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Late-breaking abstract: Nasal symptoms are common in subjects with COPD and concomitant heart disease

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Background: Systemic inflammation has been suggested as a possible link between cardiovascular (CV) disease and COPD. Also nasal symptoms have been discussed in relation to COPD and systemic inflammation. Coincident data on these conditions are scarce.
Aim: To give descriptive population based data on CV disease and nasal symptoms in COPD and non-COPD.
Methods: All subjects with COPD according to GOLD, $FEV_1/FVC<0.70$, were identified (n=993) from clinical follow-ups in 2002-04 of the OLIN (Obstructive Lung Disease in Northern Sweden) studies' cohorts together with 993 gender- and age-matched reference subjects without COPD (non-COPD, further divided into normal and restrictive lung function, Nlf and Rlf). Interview-data on nasal blocking/rhinitis and CV disease were used.
Results: CV disease (heart disease (HD), hypertension, stroke, claudicatio) was more prevalent in COPD compared to in Nlf; 50.1% vs 41.0% ($p<0.001$) and also the prevalence of HD (angina pectoris, heart failure, myocardial infarction), 18.5% and 13.7%, respectively (p=0.006). Nasal symptoms were more common in COPD compared to in Nlf, 43.1% vs 32.3%, $p<0.001$. In Rlf the prevalence of nasal symptoms, CV disease and HD was 41.0%, 59.0% and 24.4%, significantly higher compared to in Nlf (p=0.017, $p<0.001$ and $p<0.001$) and all but nasal symptoms also compared to in COPD (p=0.573, p=0.047 and p=0.017). In subjects with COPD and HD, 53.0% had nasal symptoms, while 35.8% in Nlf and 62.2% in Rlf.
Conclusion: Cardiovascular disease and nasal symptoms were common in COPD, and Rlf did also identify a population with increased CV disease burden. The overlap between heart disease and nasal symptoms was large in subjects with COPD but also in Rlf.

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Prevalence of COPD in a rural population in India

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COPD is a growing cause of morbidity and mortality across the world. However, there is little data on the burden of COPD in India, especially in the rural population.
Aim: We aimed to study the prevalence and risk factors for COPD in a rural population in India using the Burden of Obstructive Lung Disease (BOLD) study protocol.
Methods: 3600 male and female subjects above the age of 25 yrs residing in 22 rural villages near Pune were randomly selected to participate in the study. 10 trained field workers visited their homes, and after obtaining written informed consent, administered the BOLD questionnaire and performed pre and post-bronchodilator spirometry using ndd sprirometer. COPD was defined as post-bronchodilator FEV1/FVC <70%.
Results: 2699 subjects (M: 49.9%; F: 50.1%) with a mean age 43.8±14.5 yrs consented. Acceptable spirometry was obtained from 1745 subjects. The overall prevalence of COPD was found to be 5.1% (M-6.5%; F-3.4%) and 85% of these never smoked. Male gender [Adj OR: 1.93 (CI 1.2-3.3); p=0.01] and increasing age [OR: 2.01 (CI 1.7-2.4); $p<0.0001$) were strongly associated with COPD. 70% of the COPDs lived in homes that used biomass fuel for cooking compared to 30% who used liquefied petroleum gas (LPG). Tobacco smoking on its own was significantly associated with COPD [OR: 2.34 (CI: 1.2-4.3); p=0.006], however, after adjustment, the risk reduced [Adj OR: 1.88 (CI: 0.96-3.7); p=0.06]. Smokers who used biomass fuel had a 3.2-fold higher prevalence of COPD than non-smokers using LPG (p=0.01).
Conclusion: COPD is more common amongst non-smokers in the rural population in India although smoking is a risk factor for COPD. Smokers who use biomass fuel for cooking have a significant additive risk of COPD.

