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P994 Alpha1-antitrypsin deficiency in Italy: Analysis of the Italian registry

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Alpha1-antitrypsin Deficiency (AATD) is a rare hereditary disorder with a prevalence of about 1/5000 individuals in Italy. Deficient patients are at a higher risk to develop lung emphysema at an early age and liver cirrhosis. The low prevalence of AATD suggested the establishment of a registry with the aim to learn more details about the natural history and the quality of care of these patients. The Italian Registry of AATD was established in 1993. A total of 312 adult subjects with severe AATD were enrolled, namely 206 PI*ZZ, 48 PI*SZ, 3 PI*SS and 55 patients with, at least, one rare deficient allele (R). The frequency of 17.6% of PI*RR is the highest so far recorded in national registries of AATD. Clinical data have been collected: 253 were index-patients, mainly affected by lung and liver diseases (79% and 10%, respectively), and 55 were enrolled because of kinship with AATD patients. Mean age of enrollment was significantly higher (p=0.03) in index (49.6 \pm 14.4 years) than in non-index (43.5 \pm 14.5 years). The mean interval between the onset of symptoms and the final diagnosis was 8 years for patients with lung diseases, and 13 years for liver diseases. Among index patients, most of them were former-smokers (63%). From 1999, 100 patients underwent augmentation therapy with purified AAT (Prolastin); they were mainly former-smokers (75%) with panlobular emphysema (34%). Interestingly, 10% of patients receiving augmentation therapy were non-index subjects. The data of the registry allow a detailed characterization of the natural course of the disease and the levels of the patient care, and confirm the usefulness of early detection of AATD.

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The polymorphisms of C-reactive protein gene modify the association between central obesity, asthma and lung function in Taiwan

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Background: High-sensitive CRP concentrations and obesity are proposed to cause asthma and impaired lung function, but little has been reported to date on the association between CRP gene and asthma.

Objective: Three tagSNPs polymorphisms for CRP gene were selected from HapMap data, and genotyping by using TaqMan allelic discrimination assay. We studied the association of polymorphisms in CRP genes and their interactions with central obesity on asthma and lung function.

Method: A total of 814 asthmatic adults and controls were recruited in southern Taiwan. All subjects underwent questionnaire interviews, pulmonary function tests and genotyping. We detected three single nucleotide polymorphisms of *CRP* gene, and analyzed gene-obese interaction on the risk of asthma.

Results: We found that BMI and WHR were associated with hs-CRP concentrations. Although *CRP* SNPs alone and haplotypes were not associated with asthma risk, the association of asthma with central obesity, measured as the waist-to-hip ratio (WHR), seemed to be stronger in subjects who carries A/T heterozygote (p<0.05) for *CRP* SNP rs1417938 than in subjects who had the T/T genotypes. We did not find interaction effect on asthma between BMI and *CRP* SNPs.

Conclusion: The current results suggested that central obesity play an important role in asthma pathogenesis, and the effect was modified significantly by the *CRP* SNP rs1417938 in Taiwanese population.

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DNA and fatty acids oxidative stress in respiratory diseases: Preliminary results from the GEIRD study

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Among the determinants of respiratory diseases, emphasis has recently been placed on oxidative stress, but its role on the occurrence of the respiratory diseases is only partially known. The aim of this study is to investigate the oxidative stress levels in people with respiratory diseases and controls.

8-OHdG, a DNA oxidation product, and 8-isoprostane, a lipid oxidation product, were measured in spot-urine samples collected in the frame of Genes Environment Interactions in Respiratory Diseases (GEIRD) study, a nested multi-case control survey. Controls and cases of COPD, current asthma, past asthma, non-allergic rhinitis, allergic rhinitis and other respiratory conditions (n= 239, 19, 122, 70, 58, 45 and 76 respectively) were analysed to test differences in levels of urinary creatinine-corrected 8-OHdG and 8-isoprostane, using quantile regression models adjusting for age, gender, smoking habits, BMI and other potential confounders. Adjusted 8-OHdG median concentrations were significantly higher in allergic

