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ABSTRACTS

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01

Patterns of initial treatment for COPD according to clinical phenotypes in Catalonia

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BACKGROUND: The Spanish guidelines for COPD (GesEPOC) identify 4 clinical phenotypes: non exacerbator COPD, asthma-COPD overlap syndrome (ACOS), frequent exacerbator with chronic bronchitis (CB) and frequent exacerbator with emphysema. Treatment is recommended according to the clinical phenotype and severity. Despite this clasification, real world prescription patterns may differ from the current guidelines recommendations.
AIM OF THE STUDY: This study examined the adequacy of prescribing patterns for newly diagnosed COPD patients from 2007 to 2012 according to their clinical phenotype.
METHODS: Data for this retrospective population based study was obtained from the "System for Development in Research in Primary Care" (SIDIAP) that includes information of 5.8 million inhabitants, 80% of the population of Catalonia (Spain). We included newly diagnosed COPD patients (between 2007–2012) following a diagnosis algorithm and identified their clinical phenotypes. Information about demographic characteristics and the initially prescribed treatment was collected.
RESULTS: During the study period 41492 patients were diagnosed with COPD. Patients were classified as non exacerbators (28552 patients, 69%), ACOS (2152 patients, 5.2%) and frequent exacerbators with CB or emphysema (10888 patients, 27.6%). Baseline characteristics were similar in the 3 groups, although the percentage of women was higher in the ACOS group.
After the diagnosis of COPD, 8837 (21.2%) patients received no treatment. As a first treatment after diagnosis, 11595 (40.6%) of non exacerbator patients were prescribed inhaled corticosteroids, for 1140 of them (4%) in monotherapy. The majority of patients in the ACOS group (88.8%) were treated, 1490 (69.2%) patients with ICS (11.2% in monotherapy). Only 47.6% of patients in the frequent exacerbators group received any treatment and 5702 (52.4%) were on ICS.
CONCLUSIONS: Many COPD patients still remain untreated after diagnosis. Contrary to the recommendations of the COPD guidelines, the use of ICS in non exacerbator patients is widespread, however its use is higher in the ACOS patients.

02

Assessing allergic rhinitis symptom control using a simple visual analogue scale: the digital solution

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BACKGROUND: ARIA developed a visual analogue scale (VAS) as a tool to assess AR control and improve management. This has been validated to assess the burden of AR in primary care,[1] but patients and primary care physicians are not unaware of it.
AIM: To develop a digital VAS-based app for patients to document AR symptom control with their current medication.
METHODS: This app was developed by members of the ARIA Executive committee and experts in patient reported outcomes, who mutually agreed the information that should be captured and recorded. Based on this information, app wireframes were generated and a prototype developed. The content and functionality of the app were tested in both patients (n = 14) and GPs (n = 6) to assess comprehension and usability, prior to finalization.
RESULTS: The app collects information on symptoms experienced, disease type (intermittent/persistent), how symptoms impact users' lives, and type(s) of AR medication used. Users assess their daily symptom control by simply clicking on 3 consecutive VAS (i.e., general-, nose- and eye-symptom) in response to the prompt `describe your AR symptoms today', from `not at all bothersome' to `extremely bothersome'. An asthma VAS is included for those with asthma comorbidity. A push to track symptoms and take medication is an included option. VAS scores are logged and plotted over time and control assessed by predefined cut-offs; well controlled: VAS < 20 mm; partly controlled VAS > 20 mm < 50 mm; uncontrolled VAS > 50 mm. Medication taken on each day is seen by clicking each data point.
CONCLUSION: This app was well accepted by patients and physicians. It is a simple and consistent way to assess AR symptom control on currently used medication. It will allow doctors to better tailor AR medications to patients' needs. The `have you taken your medication' push function is expected to improve patient compliance. It is available for download from the app store.

REFERENCE
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03

Long-term natural course of severe asthma and the influence of early asthma control

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BACKGROUND: Little is known about the natural history of severe asthma. In addition, it is not known whether achieving clinical control of asthma can change the future course of the disease.
METHODS: A cohort of patients with incident severe asthma was identified through the British Columbia administrative health databases between 1997 and 2012. We categorized each patient-year into three severity states (mild, moderate, or severe) and two control states (uncontrolled or controlled). Partial proportional odds regression was used to estimate the annual transition probabilities across severity states as a function of baseline asthma control, adjusting for potential confounders. The transition probabilities were then used to project the ten-year course of severe asthma across the population, and G-computation was used to estimate the marginal effect of baseline control on the trajectory of severe asthma.
RESULTS: We analysed 67 218 patient-years from 13 591 unique individuals with newly classified severe asthma at baseline. After ten years, most patients eventually transitioned to mild/moderate states (83.0%) and a small proportion

