Background: Idiopathic pulmonary fibrosis (IPF) profoundly affects the quality of patients’ lives. A systematic review was performed to evaluate critically the published literature and to examine what is known about health-related quality of life (HRQL) in patients with IPF.

Methods: The MEDLINE, EMBASE, Health and Psychosocial Instruments, and Cochrane Library databases were searched to 1 April 2004. Abstracts and bibliographies of published articles were scanned and contact was made with investigators. Included studies analysed HRQL (or quality of life) in at least 10 patients with IPF. Two reviewers independently selected studies, evaluated their quality according to predetermined criteria, and abstracted data on study design, patients’ demographic and clinical characteristics, and quality of life outcome measures.

Results: Seven studies met the inclusion criteria. The studies enrolled 512 patients with IPF and used three different instruments to measure HRQL. All studies had important limitations in methodological quality; none measured longitudinal changes in HRQL over time. Patients reported substantially impaired HRQL, especially in domains that measured physical health and level of independence. Patients with IPF appear to have similar impairments in HRQL to those with chronic obstructive pulmonary disease. Measures of dyspnoea were moderately correlated with scores from domains that measured physical health (r² = 0.03–0.66) and energy/fatigue/pep (r² = 0.19–0.55), but measures of pulmonary function and gas exchange did not correlate as strongly with these and other domains.

Conclusion: Studies of HRQL in patients with IPF suggest that, in addition to the obvious effect on physical health, general health, energy level, respiratory symptoms, and level of independence are also impaired. Variability in HRQL among patients is not fully explained by measures of dyspnoea or pulmonary function, suggesting that HRQL measures provide unique information. More research is needed to identify or design appropriate measurement instruments for patients with IPF and to examine changes in HRQL over time or in response to specific treatments.

METHODS

Study identification

Systematic methods were used to identify potentially relevant studies, assess study eligibility for inclusion, and evaluate study quality. We attempted to find all published studies examining HRQL (or QOL) in patients with IPF. One investigator, with the help of a professional medical reference librarian, searched MEDLINE, EMBASE, the Cochrane Library, and the Health and Psychosocial Instruments (HAPI) databases to April 2004. To capture additional articles we manually reviewed relevant conference proceedings, meeting abstracts, and reference lists from identified studies and pertinent review articles. Studies published in any language were potentially eligible. Abstracts were considered for inclusion only when investigators provided complete information about study methods and results.

Three search strategies were developed: one for MEDLINE and EMBASE, one for HAPI, and one for the Cochrane Library database (see Appendix A available online only at thorax.bmj.com).
We included studies that measured HRQL in at least 10 patients with IPF. Studies that enrolled patients with diagnoses other than IPF were eligible for inclusion only if the HRQL data from the IPF patients were analysed separately from non-IPF patients and the results of those analyses were reported.

Study quality
We adapted the reporting guidelines of Staquet et al. and the methods of Efficace et al. to evaluate six aspects of methodological quality: (1) IPF case definition and cohort assembly; (2) clinical characteristics of the IPF subjects; (3) HRQL instrument selection; (4) HRQL end points and instrument administration; (5) methods of statistical analysis; and (6) completeness of reporting HRQL results. The complete study quality assessment instrument is presented in Appendix B (available online at http://www.thoraxjnl.com/supplemental).

Data abstraction
We abstracted data about demographic characteristics, mode of diagnosis, physiological and radiological measures of disease severity, and co-morbid conditions. We also collected data pertaining to the role of the measurement instruments in each study, how missing HRQL data were handled, the specific HRQL results observed, and the study specific psychometric properties of each instrument.

Table 1: Studies that assess HRQL or QOL in patients with IPF included in this review.