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European screening for α_1 -antitrypsin deficiency in subjects with lung disease Timm Greulich¹, Hristo Metev², Bernard Budimir³, Gyorgy Losonczy⁴ Ludmilla Borsa⁵, Dalcius Vaicius⁶, Ivan Solovic⁷, Matjaz Flezar⁸, Marcela Vigdorovici⁹, Tatyana Martynenko¹⁰, Tetyana Pertseva¹¹, Sandra Camprubí¹². ¹Department of Internal Medicine, Division for Pulmonary Disease, Hospital of the University of Marburg, Marburg, Germany, ²Department of Pulmonology, District Dispensary for Pulmonary-Phthisis Diseases with Inpatient Hospital, Russe, Bulgaria; ³Department of Pulmonology, University Hospital for Lung Diseases Jordanovac, Zagreb, Croatia; ⁴Department of Pulmonology, Semmelweis University, Budapest, Hungary; ⁵Doctors' BINI, Doctors' BINI, Ventpils, Latvia; ⁶Diagnostic Department of Internal Medicine, Vilnius University Hospital Santariskiu Clinics, Vilnius, Lithuania; ⁷Department of Pulmonology and Physiology, National Institute for Tuberculosis, Lung Diseases and Thoracic Surgery, Hagy, Slovakia (Slovak Republic); ⁸Pulmonary Function Laboratory, University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia; ⁹Tuberculosis Unit, Clinical Hospital of Pneumology Oradea, Oradea, Romania; ¹⁰Department of Pulmonology, Municipal Medical Institution City Hospital #5, Barnaul, Russian Federation; ¹¹Department of Hospital Therapy, Dnepropetrovsk State Medical Academy, Dnepropetrovsk, Ukraine; ¹²Clinical Trials and Pharmacovigilance Department, Instituto Grifols, S.A., Barcelona, Spain

Introduction: Alpha-1 antitrypsin deficiency (AATD) is a common hereditary disorder that predisposes to early-onset pulmonary emphysema. Despite its prevalence, AATD is highly underdiagnosed. According to published guidelines for AATD, a diagnostic testing is greatly recommended in symptomatic adults with emphysema, COPD, or asthma with airflow obstruction incompletely reversible after aggressive bronchodilator treatment.

Aim: To investigate AATD presence in ten European countries targeting a cohort of symptomatic subjects.

Methods: Blood samples from adult subjects with lung disease were collected as dried blood spot (DBS). Detection testing algorithm consisted of 3 steps: first, all DBS specimens were analysed for α_1 -antitrypsin (AAT) levels by nephelometry; second, only samples with AAT levels below normal range (0.83 – 2.00 g/l) were genotyped for S- and Z-alleles by polymerase chain reaction; third DBS were phenotyped by isoelectric focusing in case of PiS, PiZ and non-S non-Z allele results.

Results: A total of 5396 subjects from Bulgaria, Croatia, Hungary, Latvia, Lithuania, Romania, Russia, Slovakia, Slovenia and Ukraine were screened in 11 months. Seven hundred and eighty two (14.4%) had DBS AAT levels below the normal range. Among them, detection of S- and Z-alleles showed 16 PiZZ, 1 PiSS, 5 PiSZ, 38 PiS, 79 PiZ and 642 non-S non-Z variants. AAT phenotyping of PiZ, PiS and non-S non-Z alleles revealed 1 PiZrare, 38 PiMS, 78 PiMZ, 579 PiMM and 63 no result. Detection rate of severe AATD in symptomatic subjects was 0.41%. **Conclusions:** These data would support AATD screening programs in countries with a large number of symptomatic subjects but low awareness about this genetic condition. rhinitis (4.7ng/mg, 95%CI 3.8;5.6), current asthma (4.3ng/mg, 95%CI 3.7;4.9) and COPD cases (5.4ng/mg, 95%CI 3.8;7.1) than in controls (3.3ng/mg, 95%CI 2.8;3.8). 8-isoprostane median levels were higher, even if not significantly different, in subjects with respiratory diseases (range 0.57-0.69ng/mg) than in controls (0.51ng/mg).

While 8-isoprostane seems to be implied to a minor extent in respiratory illnesses, 8-OHdG has a significant association in COPD, asthma and allergic rhinitis.

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Does genetic ancestry modify the relationship of smoking and lung function? The MESA lung study

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Introduction: Smoking is a risk factor for COPD but little is known about whether this risk differs by genetic ancestry. The few prior studies rely on self-reported race/ethnicity.

Objectives: To test the hypothesis that genetic ancestry modifies the association of smoking and lung function.

Methods: The Multi-Ethnic Study of Atherosclerosis (MESA) is a populationbased study of adults without clinical cardiovascular disease in the United States. Principal components (PC) of ancestry were derived from genome-wide data (Affymetrix 6.0) in MESA. Spirometry was measured by ATS/ERS guidelines. We tested the interaction of PCs with packyears of smoking on FEV₁ stratified by gender and adjusted for age, height, and current smoking.