(17.0%) remained in severe asthma. Uncontrolled asthma at baseline predicted a higher risk of transitioning to more severe states (odds ratio 1.13, 95% confidence interval: 1.06, 1.21). Controlled asthma at baseline resulted in a 14% lower ten-year cumulative incidence of patient-years with severe asthma.
CONCLUSIONS: Our results indicate that the long-term prognosis of severe asthma is generally good and achieving asthma control early in the course of severe asthma can have important and underappreciated long-term effects.

04

Discrepancy between patient-perception and guideline-defined asthma control in Asia: a survey of over 2400 patients

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BACKGROUND/AIM: A recent survey (REALISE^{TM}) has revealed that patients in Europe perceive their asthma to be well-controlled despite the presence of symptoms. We report data from a similar survey of patients to assess if such discrepancy is seen in Asia.
METHODS: Online surveys were completed by patients (aged 18-50 years, ⩾2 prescriptions for asthma in the past two years), recruited via validated consumer panels from 8 countries in Asia.
RESULTS: A total of 2,467 patients participated, split across the following geographies: Mainland China (30%), Hong Kong (8%), Indonesia (7%), Korea (20%), Malaysia (6%), Philippines (6%), Singapore (8%), and Taiwan (12%). Mean age of respondents was 34 years, with relatively equal proportion of males (54%) and females (46%).
While 89% considered their asthma to be well-controlled, only 18% were classified as such according to GINA guidelines, the rest being partly controlled (32%) and uncontrolled (50%). In the past 7 days before completing the survey, 35% used their reliever inhaler ⩾3 times, 38% experienced symptoms ⩾3 days in a week, 64% had symptoms that interfere with normal activities, and 71% had night-time awakening due to asthma symptoms. In the past year, 33% have been hospitalized, 38% of the respondents had emergency visits, and 73% required oral steroids for worsening asthma. Despite symptoms and exacerbations, 82% did not consider their asthma as serious, 80% regarded their state of health as similar as or better than other people their age, and 82% described themselves as confident in managing their asthma.
Interestingly, more than 2/3 of the respondents related `control' to managing attacks rather than absence or minimal symptoms. Patients' definitions of well-controlled asthma included: attacks are controllable with medical help, reduction of attacks within a time-frame, and prevention of attacks through lifestyle modification or alternative medicines (e.g., traditional Chinese medicines).
CONCLUSION: Patients consistently overestimated their own asthma to be controlled rather than what their clinical symptoms suggested. This discrepancy may be due to fundamental difference on how patients define `control' which is currently geared towards management of exacerbation, instead of pre-defined level of symptom control. A shared understanding of such concepts between patients and physicians may help in achieving treatment goals in asthma care.
DISCLOSURE: Mundipharma Pte Ltd provided funding for the survey. The authors received an honorarium from Mundipharma Pte Ltd for their participation in REALISE Asia Working Group meetings and discussions. G Neira is an employee of Mundipharma Pte Ltd. The REALISE Asia Working Group acknowledges Professor David Price for his advice on the survey and analysis of results, and Research Partnership Healthcare Asia Pte Ltd for survey conduct and data analysis.

05

Identification of attitudinal clusters in patients with asthma: Analysis from REALISE^{TM} Asia

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BACKGROUND/AIM: Similar to the identification of clusters of patients in Europe based on survey of their attitudes towards asthma (REALISE^{TM}), we sought to understand such attitudinal groups among Asian patients.
METHODS: Online surveys were conducted among 2,467 adult patients with asthma across 8 countries in Asia. Using a two-step approach, the respondents were segmented into groups, each containing patients who were similar in their attitudes, yet distinct from those in other groups.
RESULTS: Based from GINA-defined control status (See Table 1), cluster 5 had the most number of uncontrolled patients (92%), followed by clusters 3 (79%) and 4 (74%). Meanwhile, clusters 1 and 2 had the most number of controlled patients (34 and 38% respectively). Cluster 3 had significantly higher number of days and nights when their activities are interrupted by asthma. Cluster 1 had the highest proportion of those who did not experience exacerbation in the last 12 months—no emergency visits (83%), no oral steroids (51%) and no

