# ABSTRACTS:

## Second-hand smoke in indoor hospitality venues in Pakistan

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**Background:** Second-hand smoke (SHS) constitutes a signifi cant public health threat in countries with a high smoking prevalence. However, data assessing the quality of indoor air at public venues in Pakistan are limited.
**Objectives**: To measure mean concentrations of PM2.5 (particulate matter ⩽2.5 microns in diameter), a sensitive indicator of SHS, in hospitality venues in Pakistan.
**Setting and design**: Data were collected discreetly from 39 indoor venues such as cafes, restaurants and *shisha* (water-pipe) bars from three major cities in Pakistan. Data were recorded using a portable air quality monitoring device.
**Results:** The overall mean PM2.5 value for the visited venues was 846 µg/m3 (95%CI 484–1205). The mean PM2.5 value was 101 µg/m3 (95%CI 69–135 µg/m3) for non-smoking venues, 689 µg/m3 (95%CI 241–1138) for cigarette smoking venues and 1745 µg/m3 (95%CI 925–2565) for shisha smoking venues.
**Conclusion:** The signifi cant levels of SHS recorded in this study, in particular from shisha smoking venues, could represent a major public health burden in Pakistan. Appropriate legislation needs to be enforced to protect the health of those exposed to the hazards of second-hand tobacco smoke.

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## Use of Varenicline for 4 Weeks Before Quitting Smoking: Decrease in Ad Lib Smoking and Increase in Smoking Cessation Rates.

*Hajek P, McRobbie HJ, Myers KE, Stapleton J, Dhanji AR.*

**Study Question:**
The use of varenicline alleviates post-quit withdrawal discomfort, and reduces the "reward" associated with smoking. The current treatment schedule, which commences 1 week before quitting, relies primarily on the first mechanism. Does increasing the pre-

quit medication period render cigarettes less satisfying and facilitate quitting?

**Methods:**
A total of 101 smokers attending a stop smoking clinic in London, United Kingdom, were randomly allocated to receive varenicline for 4 weeks before the target quit date (TQD) or to receive placebo for 3 weeks before the TQD, followed by varenicline for 1 week before the TQD. In both groups, standard varenicline treatment was given for 3 months after the TQD. Measures included smoking satisfaction and smoke intake before quitting, urges to smoke and withdrawal discomfort after quitting, and sustained abstinence from the TQD to 3 months.

**Results:**
There was no difference between groups for mean age of 45 years, mean cigarettes per day (15.5 vs. 18.2), previous quit attempts (2.7), partner smoking, or body mass index. Varenicline preloading reduced pre-quit enjoyment of smoking ($p = 0.004$) and smoke intake ($p < 0.001$), with 36.7% of participants reducing their cotinine concentrations by more than 50% (reducers). Varenicline preloading did not affect post-TQD withdrawal symptoms, but it increased 12-week abstinence rates (47.2% in the varenicline arm vs. 20.8% in the placebo arm, $p = 0.005$). The effect was particularly strong among the reducers in the varenicline arm (66.7% in reducers vs. 22.6% in nonreducers, $p = 0.002$). Varenicline preloading was well tolerated.

**Conclusions:**
Although several issues remain to be clarified, varenicline preloading can generate a substantial reduction in ad lib smoking and enhance 12-week quit rates. Current treatment schedules may lead to suboptimal treatment results.

**Perspective:**
The results are more robust than expected. In the large trials, the standard protocol with just 1 week of pretreatment with varenicline, the 12-week post-quit date abstinence rate is over 40% compared to the 20% in this study. This proof of principle designed protocol needs to be expanded to include long-term follow-up, a much larger cohort, and other options including longer duration of treatment. Cigarette smoking is the most preventable cause of illness, death, and excess health care costs in the United States, accounting for more than 440,000 deaths annually and $157 billion in health-related economic losses.

*Arch Intern Med* 2011;171 :770-777

## Lung diseases directly associated with rheumatoid arthritis and their relationship to outcome

*Y. Tsuchiya, N. Takayanagi, H. Sugiura, Y. Miyahara, D. Tokunaga, Y.Kawabata and Y. Sugita*

**Abstract**

The outcome and cause of death of each lung disease directly associated with rheumatoid arthritis (RA-LD) have been poorly investigated.

A retrospective study was conducted of 144 patients with RA-LD, in whom the median follow-up period after the initial visit for a respiratory examination was 4.5 yrs.