Results: Of 3229 participants, self-reported race/ethnicity was 35% white, 26% African-American, 22% Hispanic and 17% Chinese; 49% had ever smoked (median packyears 17; IQR, 6, 36). Models with PC and self-reported race/ethnicity explained the variance in FEV₁ equally well (R^2 =0.59); however adjustment for PCs rendered self-reported race/ethnicity non-significant. Packyears were associated with lower FEV₁ in all groups (p<0.001). In women, PCs did not modify the relationship of packyears to FEV₁ (p=0.86). In men, the relationship was modified by PCs (p=0.01), specifically PC2 (tracking Asian ancestry) was associated with less of a decrement in FEV₁ per packyears smoking (p=0.001).

Conclusions: Variation between European and African genetic ancestry did not modify the relationship between smoking and lung function in either gender, but this relationship may be modified by Asian ancestry in men.

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The associations between the adult asthma, central obesity and gene polymorphisms and activities of superoxide dismutase and catalase

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Background: Adult asthma is caused by interaction effects of genetic and environmental factors. Previous studies have indicated that obesity may increase the risk asthma. Therefore, our study objectives were to investigate the association between asthma and the polymorphisms of SOD or CAT, especially in central obesity.

Materials and methods: A case-control study was performed to recruit 250 asthmatic adults from a hospital and 250 age and sex-matched controls who were free from symptoms of asthma, COPD, TB, and chronic bronchitis by self-report. All subjects completed a questionnaire, waist and hip circumference measurement and lung function test were performed. Central obesity was defined as waist-to-hip ratio (WHR) >0.95 for males and >0.85 for females. We also analyzed genotyping of SOD gene Ala16Val and CAT gene C-262T.

Result: In our study, we did not find any significant association between the SOD Ala16Val and CAT C-262T and asthma. The WHR of asthmatic patients was significantly higher than the controls. The activities of SOD and CAT in new onset asthma patients were significantly different from control subjects (p<0.01). Compared with non-obesity and SOD AG/GG genotype, we found that the AOR value for obesity and SOD GG genotype is 2.68 (95%CI, 1.30-5.55).

Conclusion: The activities of SOD and CAT are significantly related to adult asthma but not for central obesity. This would enable us to further investigate the mechanism of defective antioxidant enzymes for asthma pathogenesis.

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Background: We studied the relative influence of genetic and environmental factors on the variation in susceptibility to chronic bronchitis.

Methods: In a population-based questionnaire study of 13,649 twins, 50-71 years of age, from the Danish Twin Registry, we calculated the sex-specific concordance rates and heritability of chronic bronchitis.

Results: The prevalence of CB was 9.3% in men and 8.5% in women. The concordance rate for chronic bronchitis was higher in monozygotic twins than in dizygotic twins among women; 0.30 vs. 0.17, but not among men; 0.15 vs. 0.18. The heritability of chronic bronchitis adjusted for smoking and age was 50% (30-67%) in women, whereas familial aggregation of chronic bronchitis in men was ascribable to 25% (8-41%) familial environment but not to genetic factors. **Conclusions:** Chronic bronchitis shows moderate familial aggregation, particularly in women. Increased respiratory morbidity and mortality among female smokers relative to male smokers may have a genetic origin.

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Birth mode and gut microbiota influence the risk of allergies and asthma – The KOALA birth cohort study

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Background: Gut microbiota (GM) composition and birth mode have been linked to allergies. However, results are inconsistent and the hypothesized intermediate role of GM in the association between birth mode and allergies has not been studied yet.

Aim: To study the relationship between GM composition, birth mode and allergic manifestations.

Methods: The KOALA-study includes data on birth mode and on allergic symptoms from birth untill age 6 years. Faecal samples were collected at age 1 month (n=1176) to determine GM composition using qPCR. Blood samples were collected at ages 1, 2, and 6 years to determine specific IgE levels against common allergens.

Results: Infants born by caesarean (C-)section had lower numbers of bacteroides. *C. difficile* prevalence was highest in infants born by C-section (42%), followed by infants born vaginally in the hospital (26%) and at home (19%). Colonisation by *C.difficile* was associated with an increased risk of eczema, wheeze and sensitisation throughout the first 6 years of life and with asthma (OR: 2.02, 95%CI: 1.15-3.56) at 6 years. Regarding mode and place of delivery, only children with atopic parents had an increased risk of asthma (2.06, 1.27-3.35) and sensitisation to food allergens (1.91, 1.29-2.84) when they had been vaginally delivered in hospital, when compared to vaginal delivery at home. C-section also increased the risk of sensitisation to food allergens (2.16, 1.21-3.86) compared to infants delivered at home.

Conclusion: Birth mode strongly influences the GM composition and both are associated with allergic manifestations, including asthma. More extensive microbial profiling is needed to examine whether *C.difficile* reflects other shifts in GM.