<table>
<thead>
<tr>
<th>Study no</th>
<th>Investigators</th>
<th>Study objectives</th>
<th>Measurement instruments used</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>De Vries et al*</td>
<td>(1) Identify life domains relevant to patients with IPF</td>
<td>SGRQ* WHOQOL-100*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) Determine whether the SGRQ or WHOQOL-100 was preferred for assessing these aspects</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Martinez et al</td>
<td>(1) Examine associations between HRQL and measures of dyspnoea and pulmonary function</td>
<td>SF-36†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) Compare HRQL in patients with IPF and healthy people</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>De Vries et al*</td>
<td>(1) Assess QOL in IPF patients</td>
<td>WHOQOL-100*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) Identify clinical parameters related to QOL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3) Determine clinical predictors of QOL scores</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Martinez et al</td>
<td>Examine association between HRQL and multiple dyspnoea scales</td>
<td>SF-36†</td>
</tr>
<tr>
<td>5</td>
<td>Nishiyama et al</td>
<td>(1) Identify the association between clinical markers of disease severity and HRQL</td>
<td>SGRQ‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) Examine the relationship between HRQL and both dyspnoea and exercise capacity</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Douglas et al†</td>
<td>Clinical trial of calcitriol versus prednisone</td>
<td>SF-36</td>
</tr>
<tr>
<td>7</td>
<td>Raghu et al*</td>
<td>Clinical trial of interferon-γ versus placebo</td>
<td>SGRQ</td>
</tr>
</tbody>
</table>

SGRQ, St George’s Respiratory Questionnaire; SF-36, Medical Outcomes Study Short Form-36; WHOQOL-100, WHO Quality of Life 100 Item Instrument.
* Dutch version; † Portuguese version; ‡ Japanese version.

Statistical analysis
Median values and ranges for summary statistics are reported based on information provided by each of the primary study authors. We did not attempt to pool data across studies because the number of studies was small and there was substantial heterogeneity in patient characteristics and choice of measurement instruments. An overall kappa (κ) coefficient was calculated to assess inter-rater agreement on study inclusion, and κ coefficients were calculated for each individual study to assess agreement on study quality ratings. Correlation coefficients were squared for pairwise relationships between certain clinical variables and HRQL/QOL scores, thus generating R² values or coefficients of determination for those relationships. The resulting value (R²) is interpreted as the proportion of variability in one variable (such as HRQL score) that is explained by the other variable (such as forced vital capacity), regardless of the direction (positive or negative) of the correlation.

RESULTS
We reviewed 2442 citations of peer reviewed articles and excluded 2432 after carefully reviewing their titles and abstracts. The full reports of the remaining 10 articles were examined for inclusion in the review; of these, six met our criteria for inclusion (table 1). Two studies that enrolled substantial numbers of patients with diseases other than IPF and did not provide separate data for IPF patients were excluded11 12 together with two studies that enrolled fewer than 10 patients with IPF.14 15 We determined that one of three potentially relevant abstracts was eligible after the investigators provided complete details about study methods and results.16 We excluded an abstract of a study that enrolled several patients with usual interstitial pneumonia (UIP) patterns of lung injury because the number of patients with IPF as the cause of the UIP pattern was not specified.17 Another abstract that otherwise met eligibility criteria was excluded because the investigators did not provide complete details about study methods and results.18 For the interested reader, the results of this study are summarised in Appendix C (available online at http://www.thoraxjnl.com/supplemental).
Table 2 Characteristics of included studies and their participants with IPF

