P3385
Self-reported race and ethnicity affect FeNO values in healthy individuals
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Background: Race and ethnicity are known factors of variation in pulmonary function. We aim to determine if self-identified race/ethnicity affect the values of exhaled nitric oxide (FeNO) in healthy and asthmatic individuals in a population setting.

Methods: We analyzed the validated FeNO measurements (NIOX MINO) recorded in the National Health and Nutrition Examination Survey 2007-10 (n=13,275; age 6-79 years). Race/ethnicity is coded as Mexican American (20%), Other Hispanic (11%), Non-Hispanic White (43%), Non-Hispanic Black (20%) and Other Race - Inc. Multi-Racial (5%). Adjustments were made using multiple-linear regression models.

Results: Non-Hispanic Whites have the lowest FeNO values (mean 15.8 ppb, 95%CI 15.4; 16.1) and Other Race - Including Multi-Racial the highest (20.0 ppb (18.6; 21.4)). Race and ethnicity significantly affect FeNO values even after adjusting for age, gender, BMI and reported hay fever in non-asthmatic subjects (B=0.30, p<0.01), but not in individuals with self-reported asthma (B=0.09, p=0.83). However, the mean difference between race/ethnicity categories was reduced after excluding subjects with hay fever.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Mean FeNO (ppb)</th>
<th>Mean difference to reference category (Non-Hispanic white)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td>18.2</td>
<td>14.8</td>
</tr>
<tr>
<td>Mexican American</td>
<td>18.5</td>
<td>16.5</td>
</tr>
<tr>
<td>Other Hispanic</td>
<td>20.9</td>
<td>17.1</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>22.7</td>
<td>17.9</td>
</tr>
<tr>
<td>Other Race - Inc. Multi-Racial</td>
<td>25.1</td>
<td>18.5</td>
</tr>
</tbody>
</table>

Conclusion: Race and ethnicity are significant factors for FeNO in healthy individuals. Hay fever seems to play an important role in the mean difference between race/ethnicity categories. An objective measurement of atopy is probably needed to clarify this relationship.

P3386
Volatile organic compounds exposure and respiratory function in preschoolers from mothers participated in a randomized clinical trial during pregnancy
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Background: Early exposure to air pollution is crucial in the development of the immune response and monitoring of respiratory function is important in the diagnostic and management of respiratory diseases.

Objective: To determine the impact of air pollution on respiratory function in preschool-aged Mexican children and evaluate the interaction between supplementation with omega-3 fatty acids and air pollution exposure in this population.

Methods: The forced oscillation technique (Respiratory resistance (Rrs 6, 8Hz) and reactance (Xrs 6, 8Hz) using Cosmed Quark 12m, Italy) were used to measure respiratory function in 585 children (292 males) 3-5 years old once as part of the Omega-3 Supplementation Study in Mexico. Measurements were performed according to ATS/ERS standards. For environmental exposure, we conducted local monitoring of Volatile Organic Compounds air concentrations (Benzene, toluene, xilene, heptanes and hexane) in diferent parts of the city and the association between respiratory function and air pollution exposure were analyzed using lineal regression models.

Results: The lung function did not differ significantly between groups of supplementation. The volatile organic compounds (BTX, heptanes, hexane) air concentrations were significantly inverse related to respiratory function (Rrs 6, 8Hz and Xrs 6, 8Hz) (p<0.05). We did not observe a potential interaction between treatment groups and air pollution exposure.
Conclusions: Exposure to volatile organic compounds air concentrations in the general environment decrease the respiratory function in Mexican Preschoolers.

P3387 Effects of short-term exposure to air pollution on the levels of exhaled nitric oxide among adults – Results from the ADONIX study in Gothenburg, Sweden

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The fraction of exhaled nitric oxide (FENO) is a marker of airway inflammation, used clinically to diagnose and monitor asthma. FENO can be measured at different exhalation flows to monitor different parts of the airways. Air pollution is known to cause adverse health effects, and inflammation has been suggested as a main pathway in this study we examined whether short-term exposure to ozone (O₃), nitric oxides (NOₓ) or particulate matter less than 10 μm (PM₁₀) are related to increased levels of FENO.

From 2001 through 2008, 5841 randomly selected adults aged 25-75 years in Gothenburg, Sweden, were clinically investigated. FENO was measurement at three different flow-rates, and in this study we included FENO measured at the highest (230ml/s) and lowest (50ml/s) flows. Air pollution data were collected from an urban and background station, and we studied the effects of the 3,24 and 120 hour averages preceding the clinical examination. Log-linear regression was applied to estimate the associations of air pollution on FENO.