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Patterns of sensitization in early childhood in farming environment: A French part of the PASTURE/FORALLVENT European birth cohort study Anne Leydier¹, Vincent Kaulek², Amandine Chauveau¹, Flora Metzger² Erika von Mutius³, Dominique Angèle Vuitton⁴, Jean-Charles Dalphin², Marie-Laure Dalphin¹. ¹Pediatry, University Hospital, Besançon, France; ² Respiratory Diseases, University Hospital, UMR CNRS 6249, Besançon, ² France; ³ Pediatry, University Children's Hospital, Munich, Germany; ⁴ University of Franche-Comté, EA 3181, Besançon, France

Background: Cross sectional studies have repeatedly shown that children growing up on a farm had a significantly lower prevalence of atopic sensitization measured by specific IgE (IgEs) in serum but very little is known regarding sensitization tested by skin prick-tests (SPT).

Objective: To compare SPT-tested sensitization during the first 4.5 years of life in children born and living on dairy farms (F) and in children of families from the same rural region, but not born and not living on farms (non-F).

Methods: 168 children at 1 yr (49% F; 49% boys) and 155 at 4.5 yrs (52% F; 52% boys) were tested by SPT using a battery of 11 (1 yr) and 16 (4.5 yrs) age-and areaadapted allergens. Correspondent serum specific IgEs were measured at both ages Results: Prevalence of at least one positive SPT was of 8.5% (1 yr), 9.6% (4.5 yrs) in F and 11.6% (1 yr), 19.5% (4.5 yrs) in non-F groups (p=0.05). In the whole population, positive SPT were mainly against food allergens at 1 yr (13/17, 12 for egg antigen) and against aeroallergens at 4.5 yrs (24/26, 15 for seasonal antigens). At 1 yr, 17% of girls had positive SPT, versus 3.5% of boys, compared with 4.5 yrs (10.7% vs 17.5%). No relationship between IgEs-and SPT-tested sensitization was observed at 1 yr. Such a relationship was demonstrated at 4.5 yrs considering all antigens as well as categories (food, seasonal, perennial) but not for each single antigen.

Conclusions: The prevalence of positive skin prick tests is significantly lower in children growing up on a dairy farm than in their rural peers. At one year, there is no correlation between SPT-and IgEs-tested sensitizations.

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Air pollution and development of respiratory system: A 19-year cohort study among children in Ptolemaida, Greece

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Aim: Diachronic study of the function of the respiratory system among children in the city of Ptolemaida.

Methods: Concentrations of airborne particles with an aerodynamic diameter < $10\mu m$ (PM₁₀) were measured regularly during the study period. Participants of the study were children 10-12 year old who completed a questionnaire about respiratory diseases (Ferris BG), underwent spirometry and anterior rhinomanometry during the first visit (1990-1) and at follow-up (2008-9) (mean follow-up: 19 ± 1.1 years)

Results: The average annual concentration of PM10 was always above the permissible levels. A total of 1086 children were studied initially while 312 of them were examined during the follow-up visit. All were permanent residents in Ptolemaida. Based on the answers to the questionnaire: the prevalence of asthma has remained constant (5.4 vs 6.1%, p=0.85), allergic symptoms increased (16 vs 47.8%, p<0.001) and nasal symptoms were common (92.9 vs 47.3%, p<0.002). Lung function parameters were within predicted values at both visits (FVC: 98.9±12 vs 107.3±14.4% pred., p <0.001, FEV1: 98.2±12.5 vs 111.1±15.1% pred., p<0.001 and FEF₂₅₋₇₅: 96.7±22.7 vs 121.8±34.6%pred., p<0.001). On the other hand, nasal flows were extremely low (flow sum: 302.5±119.7 and 511.1±252.6 ml/sec at follow-up) while 47.1% of the adult group had severe nasal obstruction (flow sum < 500ml/sec). 45.8% of the adults were current smokers. The incidence of asthma, FEV1%pred. and nasal flows were not different between smokers and non-smokers

Conclusions: Lung function of children in Ptolemaida developed within predicted values while severe nasal obstruction was particularly frequent among young adults.

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Weather, pollution and topography in COPD exacerbations: An observational study in Worcester and Dudley, UK

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Background: Chronic respiratory symptoms are high in the UK compared to other countries where smoking is more common. The British climate may play a role. Objectives: To examine the combined effect of weather, pollution and topography on symptoms in COPD subjects residing in river valley locations.

