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# 207. COPD: risk factors, biomarkers and diagnosis

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### Respiratory health at the extremes of the ageing population: Initial results of the UK Newcastle 85+ study

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People aged 85+ years are demographically the fasting growing age group worldwide increasing the burden on healthcare resources. In the Newcastle 85+ study subjects born in 1921, recruited from the Newcastle area, underwent domiciliary health assessment, including respiratory history, symptoms, spirometry and review of general practitioner (GP) records for pre-existing disease. 845 participants (319 Male: 526 Female) took part, regardless of current health status.

Significant occupational exposure to heavy industry was reported by 42% men and 17% women. 71% men and 52% women were current or ex- regular smokers. Review of GP records showed 18% men and 16% women had a diagnosis of Chronic Obstructive Pulmonary Disease (COPD); 7% men and 13% women a diagnosis of Asthma; and 10% men and 7% women had other primary respiratory diagnoses.

92% performed reproducible spirometry. 28% males had normal spirometry, 13% restrictive and 59% obstructive spirometry (Mild 36%; Moderate 46%; Severe 15% and very severe 3%). In the females, 33% had normal spirometry, 16% restrictive and 51% obstructive spirometry (Mild 44%; Moderate 43%; Severe 11% and very severe 2%). The MRC Dyspnoea score was  $\geq 2$  in 38% men and 40% women.

This study presents data on a large population of very elderly people. It shows a high prevalence of diagnosed airways diseases with 25% men and 29% women having asthma or COPD. Obstructive spirometry was reported in 59% men and 50% women with significant disability shown by MRC-dyspnoea score. These initial results suggest a significant burden of respiratory compromise with potential for significant impact on health care services in the coming years.

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#### Passive smoking and COPD – More dangerous than believed <u>Stig Hagstad</u><sup>1,2</sup>, Linda Ekerljung<sup>1</sup>, Anders Bjerg<sup>1,2</sup>, Anne Lindberg<sup>2,3</sup>, Eva Rönmark<sup>2,3</sup>, Bo Lundbäck<sup>1,2</sup>. <sup>1</sup>Krefting Research Centre, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden; <sup>2</sup>The OLIN Studies, Norrbottens Läns Landsting, Luleå, Sweden; <sup>3</sup>Department of Public Health and Clinical Medicine, University of Umeå, Sweden

**Background:** Passive smoking has been identified as a risk factor for cardiac diseases, asthma, lung cancer and with detrimental effects on lung function, but the relationship between passive smoking and COPD is not fully established. Aim: To study environmental tobacco smoke (ETS) as a risk factor for COPD in never-smokers.

**Methods:** Data from three cross-sectional studies from the Swedish OLIN database were pooled. Only never-smokers were included in the analyses, and 2118 never-smokers had completed structured interviews and lung function tests of acceptable quality. COPD was defined according to the GOLD criteria. Risk analysis was performed by using multiple logistic regression analysis.

**Results:** Exposure to ETS at home was associated with COPD (OR 1.5, 95% CI 1.0-2.2). ETS at current or past workplace was also associated with COPD. The relationship was more pronounced in subjects who reported exposure to ETS at both past and current workplace (OR 2.4, 95% CI 1.5-4.0). Current exposure to ETS at home in combination with ETS at both current and previous workplace was strongly related to COPD (OR 3.6, 95% CI 1.6-8.5). There was a strong relationship between increasing amount of exposure to ETS in various settings and the prevalence of COPD, especially among women. Interestingly, of the 14 women aged  $\leq$ 65 years who had reported current exposure to ETS at home and at both previous and current workplace, 7 had COPD.

**Conclusion:** ETS was found to be an independent risk factor for COPD. This relationship was stronger in women and the association was stronger with increasing degree of exposure.

The effect of body mass on COPD in non-smoking women

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Rationale: Smoking is the strongest COPD risk factor, however it has been recognised that a substantial proportion of COPD cases arises in non-smokers. Many studies suggest that obesity is more prevalent in patients with COPD, but it has not been elucidated whether this is also true for never-smokers. Aim of the current study was to assess the effect of change in BMI on incidence and persistence of COPD in never smoking women.

**Methods:** The current study used pooled data from the population based SAPAL-DIA and SALIA cohorts. Weight status was defined based on BMI at baseline and change in BMI. Pre-bronchodilator ratio of forced expiratory volume in one second over forced vital capacity (FEV1/FVC) was measured in both studies at baseline and follow-up. COPD was defined according to the GOLD criteria or having FEV1/FVC<lower limit of normal and percent predicted FEV1<80%.

Mixed regression models with random intercept for study area were used to assess the association between BMI change and COPD prevalence and incidence in non smoking women after adjustment for selected confounders.