<table>
<thead>
<tr>
<th>Investigators</th>
<th>N</th>
<th>Modality of IPF diagnosis</th>
<th>Mean (SD) years since diagnosis</th>
<th>Mean (SD) age (years) % Male</th>
<th>Mean (SD) FVC%</th>
<th>Mean (SD) TLco%</th>
<th>Mean PaO2 at rest (kPa)</th>
<th>Taking oral medication for IPF at time of study (%)</th>
<th>Using supplementary oxygen at time of study (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Vries²⁰</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nishiyama²¹</td>
<td>41</td>
<td>biopsy proven IPF</td>
<td>5.8 (5.4)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Raghu²²</td>
<td>330</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>64 (9)</td>
<td>64 (20)</td>
<td>64 (20.4)</td>
<td>69.6 (16.8)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>De Vries²²</td>
<td>30</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>63.5</td>
<td>65 (2.0)</td>
<td>61.9 (3.2)</td>
<td>8.1 (0.3)</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>Martinez²³</td>
<td>26</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>68 (15)</td>
<td>78 (2.0)</td>
<td>69 (16.1)</td>
<td>68 (2.0)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Martinez²³</td>
<td>34</td>
<td>biopsy proven IPF</td>
<td>5.5 (10.9)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Martinez²³</td>
<td>25</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>65.9</td>
<td>65 (2.0)</td>
<td>69 (3.2)</td>
<td>8.1 (0.3)</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>Martinez²³</td>
<td>117</td>
<td>clinical IPF</td>
<td>NR</td>
<td>64 (20)</td>
<td>64 (20.4)</td>
<td>68 (2.0)</td>
<td>7 (8.3)</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>Douglas²⁴</td>
<td>213</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>64 (9)</td>
<td>64 (20)</td>
<td>64 (20.4)</td>
<td>69.6 (16.8)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Douglass²⁴</td>
<td>5</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>15 (15)</td>
<td>15 (15)</td>
<td>15 (15)</td>
<td>15 (15)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>De Vries²²</td>
<td>30</td>
<td>biopsy proven IPF</td>
<td>NR</td>
<td>63.5</td>
<td>65 (2.0)</td>
<td>61.9 (3.2)</td>
<td>8.1 (0.3)</td>
<td>80</td>
<td>100</td>
</tr>
</tbody>
</table>

FVC, forced vital capacity; TLco, carbon monoxide transfer factor; PaO2, arterial oxygen tension.
*Duration of symptoms rather than time since diagnosis.
†Slow vital capacity.
NR = not reported.
Numbers in parentheses are standard deviation (SD) and are reported where available.

Study description

Two studies measured QOL by administering the World Health Organization’s Quality of Life 100-item instrument (WHOQOL-100),¹⁹ ²⁰ three studies measured HRQL by administering the Medical Outcomes Study Short Form 36-item instrument (SF-36),²¹–²³ and two studies measured respiratory disease-specific HRQL by administering the St George’s Respiratory Questionnaire (SGRQ).¹⁶ ¹⁹ ²⁴ Further details of these instruments are shown in Appendix D (available online at http://www.thoraxjnl.com/supplemental).

Five of the studies were cross sectional in design. DeVries and colleagues²⁰ performed a semi-qualitative study of 10 patients with moderately severe IPF. Although a formal qualitative analysis was not performed, the investigators reported findings from three focus groups. Participants in this study also completed the SGRQ and the WHOQOL-100 and discussed the merits and limitations of these instruments in the context of the focus groups. Martinez et al²¹ used the SF-36 to compare HRQL in 34 patients with moderately severe IPF with 34 age and sex matched control subjects. Twenty seven of the IPF patients in this study had their diagnoses confirmed by open lung biopsy and all 34 were taking daily prednisone (dose range 10–60 mg). In another study, DeVries and colleagues²¹ used the SF-36 to compare HRQL in 34 patients with biopsy proven IPF with 41 age and sex matched controls. The mean carbon monoxide transfer factor (TLco) in the IPF group was 45.3% of the normal predicted value and 14 IPF patients were using supplemental oxygen (table 2).

Two other studies were controlled clinical trials. Douglas and colleagues²⁻¹ performed a randomised prospective study at a single large tertiary referral centre. They randomly assigned 26 IPF patients (one biopsy proven) to receive either prednisone or colchicine. There was no difference between the two groups in the composite primary end point (death, significant deterioration in pulmonary function, intolerance or adverse event due to the study drug requiring cessation of treatment, addition of a second drug for the treatment of IPF, and study drop out for any reason) or in HRQL scores from the SF-36. Raghu et al²² reported the results of an international, multicentre, randomised, double blind trial of interferon γ-1b that enrolled 330 patients with IPF. Compared with placebo, interferon γ-1b did not significantly affect progression-free survival, measures of pulmonary function, gas exchange, or HRQL as measured with the SGRQ.