One inter-quartile range (IQR) increase of ozone O₃, NOₓ or particulate matter less than 10 μm (PM₁₀) was associated with a 5.1% (95% CI 1.7-8.5) increase in FENO₂₇₀ and 3.6% (95% CI 0.4-3.4) increase in FENO₉₀. For NOₓ, a small effect was seen for the 24- and 120-hour average FENO₉₀, whereas no clear effect was seen for PM₁₀. The effect of ozone on FENO₉₀ and FENO₂₇₀ was significantly lower among asthmatic subjects; however the effect on asthmatics could not be separated from null.

In summary, short-term exposure to O₃ gives rise to a small increase in FENO₂₇₀ and FENO₉₀ measures of inflammation in the distal and proximal airways.

P3388 Estimated short-term effects of air pollutants on daily respiratory emergency department visits in three Swedish cities

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Large number of epidemiological studies has found associations between daily changes in ambient particulate air pollution and different kinds of health outcomes. Our aim was to estimate the short-term effects of different air pollutants on daily emergency department visits for respiratory diagnoses in three largest cities in Sweden to find the effects in different environments. Data on daily number of visits from 2001 through 2008 in Stockholm, Gothenburg and Malmö were collected from the national Patient Register and data on daily air pollution concentrations (PM in urban and background station, and we studied the effects of the 3, 24 and 120 hour averages preceding the clinical examination. Log-linear regression was applied to estimate the associations of air pollution on FENO.

To evaluate the association between ambient air pollution (NOₓ, O₃, PM₁₀, H₂S) and H₂S from The City of Reykjavík, and The Environment Agency of Iceland. A case-crossover design was used and the study period was January 1st 2005 to December 31st 2009.

Results: Exposure to air pollution was associated with the dispensing of drugs for cardiovascular disease (C01DA). For each 10 μg/m³ increase in NOₓ concentrations the dispensing of glyceril trinitrates (sub-group C01DA02) increased by 11.6% (at lag 0) and 7.1% (at lag 1). Similarly, an increase by 10 μg/m³ of O₃ concentration was associated with 9.0% (at lag 0) and 7.2% (at lag 1) increase in glyceril trinitrate dispersions.

Conclusion: The findings indicate that increased air pollution levels are associated with increased dispensation of glyceril trinitrate. We caution that this is the first study to examine the association between ambient air pollution and dispensation of drugs for angina pectoris, hence further evidence is needed for definite conclusions of this association. Drug dispensing may potentially be a sensitive indicator of health when estimating the effects of air pollution.

P3391 Occupational air pollutants – More hazardous for respiratory health than smoking? Results from the obstructive lung disease in northern Sweden studies

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Background: Both smoking and occupational air pollutants (OAP) are risk factors for impaired respiratory health. Comparisons of their effects and how they interact are scarce.

Aim: To compare the effects of ever smoking and ever OAP on non-malignant respiratory disorders and to assess their interactions.

Material and methods: In a population-based incidence study of asthmatic and bronchitic disorders in northern Sweden, 5896 subjects answered a postal questionnaire in 1996 and in 2006 (79% of the responders in 1996). Cumulative incidences were calculated. Risk factors were analyzed in multiple logistic regressions adjusted for possible confounders and the results are presented as odds ratios (OR).

Results: Never/ever smoking (S) and never/ever OAP were used as a combined variable with four categories or as dichotomous variables, respectively.

Conclusion: Occupational air pollutants are a risk factor for impaired respiratory health. Comparisons of their effects and how they interact are scarce.

P3395 Air pollution in Reykjavík and dispensation of drugs for angina pectoris

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Introduction: Ambient air pollution is associated with increase in morbidity from heart diseases. Air pollution concentrations in the Reykjavik area are known to exceed official European health limits several times every year.

Objectives: To evaluate the associations between ambient air pollution (NOₓ, O₃, PM₁₀, H₂S) and emergency department visits in three Swedish cities

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Abstract printing supported by Chiesi Visit Chiesi at Stand B2.10

Conclusion: Our results suggest that O₃ has an acute effect on child lung function in Guadeloupe even with value levels inferior to WHO guidelines.
P3392 Urban living is a risk factor for allergic sensitization among adults in northern Sweden

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Aim: To assess prevalence and risk factors for allergic sensitization based on skin prick test (SPT) and specific IgE in adults.