A total of 57 patients were identified with usual interstitial pneumonia (UIP), 31 with bronchiectasis, 16 with nonspecific interstitial pneumonia (NSIP), 11 with bronchiolitis, five with organising pneumonia (OP), five with diffuse alveolar damage (DAD) and 19 with combined disease. The 5-yr survival rates were 36.6% in the UIP group, 87.1% in the bronchiectasis group, 93.8% in the NSIP group, 88.9% in the bronchiolitis group, 60.0% in the OP group and 20.0% in the DAD group. Survival of patients with DAD was worse than that of patients with UIP. Overall, survival of patients with UIP was worse than that of patients with bronchiectasis, NSIP or bronchiolitis. Of the 144 patients, 71 (49.3%) died, of whom 58 (81.7%) died due to respiratory lesions.

Of patients with RA-LD, patients with DAD experienced the highest mortality, and the survival of patients with UIP was worse than that of patients with NSIP.

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## Alterations in the pulmonary function tests of inflammatory bowel diseases.

*Ateş F, Karincaoğlu M, Hacievlıyagıl SS, Yalniz M, Seçkın Y*.

**Background/aims**: We aimed to determine the changes in the pulmonary function tests of the patients with inflammatory bowel diseases.

**Methods:** Forty inflammatory bowel dieases patients; 30 ulcerative colitis and 10 Crohn's disease, and ageand sex-matched control group, consisting of 30 healthy persons, were included in the study. Disease activity in patients with ulcerative colitis was assessed by Truelove and Witts Criteria and in Crohn's disease patients by Chron's Disease Activity Index.

**Results**: Pulmonary function tests were found abnormal at least in one parameter in 17/30 ulcerative colitis patients (56%) and in 5/10 Crohn's disease patients (50%) in the activation period and in 5/30 ulcerative colitis patients (17%) and in 2/10 Crohn's disease patients (20%) in the remission period of the diseases of the same patients. Forced vital capacity, first second, residual volume/total lung capacity, diffusing capacity of the lung for carbon monoxide and diffusing capacity of the lung for carbon monoxide per liter alveolar volume values were found significantly impaired in the activation period in comparison with the values of the same patients in the remission period ($p<0.01$). It was found that pulmonary function test values in patients with inflammatory bowel dieases were not affected by either the type of disease or treatment with 5-aminosalicylic acid. However, they were affected notably by the disease activity. **Conclusion**: Pulmonary function test abnormalities were found frequently in patients with inflammatory bowel dieases without presence of any respiratory symptoms and lung radiograph findings. The severity and frequency of these pulmonary function test abnormalities which were detected even in the remission periods increase with the activation of the disease. Therefore, pulmonary function test may be used as a non-invasive diagnostic procedure in determining the activation of inflammatory bowel dieases and might aid to the early diagnosis of the latent respiratory.

*Turk J Gastroenterol. 2011 Jun;22(3):293-9.*

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## Transbronchial needle aspiration "by the books".

*Kupeli E, Memis L, Ozdemirel TS, Ulubay G, Akcay S, Eyuboglu FO.*

**Abstract:**

**Background:**

Training for advanced bronchoscopic procedures is acquired during the interventional pulmonology (IP) Fellowship. Unfortunately a number of such programs are small, limiting dissemination of formal training.

**Objective*:***

We studied success of conventional transbronchial needle aspiration (C-TBNA) in the hands of physicians without formal IP training.

**Methods*:***

A technique of C-TBNA was learned solely from the literature, videos and practicing on inanimate models at "Hands-On" courses. Conventional TBNA with 21 and/or 19 gauge Smooth Shot Needles (Olympus(®), Japan) was performed on consecutive patients with undiagnosed mediastinal lymphadenopathy.

**Results*:***

Thirty-four patients (male 23), mean age 54.9 ± 11.8 years underwent C-TBNA. Twenty-two patients had nodes larger than 20 mms. Suspected diagnoses were malignancy in 20 and nonmalignant conditions in 14. Final diagnoses were malignancy 17, sarcoidosis 4, reactive lymph nodes 12, and tuberculosis 1. Final diagnosis was established by C-TBNA in 14 (11 malignancy, 3 sarcoidosis; yield 41.1%), mediastinoscopy in 14, transthoracic needle aspiration in 3, peripheral lymph node biopsies in 2 and by endobronchial biopsy in 1. Nodal size had an impact on outcome (P = 0.000) while

location did not (P = 0.33). C-TBNA was positive in 11/20 when malignancy was suspected (yield 55%), while 3/14 when benign diagnosis was suspected (yield 21.4%) (P = 0.05). Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 66.6%, 100%, 100%, 65%, and 79.4%, respectively. There were no complications or scope damage.