Method: For one year, 52 subjects recorded daily respiratory symptoms. These were compared to corresponding 24-hour means for selected weather and pollution variables. Exacerbation frequencies were correlated with altitude and distance from river valleys

Results: Statistically significant (p<0.05) relationships were recorded between altitude and exacerbations frequency (r=-0.33 to -0.44). Relative humidity (r=0.19 to 0.43), temperature (r=-0.08 to -0.58), dew point (r=-0.13 to -0.42), and the difference between temperature and dew point (r=-0.19 to -0.46) showed predominantly statistically significant relationships with symptoms. Particulates showed some of the strongest correlations with symptoms (r=0.11 to 0.44). Generally, an adjustment of data for infectious exacerbations led only to minor changes in the results.

Conclusion: Our study provides for the first time evidence of increased respiratory symptoms in lower altitude areas of river valleys. The correlation results demonstrate a combined effect of certain weather conditions on acute exacerbations, especially those which result in airborne water droplet formation. The deleterious influence of pollution is also confirmed. Particles can serve as nuclei for airborne water droplets formation and an increased retention of particles and pollutants under these weather conditions is suggested.

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Spatial distribution of COPD in a rural population in India using geographic information system (GIS)

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GIS mapping is a useful tool to study the spatial distribution of diseases and examine their association with geographic risk factors.

Aim: We used GIS to determine spatial distribution of COPD in 22 rural villages spread across an area of 232 km², and study the association between proximity to highways and prevalence of COPD.

Methods: 3,592 randomly selected individuals were administered a respiratory health questionnaire and underwent pre and post bronchodilator spirometry (ndd Spirometer) according to the ATS/ERS standards. COPD was defined as postbronchodilator FEV1/FVC<0.7. Each individual's residence was mapped using Global Positioning system (Garmin eTrex, USA). Spatial distribution of all individuals and the association between proximity to highway and prevalence of COPD were performed using ArcGIS software version 9.3, USA.

Results: A significant cluster of COPD subjects were found residing <500m from the highway (Moran's Index = 0.07; p<0.01). 90% of individuals residing <500m from the highway used liquefied petroleum gas for cooking and in this population a strong positive correlation was found between proximity to highways and COPD prevalence (r2= 0.946; p<0.04). Individuals who resided > 500m from the highway had a higher prevalence of COPD and this was strongly associated with the use of biomass fuel [OR: 1.46 (CI: 1.06-2.0); p<0.01].

Conclusion: Residing <500m from the highway was strongly and positively associated with COPD. The prevalence of COPD was three-fold higher amongst those living >500m from the highway and this was significantly associated with the use of biomass fuel

P1005

Effect of urban vehicular traffic pollution on respiratory symptoms and pulmonary function in schoolchildren

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Our aim was to evaluate the relationship between pollution from urban traffic on respiratory symptoms and function in adolescents. In 2005-2006 we performed a survey on 2150 schoolchildren (10-17 yrs) from 16 junior high schools in the city of Palermo, Italy. Subjects fulfilled an ISAAC questionnaire and underwent spirometry and skin tests. The geographic location of each residence was geo-coded by Geographic Information System. A vehicular traffic model computed the daily average traffic of 2561 road segments in the city and was used for estimating the amount of traffic close to each dwelling. We identified 3 areas with progressively increasing traffic: A (in the West side close to the hills around the city - 14.8% of subjects); B (central - 53.7%); and C (the outskirts in the North and South of Area B - 31.5%). Prevalence of respiratory conditions was: wheeze ever (WE), 15.8% in Area A, 22.1% in Area B, and 23.3% in Area C (p=0.02); asthma ever (AE), 8.1%, 12.4%, and 13.0%, respectively (p=0.068); impaired lung function (ILF) was present in 1.7% of subjects, in 4.1%, and in 5.2%, respectively (p=0.037). In a logistic regression model, Odds ratios (OR) with 95% confidence intervals (CI) were calculated with Area A as reference and corrected for confouders: Area B was significant risk factor for WE (OR 1.66, IC 1.17-2.36), AE (OR 1.83, IC 1.15-2.91), and ILF (OR 2.71, IC 1.06-6.89). The corresponding OR for Area C were 1.66 (IC 1.16-2.40), 1.72 (IC 1.06-2.80), and 3.42 (IC 1.32-8.84), respectively. Our results point out that children exposed to increased levels of urban vehicular traffic near the house of residence are at higher risk for asthma and impaired lung function.

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Long-term effect of urban air pollution on lung function

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Background: Long-term effects of air pollution on lung function remain uncertain particularly for adults.

