms (increase in dyspnea, sputum purulence, or sputum volume) or an increase in 1 “major” and 1 “minor” symptom (increase in nasal discharge, wheeze, sore throat, cough, or fever)
- Data were collected over 4 years

Baseline Characteristics

Baseline Demographics for the 32 Patients Recording Daily FEV₁

	Median	Interquartile Range
Age, years	66.8	60.7-73.7
Gender, % male	90.6	—
FEV ₁ , % predicted	36	24.7-50.2
Smoking, years	40	30-46
Smoking at recruitment, %	31.2	—
Taking inhaled corticosteroids, %	87.5	—

Frequency of Exacerbations Is Associated With a Decline in Lung Function



Results based on a secondary analysis of 32 patients who recorded daily FEV₁. The median rate of exacerbations seen at clinic was 1.5 per patient per year.

Donaldson GC, et al. *Thorax*. 2002;57:847-852.

Evaluation of the Relationship Between Exacerbations and Quality of Life

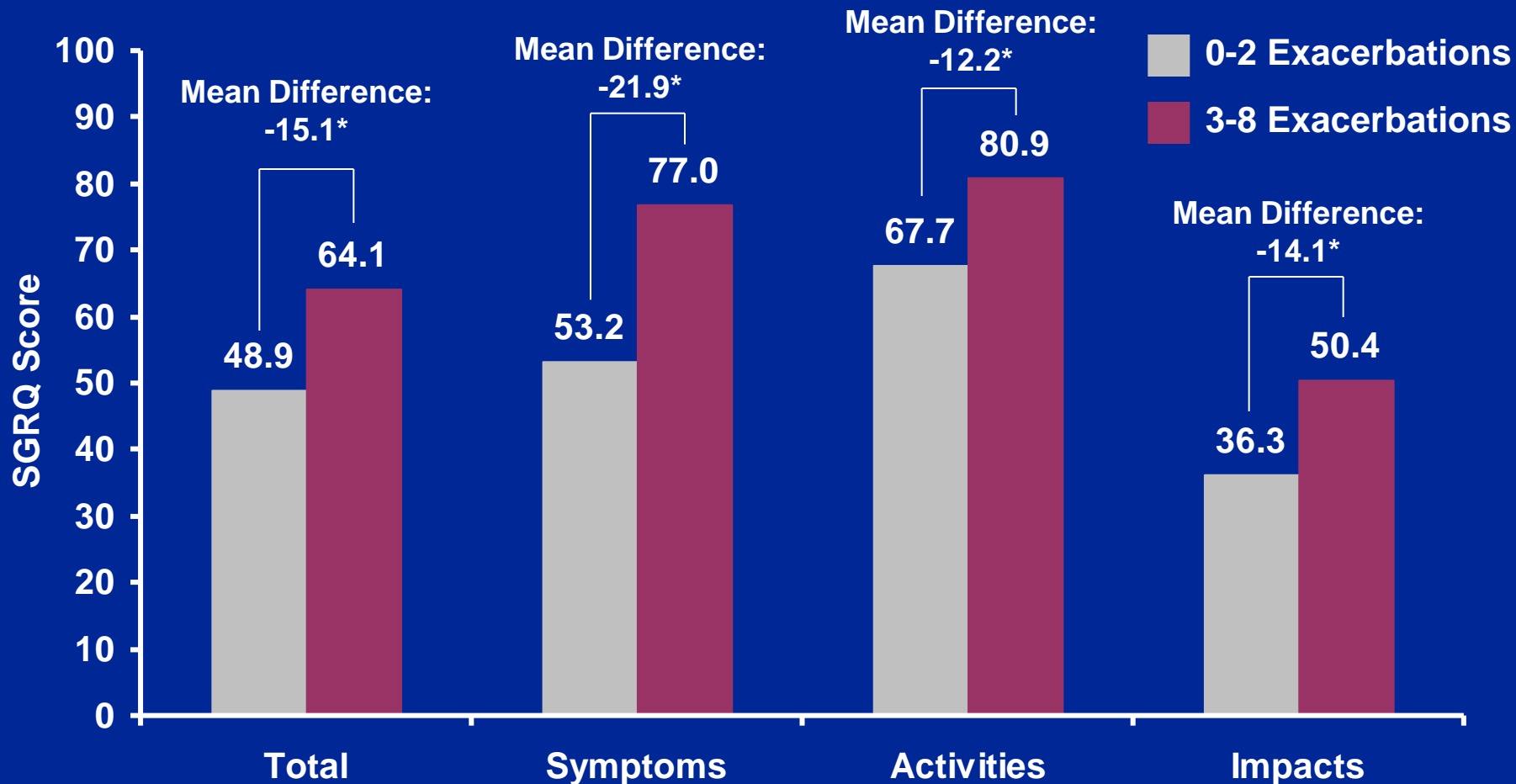
Objective:

- Evaluate the effect of the severity and frequency of exacerbations on quality of life

Study Design:

- Included 73 patients with COPD attending outpatient clinics ($FEV_1 < 70\%$ of predicted)
- Patients measured daily PEF and respiratory symptoms for 1 year
- Exacerbations were diagnosed at an acute visit by the investigator or based on review of diary cards
 - Exacerbations were defined as the presence of ≥ 2 consecutive days of increase in any 2 “major” symptoms (increase in dyspnea, sputum purulence, or sputum volume) or an increase in 1 “major” and 1 “minor” symptom (increase in nasal discharge, wheeze, sore throat, cough, or fever)
- Patients completed St. George’s Respiratory Questionnaire (SGRQ) at their last clinic visit

Patients With Frequent Exacerbations Had Significantly Worse Quality of Life



* $P \leq 0.002$

Evaluation of Reporting of COPD Exacerbations

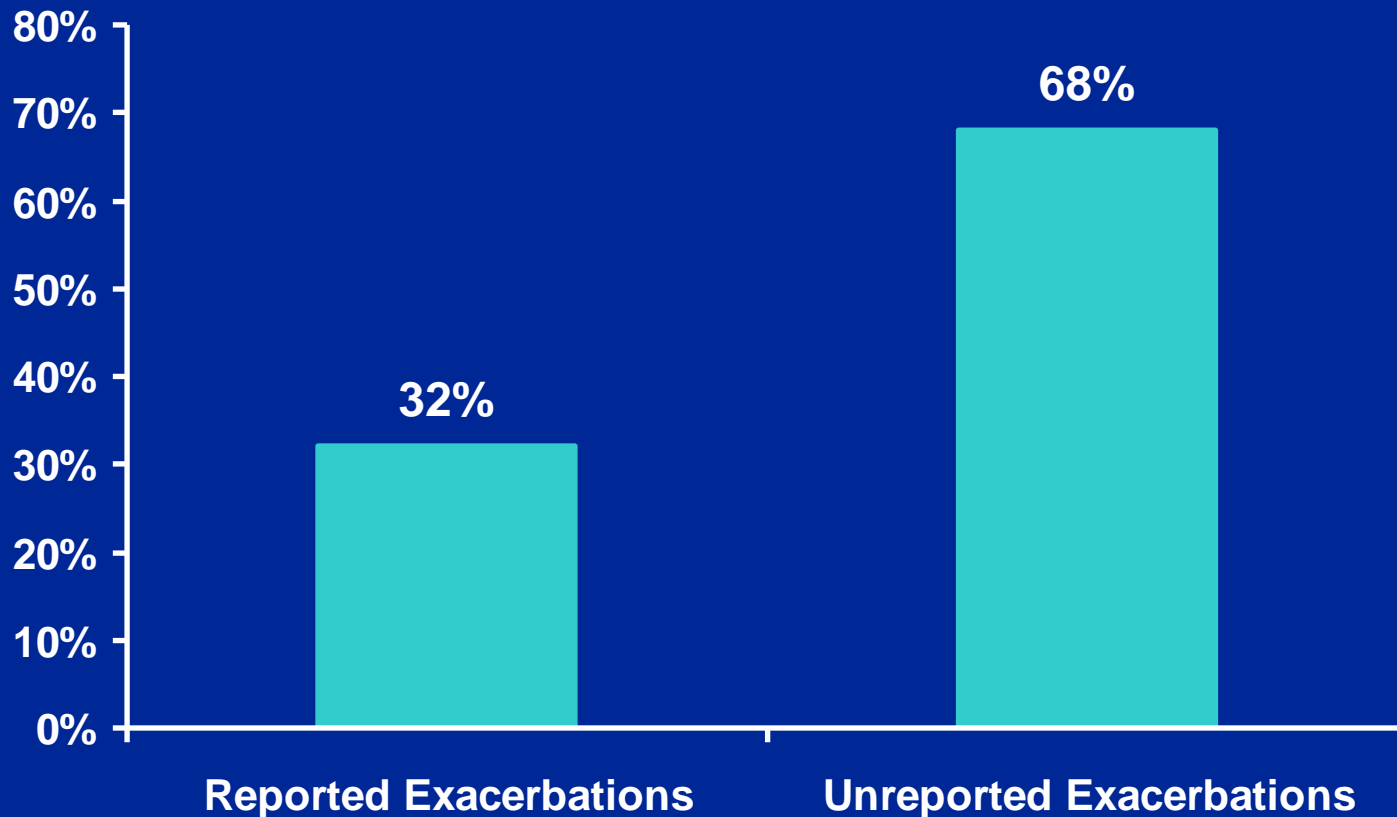
Objective:

- To determine the incidence of reported and unreported exacerbations and identify predictors of underreporting
- To compare the effect of reported and unreported exacerbations on health status

Study Design:

- A secondary analysis of an open-label, 6-month, prospective cohort study including 421 patients with COPD
- Patients included had an FEV_1 <70% predicted and a history of ≥ 2 exacerbations in the previous 3 years
- Patients recorded daily symptoms in a diary and were instructed to report a sustained (≥ 24 hours) worsening of any symptom to the study center
- Exacerbations were defined as a worsening of 1 key symptom (dyspnea, sputum amount, sputum color) occurring for ≥ 2 consecutive days

Patients Were Twice as Likely to Not Report a COPD Exacerbation



Reported exacerbations were defined as exacerbations reported by patient phone calls or reports of healthcare utilization for the event.

Unreported exacerbations were defined as exacerbations based on diary symptoms and were not matched to any reported exacerbation.

Patients With Reported and Unreported Exacerbations Experienced a Decline in Quality of Life

Median Change in Health Status (SGRQ) Between Visits 1 and 3 Months

SGRQ	Stable* Disease (n=212)	Unreported† (n=37)	Reported‡ (n=44)
Total Score	-2.3	3.4§	4.3§
Symptom	-1.0	2.8	10.3
Activity	0	0	2.8
Impact	-0.9	0.7	3.5

*No reported or unreported exacerbation between 1- and 3-month visits.

†Only unreported exacerbation(s) between 1- and 3-month visits.

‡At least 1 reported exacerbation between 1- and 3-month visits.

Statistically significant difference in total SGRQ score among those with reported and unreported exacerbations compared with no exacerbations ($P<0.05$).

SGRQ=St. George's Respiratory Questionnaire.

Langsetmo L, et al. *Am J Respir Crit Care Med*. 2008;177:396-401. Used with permission from OFFICIAL JOURNAL OF THE AMERICAN THORACIC SOCIETY. © AMERICAN THORACIC SOCIETY.