Characteristics of study participants

The studies included a total of 512 subjects with IPF (median 34, range 10–330). The range of mean subject ages was 58–68 years. Overall, 64% of IPF subjects were male (range 37–85%).

In six studies that provided information about the mode of diagnosis, IPF was confirmed by surgical lung biopsy in 3.8–100% of subjects. Overall, 68% (range 0–100%) of IPF subjects (N = 350) were taking oral corticosteroids. For the five studies with available data, 0–36% of IPF subjects were using supplemental oxygen (table 2).

Study quality

The seven studies met a mean (SD) of 46 (10)% of the predetermined quality criteria. The greatest percentage of quality criteria met by any one study was 61%. The median κ coefficient for inter-rater reliability was 0.85, indicating very good agreement between investigators on their ratings of study quality. Studies rarely met the arbitrary cut off value of at least 65% of the criteria in each of the six predefined quality domains (fig 1). Ten individual quality items were not met by any study (see Appendix E available online at http://www.thoraxjnl.com/supplemental).

Study data

Domains impacted

IPF patients demonstrated impaired HRQL in many life domains but physical health was most negatively impacted. Other domains that were rated consistently lower by IPF patients relative to either healthy controls or large samples of the general population included those that assessed...
HRQL and QOL scores: correlations with clinical parameters

Four studies examined the associations between HRQL (or QOL) instrument scores and results of pulmonary function tests (including arterial blood gas tensions), non-invasive measures of oxygenation, and breathlessness as measured by several dyspnoea indexes (see Appendix F available online at http://www.thoraxjnl.com supplemental).
In general, HRQL scores correlated with pulmonary function tests in the expected directions, but many of the correlations were not statistically significant. Most correlation coefficients had absolute values of <0.4. Dyspnoea consistently correlated better with HRQL and QOL than any other disease symptom or clinical severity measure. The strongest correlations were between dyspnoea and domains assessing aspects of physical health (for example, the SF-36 Physical Functioning domain).

Across studies, the strongest associations were between dyspnoea and physical health ($R^2 = 0.03-0.66$). Relative to the other pairwise associations, dyspnoea was also strongly associated with domains that assess energy, fatigue, or pep ($R^2 = 0.19-0.55$). The association between dyspnoea and emotional health was much weaker, and the associations between either pulmonary function or oxygenation and HRQL were, in general, weaker still (fig 3).

HRQL and investigational drugs

Two trials that enrolled a total of 356 IPF patients met the inclusion criteria. In both of these trials the study drugs (colchicine or interferon-γ-1b) did not improve HRQL.

DISCUSSION

This systematic review included seven studies that evaluated HRQL (QOL) in IPF patients. In these studies, patients with IPF were found to have impaired HRQL in nearly every life domain, but domains related to physical functioning, symptoms, and level of independence were affected most. In general—to the extent that obstructive lung disease specific instruments are capable of accurately measuring HRQL in patients with IPF, and to the extent that generic instruments are capable of accurately measuring HRQL in patients with severe diseases such as IPF or COPD—patients in comparable stages of IPF and COPD appear to have similar impairments in HRQL. Some scores from the three measurement instruments used in the studies included in this review correlated significantly and in the expected directions with selected measures of IPF severity—both physiological measures and self-report measures that involve patient perception (such as dyspnoea).

The strongest correlations were seen between dyspnoea and HRQL domains that tap overall health or aspects of physical health. The correlations between these same domains and measures of pulmonary function (FVC, TLC, or oxygenation (PaO₂)) were much weaker. In fact, many of the correlations reported in these studies, including many of those that achieved statistical significance, might be considered weak in other arenas. However, the impetus for assessing HRQL is the clinical observation that patients with objectively equal physiological parameters can have very different quality of life. A very strong correlation between such parameters and HRQL scores would suggest that there is no need to measure HRQL; knowing the patients’ physiological status would suffice.

