P1755

Development and validation of a new comorbidity index for COPD
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Comorbidities influence outcome in COPD, but their role remains poorly described. We studied the impact on survival of COPD related comorbidities and developed a COPD specific comorbidity (COTE) index. We also compared COTE with the Charlson Comorbidity Index (CCI) and BODE.

Methods: We followed 1664 COPD subjects for over 4 years. Systematically, 80 possible comorbidities were recorded including conditions listed in CCI. In a randomly selected 2/3 of the cohort we calculated their prevalence. Using Cox proportional hazard, 6 of these comorbidities were independently associated with mortality. We then assigned points to the 6 comorbidities and constructed the COTE index based on likelihood ratios for death.

Comorbidities predictive of mortality

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>HR (95% CI)</th>
<th>COTE points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Localized</td>
<td>1.26 (1.05, 1.51)</td>
<td>2</td>
</tr>
<tr>
<td>Cancer Metastatic</td>
<td>1.20 (1.00, 1.43)</td>
<td>6</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>3.05 (1.20-6.28)</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>2.16 (1.67-2.52)</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>1.60 (1.08-2.28)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Fibrosis</td>
<td>1.55 (1.18-2.01)</td>
<td></td>
</tr>
<tr>
<td>A Fibillation</td>
<td>1.42 (1.15-1.75)</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>1.38 (1.12-1.69)</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1.60 (1.02-2.39)</td>
<td></td>
</tr>
</tbody>
</table>

The COTE index was then validated in the rest (1/3) of the cohort. Finally, we compared the value of COTE,Charlson and BODE index to predict mortality in the whole population.

Results: 23 of 80 comorbidities differed in prevalence between survivors and non-survivors. The COTE index was superior to Charlson in mortality prediction: HR (95%CI) of [1.22 (1.17,1.27, p<0.001) vs 1.03 (0.99,1.07, p =0.126)] and complementary to BODE [1.32 (1.28,1.36, p<0.001)].

Conclusion: Comorbidities are prevalent in COPD and a subset of them influences survival. The COTE is simpler and more accurate than the Charlson index to predict survival. The COTE also adds independent predictive power to the BODE index.

An association between COPD and subclinical atherosclerosis that persisted after adjusting for cardiovascular risk factors has been reported. This may explain the excess cardiovascular mortality seen in patients with COPD.

Objective: To investigate the association between lung function and subclinical atherosclerosis in a population of obese adults with a normal lung function.

Methods: This is a cross-sectional analysis of the NEO (Netherlands Epidemiology of Obesity) study, a cohort of adults aged 45 to 65 years with a Body Mass Index (BMI) <27 kg/m². The association between FEV1 and subclinical atherosclerosis (mean maximal common carotid intima-media thickness [cIMT]) measured by ultrasound was assessed using linear regression.

Results: 1115 adults were included with a mean (25th-75th percentiles) age of 56 (51-61) y, BMI of 31 (28-32) kg/m², FEV1 of 104% (94-113) and 48.7% men. One percent FEV1% increase was associated with 0.001 mm (95% CI =0.001, -0.002) decrease in mean maximal cIMT.

After adjustment for age, sex, pack years and BMI the β was 0.001 (95%CI =0.000, 0.000).

Conclusion: The association between lung function and subclinical atherosclerosis in obese subjects with a normal lung function is weak and a great part of the initial association is explained by confounders. The small association is probably due to residual confounding.
**P1758**

**Fatigue in COPD and the impact of heart disease comorbidity:**

Aim: To describe fatigue in COPD by disease severity according to GOLD, and the impact of self-reported heart disease.

Methods: The Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale was used to assess fatigue; lower scores represent worse fatigue (0-52).

Results: Median FACIT-F score was 44.0 in COPD subjects, significantly lower than those without heart disease at all severities of COPD (non-COPD: 42.0 vs 47.0, p<0.001, stage I: 40.5 vs 48.0, p=0.008 and stage III-IV: 30.5 vs 38.5, p=0.051).

Conclusion: Fatigue increases with GOLD-defined disease severity, but the score is not significantly different from non-COPD until stage II. Heart disease increases fatigue in both COPD and non-COPD.

**P1759**

**Reduced lung function is an independent risk factor for the development of impaired glucose tolerance?**

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Objectives: Whether reduced pulmonary function is a risk factor for the development of impaired glucose tolerance (IGT) has yet to be determined. The aim of the present study is to obtain more information on this point in Japanese males.