**Conclusion*:***
Conventional-TBNA can be learned by the books and by practicing on inanimate models without formal training and results similar to those published in the literature could be achieved.

*Ann Thorac Med. 2011 Apr;6(2):85-90.*

## F(1) /F(O) ATP synthase-dependent CO(2) gas excretion from human pulmonaryarteriolar endothelial cells.

*Kawai Y, Yoshida K, Kaidoh M, Yokoyama Y, Ohhashi T.*

**Abstract:**
We studied the physiological role of flow through pulmonary arterioles in CO(2) gas exchange. We previously established human pulmonary arteriolar endothelial cells (HPA○EC). The cells demonstrated marked immunocytochemical staining of PECAM-1, VEGF R2, ACE-1, and CA type IV on their cell surface. Ten seconds shear stress stimulation caused the co-release of H+ and ATP via the activation of F(1) /F(O) ATP synthase on the HPAoEC. F(1) /F(O) ATP synthase was immunocytochemically observed on the cell surface of non-permeabilized HPA○EC. In the shear stress-loaded HPA○EC culture media supernatant, ATPase activity increased in a time-dependent manner. The HPA○EC were strongly stained for NTPDase 1, which partially co-localized with purinergic P2Y1. The purinergic P2Y1 receptor agonist UTP (10(-6) M) significantly potentiated the shear stress-induced increase in ATPase activity in the culture medium supernatant. Ten seconds shear stress stimulation also produced stress strength-dependent CO(2) gas excretion from the HPA○EC, which was significantly reduced by the inhibition of F(1) /F(O) ATP synthase or CA IV on the endothelial cell surface. In conclusion, we have proposed a new concept of CO(2) exchange in the human lung, flow-mediated F(1) /F(O) ATP synthase-dependent H(+) secretion, resulting in the facilitation of a dehydration reaction involving HCO(3) - in plasma and the excretion of CO(2) gas from arteriolar endothelial cells. J. Cell. Physiol. © 2011 Wiley-Liss, Inc.

*J Cell Physiol. 2011 Jul 18. doi: 10.1002/jcp.22937*

## Smoking and pulmonary fibrosis: novel insights.

*Samara KD, Margaritopoulos G, Wells AU, Siafakas NM, Antoniou KM.*

**Abstract:**
The relationship between smoking and pulmonary fibrosis is under debate and intense investigation. The aim of this paper is to review the existing literature and identify further areas of research interest. Recently the negative influence of cigarette smoking on IPF outcome was highlighted, as non-smokers exhibit a better survival than ex-smokers and combined current- and ex-smokers. In patients with non-specific interstitial pneumonia (NSIP), a high prevalence of emphysema was recently demonstrated, providing an indirect support for a smoking pathogenetic hypothesis in NSIP. The coexistence of pulmonary fibrosis and emphysema has been extensively described in a syndrome termed combined pulmonary fibrosis and emphysema (CPFE). Connective tissue disorders (CTDs) are a group of autoimmune diseases which affect the lung, as one of the most common and severe manifestations. However, the relationship between smoking and autoimmune disorders is still conflicting. Rheumatoid arthritis results from the interaction between genetic and environmental factors, while the best established environmental factor is tobacco smoking. Smoking has also a negative impact on the response of the RA patients to treatment. The aforementioned smoking-related implications give rise to further research questions and certainly provide one more important reason for physicians to advocate smoking cessation and smoke-free environment.

*Pulm Med. 2011;2011:461439. Epub 2011 Jun 15.*

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## Clinical pathway for acute exacerbations of chronic obstructive pulmonary disease: method development and five years of experience.

*Nishimura K, Yasui M, Nishimura T, Oga T.*.

**Background:**
Randomized controlled trials, evidence-based **medicine**, clinical guidelines, and total quality management are some of the approaches used to render science-based health care services. The clinical pathway for hospitalized patients suffering from acute exacerbations of chronic obstructive **pulmonary** disease (AECOPD) is poorly established, although a clinical pathway is an integral part of total quality management.