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Using the lower limit of normal to classify lung disease misses at risk people

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Background: The Global Initiative on Obstructive Lung Disease (GOLD) stages for chronic obstructive pulmonary disease (COPD) uses a fixed ratio of the post-bronchodilator forced expiratory volume in one second (FEV1)/ forced vital capacity (FVC) of 0.70 as a threshold to define obstruction. Some advocate using lower limit of normal (LLN) for the FEV1/FVC ratio, FEV1, and FVC to define abnormality.
Objective: To determine mortality in a representative sample of the U.S. adult population comparing abnormality determined using GOLD criteria to that determined using LLN criteria.
Methods: We used baseline data from the Third National Health and Nutrition Examination Survey (NHANES III) and follow-up mortality data. We classified subjects as obstructed, restricted, or normal based on the GOLD vs. the LLN criteria. We used Cox proportional hazards models to determine the relation between diagnosed lung disease and mortality, adjusting for covariates.
Results: Our study sample included 13,847 subjects, of whom 3,774 died during the follow-up period. Of subjects classified as obstructed and restricted using GOLD criteria, 20.9% and 18.0% were classified as normal using the LLN. Mortality was increased in the obstructed (hazards ratio [HR] 1.48, 95% confidence interval [CI] 1.21, 1.80) and restricted (HR 2.03, 95% CI 1.67, 2.45) subjects classified as normal using the LLN, but abnormal using the GOLD criteria.
Conclusion: In the nationally representative NHANES III data, subjects classified as normal using the LLN criteria but obstructed or restricted using the GOLD criteria have a higher risk of mortality.

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Ten-year trend in the prevalence of chronic cough and phlegm among young adults in Italy

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The presence of chronic cough and phlegm (on most days for a minimum of 3 months a year and for at least 2 successive years) identifies a subgroup of subjects with a high risk of developing COPD, independently of smoking habits. We sought to evaluate the ten-year trend in the prevalence of these symptoms among young adults in Italy.
In 1998/2000, a screening questionnaire was mailed up to 3 times to general population samples of 20-44 year-old subjects, and eventually given over the phone to the remaining non-responders, in the Italian Study on Asthma in Young Adults (ISAYA) (9 centres; response rate = 72.7%). The same procedure was repeated in the Gene Environment Interactions in Respiratory Diseases (GEIRD) study in 2007/2010 (7 centres; response rate = 57.2%).
In the 4 centres (Pavia, Sassari, Turin, Verona) involved in both the studies, the adjusted percentage* of current smokers has decreased (from 34.3 to 27.4%; $p<0.001$) during the past decade. The adjusted prevalence* of chronic cough and phlegm (with the 95%CI) is reported in this table:

	ISAYA (1998/2000) (n=8,931)	GEIRD (2007/2010) (n=5,162)	p-value
Non-smokers	7.5% (7.1–7.9)	9.1% (8.2–10.1)	0.01
Past smokers	11.2% (10.6–11.9)	10.4% (9.9–10.9)	0.11
Current smokers	19.3% (18.4–20.2)	21.2% (18.4–24.3)	0.32
Total	12.4% (11.9–12.8)	12.6% (11.5–13.9)	0.74

*Adjusted for centre, type of contact (telephone vs mail), cumulative response rate, season of response, sex, age.

The overall prevalence of chronic cough and phlegm has not changed during the past decade among young adults in Italy, but a decrease is expected due to the observed reduction in the percentage of current smokers. The increase in the prevalence among non-smokers deserves further investigation.