Aims: To investigate the association between exposure to nitrogen dioxide (NO₂) - used as a marker for local traffic-related pollution - and particulate matter <10 microns (PM₁₀) in the urban area of Grenoble (France) and lung function in adults. Methods: Lung function parameters (FEV1, FVC and FEV1/FVC% predicted assessed using the Stanojevic equations) were assessed between 2001-2007 for 450 adults living in Grenoble (120 asthmatics and 330 non asthmatics), in the frame of the follow-up of two epidemiological studies, EGEA (Epidemiological study on the Genetics and Environment on Asthma) and ECRHS (European Community Respiratory Health Survey). The annual means of NO2 (2004) and PM10 (2008) levels were estimated at the home addresses using a dispersion model and were combined to time-specific measures from the permanent air quality monitoring stations to capture temporal variations in exposure (the year before the lung function measurement). Linear regression models were stratified by asthma and adjusted for sex, age, BMI, active and passive smoking, occupational group, atopy, study and for asthmatics inhaled corticosteroids.

Results: Medians concentrations (μ g/m³) were 34 (IQR 31-38) for NO₂ and 31 (IQR 29-33) for PM_{10} . In non asthmatics, for a 10μ g/m³ increase in NO₂ and PM₁₀, FVC% predicted decreased by 3.7 (p=.01) and 11.7 (p=.03) and FEV₁% predicted by 3.3 (p=.02) and 9.0 (p=.07) respectively. Similar but not significant negative trends were observed in asthmatics.

Conclusion: Results suggest negative associations of home outdoor NO_2 and PM10 with lung function in non asthmatics.

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Effects of smoking habits on annual change in FEV1: A 12-year follow-up study

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Background: The rate of forced expiratory volume in 1 second (FEV1) decline is a marker of chronic obstructive pulmonary disease risk. To date, limited longitudinal data exist on airflow obstruction (COPD) and FEV1 decline in Japan. Aims and objectives: The aim of this study was to investigate the rate of FEV1

decline by smoking habits over a 12-year periods in Japanese males.

Methods: The study included 913 male subjects, aged 30-76 years at baseline, who underwent lung function tests at a medical check-up in 1994 (baseline), 1999, and 2006. The study group consisted of 263 persistent never smokers, 296 early quitters (those who stopped smoking between 1994 and 2006), 117 late quitters 8those who stopped smoking between 1999 and 2006), and 237 persistent smokers without airflow obstruction at baseline. Airflow obstruction (AO) was defined as FEV1/FVC<0.7 and 5th percentile lower limit of normal (FEV1/FVC<LLN).

Results: Mean annual decline in FEV1 over a 12-year periods were -35.0 ml/yr in persistent never smokers, -37.9 ml/yr in early quitters, -40.7 ml/yr in late quitters, and -44.8 ml/yr in persistent smokers. Mean annual decline in FEV1 over a 12-year periods defined using the fixed criteria and the LLN criteria were -34.6 ml/yr, -34.3ml/yr in persistent never smokers without AO, -42.3 ml/yr, -42.3 ml/yr in persistent smokers without AO, -60.3 ml/yr, and -56.7 ml/yr in persistent smokers with AO, respectively.

Conclusions: Persistent smokers with AO had a significant reduced FEV1 decline compared with those in persistent never smokers and current smokers without AO. Our study confirmed that early cessation of smoking may reduce the FEV1 decline and prevent the development of AO among smokers.

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Influences of smoking on FEV1 remain over the long-term after cessation Shinobu Osanai, Mie Aoki, Toshiyuki Ogasa. Cardiovascular Respiratory and Neurology Division, Department of Internal Medicine, Asahikawa Medical University, Asahikawa, Hokkaido, Japan

Backgrounds and objectives: Natural course of forced expiratory volume in on second (FEV1) after smoking cessation is still unclear. We sought to assess influences of smoking habits to FEV1 in subjects without obstructive pulmonary disorders

Subjects and methods: Subjects were recruited from patients who attended to rural primary care clinics except for respiratory disorders. Each participant was asked to answer a questionnaire including smoking history and measure forced vital capacity (FVC) and FEV1. Results are presented as mean \pm SD.

Results: In the present study, 408 of male (61.2 ± 13.7 years-old) and 500 of female (60.2 ± 15.6 years-old) were analyzed. There was no significant difference in smoking duration between current smokers (28.1±23.9 pack/year) and ex-smokers $(31.3\pm30.8 \text{ pack/year})$. In the ex-smokers, duration after smoking cessation was 14.3±13.0 yr. Both %FEV1 (measured FEV1/predicted FEV1 (%)) in current smokers (95.3±14.8, n=253) and %FEV1 in ex-smokers (93.7±15.4, n=269) were lower than %FEV1 in non-smokers (103.2 \pm 16.5, n=386) (P<0.01). There was no difference in%FEV1 among the subgroups divided by age both in current smokers and ex-smokers. Also, there was no difference in %FEV1 among the subgroups divided by duration of smoking cessation in ex-smokers. The ex-smokers under 40 years-old had lower %FEV1 comparing to non-smokers under 40 years-old. The ex-smokers who stopped smoking more 20 years had still lower %FEV1 than that in non-smokers.