**Results:** Lung function data and information on potential confounders were available in 9662 women. The majority of women were never smokers (62.5%). The average BMI between baseline and follow-up ranged between 15.48-53.89 kg/m<sup>2</sup>. The incidence of COPD according to the GOLD criteria stage 1 was 3.2% and the incidence in the combined stage 2 and higher was 2.52%. The odds of developing COPD stage 2 increased by a factor of 1.3 per unit increment in BMI. Menopausal status did not influence this association.

**Conclusion:** The results of our analysis suggest that a change in BMI influences the development of COPD in non-smoking women.

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### COPD - Prevalence and risk study from rural north India

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**Background:** The increasing impact of Chronic Obstructive Pulmonary Disease (COPD) on health care resources is now being recognized as a major public health problem and is projected to be the third leading cause of death worldwide by 2020. **Aims and objectives:** To estimate the prevalence and assess the risk factors for COPD in adults using spirometry (GOLD criteria).

**Methods:** A community-based, cross sectional, multiphasic survey was conducted on 2112 adults, age >35 years. COPD was diagnosed using fixed ratio post bronchodilator FEV1/FVC<70% on spirometric evaluation conducted on participants who screened positive using clinical (by validated respiratory questionnaire) or PEF criteria.

**Results:** The overall prevalence of COPD was 8% (10.8% in males and 5.1% in females). The prevalence of COPD was 15.3% in the ever smokers and were at 3.54 times higher risk (95% CI 2.6-4.9) compared to non smokers. The exposure to high risk occupation showed an increased risk for development of COPD [OR 3.983, 95% CI 2.87-5.52] than the non exposed individuals. Among females, the prevalence was highest for the heavy kitchen smoke exposure (8.2%). On logistic regression the factors related with COPD were age >65 years [OR 1.079 95% CI 1.064-1.095], exposure to high risk occupation [OR 2.395 95% CI 1.485-3.861] and smoking [OR 2.263 95% CI 1.467–3.492]. Other factors as exposure to passive tobacco smoke, education, socio economic status did play a role independently, however no significant higher risk was observed using multivariate statistical model.

**Conclusion:** Ageing, smoking, occupation and biomass smoke exposure certainly explain the web of causation on the background of other risk factors as passive smoking, education and socioeconomic status.

### 1680

## Association between serum levels of clara cell secretory protein and lung function in adults from ECRHS

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The 16-kD Clara cell secretory protein (CC16) has anti-inflammatory properties and protective effects from oxidative stress on the respiratory tract and has been proposed as a biological marker of pulmonary health. Whether CC16 is associated with lung function and airflow limitation in the general population remains unknown.

We measured CC16 in serum samples of 851 participants (mean age 41 yrs; 51% women) of 3 Spanish ECRHS centres using an immunoassay. Lung function parameters (FEV1% and FVC% predicted and FEV1/FVC), airflow limitation (AL) defined by Gold criteria (FEV1/FVC<0.70) were considered. All the analyses were adjusted for center, sex, age, smoking, pack-years, body mass index (BMI), and height. Mean CC16 level was 5.8 (sd=2.9), ranging from 0.4 to 19  $\mu$ g/l. FEV1% predicted and FEV1/FVC increased with increasing CC16 levels.

Lung function (dependent var, n=851)	Adjusted* ß (95% CI)	р
FEV1, % pred	1.85 (0.87, 2.83)	< 0.001
FVC, % pred	0.83 (-0.03, 1.70)	0.06
FEV1/FVC	0.77 (0.30, 1.23)	0.001

\*Estimates from linear regression models, adjusted for centre, age, BMI, smoke, pack-years (sex and height for FEV1/FVC).

This association was stronger in asthmatics (2.6% increase (95% CI 0.6-4.5) in FEV1/FVC) as compared to non-asthmatics (0.6%; CI 0.1-1.0) (p for interaction 0.01). CC16 levels were lower in subjects with moderate/severe AL (4.1 µg/l, p from multivariate multinomial regression=0.04), but not in those with mild AL (5.7 µg/l, p=0.9) compared to subjects with no AL (5.9 µg/l). This study shows that reduced CC16 levels are associated with lower lung function and moderate/severe airflow limitation in the general population.

Funded by Spanish FIS ISCIII PS09/01354 and ERS fellowship 123-2011.