Methods: First, 973 men showing normal lung function without respiratory disease were recruited in cross-sectional research. All the subjects were divided into quartiles according to baseline%FVC,%FEV1, and FEV1,% and analyzed the ratio of IGT and DM. Next, 511 men showing normal pattern in 75g OGTT were recruited in longitudinal research. The subjects were divided into%FVC,%FEV1, and FEV1,% quartiles, we compared the cumulative incidence rates of IGT among the four groups, and analyzed the risk factors for the development of IGT.

Results: In the cross-sectional research, the rates of IGT and DM for each quartile at first examination were significantly associated with lower%FVC and%FEV1 quartile, but not significantly with lower FEV1,% quartile. During the mean follow-up period of 28.4±6.0 months, 89 (17%) among 511 men showed IGT. The cumulative incident rates of IGT for each quartile were significantly higher in lower%FVC and%FEV1 group, but not significantly with lower FEV1,% quartile. In a Cox proportional hazards model, lower FEV1,% quartile was an independent risk for development of IGT adjust for age, BMI, systolic BP, total cholesterol, CRP, and pack-year smoking.

Conclusions: Not reduced%FEV1, and FEV1,% but reduced%FVC is an independent risk factor for the development of IGT in Japanese males.

**P1760**

**Lung function, bronchial hyperresponsiveness (BHR) and metabolic risk factors in adults: Preliminary results from the gene environment interaction in respiratory disease (GEIRD) survey**

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Background: Lung function, bronchial hyperresponsiveness (BHR) and metabolic risk factors are strongly associated with cardiovascular diseases, mortality, and is associated with insulin resistance and type 2 diabetes mellitus. It is well known that a common mechanism, such as insulin resistance and obesity, underlies metabolic syndrome (MS).

Our aim was to assess the association between lung function and MS in the GEIRD study, a nested multi-case control survey, in Verona, Italy. The study population included 1117 subjects (aged 20-66 years) who underwent spirometry (n=1113) and methacholine challenge (n=472). MS was defined according to the presence of 3 or more of the following factors: blood pressure of 130/85 mmHg or higher, abdominal obesity (waist girth: men>=102, women>=88cm), self reported dyslipidemia, self reported diabetes. We studied the association of FEV1, FVC (% predicted), FEV1/FVC (%), and BHR (as defined in a PD20<15mg/ml) with MS and each of its components (using multiple linear or logistic regression adjusted for age, sex, height, smoking habits and case-control status).

MS was associated with reduced FEV1 predicted (b=-4.3, 95%CI:-8.8,0.2) and not with FEV1/FVC (%)(b=0.2,95%CI:-1.6,1.2). A negative but not statistically significant association between MS and FVC% predicted (b=-2.3, 95%CI:-8.8,0.2) was found. A positive association emerged between MS and BHR (OR=8.7, 95%CI: 2.3-33.8). Among MS components, only abdominal obesity was related with a reduced FVC% predicted (b=-3.5, 95%CI:-6.0,-0.0).

Our data indicate the low FEV1% predicted and BHR are associated with MS. The results of the present analysis deserves further investigation.

**P1761**

**Axiological analysis of the association between lung function and metabolic syndrome (MS) in asthma and respiratory disease (GEIRD) survey**

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Lung function, bronchial hyperresponsiveness (BHR) was assessed in 933 subjects of the GEIRD study according to the presence of 3 or more of the following factors: blood pressure of 130/85 mmHg or higher, abdominal obesity (waist girth: men>=102, women>=88cm), self reported dyslipidemia, self reported diabetes. We studied the association of FEV1, FVC (% predicted), FEV1/FVC (%), and BHR (as defined in a PD20<15mg/ml) with MS and each of its components (using multiple linear or logistic regression adjusted for age, sex, height, smoking habits and case-control status).

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Our data indicate the low FEV1% predicted and BHR are associated with MS. The results of the present analysis deserves further investigation.
Asthma and caries: A systematic review and meta-analysis

P1763

Asthma and caries: A systematic review and meta-analysis
Maritta S. Jaakkola1, Salla Alavaikko2, Leo Tjaderhane 3, Jouni J.K. Jaakkola 2.

Objective: We conducted a systematic review and meta-analysis to synthesize the evidence on the relation between asthma and caries.

Methods: An Ovid Medline database search was performed from 1950 through May 2010 using the MeSH terms "asthma" and "caries". Summary effect estimates were calculated with fixed- and random-effects models and determinants of heterogeneity were studied in meta-regression analysis.

Results: The meta-analysis was based on 11 articles providing effect estimates of asthma on primary dentition and 14 articles on permanent dentition. The summary effect estimates of the relation between asthma and caries from the random-effects model were 2.73 (95% CI 1.61, 4.64) and 2.04 (95% CI 1.41, 2.89), respectively.