The strong associations between dyspnoea and HRQL domains that assess either overall or physical health are not surprising because a measure of an individual’s perception of something—that is, a self-report measure like his assessment of his own physical health—may tend to be more highly correlated with other perception based measures such as reported dyspnoea or with closely associated reliable functional measures such as exercise capacity (as evaluated, for example, by the 6 minute walk test) than with nonperception based measures.

The modest correlations in these studies are also not entirely unexpected because HRQL measures are not perfectly reliable. Such less than perfect reliability can impose an upper bound on the correlations with other measures, however reliable these other measures themselves may be. A labile physiological measurement at a particular point in time and a perception based measure (which generally takes into account a person’s typical circumstance over a longer time period) appear likely not to be very highly correlated by conventional standards, even if the physiological process being measured had a marked role over time in determining the perception based measure. However, assuming that nonperception based measures such as pulmonary function and oxygenation are not particularly labile measures in stable IPF patients, and that HRQL (or QOL) instruments have adequate reliability, the modest correlations observed in these studies suggest that measuring HRQL provides unique information about IPF patients that is not captured by measures of pulmonary function, gas exchange, or dyspnoea.

With regard to study quality, the scores on quality dimensions related to the adequacy of reporting of baseline demographic and clinical characteristics were higher than the scores related to HRQL instrument selection, HRQL data analysis, and HRQL results reporting. Some studies measured HRQL but did not report scores, and investigators frequently did not report their rationale for choosing the instruments used in their studies. This, of course, does not pertain to instrument validation studies since their primary goal is to support the inference that there is a sound rationale for using that instrument for a given purpose in a certain population. For all other studies, however, and particularly for drug trials, a sound rationale for choosing a certain instrument should be described. Data to support the instrument selection for a particular study should be presented, or it should be clear that the study will itself yield data capable of either providing or supplementing such support.

Very little is known about the reliability and validity of existing measurement instruments in patients with IPF. McHorney and Tarlov have summarised instrument
measurement standards and usefulness criteria to help investigators choose appropriate instruments for their studies. Besides being brief and easily administered, a measurement instrument should have: (1) minimal floor and ceiling effects (that is, a low proportion of respondents in the target population who have scores at either the lowest possible or highest possible value); (2) acceptable internal consistency reliability and known standard errors of measurement; (3) adequate test-retest reliability and a reliable change index; and (4) validity and sensitivity to clinical change for both the population and purpose for which it is to be used. This last criterion is particularly important for studies in which HRQL is measured over time (as sometimes occurs in clinical trials), but no study has specifically addressed instrument longitudinal validity or sensitivity to change in patients with IPF.

As with any review article, the possibility of publication bias exists. However, one strength of our study—the comprehensive literature search performed with the assistance of a professional medical librarian—ensured that we captured relevant published articles. While our inclusion criteria were relatively lenient, we identified only seven eligible studies. We also identified one abstract in which investigators measured HRQL in patients with IPF, but we chose not to include in the review this incomplete report that has not undergone peer review.14 Other published studies of HRQL that enrolled patients with a variety of diffuse lung diseases including IPF did not meet our entry criteria.12–14

The paucity of data related to quality of life in IPF leaves several gaps in our understanding and provides opportunities for future research. For example, it will be important to examine the psychometric properties of existing instruments in this population and to define the most appropriate instrument to use in particular studies. Because they are developed for use in specific patient populations, disease-specific instruments contain items of particular relevance and are very likely to be more sensitive to changes in HRQL over time than other instruments.20 Instruments that are sensitive to change are needed to evaluate the impact of investigational pharmacological and non-pharmacological interventions. Currently, there is no disease specific instrument to measure HRQL in patients with IPF, but one that is properly developed and rigorously tested would be expected to be more relevant and therefore more sensitive than existing generic or respiratory disease specific HRQL instruments for studies of patients with IPF.