Conclusion: In conclusion, influence of smoking on FEV1 starts under 40 yearold, and decrease of FEV1 remain over 20 years after cessation in subjects without obstructive pulmonary disorders.

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Reduced body mass index is associated with the presence of airflow

obstruction in a rural Indian setting Biswajit Chakrabarti¹, Sabita Purkait², Punybrata Goon², Vicky Moore³, Christopher Warburton¹, Peter Calverley⁵, Justin Zaman⁴, Rahul Mukherjee³ Aintree Chest Centre, University Hospital Aintree, Liverpool, United Kingdom; ²Moitri Swasthya Kendra, Shramajibi Swasthya Udyog, Chengail, West Bengal, India; ³Department of Respiratory Medicine & Physiology, Birmingham Heartlands Hospital, Birmingham, United Kingdom; 4 Epidemiology & Public Health, Div of Population Health, University College London, United Kingdom; ⁵Clinical Sciences Centre, University Hospital Aintree, Liverpool, United Kingdom

Background: Respiratory conditions remain a significant source of morbidity globally. We wished to understand factors associated with the development of airflow obstruction (AFO) within a rural Indian setting. We hypothesised that being significantly underweight (BMI less than 18.5) could be linked to the development of AFO (FEV1/FVC less than 0.7).

Methodology: Patients greater than 35 years old attending a primary care outpatient clinic at Chengail, West Bengal, India underwent: 1. A structured questionnaire 2. Measurement of BMI 3.Spirometry (analysed by a Respiratory Clinical Physiologist).

Results: 416 patients (mean age 51 years; 47% male; 62% never smokers) completed the study; spirometry deemed valid for analysis in 286 (69%). 47 (16%) of all subjects were noted to exhibit AFO; GOLD stage 1 (15%); GOLD stage 2 (49%); GOLD stage 3 (26%);GOLD stage 4 (10%). Never smokers comprised 43% (20/47) of all AFO cases. On logistic regression, factors associated with AFO were: Increasing age (95% CI 0.004-0.011; p=0.005), smoking status (95% CI 0.07-0.174; p=0.006), male gender (95% CI 0.19-0.47; p=0.012), reduced BMI (95% CI 0.19-0.65; p=0.02) and occupation (95% CI 0.12-0.84; p=0.08). Mean BMI was significantly lower in the 47 patients with AFO (20.11 v 21.62; p=0.02). AFO was observed in 27% (18/66) of subjects with a BMI less than 18.5 falling to 13% (29/220) of subjects with BMI greater than 18.5 (p=0.013). In those underweight ever smokers, airflow obstruction was identified in 25% (13/52) rising to 32% (14/44) in ever smokers with a BMI greater than 18.5.

Conclusion: Our study suggests that being underweight is associated with the presence of AFO in a rural Indian setting.

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Risk factors for obstructive lung function in morbidly obese patients

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Background: Morbidly obese patients are not only at risk for asthma but also for pulmonary complications related to bariatric surgery.

Aim of the study: To calculate a risk score for obstructive lung function in morbidly obese patients as pre-surgical screening tool before bariatric surgery, and relating pulmonary complications to this score.

Methods: 39 of the 342 patients (11.4%) had an obstructive lung function. A history of asthma (adj.OR 3.2; 95%CI:1.4-7.5), >5 pack years (adj.OR 2.8; 95%CI:1.2-6.3) and abdominal circumference >120cm (adj.OR 7.0; 95%CI:1.6-31.0) were associated with an obstructive lung function (multiple logistic regression). The risk of obstructive lung function was calculated (1, 1 and 2 points respectively). At the cut of point of \geq 2 sensitivity was 0.968 and specificity 0.315 (ROC analysis, area under the curve 0.764). Inhalation medication after pulmonary screening was

prescribed in 35 patients, of whom 34 (97%) had a risk-score of ≥ 2 (p<0.000). Only 5 pulmonary complications occurred, however all pulmonary complications were in risk-score ≥ 2 group (p=0.325).

Conclusion: Abdominal circumference is a better predictor than BMI for obstructive lung function in morbidly obese patients undergoing bariatric surgery. Although the incidence of pulmonary complications after bariatric surgery is low, pre-surgical risk factor analysis could identify patients at risk for obstructive lung function and pulmonary complications.

