severity is a common source of bias. Consequently, failure to properly control for the bias could lead to serious flaws in the study. **METHODS:** We used a novel approach for identifying comorbidities associated with COPD by mapping the incident comorbidity patterns in the pre-COPD diagnosis period as well as over the course of the disease using a retrospective cohort of patients aged 50+ in the UK General Practice Research Database. Each patient was matched to another without COPD on year of birth, sex, general practice and completed years of medical records up to at least a year after the index date for COPD between 1990 and 1998. We identified 24,000 such pairs that also satisfied a requirement for at least one medical consultation and at least one prescription for any drug in the year prior to the index date for COPD. **RESULTS:** Based on trends in rate ratios, we found significant time-dependent associations between the incident COPD diagnosis and incident comorbid conditions such as lung cancer, myocardial infarction, pneumonia, cardiac disorders, osteoporosis, fractures, skin bruises, psychiatric disorders and respiratory infections. **CONCLUSIONS:** The results indicated interesting associations which could help improve our understanding of the natural history of COPD and its burden. This methodology can be used to identify important comorbidities for effective comparative assessments.

PRS4

EFFECTIVENESS OF VARENICLINE COMPARED TO BUPROPION AND NICOTINE REPLACEMENT THERAPY (NRT) FOR SMOKING CESSATION IN TWO SMOKING SPECIALIZED UNITS OF THE SPANISH PRIMARY CARE SETTING

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OBJECTIVES: The objective of this study was to estimate the effectiveness of varenicline, bupropion and nicotine replacement therapy (NRT) in smoking cessation in two specialized smoking units belonging to primary care centers. **METHODS:** A multicenter longitudinal observational study was designed. Patient's data were collected retrospectively based on their clinical records. Patients over the age of 18, who initiated treatment of smoking cessation between January 1, 2006 and January 12, 2008 with varenicline, bupropion or NRT were included in the analysis. Patient's follow-up was conducted from time-baseline (day 1) and assessed at 6 and 12 months. Main variables included in the study were: comorbidities, effectiveness (continuous abstinence) and pharmacological tolerability. Statistical analysis was performed by Kaplan-Maier survival curves; $P < 0.05$. **RESULTS:** A total of 957 smokers patients treated with NRT (53.0%), bupropion (25.1%) and varenicline (21.9%) were included in the analysis. The mean age of participants was 47.6 (11.3) years and 58.6% were men. The average duration of smoking was 19.5 (6.7) years. At 6 months, 61.2% (95% CI: 54.6–67.8%) of participants in the varenicline group were continuously abstinent from smoking compared with 56.9% (95% CI: 50.6–63.2%) in the bupropion group and 52.3% (95% CI: 48.0–56.6%) in the NRT group; p = 0.003. At 12 months, the rate of continuous abstinence was 57.4% (95% CI: 50.7–64.1%) in the varenicline group compared with 52.9% (95% CI: 46.6–59.2%) in the bupropion group and 47.1% (95% CI: 42.8–51.4%) in the NRT group; p = 0.002. Pharmacological tolerability was similar between groups except for symptoms of irritability which were lower in the varenicline group: 4.3% compared to 8.3% in the bupropion group and 10.3% in the NRT group. **CONCLUSIONS:** Varenicline appeared to be an effective and safety alternative compared with bupropion and NRT on smoking cessation in the primary care setting.

PRS5

BUDESONIDE/FORMOTEROL PLUS TIOTROPIUM (BUD/FORM + TIO) VS. SALMETEROL/FLUTICASONE PLUS TIOTROPIUM (SALM/FLU + TIO): A SYSTEMATIC REVIEW AND ADJUSTED INDIRECT COMPARISON BETWEEN TWO ALTERNATIVE TRIPLE TREATMENTS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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OBJECTIVES: Use of triple therapy (long-acting beta$_2$ agonist [LABA], inhaled corticosteroid [ICS] and long-acting muscarinic antagonist [LAMA]) for the treatment of COPD has doubled in the UK over the past 5 years for all severities of the disease. This research was designed to compare the two most commonly prescribed combination inhalers (BUD/FORM and SALM/FLU) as the basis of triple therapy with TIO, the most widely used LAMA. **METHODS:** Systematic review of CENTRAL, EMBASE and MEDLINE for randomised controlled trials (RCTs) in patients with COPD treated with BUD/FORM+TIO or SALM/FLU+TIO was conducted in May 2010. Mixed treatment comparison (MTC) using TIO as a common comparator was conducted using a Bayesian Markov Chain Monte Carlo simulation. Fixed- and random-effects models were explored with the preferred model selected based on the Deviance Information Criterion (DIC). Data was extracted from relevant trials on severe exacerbations (a composite of oral corticosteroids, hospitalizations and A&E visits due to worsening symptoms). Summary effect estimate was calculated as odds ratio (OR) with 95% credible interval (95% CrI) where OR < 1 favoured BUD/FORM+TIO and OR > 1 favoured SALM/FLU+TIO. **RESULTS:** Of the 124 papers identified in the literature search, 3 RCTs had comparable patient populations and were able to supply data for analysis (1 BUD/FORM+TIO [N = 660] and 2 SALM/FLU+TIO [N = 301 and N = 60]). The exclusion of papers was based on not meeting all of the following inclusion critieria: RCTs of the chosen comparators; COPD patient population; reporting exacerbations; English-language full publication; and non-duplicates. When the fixed- and random-effects MTC models were compared the fixed-effects MTC had the lowest DIC. The results indicate a 55% relative reduction in severe exacerbations with BUD/FORM+TIO compared to SALM/FLU+TIO (OR 0.45, 95% CrI: 0.22 to 0.83). **CONCLUSIONS:** This MTC suggests that BUD/FORM-based triple therapy is significantly more effective at reducing severe exacerbations than SALM/FLU-based triple therapy.