#### 1681

### Screening of citizens with suspicion of COPD in eight municipalities in Denmark

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**Background:** Around 430,000 Danes suffer from chronic obstructive pulmonary disease (COPD) with one-third diagnosed today. Danish National Board of Health (NBH) recommends early detection of COPD, focusing on smokers/ex-smokers (or high-risk occupation) above 35 years with >1 respiratory symptom. Municipalities have been suggested to be responsible for early detection. A pilot study found early detection in municipalities to be feasible and reliable in terms of citizens ending up with the final diagnosis of COPD at their GP.

Aim and objective: To investigate the success of screening for COPD in eight Danish municipalities.

**Methods:** Eight municipalities (430,000 inhabitants) offered spirometry to citizens (self-referral) with no previous COPD diagnosis fulfilling the NBH criteria. Citizens with airway obstruction (fixed ratio:  $FEV_1/FVC < 70\%$ ) were requested to visit their GP for diagnosis. Data, including spirometry and smoking habits, were recorded in a secure database.

**Results:** 950 citizens in the risk group of COPD were included (55% females, 58 years, 45% smokers, 30 pack-years, 1-2 lung symptoms, MRC 1.6). Of the sample 34% (323) (22-44% in different municipalities) had indication of airway obstruction. Screening spirometry suggested 86% had mild to moderate COPD. With evidence from the pilot study: 85% detected by municipality screening end up diagnosed with COPD at their GP. This suggests that 29% (275) of the patients in the present sample were COPD patients. After screening 65% of smokers were interested in quitting smoking.

**Conclusions:** Early detection of COPD at the municipality level seems to be worthwhile and successful. Together with the GP-level this might identify undiagnosed COPD patients.

#### 1682

## Is spirometry properly used to diagnose COPD? Results from the population-based BOLD study in Salzburg, Austria

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**Background & objective:** Current guidelines reccommend post-bronchodilator spirometry to confirm a diagnosis of COPD. We investigated whether a selfreported diagnosis of COPD was associated with prior spirometry and, whether a correct diagnosis of COPD was more likely when spirometry was reported. **Methods:** We used data from the population-based Austrian BOLD study. Participants were aged  ${>}40$  years, and completed the BOLD questionnaire and post-bronchodilator spirometry.

Reported COPD diagnosis and reported prior lung function test were based on questionnaire. Non-reversible airways obstruction (AO) was defined as post-bronchodilator FEV1/FVC < 0.7.

A correct diagnosis of COPD was defined, when subjects reported a prior COPD diagnosis and demonstrated non-reversible airways obstruction on postbronchodilator spirometry.

**Results:** 68 (5.4%) of 1258 participants reported a prior physician's diagnosis of COPD. Among those only 25.0% (17/68) reported a lung function test within the past 12 months, and 67.6% (46/68) at any time in the past. The likelihood for a correct COPD GOLD stage I+ diagnosis was similar among subjects reporting (likelihood ratio 2.07 [95% CI; 0.89 – 5.50 C.I.]) and subjects not reporting (likelihood ratio 2.78 [95% CI; 1.58 – 4.87]) a lung function during the last 12 months. Similar likelihood ratio were seen when GOLD stage II+ was investigated and, when lung function was reported at any time in the past.

**Conclusion:** One third of subjects with a reported diagnosis of COPD never had a lung function test. When spirometry was reported, this did not increase the likelihood for a correct COPD diagnosis.

#### 1683

### Inhaled corticosteroids and the risk of pneumonia in Medicare patients with COPD

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**Background:** A growing number of studies have found a positive association between the use of inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD) and the risk of pneumonia.

**Objective:** To determine the relationship between ICS use and risk of pneumonia in the Medicare population with COPD.

Methods: We performed a nested case control analysis to study the relationship between ICS use and risk of pneumonia in a cohort of Medicare Advantage members with COPD. We designated a case to be a member's first inpatient or outpatient episode of pneumonia. Cases were matched to controls of the same age and sex who entered the COPD cohort at the same time but had not yet contracted pneumonia by the case's event date. We estimated the association between ICS use and pneumonia using logistic regression analysis. Adjusted models controlled for age, sex, race, use of other COPD medication classes, markers of COPD severity, receipt of the pneumococcal vaccine, and comorbidities.

**Results:** Out of a COPD cohort of 83,455 members, we identified 13,778 episodes of pneumonia, which were matched to 36,767 controls. Adjusting for covariates, we found that having used any ICS during the past year is associated with an increased risk of a pneumonia episode (OR 1.11, 95% CI: 1.05-1.18). In alternative specifications, we found the risk of pneumonia is highest for current ICS users (OR 1.26, 95% CI: 1.16-1.36) and current high-dose users (OR 1.55, 95% CI: 1.25-1.92), compared to non-users.

**Conclusion:** Our study confirms the finding of previous studies that ICS use – especially current use and high-dose use – is associated with an increased risk of pneumonia.