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Associations of different serum 25(OH)D levels to parameters of respiratory health in COPD patients

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Recent studies show a high prevalence of vitamin D deficiency in COPD patients. Optimal vitamin D levels may differ for different physiological processes. There is no current consensus on the optimal level for respiratory health and lung function. **Methods:** Serum 25(OH)D in 426 COPD patients, GOLD stage II-IV, aged 40-76, from the Bergen COPD Cohort study, were determined by liquid chromatography double mass spectrometry. Examined explanatory variables were sex, age, body mass index (BMI), smoking habits, FEV1, exacerbation frequency, PaO2, respiratory symptoms, use of inhaled steroids, CRP, total white blood (WBC) count and seasonality. Vitamin D levels were categorised into 5 groups (A,B,C,D,E): A: <10ng/ml; B: 10-20ng/ml; C: 20-30ng/ml; D: 30-40ng/ml; and E: 40-52ng/ml. Associations were tested with chi-square and Kruskal Wallis.

Results: The prevalence of subjects in vitamin D categories, A to E, were 6.8%, 26.5%, 33.1%, 27.0%, and 6.6% respectively.

The percentage of daily smokers in group A through E: 58.6%, 53.1%, 39.7%, 38.3%, and 58.6% (p=0.046).

Mean FEV1 was 42%, 43%, 51%, 51%, 51%, and 56% in group A through E (p<0.001). Resting PaO2 varied between 8.9kPa in group B to 9.7kPa in group E (p=0.008). Mean WBC counts were 8.5, 8.3, 7.5, 7.6, and 7.1 in group A through E (p=0.017). In group A, 24.1% were obsec compared with 3.6% in group E (p=0.14). 27.6% of subjects in group A had high exacerbation frequency (>2/year) compared with 13.5% in group C (p=0.21).

Conclusion: Vitamin D deficiency (<20ng/ml) was common in COPD patients and significantly related to important disease phenotypes, but the critical cutoff level of vitamin D varied between the different respiratory health variables.

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Microbial evaluation of proton pump inhibitors and the risk of pneumonia Sabine Meijvis¹, Marie Claire Cornips², Paul Voorn³, Patrick Souverein², Henrik Endeman⁴, Douwe Biesma^{1,5}, Hubert Leufkens², Ewoudt van de Garde^{2,6}. ¹ Department of Internal Medicine, St. Antonius Hospital, Nieuwegein, Netherlands; ² Pharmacoepidemiology and Clinical Pharmacology, Utrecht University, Utrecht, Netherlands; ³ Medical Microbiology and Immunology, St. Antonius Hospital, Nieuwegein, Netherlands; ⁴ Department of Intensive Care Medicine, Onze Lieve Vrouwe Gasthuis Amsterdam, Amsterdam, Netherlands; ⁵ Department of Internal Medicine, University Medical Centre Utrecht, Utrecht, Netherlands; ⁶ Department of Clinical Pharmacy, St. Antonius Hospital, Nieuwegein, Netherlands

Background: Recent initiation of proton pump inhibitor (PPI) treatment may increase the risk of community-acquired pneumonia (CAP), hypothetically by allowing colonization of the oropharynx by gastrointestinal bacteria. Aim of this study was to assess the causal pathway by considering microbial etiology of pneumonia and indications for initiation of PPI treatment.

Methods: This was a population-based case-control study with 430 cases with pneumonia and 1720 matched controls. An elaborate diagnostic protocol was used to identify the causative microorganism of pneumonia. For patients recently starting PPI treatment, indications for treatment were assessed.

Results: Recent initiation of PPI treatment (<30 days) was associated with an increased risk of CAP (adjusted OR 3.2, 95% CI 1.4 – 7.2). Oropharyngeal bacteria were evenly distributed among current, past and non-users of PPIs (p=0.41). Only in 5 patients (1.2%) with pneumonia (2 current users and 3 non users), gastrointestinal bacteria were identified. Excluding patients who possibly were prescribed PPI treatment for early symptoms of pneumonia (protopathic bias) did not alter the study findings.

Causal Pathogens of CAP in relation to PPI use

	All n=430 (%)	Non n=307 (%)	Current n=103 (%)	Past n=20 (%)
Oropharyngeal bacteria*	166 (39)	119 (39)	42 (41)	5 (25)
Gastrointestinal bacteria [†]	5 (1.2)	3 (1.0)	2 (1.9)	0 (0.0)

*S. pneumoniae, H. influenzae, S. aureus, H. parainfluenzae and other streptococci. [†]E. coli and K. pneumoniae.

Conclusions: This study reaffirmed that use of PPIs is associated with an increased

risk of CAP, especially when treatment is started recently. Protopathic bias nor shifts in microbial aetiology seem to explain the association.