**Aim:**
To evaluate the outcomes of patients hospitalized with AECOPD in Japan, treated with a clinical pathway following published guidelines.

**Methods*:***
Prospective data were collected for patients with AECOPD admitted to a general hospital over a 5-year period since 2003. The clinical pathway was designed to establish general rules for the entire treatment protocol. The clinical pathway indicates which treatments and interventions should be performed, and when. In this study, health

care providers were required to check the clinical pathway sheets to determine the next step of treatment.

**Results*:***
This study analyzed 276 hospitalizations in 165 patients. The clinical pathway was interrupted and defined as a dropout in 45 cases (16.3%). Nine patients died during hospitalization (3.3%). Oxygen was administered in 232 hospitalizations (84.1%). Noninvasive positive pressure ventilation (NPPV) treatment was administered in 110 hospitalizations (39.9%). The rate of intubation in those cases where NPPV treatment had been administered was 8.2% (9 cases out of 110). The average length of stay (LOS) was 20.3 days, and the median value was 15 days. The LOS was longer than 30 days in 34 admissions (12.3%), mainly due to complications.

**CONCLUSION:**
AECOPD can be managed using a clinical pathway. This clinical pathway could fill the gap between guidelines and clinical practice.

*Int J Chron Obstruct Pulmon Dis. 2011;6: 365-72. Epub 2011 Jun 29.*

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## Efficacy of two corticosteroid regimens in acute exacerbation of chronic obstructive pulmonary disease.

*Aggarwal P, Wig N, Bhoi S.*

**Background:**
Studies comparing corticosteroids in the management of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) are lacking.

***OBJECTIVE:***
To compare intravenous (IV) methylprednisolone (MP) followed by oral MP with IV hydrocortisone (HC) followed by oral prednisolone in patients with AECOPD.

**Methods*:***
Ninety-seven patients with AECOPD were randomly allocated to Group A (n = 50) or Group B (n = 47). Group A patients were administered HC 200 mg 6 hourly until discharge, followed by prednisolone 0.75 mg/kg/day for 2 weeks; Group B patients were administered IV MP (125 mg bolus, followed by 40 mg 6 hourly) and then oral MP 0.6 mg/kg/day for 2 weeks. Clinical variables, peak expiratory flow (PEF) and forced expiratory volume in 1 second (FEV(1)) were assessed until discharge and again 2 weeks after discharge.

**Results*:***
Baseline characteristics were comparable. Mortality, need for mechanical ventilation and acute exacerbation within 2 weeks of discharge were not significantly different between the two groups. However, at 2 weeks, Group B showed significant improvement over Group A in FEV(1) and PEF.

**Conclusion:**
This study suggests that in AECOPD, IV MP followed by oral MP produced greater improvement in FEV(1) and PEF than IV HC followed by oral prednisolone, although there were no differences in need for ventilator support or in recurrence of exacerbation.

*Int J Tuberc Lung Dis. 2011 May;15(5):687-92.*

**Corticosteroids and ARDS: A review of treatment and prevention evidence.**

*Khilnani GC, Hadda V*.

**Abstract:**

To systematically review the role of corticosteroids in prevention of acute respiratory distress syndrome (ARDS) in high-risk patients, and in treatment of established ARDS. Primary articles were identified by English-language Pubmed/MEDLINE, Cochrane central register of controlled trials, and Cochrane systemic review database search (1960-June 2009) using the MeSH headings: ARDS, adult respiratory distress syndrome, ARDS, corticosteroids, and methylprednisolone (MP). The identified studies were reviewed and information regarding role of corticosteroids in prevention and treatment of ARDS was evaluated. Nine trials have evaluated the role of corticosteroid drugs in management of ARDS at various stages. Of the 9, 4 trials evaluated role of corticosteroids in prevention of ARDS, while other 5 trials were focused on treatment after variable periods of onset of ARDS. Trials with preventive corticosteroids, mostly using high doses of MP, showed negative results with patients in treatment arm, showing higher mortality and rate of ARDS development. While trials of corticosteroids in early ARDS showed variable results, somewhat, favoring use of these agents to reduce associated morbidities. In late stage of ARDS, these drugs have no benefits and are associated with adverse outcome. Use of corticosteroids in patients with early ARDS showed equivocal results in decreasing mortality; however, there is evidence that these drugs reduce organ dysfunction score, lung injury score, ventilator requirement, and intensive care unit stay. However, most of these trials are small, having a significant heterogeneity regarding study design, etiology of ARDS, and dosage of corticosteroids. Further research involving large-scale trials on relatively homogeneous cohort is necessary to establish the role of corticosteroids for this condition.