Methods: In 2009 a random sample of 737 adults in ages 20-69 years was invited for examinations including SPT and blood sampling for specific IgE. SPT with ten common airborne allergens were performed in 463 subjects aged 20-60 years. A wheal ≥3 mm was considered as a positive reaction. Blood samples for specific IgE were collected in 692 subjects, and specific IgE was analysed for the same allergens as tested in the SPT. An elevated level of specific IgE was defined as ≥0.35 IU/ml.

Results: In general, the prevalence of allergic sensitization based on SPT and specific IgE, respectively, yielded similar results. The prevalence of any positive SPT was 39% versus 35% for any elevated IgE. p=0.23. The prevalence of sensitization to cat and dog was significantly lower based on IgE compared to SPT, while sensitization to other allergens showed almost identical figures irrespective of method used. The risk factor analyses based on SPT and IgE, respectively, yielded similar results. The prevalence decreased significantly by increasing age. Having a family history of rhinitis (OR 3.1; 95% CI 2.0-4.8 for any positive SPT, OR 2.7; 95% CI 1.8-4.0) and urban living (OR 1.7; 95% CI 1.1-2.7 for any positive SPT and OR 1.5; 95% CI 1.0-2.3) were significant risk factors for allergic sensitization.

Conclusion: A similar sensitization pattern was observed when assessing the prevalence of allergic sensitization by SPT and specific IgE, respectively. Young age, a family history of allergic rhinitis and urban living were significant risk factors for allergic sensitization among adults.

P3393 Normal antioxidative enzyme activities in several genes are associated with less bronchial hyperresponsiveness (BHR) among young Danes

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Background and aim: BHR might be associated to the oxidative defense. We hypothesize that genotypes coding for normal antioxidative enzyme activity (AEA) influence the occurrence of BHR.

Methods: In a cross sectional study 7,271 subjects aged 20-44 year (73% response rate) were recruited using an asthma screening questionnaire. All subjects with asthma (n = 460) and a 20% random sample (n= 728) were clinically investigated, including a bronchial provocation test, skin prick test (SPT) with 13 aeroallergens, and a blood sample. The bronchial provocation test was available for 956 subjects, and BHR was defined as at least 20% drop in baseline FEV1. Variants in 13 genes including glutathione S-transferases; GSTP1 (Ile105Val, rs1695), GSTT1 (gene copy nr) and 3 glutathione S-transferases; GSTPI (Ile105Val, rs1695), GSTT1 (gene copy nr) and GSTM1 (gene copy nr).

Results: The frequency of BHR was 12.8% in the random sample and 42.6% in the asthma sample. Logistic reg. models showed a neg. association between being BHR and having at least 4 genotypes coding for normal AEA compared to no normal genotype, OR 0.24 (0.06-0.94) adj, for smoking, FEV1, sex, atopy, height2 and SPT-size of HDM. The result were similar after further adjustments for BMI, county and sample (random/case), OR 0.25 (0.06-1.06). ORs for BHR were decreased for 1 – 3 genotypes with normal AEA compared to no normal genotype, but not significantly so and no clear dose-response relations were seen.

Conclusion: This study suggests, that a combined effect of several genotypes including a bronchial provocation test, skin prick test (SPT) and specific IgE in adults.

Alternatively, increasing BMI may lead to an increase in airway oxidative stress and obesity increases the risk for developing new onset asthma in adults and children. Enhaled breath condensate (EBC) collection is a noninvasive method to investigate pulmonary oxidative stress biomarkers.

Methods: We measured exhaled nitrites and nitrites, 8-isoprostanes, pH and oxidized (GSSG) glutathione, to assess alveolar oxidative stress in obese patients (52 asthmatics and 135 non-asthmatics) and 118 nonobese (52 asthmatics and 135 non-asthmatics). EBC was collected over 10 min using a refrigerated condenser according to European Respiratory Society/American Thoracic Society guidelines for recommendations.

Results: We found an increase in the concentrations of GSSG and 8-isoprostanes in both groups of obese patients (both asthmatic and non-asthmatics) compared with nonobese patient (asthmatic and non asthmatic) (p <0.001) and a slight decrease in the pH of EBC in obese patients with asthma compared with the rest (p <0.05). In relation to nitrites and nitrates were statistically lower in obese patients with asthma and without asthma than the total non-obese patients.