Evaluation of Recovery Time for Lung Function and Symptoms Following Exacerbations

Objective:

- To evaluate the recovery of lung function and symptoms following an exacerbation

Study Design:

- A cohort of 101 patients with COPD ($FEV_1 < 70\%$ of predicted) were followed over 2.5 years
- Patients recorded daily PEF and symptoms on diary cards
- Exacerbations were diagnosed at an acute visit by the investigator or based on review of diary cards
 - Exacerbations were defined as the presence of ≥ 2 consecutive days of increase in any 2 “major” symptoms (increase in dyspnea, sputum purulence, or sputum volume) or an increase in 1 “major” and 1 “minor” symptom (increase in nasal discharge, wheeze, sore throat, cough, or fever)
- 91 patients had a total of 504 exacerbations

Recovery of Lung Function and Symptoms Following an Exacerbation Is Often Prolonged and Sometimes Incomplete

	PEF	Symptoms
Time to recovery,* median days (IQR)	6 (1-14)	7 (4-14)
Exacerbations recovering within 35 days	75.2%	86.1%
Exacerbations recovering within 91 days	80.2%	90.9%
Exacerbations that did not recover within 91 days	7.1%	4.6%

*Recovery time was defined as the time for the parameter (PEF or symptoms) to return to baseline from the onset of the exacerbation. Baseline was defined as the 8- to 14-day period preceding the exacerbation.

Data are not shown for the percentage of exacerbations where recovery time could not be determined and where the next exacerbation occurred before complete recovery.

IQR=interquartile range.

**What Are the Guideline
Recommendations Regarding
Exacerbations?**

Recommendations From COPD Management Guidelines

- **ATS guidelines recommend clinicians educate patients on the signs/symptoms of an exacerbation¹**
- **GOLD guidelines state preventing exacerbations is key goal in disease management²**

1. American Thoracic Society/European Respiratory Society. *Standards for the diagnosis and management of patients with COPD [Internet]. Version 1.2. www.thoracic.org/go/copd. Accessed June 2, 2010.*
2. Global Initiative for Chronic Obstructive Lung Disease. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease – Updated 2009. www.goldcopd.org. Accessed June 2, 2010.*

Summary

- Significant burden associated with COPD and exacerbations
 - 672,000 hospitalizations¹, 16.3 million office visits²
 - 50%-75% of all COPD costs are for services associated with exacerbations³
- Exacerbations are a common occurrence
 - 77% of patients experienced at least 1 exacerbation in last 12 months⁴
 - The frequency of exacerbations per year increases with worsening COPD disease severity⁵
 - 68% of COPD exacerbations are unreported⁶
- Frequent COPD exacerbations are associated with:
 - Higher rate of decline in lung function^{7,8}
 - Lower quality of life,⁹ for both reported and unreported exacerbations⁶
 - Prolonged and incomplete lung function recovery and symptom improvement following an exacerbation⁹

1. American Lung Association. *Trends in chronic bronchitis and emphysema: morbidity and mortality*. February 2010. www.lungusa.org. Accessed June 2, 2010.

2. National Institutes of Health, National Heart, Lung & Blood Institute. *Morbidity and Mortality: 2009 chart book on cardiovascular, lung and blood diseases*. www.nhlbi.nih.gov/resources/docs/cht-book.htm. Accessed June 2, 2010.

3. American Thoracic Society/European Respiratory Society. *Standards for the diagnosis and management of patients with COPD [Internet]*. Version 1.2. www.thoracic.org/go/copd. Accessed June 2, 2010.

4. O'Reilly J, et al. *Prim Care Respir J*. 2006;15:346-353.

5. Miravittles M, et al. *Respir Med*. 1999;93:173-179.

6. Langsetmo L, et al. *Am J Respir Crit Care Med*. 2008;177:396-401.

7. Donaldson GC, et al. *Thorax*. 2002;57:847-852.

8. Makris D, et al. *Respir Med*. 2007;101:1305-1312.

9. Seemungal T, et al. *Am J Respir Crit Care Med*. 2000;161:1608-1613.