Lung India. 2011 Apr;28(2):114-9.

# Symptomatic oxygen for non-hypoxaemic chronic obstructive pulmonary disease.

*Uronis H, McCrory DC, Samsa G, Currow D, Abernethy A.*

**Background:**

Dyspnoea is a common symptom in chronic obstructive pulmonary disease (COPD). People who are hypoxaemic may be given long-term oxygen relief therapy (LTOT) to improve their life expectancy and quality of life. However, the symptomatic benefit of home oxygen therapy in mildly or non-hypoxaemic people with COPD with dyspnoea who do not meet international funding criteria for LTOT (PaO(2)< 55 mmHg or other special cases) is unknown.

**Objectives:**

To determine the efficacy of oxygen versus medical air for relief of subjective dyspnoea in mildly or non-hypoxaemic people with COPD who would not otherwise qualify for home oxygen therapy. The main outcome was patient-reported dyspnoea and secondary outcome was exercise tolerance.

**Search strategy:**

We searched the Cochrane Airways Group Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE, to November 2009, to identify randomised controlled trials. We handsearched reference lists of included articles.

**Selection criteria:**

We only included randomised controlled trials of oxygen versus medical air in mildly or non-hypoxaemic people with COPD. Two review authors independently assessed articles for inclusion.

**Data collection and analysis:**

One review author completed data extraction and methodological quality assessment. A second review author then over-read evidence tables to assess for accuracy.

**Main results:**

Twenty-eight trials on 702 patients met the criteria for inclusion; 18 trials (431 participants) were included in the meta-analysis. Oxygen reduced dyspnoea with a standardized mean difference (SMD) of -0.37 (95% confidence interval (CI) -0.50 to -0.24, P < 0.00001). We observed significant heterogeneity.

**Author's conclusions:**

Oxygen can relieve dyspnoea in mildly and non-hypoxaemic people with COPD who would not otherwise qualify for home oxygen therapy. Given the significant heterogeneity among the included studies, clinicians should continue to evaluate patients on an individual basis until supporting data from ongoing, large randomised controlled trials are available.

*Cochrane Database Syst Rev. 2011 Jun 15;6:CD006429.*

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## Assessing evidence of interaction between smoking and warfarin: a systematic review and meta-analysis.

*Nathisuwan S, Dilokthornsakul P, Chaiyakunapruk N, Morarai T, Yodting T, Piriyachananusorn N*

**Background:**

Chronic smoking, theoretically, can interfere with warfarin metabolism through enzyme-inducing effects of polycyclic aromatic hydrocarbons. However, clinical evidence of interactions between warfarin and smoking are inconclusive. This study aimed to systematically review all relevant clinical evidence of this interaction.

**Methods:**

We performed a systematic search using computerized databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials, CINAHL, Allied and Complementary Medicine, PsycINFO, International Pharmaceutical Abstracts, and ClinicalTrials.gov from 1966 to December 2008. Keywords included "warfarin" with "smoking," "tobacco," "cigarette," and "polycyclic aromatic hydrocarbons." Original articles reporting interaction between warfarin and smoking were included. All articles were reviewed independently by two investigators for study design, population, outcomes, and quality of evidence.

**Results:**

Of the 1,240 studies retrieved, one experimental pharmacokinetic study and 12 cross-sectional studies were included. The pooled analyses of multivariate studies suggested that smoking was associated with a 12.13% (95% CI, 6.999-17.265; P < .001) increase in warfarin dosage requirement and an additional 2.26 mg (95% CI, 2.529-7.042; P = .355) per week compared with nonsmoking. Additional sensitivity analysis of four multivariate studies with adjustment for pharmacogenomic factors suggested that smoking was associated with a 13.21% (95% CI, 8.59%-17.83%; P < .001) increase in warfarin dosage requirement compared with nonsmokers. Results of an experimental pharmacokinetic study lend theoretical support to the findings.

**Conclusions:**

Evidence suggests that smoking may potentially cause significant interaction with warfarin by increasing warfarin clearance, which leads to reduced warfarin effects. Close monitoring of warfarin therapy should be instituted when there is a change in smoking status of patients requiring warfarin therapy.

*Chest. 2011 May;139(5):1130-9.*

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