Conclusions: Our results suggest that obesity leads to an increase proinflammatory mechanisms that could be associated with increased systemic inflammation and oxidative stress and may affect the status or condition of asthma.

Figure 1. OR for wheeze in relation to age of smoking debut in women and men. Estimated from GAM models.

Conclusions: Exposure to tobacco smoking affects adult respiratory health, with women being more susceptible than men to early smoking debut and amount of pack years.

P3396 Bone mineral density is associated with the risk of non-small cell lung cancer, the HUNT study

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Background: The overall survival in lung cancer is poor. The highest survival has been observed for cancers diagnosed in early stages, so early identification of patients at risk is important. Estrogen receptors have been found in non-small cell lung cancer. This may indicate that estrogen promote carcinogenesis. Estrogen level is associated with bone mineral density (BMD). Hence, BMD might be used as surrogate measure of long term estrogen exposure.

Aim: To investigate whether low BMD is associated with lower risk for lung cancer.

Method: We analyzed data from a cohort study, the Nord-Trøndelag Health Study (HUNT-study) linked to the Norwegian Cancer Registry. 18156 subjects under-
went bone densitometry of the forearm. The results were reported as z-scores and categorized into tertiles. All analyses were stratified by sex. Body mass index (BMI), lung function and smoking were tested as confounders in logistic regression models. BMI and lung function changed the odds ratio less than 10% and were not included in the final model.

**Results:** 72% of the 18156 participants were females. In the low z-score group we found more ever smokers (P < 0.01) but no differences in age and sex distribution between the three z-score groups. In all 194 cases with non-small cell lung cancer were identified. Among these 56% were females, 87% were ever smokers and the mean age was 72.2±11 years.

**In men, low compared to high z-score was associated with a higher risk of lung cancer, OR 3.3 (95% CI: 1.85-5.99) and adjusted for smoking OR 2.93 (95% CI: 1.62-5.36).**

In women no association with BMD was seen.

**Conclusion:** Low bone mineral density is associated with a higher risk of lung cancer, in men, but not in women.

**P3397**

**Individual decline of FEV1 show diversity in COPD**

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**Aim:** To develop methods to gain better understanding of individual development of lung functions in COPD sub-phenotypes.

**Results:** The patients (N=600) have been recruited from two Finnish University Hospitals. Their medical records have been carefully evaluated including spirometry results. A multivariate modeling was used to find differences in factors affecting the inter-individual development of FEV1. To manage the within-patient variation of consecutive measures, simulation methods were used to determine which patients were presenting significant changes in lung function over time. Logistic regression analysis was conducted to determine the characteristics of decliners.

The COPD patients represent all stages of the disease. Mean follow-up time was 5.9 years (range 2-12) and with mean 9.4 spirometries (range 3-36) per patient. Twelve percent of patients were identified as constant decliners. The decliners had a mean rate of decline of -101 (95% CI, -58 to -171) ml/year, whereas residual patients had mean rate of -35 (95% CI. 25 to -88) ml/year. When numerous co-morbidities and clinical characteristics were tested, only mental disorders (OR=1.75) were shown to associate with poor development of FEV1. Patients who had been able to stop smoking and whose diagnosis had been done at early stages (better FEV1 baseline level) of the disease, showed protective effect (OR=0.52 and OR=0.98/% decline). Our preliminary results suggest that COPD patients show diversity in their risk of future FEV1 decline. Development of robust screening protocols at early stages of COPD might be of value in revealing the rapid decliners.

**P3398**

**Age of menarche and risk of asthma: Systematic review and meta-analysis**

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**Aim:** To conduct a systematic review and meta-analysis of the relationship between the age at menarche and risk of asthma.

**Methods:** A prespecified literature search strategy was used to identify all articles directly concerning the relationship between asthma and age at menarche. We were interested in studies with asthma defined as self reported asthma, diagnosed asthma or asthma symptoms in studies defining early menarche as menarche before the age of 12 years of age or younger. Further, we were interested in controlled trials, prospective and retrospective cohort studies, case-control-studies and cross-sectional studies with or without modelling.

**Results:** We identified 34 articles of which 8 matched the inclusion criteria (two cross-sectional studies, three case-control studies, two retrospective studies, and one prospective study) with a total of 18124 patients. All articles were consistent in their results, showing a clear positive relationship between asthma and age at menarche. Estimates from the selected studies showed that the risk of asthma was increased between 1.13 and 2.34 times in girls with early menarche.