As with any instrument, the validity of a disease specific instrument for measuring HRQL over time and its sensitivity to change can only be assessed through a longitudinal study. A longitudinal study in patients with IPF would also improve our understanding of the disease by allowing us to assess HRQL in relation to disease progression. Such a study might also enable us to determine whether and how IPF patients adapt to this disabling disease.

In conclusion, we identified seven studies that examined HRQL or QOL in patients with IPF. The studies had several limitations, including inadequately explaining the rationale for measurement instrument selection and incomplete HRQL data analysis and reporting of results. Patients with IPF have impaired HRQL in many life domains, but domains that reflect aspects of physical health are most negatively impacted. More research is needed to learn about how this disease affects patients, whether and how IPF patients adapt to their disease over time, and whether existing measurement instruments are reliable and valid for assessing HRQL over time in this patient population.

ACKNOWLEDGEMENTS

The authors thank Desmond Sjaunjockley for reviewing non-English language studies; Lori Nelson for helping to develop the quality criteria for included studies; Abby King for her thoughtful review of a previous version of this manuscript; and Christopher Stave for his guidance and assistance with the literature searches.

Appendices A–F are available online on the Thorax website at http://www.thoraxjnl.com/supplemental

Authors’ affiliations

J J Swigris, W G Kuschner, S S Jacobs, S R Wilson, M K Gould, Division of Pulmonary and Critical Care Medicine, Stanford University, Stanford, CA, USA

W G Kuschner, M K Gould, VA Palo Alto Health Care System, Palo Alto, CA, USA

S R Wilson, Palo Alto Medical Foundation Research Institute, Palo Alto Medical Foundation, Palo Alto, CA, USA

Dr Swigris received support from an NIH training grant (T32 HL07948-01A1). Dr Gould received an Advanced Research Career Development Award from the VA Health Services Research and Development Service. The views expressed in this article are those of the authors and not necessarily the views of the Department of Veterans Affairs.

REFERENCES


www.thoraxjnl.com
Severity of COPD is linked to decreased histone deacetylase activity


Histone acetylation status depends on the equilibrium between the activities of histone acetyltransferase (HAT) and histone deacetylase (HDAC). Acetylation prompts unwinding of histone and allows DNA transcription and production of cytokines. In alveolar macrophages HDAC is a key molecule in repressing the production of pro-inflammatory cytokines.

In this study the authors attempted to correlate changes in HDAC activity and expression with the severity of chronic obstructive pulmonary disease (COPD) as measured by spirometry. HDAC and HAT activities were measured in nuclear extracts of surgical lung specimens from non-smokers and patients with pneumonia, cystic fibrosis, or COPD. Alveolar macrophages from non-smokers, healthy smokers, and patients with COPD or asthma were also examined. RNA was used for quantitative reverse transcriptase polymerase chain reaction assay of HDAC1-8 and interleukin-8 (IL-8). Histone-4 acetylation at the IL-8 promoter was evaluated with chromatin immunoprecipitation.

HDAC activity was decreased in the peripheral lung tissue, alveolar macrophages, and bronchial biopsy specimens of COPD patients compared with healthy non-smokers. Lung HDAC activity was reduced in more severe COPD. Increases in histone-4 acetylation at the IL-8 promoter and expression of IL-8 messenger RNA were correlated with increased severity. However, there was no relationship between total HAT activity and severity of COPD. Bronchial biopsy specimens from mild asthmatics and healthy smokers had lower HDAC activity than those from non-smokers. There were further reductions in patients with COPD. Asthmatic patients had increased HAT activity compared with non-smokers, but there was no change in HAT activity in those with COPD.

The authors conclude that patients with COPD have progressive reduction in total HDAC activity that reflects the severity of the disease. In both asthma and COPD the balance between HAT and HDAC is shifted towards hyperacetylation, but by different mechanisms. These findings may have therapeutic implications.

S A Nachman
Assistant Professor of Clinical Medicine, Columbia University/Harlem Hospital Center, New York, NY, USA; san14@columbia.edu