Conclusion: LDS for FEV₁ increases with the number of asthma symptoms, but in non-atopic females this association is weaker than in atopic females and in men. It remains unclear whether this is due to higher perception of asthma symptoms among non-atopic females.

P1764

Are systemic inflammatory markers predictive of loss of lean body mass in COPD patients?

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Background: Previous studies suggest a relationship between systemic inflammation and body composition in COPD. We examined the relationships between four plasma inflammatory markers, C-Reactive Protein (CRP), Tumor Necrosis Factor (TNFα), and interleukins IL-1 and IL-6, and body composition (fat free mass index (FFMI, kg/m²)) and fat mass index (FMI, kg/m²) in 409 stable COPD patients (aged 40-75, GOLD categories II-IV, 249 male) from the Bergen COPD Cohort Study in Western Norway.

Methods: Levels of the four plasma markers were determined by enzymeimmunoassays (ELAs) from samples taken at baseline, and after one and two years of follow-up. FFMI and FMI were measured by bioelectrical impedance at baseline, and after one and two years of follow-up. CRP was significantly associated with FMI at baseline, where mean (SD) FMI in the three CRP categories 0-1 ug/mL, 1-4 ug/mL, and 4+ ug/mL was 8.1 (2.4), 10.8 (4.3), and 12.5 (5.5) in men and 6.6 (1.7), 7.4 (2.7), and 8.4 (3.0) respectively. TNFα, IL-1, and IL-6 showed no association with baseline FMI.

Results: Of the four systemic inflammatory markers CRP, TNF, IL-1, IL-6; CRP only was related to body composition (FMI, not FFMI) at baseline. No marker predicted change in FFMI or FMI.

Prediction of SpO₂ ≤ 95% in a cross-sectional population based survey
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Background: Pulse oximetry has become an important tool in evaluating, and monitoring pulmonary diseases. There is limited knowledge on distribution of SpO₂ values in a screened population.

Aims and objectives: We wanted to determine independent predictors of low pulse oximetry values in a screened population.

Methods: A cross-sectional population based survey was performed in the city of Tromsø, Norway, in 2007-2008. Valid spirometry and pulse oximetry (SpO₂) were performed in 6320 participants aged 38-87 years (57% women). The examination included questionnaires and readings for hemoglobin, C-reactive protein (CRP), pulse, weight and height. We considered resting oxygen saturation ≤ 95% as an abnormal value. Predictors of SpO₂ ≤ 95% with a statistical significance of p<0.05 were entered into a logistic regression model. In the final model we included predictors with p≤0.05.

Results: We found SpO₂ ≤ 95% in 400 participants (6.3%) and SpO₂ ≤ 92 in 30 (0.5%). The strongest predictors in the logistic regression (p<0.001) were increased BMI, reduced FEV₁% predicted, and increased age, hemoglobin and CRP.
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Short-term variation in air pollution triggers acute reaction after lung transplantation

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Epidemiological studies demonstrated that fine particulate air pollution (PM) can trigger adverse health outcomes. Recently, we demonstrated that chronic exposure to air pollution is associated with increased risk of chronic rejection and mortality after lung transplantation. In the present study, we investigated whether short-term elevations in ambient PM10 increased the risk of acute rejection after lung transplantation.

All transbronchial biopsies from a routine follow-up of 355 transplanted patients at the University Hospital Leuven were included. Acute perivascular and peribronchial rejection was scored and BAL neutrophils and serum CRP were assessed. We used land use data to calculate the background level of PM10 for each participant’s home address using a kriging interpolation method. We estimated BAL neutrophils, serum CRP and the risk of acute rejection in relation with outdoor PM10 concentrations on the day of tissue sampling and up to five days before. The model was adjusted for covariates such as age, sex, post-operative day (POD) and daily temperature.

The odds of acute rejection increased by 30% (95% CI 4.6-11.6%) for each 10 μg/m³ increment in ambient PM10 concentration three days before the day of biopsy (lag day 2). Log-transformed neutrophils and serum CRP were significantly related to PM10 as well. For each 10 μg/m³ increment in ambient PM10 concentration on lag day 2, BAL neutrophils increased by a factor 1.09 (95%CI 1.01-1.18) and serum CRP increased by a factor 1.10 (95%CI 1.02-1.18). We showed that short-term ambient air pollution acts as a trigger of acute rejection after lung transplantation, probably mediated by a pro-inflammatory response.

P1768

Health related quality of life and its effect on lung function

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Background: SF-12 is a validated questionnaire for measuring patient-reported functional health and well-being. There is a paucity of knowledge on whether the physical component scale, PCS, part of the SF-12, could predict lung function longitudinally.