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Costs of COPD by disease severity

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Background: Chronic obstructive pulmonary disease (COPD) is one of the most common chronic and disabling diseases worldwide, and the societal costs are high.
Aim: To estimate the societal costs of COPD in Sweden and to examine the relationship between disease severity and costs.
Methods: The study sample was identified in earlier clinical examinations of general population cohorts within the OLIN (Obstructive Lung Disease in Northern Sweden) studies. The cohort consisted initially of 993 subjects fulfilling COPD spirometric criteria (GOLD). In 2009-2010, telephone interviews on resource utilization were made to a sample of 244 subjects, stratified by disease severity. Interviews were performed quarterly to minimize the risk of recall bias. A non-parametric Mann-Whitney U-test was used to test cost differences between groups; p-values adjusted by Bonferroni correction. Unit costs from 2010 were applied.
Results: A highly significant relationship was found between disease severity and costs. The mean annual total cost per patient in relation to disease severity (GOLD) was: stage I €811; II €2,660; III €7,068; and IV €20,665. Indirect costs were higher than direct costs in all severity stages. For direct costs, main cost drivers were hospitalizations in stage III and IV, and drugs in stage I and II, respectively. The main cost driver in indirect costs was productivity loss due to early retirement, except in stage I where the driver was sick-leave. In comparison with a similar study performed in 1999 a numerical increase in mean annual total costs per patient was observed (ns).
Conclusions: The results indicate that the societal costs of COPD in Sweden are substantial, and the costs increase considerably by disease severity.

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Associations between quantitative computed tomography (qCT) measures of emphysema and mortality

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Background: Knowledge is limited regarding associations between qCT measures of emphysema and mortality.
Aims: To examine 6-year mortality (all-cause and chronic lower airway diseases (ICD-10 codes J40-J47)) in relation to qCT measures of emphysema.
Methods: In the Norwegian GenKOLS study 2003-05, 947 ever-smokers (49% with COPD) aged 40-85 years performed spirometry and qCT examination. Lung inflation level was obtained by dividing CT measured lung volume by predicted TLC. CT emphysema was estimated using% of lung voxels with X-ray attenuation values less than -950 Hounsfield units (% low-attenuation areas (LAA)), expressed in population quintiles. Mortality data from 2003-09 were gathered from the Norwegian Cause of Death Registry. Gender-stratified Cox proportional hazards were modelled, adjusting for FEV1, COPD status, age, BMI, smoking, inflation level.
Results: Both all-cause (n=106) and chronic lower airway diseases mortality (n=31) increased with%LAA: from 3% and 0.5% in the lowest quintile to 32% and 12% in the highest quintile. Unadjusted hazard ratios (HR) (95% CI) for all-cause mortality were 14.1 (6.2, 32.0) for the highest quintile for women, and 8.4 (4.4, 16.1) for men. After adjustment, the trends remained the same, but were (borderline) significant only for women (HR 3.7 (95% CI 0.9, 14.3). For chronic lower airway mortality, the highest quintile%LAA had HR (95%CI) 47.2 (6, 377) for women, and 39.7 (5, 301) for men. After adjustment, upper%LAA quintile had HR 17.6 (95%CI 1, 308) for women and 2.5 (0, 47) for men.
Conclusions: qCT measures of emphysema are related to mortality, especially in women. Subjects with high%LAA have a substantially elevated mortality risk.

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Impact of comorbidities on survival of patients with COPD according to GOLD stages

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Introduction: In COPD patients the impact of comorbidities on patient's outcomes is gaining interest. The aim of our study is to describe the role of comorbidities on mortality according to COPD GOLD stages.
Methods: We enrolled and followed 1664 patients from the BODE cohort over 10 years in five tertiary centers in the USA and Spain.
Demographics, anthropometrics, physiological, comorbidities and survival with cause of death were recorded systematically. Patients were grouped according to GOLD stages I-II, III and IV. Tukey's test was used to compare means among groups. A multivariate analysis was used to select those comorbidities associated with mortality. The effect of comorbidities over survival time was explored using Cox proportional hazard.
Results: Groups characteristics and differences are shown in table 1. GOLD IV subjects were significantly younger, had fewer comorbidities and higher mortality. Furthermore comorbidities did not influence mortality in these subject and they died mainly from COPD (Table 2 and 3).