**Conclusions:** Early age at menarche is associated with increased risk of asthma. Hormonal, immunological, genetic, and environmental factors may act in a developmental context to explain this relationship.

**P3399**

**HRT, lung function, respiratory symptoms and menopausal status**

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**Background:** The relation of HRT (hormonal replacement therapy) with respiratory symptoms is not understood; women using HRT appear to have more respiratory symptoms but better lung function.

**Methods:** This analysis included 1686 women 45-56 years participating in ECRHS II. Logistic and linear regressions were conducted to investigate the association between HRT and lung function and respiratory symptoms while adjusting for BMI, age, smoking, center and height.

**Results:** Menopausal women using HRT had higher FEV1 (adj diff 70 ml (95%CI=4 to 136)) but no increase in respiratory symptoms (OR=1.00 (0.68 to 1.48)) compared to menopausal women not using HRT. Premenopausal women using HRT had indicated more asthma symptoms (OR=1.65 (0.86 to 3.18)) and indicated lower FVC (adj diff -103 to 161) than premenopausal women not using HRT.

**Conclusions:** The association between HRT and respiratory health was modified by menopausal status. In this population of women in the perimenopause, HRT appeared to be beneficial for respiratory health among menopausal women, but possibly led to adverse respiratory outcomes among those still menstruating. The conflicting evidence in the field might be due to lack of account for menopause status when investigating effects of HRT.

**P3400**

**At onset and persistence of eczema and the subsequent risk of asthma and allergic rhinitis**

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**Background:** Few studies have simultaneously addressed the importance of age at onset and persistence of eczema for the subsequent development of asthma and allergic rhinitis in children.

**Objective:** To examine age of eczema onset and eczema persistence as predictors for childhood asthma and allergic rhinitis at ages 6, 7, and 12 years.

**Methods:** A prospective birth cohort was recruited comprising 620 infants with a family history of allergic diseases. Telephone interviews were conducted 18 times in the first two years of life, annually from age 3 to 7, and at 12 years to document any episodes of current asthma. Current asthma and allergic rhinitis were assessed at ages 6, 7, and 12.

**Results:** Very early-onset (<6 months) persistent eczema was related to current asthma (adjusted OR=6.9, 95%CI 2.4-14.7) and allergic rhinitis (aOR=4.5; 95%CI 1.9-10.9) at age 12 years. Adjustment for asthma and atopic sensitisation had a small but a significant effect on these associations. There was no evidence that early-onset remitting eczema (only present < 2 years) or late-onset eczema (onset > 2 years) were associated with current asthma and allergic rhinitis. These results were consistent with the 6-7 year findings.

**Conclusion:** Eczema which commences very early in life and persists into toddler years is strongly associated with childhood asthma and allergic rhinitis, and is possibly mediated by atopy-allergen sensitisation. However remitting and late-onset eczema do not appear to be related to these outcomes. With effective early intervention, the risk of diseases associated with early-onset eczema might be reduced.
Asthma and obesity are important health issues in industrialized countries and obesity is a risk factor for asthma. Our study was aimed at investigating the effect of body mass index (BMI) on lung function in a large sample of healthy children enrolled in two cross-sectional surveys performed on random samples of children, aged 10-17 years, living in the city of Palermo, Southern Italy. At school, all the subjects completed self-administered questionnaires regarding past and current respiratory symptoms and personal information, and performed spirometry. On a total of 3,200 children, 807 reporting wheeze ever, nocturnal cough, or exercise-induced cough were excluded from the analysis. 2,393 subjects (49% M) were evaluated. Height-adjusted lung function measures were plotted against BMI Z-score for each gender and age class, and slope values were computed by linear regression analysis. Height-adjusted FVC and FEV1 were positively correlated to BMI Z-score in both males and females. Slope values (L/BMI Z-score unit) were 0.057 in males and 0.114 in females for FVC and 0.022 and 0.072 for FEV1, respectively, being significantly steeper among females in each age class. FEV1/FVC ratio was inversely correlated to BMI Z-score with similar slope values for male and females. FEF25-75%/FVC ratio was negatively correlated to BMI Z-score: the slope values were steeper among females in each age group. In conclusion, despite both FVC and FEV1 are positively correlated to BMI, their disproportionate increase as BMI increases could cause a reduction of relative airway size as measured by the FEF25-75%/FVC at higher BMI values. This could, at least in part, contribute to the reported association between overweight-obesity and asthma.