Methods: In the Hordaland County Cohort Study, 1527 subjects, 52% men, aged 26-82 years at baseline performed post bronchodilator spirometry in 1996-97 and in 2003-05. SF-12 was used as measurement of health related quality of life and PCS score was main predictor. We performed linear regression analyses of PCS and post BD FEV1 in 2003-05, and adjusted for sex, age, height, educational level, occupational exposure, smoking habits, packyears and baseline FEV1.

Results: Mean FEV1 in 2003-2005 was 3.11L (SD 0.9). Mean baseline FEV1 was 3.46L (SD 0.9), and mean PCS score of the SF 12 was 50.4 (SD 8.4). Coefficients (95% CI) for significant predictors in the multivariate model were; -0.03 (-0.03, -0.027) for age, 0.089 (0.02, 0.16) for ex smokers vs never smokers, 0.025 (0.05, 0.11) for current smokers vs never smokers, 0.43 (0.36, 0.50) for men vs women, 0.14 (0.07, 0.21) for intermediate vs lower education, 0.14 (0.06, 0.23) for higher vs lower education, -0.01 (-0.02, -0.01) for packyears and 0.008 (0.005, 0.011) for PCS score. PCS was a significant risk factor for lower FEV1, but the significance did not remain when adjusting for baseline FEV1.

Conclusion: The physical sum score of the SF-12 predicts lower lung function at follow up. The effect did not remain after adjusting for baseline lung function. However, this result shows that in absence of spirometry, SF-12 may serve as a simple and effective tool to identify persons at risk of COPD.

P1769

Health-related quality of life in subjects with respiratory diseases: Preliminary results from the GEIRD study

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Health-related quality of life (HRQL) is an important outcome measure in patients with respiratory diseases. This study aims at investigating HRQL in different respiratory disorders.

Controls and cases of COPD, current asthma, past asthma, non-allergic rhinitis, allergic rhinitis and “Other Respiratory Conditions” (ORC) (n= 321, 224, 125, 79, 130, and 148 respectively) were recruited in the frame of the nested multi-case control Genes Environment Interactions in Respiratory Diseases (GEIRD) study. HRQL was measured using SF-36 questionnaire. Medians of physical and mental component scores (PCS and MCS respectively) were estimated by quantile regression models adjusting for potential confounders. PCS and MCS median scores of controls were respectively 54.8 (95% CI 54.2-55.3) and 52.0 (95% CI 50.9-53.2) and were significantly different from all phenotypes except rhinitis and past asthma cases; in particular, PCS median score ranged from 49.4 (95% CI 47.6-51.2) for COPD cases to 53.0 (95% CI 52.2-53.9) for current asthma cases and MCS score from 47.9 (95% CI 44.3-51.5) for COPD cases to 49.9 (95% CI 48.6-51.2) for current asthma cases (Table 1).

Table 1: Adjusted median (95% CI) and statistical significance of PCS and MCS score in respiratory disease cases compared to controls

<table>
<thead>
<tr>
<th>Disease</th>
<th>PCS Median (95% CI)</th>
<th>p-value (vs controls)</th>
<th>MCS Median (95% CI)</th>
<th>p-value (vs controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>54.8 (54.2-55.3)</td>
<td></td>
<td>52.0 (50.9-53.2)</td>
<td></td>
</tr>
<tr>
<td>Non-allergic rhinitis</td>
<td>3.05 (3.00-3.10)</td>
<td>0.045</td>
<td>3.05 (3.00-3.10)</td>
<td>0.061</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>5.03 (4.95-5.11)</td>
<td>0.140</td>
<td>5.10 (4.95-5.29)</td>
<td>0.439</td>
</tr>
<tr>
<td>Other respiratory symptoms</td>
<td>3.05 (3.00-3.10)</td>
<td>0.0001</td>
<td>3.05 (3.00-3.10)</td>
<td>0.007</td>
</tr>
<tr>
<td>Post allergia</td>
<td>5.03 (4.95-5.11)</td>
<td>0.003</td>
<td>5.03 (4.95-5.11)</td>
<td>0.007</td>
</tr>
<tr>
<td>Current asthma</td>
<td>3.05 (3.00-3.10)</td>
<td>0.0001</td>
<td>3.05 (3.00-3.10)</td>
<td>0.007</td>
</tr>
<tr>
<td>COPD</td>
<td>49.1 (47.6-50.6)</td>
<td>0.0001</td>
<td>49.1 (47.6-50.6)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

To our knowledge, this is the first study to perform a direct and simultaneous comparison of quality of life in several respiratory disorders. Subjects who suffer from COPD, current asthma and ORC had poorer HRQL than controls.