Table 1: Sub groups of patients according to GOLD

	GOLD I-II	GOLD III	GOLD IV
n total	730	640	294
n died (%)*	179 (25)	259 (41)	190 (65)
Age (X±STD)**	66.5 ± 9.4	68 ± 9	65 ± 8.9
BODE (X±STD)*	1 ± 1.6	4 ± 1.9	7 ± 1.96
FU months**	52.3 (±32)	54.9 (±32)	46 (±30)
# of comorbidities X (SD)**	6.2 ± 3.7	6.2 ± 3.5	5.6 ± 3.3

(*) p<0.001 among groups (**) p< 0.001 I-II vs IV y III vs IV

Table 2: Impact of comorbidity on survival

Diseases GOLD I-II	COX (IC) p*
Lung cancer	4.26 (3.02-5.94) p< 0.0001
Pulmonary fibrosis	2.78 (1.82-4.1) p< 0.0001
Pancreatic cancer	18.12 (4.40-49.3) p= 0.0007
Bladder cancer	2.46 (1.28-4.30) p= 0.0091
Liver cirrhosis	2.5 (1.03-5.14) p= 0.0429
AF - flutter	1.69 (1.13-2.47) p= 0.0108
CHF	1.74 (1.21-2.46) p= 0.0033
Diseases GOLD III	**COX (IC) p***
Lung cancer	1.97 (1.41-2.69) p= 0.0001
Diseases GOLD IV	**COX (IC) p***
None	

Table 3: Causes of death by GOLD stages

	GOLD I-II	GOLD III	GOLD IV
COPD	46 (26%)	104 (40%)	118 (62%)
Cardiovascular	22 (12%)	21 (8%)	8 (4%)
Cancer	71 (40%)	57 (22%)	16 (8%)
Respiratory	11 (6%)	29 (11%)	19 (10%)
Other	11 (6%)	13 (5%)	5 (3%)
Unknown	18 (10%)	35 (14%)	24 (13%)
Total	179 (100%)	259 (100%)	190 (100%)

In contrast, in patients in GOLD I-II and III several comorbidities influence survival with lung cancer being the most important.(Table 3).
Conclusion: Different comorbidities have an impact in mortality at different COPD GOLD stages. We suggest the inclusion of those comorbidities as part of the evaluation of COPD patients.

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Glitazones are associated with reduced risk of COPD exacerbations and mortality among patients with diabetes

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Introduction: Moderators of systemic inflammation may reduce risk of exacerbations among patients with COPD. Glitazones, used in the treatment of diabetes, also have anti-inflammatory properties. We sought to assess whether glitazones were associated with a decreased risk of COPD exacerbations and mortality.
Study design: We performed a cohort study between 10/2005-09/2006 of all US veterans who received an oral antihypoglycemic medication (sulfonureas, biguanides, or glitazones) on more than one occasion. Our outcome measures included outpatient COPD exacerbations, hospitalization for COPD, and all cause mortality. Our primary exposure was glitazone use compared to sulfonureas and/or biguanides. We used GEE to estimate the effect of glitazones and to adjust for potential confounding factors.
Results: We identified 600,366 patients. Adjustment for age, sociodemographic characteristics, comorbidity, and markers of COPD severity had minimal effects on the point estimates. In comparison to either a sulfonylurea or biguanide, glitazones were associated with a significantly reduced risk of outpatient exacerbation (Adjusted relative likelihood (Adj-RL), 95%CI: 0.79 (0.72-0.86), hospitalization for COPD exacerbation (Adj-RL, 95%CI: 0.82 (0.69-0.97)) and all cause mortality (Adj-RL, 95%CI: 0.89 (0.85-0.93)). These estimates were robust to sensitivity analyses that imposed increasingly strict definitions of COPD.
Conclusion: Glitazones were associated with a significant reduction in COPD exacerbations and all cause mortality. We hypothesize that this association may be mediated through the anti-inflammatory properties of glitazones.
Funding: Gilead Sciences, Inc., & VA HSRD