PRS6

DEVELOPING AND APPLYING A STOCHASTIC DYNAMIC POPULATION MODEL FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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OBJECTIVES: Modeling a chronic disease like COPD is useful to extrapolate (intermediate) treatment effects observed in short-term randomized trials to the medium or long term. This study aimed to extend an existing dynamic population model of COPD progression by including exacerbations and making the model stochastic. **METHODS:** The COPD model starts with COPD prevalence in the Dutch population specified by age, gender, disease severity (four severity stages) and smoking status. Each following year the model simulates the changes in the prevalence and COPD-related health care costs due to incidence, mortality and disease progression, i.e. annual decline in FEV_1% predicted.The structure was adjusted to include moderate and severe exacerbations and the following input parameters were estimated by quantitative meta-analyses: the frequency, case-fatality, lung function decline, quality of life loss and costs of exacerbations. The model was made stochastic by specifying probability distributions around all important model parameters. The adapted model can be used to assess the impact of interventions that influence COPD incidence, disease progression, frequency and/or severity of exacerbations, mortality, quality of life or combinations of these effects. To illustrate the potential use of the model, long- term costs and effects were projected for four different COPD interventions, two on pharmacotherapy, one on smoking cessation therapy and one on pulmonary rehabilitation. **RESULTS:** Compared to a reference scenario representing minimal treatment, the cost-effectiveness of the four interventions ranged from €6,100 to €12,200 per QALY gained. The probability of the interventions to be cost-effective at a ceiling ratio of €20,000 varied from X to Y%. **CONCLUSIONS:** The extended COPD model can provide policy makers with information about long-term costs and effects of interventions over the entire chain, from primary prevention to care for very severe COPD. Moreover it describes the uncertainty of the outcomes.

PRS7

A COMPARISON OF CLINICAL EFFICACY AND SAFETY OF CICLESONIDE WITH FLUTICASONE IN 1:1 AND 1:2 DOSE RATIOS IN THE TREATMENT OF BRONCHIAL ASTHMA

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OBJECTIVES: This study compared efficacy and safety of ciclesonide (CIC) with fluticasone (FP) in the treatment of bronchial asthma. **METHODS:** Comparison was based on randomized controlled trials (RCTs) identified by means of systematic review, carried out according to the Cochrane Collaboration guidelines. The most important medical databases (EMBASE, MEDLINE, CENTRAL) were searched. Two reviewers independently selected trials, assessed their quality and extracted data. Meta-analysis of head-to-head trials was performed. **RESULTS:** Ten RCTs directly comparing CIC vs. FP were identified and included in the analysis. Comparisons of both interventions in 1:1 and 1:2 dose ratios were assessed in 8 and 5 trials, respectively. Efficacy of CIC was comparable to FP in both, 1:1 and 1:2 dose ratios with respect to reduction in risk of asthma exacerbations, improvement in proportion of symptom-free days, rescue medication-free days and improvement in asthma symptoms. Moreover, CIC and FP showed similar improvement in spirometric parameters. Comparison between CIC and FP in 1:1 dose ratio revealed that treatment with CIC was associated with statistically significant risk reduction of adverse events possibly related to study medication (RR = 0.57 [0.39; 0.83]; NNT = 16.89 [10.24; 48.18]) and candidosis (RR = 0.31 [0.17; 0.56], NNT = 32.74 [22.23; 61.99]), while the differences between groups were not significant for 1:2 dose ratio. There were no statistically significant differences between CIC and FP in either dose ratio with respect to the risk of any adverse events, upper respiratory tract infections, pharyngitis and dysphonia. **CONCLUSIONS:** Ciclesonide is a therapeutic option for patients with bronchial asthma showing comparable efficacy to fluticasone in both 1:1 and 1:2 dose ratios and provides concomitant risk reduction of candidosis and adverse events related to study medication.

PRS8

A COMPARISON OF CLINICAL EFFICACY AND SAFETY OF CICLESONIDE WITH BUDESONIDE IN 1:1 AND 1:2 DOSE RATIOS IN THE TREATEMENT OF BRONCHIAL ASTHMA

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OBJECTIVES: This study compared efficacy and safety of ciclesonide (CIC) with budesonide (BUD) in the treatment of bronchial asthma. **METHODS:** Comparison was based on randomized controlled trials (RCTs) identified by means of systematic review, carried out according to the Cochrane Collaboration guidelines. The most important medical databases (EMBASE, MEDLINE, CENTRAL) were searched. Two