P1770

The costs of adult asthma in Denmark

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Introduction and background: Asthma is often associated with health deterioration and reduced working capacity resulting in health-related and productivity costs. Population-based studies on the economic burden of asthma on society and individuals are limited.

Aims and objectives: To estimate the extra costs to society due to adult asthma in Denmark.

Methods: In a population-based cross-sectional asthma survey, 6,950 (70%) individuals aged 20-44 completed an extended ECRIHS screening questionnaire. Subjects with current asthma were identified by questions on currently taking any asthma medication, having had an attack of asthma or doctor diagnosed asthma plus asthma-like symptoms during the last 12 months. Employment status was defined by current or last held job. The analyses were based on data on individual level extracted from national registers. The direct (health care) costs were estimated by means of multiple regression models. The productivity costs due to absenteeism were estimated using the human capital approach.

Results: The prevalence of current asthma was 7.7% in males and 10.6% in females. The total average annual extra costs per asthmatic subject in comparison with non-asthmatic subjects were € 2,081 and € 1,922 for males and females, respectively. Productivity costs were the major component accounting for 85% in males and 70% in females. Hospital care expenditures accounted for the greatest percentage of the direct costs in both gender. We extrapolated the average annual costs associated with current asthma to € 352 million in the entire Danish population aged 20-44.

Conclusions: The economic burden of asthma in Denmark is substantial and primarily due to productivity costs accounting for three quarters of the total costs.
P1771
Socioeconomic position and use of drugs in chronic obstructive pulmonary disease (COPD): A population-based cohort study in Rome, Italy
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Introduction: Little is known about “real-life” use of evidence-based recommended drugs in COPD. We tested the hypothesis that drug prescription vary according to socioeconomic position.

Methods: All people (35-64 years old) discharged in 2006-07 with a diagnosis of COPD exacerbation, resident in Rome (2.700.000 inhabitants) were selected from Hospital Information System (standardized ICD-9-CM coding). Drugs were retrieved from the regional drug prescription registry based on ATC codes (12-months follow-up after discharge). An area-based (census block) socioeconomic position (SEP) index was used for each patient (quintiles: I well off, V disadvantaged). Logistic regression was performed to take into account gender, age and comorbidities.

Results: 779 individuals were studied (mean age 58.1, 58% men). 55% were in the lower SEP levels. Disadvantaged people were more likely to have respiratory failure, diabetes, ischemic heart disease and heart failure. Proportions of people with at least two prescriptions during 12 months after discharge were: long-acting inhalants 70%, short-term inhalants 45%, xanthines 23%. No statistically difference was observed across SEP groups for long-acting (OR= 1.20, 95% IC=0.67-2.16) or short-acting inhalants (OR=1.55, 95% IC= 0.90-2.68), while xanthines were more frequently prescribed for low SEP people (SEP-V vs. SEP-I OR=2.17, 95% IC=1.03-4.57; p trend < 0.05).

Conclusions: Disadvantaged COPD patients seem more exposed to xanthines whose effectiveness is less clear in comparison to inhalant drugs. We highlight the need for improving outpatient care programmes to reduce disparity in health.

P1772
Examination of multiple emergency inpatient admissions for asthma in England from hospital episode statistics (HES) 2005-2009
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Objective: We described emergency asthma inpatient admissions in England from 2005-2009 and characterised factors associated with multiple asthma admissions.

Methods: This was a GSK-funded retrospective analysis (WEUSRTP5083) using HES population data from England (©) 2010, re-used with permission). Patients with at least one emergency hospital admission where asthma was the primary diagnosis (ICD-10 J45, J46) on the first consultant episode within an admission were included. Using a backward elimination strategy, time to event modeling was employed to identify factors in the first asthma hospital record (length of stay [LOS], co-morbidities by ICD-10 chapter, gender) associated with a second asthma admission (occurring >5 days from first).

Results: There were 249,206 emergency admissions for asthma among 176,323 patients during the 4-year period. One-fifth of patients experienced >1 admission for asthma, where multiple admissions decreased with increasing age (27% age <18; 16% age 45+). Median time to second admission was 6-7 months for each age group (<18, 18-44, 45+). Among adults, factors significantly associated with the second asthma hospital admission (p<0.05) included LOS >4 days (first admission), being female and co-morbidities (endocrine/metabolic, mental/behavioral, nervous system, circulatory).

Conclusions: The burden of asthma exacerbation requiring hospitalisation in England is substantial; one-fifth of patients admitted for asthma experienced multiple admissions (2005-2009). Co-morbidities were associated with a second admission for asthma in adults, suggesting that other health conditions may contribute to asthma morbidity.