Table 1. Five attitudinal clusters were uncovered

Clusters	*%*	*Characteristics*
1. 'Well-adjusted'	29	Generally cope well with their asthma Asthma has minimal impact on their daily lives Happy to go along with doctor's advice No problem using their inhaler, reflecting carefree attitude and lower stress levels
2. 'Rejectors'	17	Refuse to accept asthma label Yet to come to terms with emotional burden of living with asthma Deprioritise their health despite some concerns about their asthma High social consciousness about using inhaler
3. 'Lost'	14	High level of stress and anxiety about their asthma Asthma has high impact on their daily lives Avoid thinking about their health High asthma information seeking frequency but do not know where to turn for answers
4. 'Endurers'	29	Accept their condition and that they do not have control over it High acceptance of condition means they do not allow asthma to have a major impact on their daily life Low level of confidence in managing their asthma Less interested in seeking information than other uncontrolled patient types
5. 'Worriers'	11	Asthma is a constant worry on their mind Accept their condition but live with a high level of stress and anxiety about their asthma Exhibit high asthma information seeking frequency due to their concern

antibiotics (42%) for asthma. In contrast, 95% of patients in cluster 5 had >1 course of antibiotics for asthma-related problems in the past year.
CONCLUSION: Asian patients can be grouped into five clusters based on their concerns about their asthma and its management. The recognition of the clusters, offers an opportunity to customize management approaches for patients and leverage on their attitudes to improve asthma control.
DISCLOSURE: Mundipharma Pte Ltd provided funding for the survey. The authors received an honorarium from Mundipharma Pte Ltd for their participation in REALISE Asia Working Group meetings and discussions. G Neira is an employee of Mundipharma Pte Ltd. The REALISE Asia Working Group acknowledges Professor David Price for his advice on the survey and analysis of results, and Research Partnership Healthcare Asia Pte Ltd for survey conduct and data analysis.

06
Predicting patients with COPD who are likely to exacerbate- Is it feasible in primary care?

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BACKGROUND: COPD exacerbations and admissions continue to rise in certain parts of the UK, despite improved management in Primary Care and many initiatives in Primary and Secondary Care to reduce them. This study sets out to find easily identifiable risk factors for COPD.
METHODS: Suitable patients were identified from the OPC (Optimum Patient Care Research Database), 3,713 patients with airways obstruction defined as FEV_1/FVC < 0.7 were identified who also had records continuously for the baseline year and one outcome year during which COPD exacerbations and or admissions were identified. The risk factors identified were chosen as those easily identified from routine GP data and included: age, sex, BMI (body mass index), spirometry, CAT (COPD Assessment Test), mMRC (modified Medical Research Council) dyspnoea score, smoking status, blood eosinophils, presence of asthma, hay fever or eczema, nasal polyps, diabetes, heart disease, GERD and depression/anxiety. Logistic regression analysis was used to estimate the area under the curve (AUC) and confidence intervals to predict ⩾2 exacerbations.
RESULTS: 19% of the patients had ⩾2 exacerbations in the outcome year. Factors which predicted COPD exacerbations and admissions included, female gender, asthma, eosinophilia (⩾450/μl) in non-smokers, nasal polyps and CAT score. The AUC was significantly better than DOSE (Dyspnoea/Obstruction/Smoking/Exacerbations) index or the GOLD groups for predicting exacerbations and admissions relating to COPD.
CONCLUSIONS: Patients at increased risk of COPD exacerbations or admissions can be identified from analysis of data which is routinely available from most UK Primary Care clinical computer systems.
DISCUSSION: This exciting study suggests that the development of a risk assessment tool for COPD may be achievable and deliverable within Primary Care, the next steps are to perform a pilot study (ideally in one group of practices such as a Clinical Commissioning Group) to ensure the project is deliverable in terms of acceptability to practices and to look at how this information can be best used to improve care for our patients and costs for the Health Service.

07
Investigating the proportion of community-based patients with COPD who meet eligibility criteria for published clinical trials of long-acting bronchodilator therapy for COPD: Pilot phase

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BACKGROUND: Limited information exists regarding whether patients enrolled in randomised control trials (RCTs) are representative of people with COPD in the community at large. We have initiated a detailed comparison of RCT eligibility criteria with characteristics of patients included in a quality-controlled, primary care research database.
AIM: To demonstrate proof of principle (exploratory phase) using eligibility criteria from the UPLIFT (Understanding Potential Long-Term Improvements in Function with Tiotropium) RCT,[1] the first of approximately 20 RCTs selected for study based on predefined criteria.
METHODS: The Optimum Patient Care Research Database (OPCRD) contains anonymous, longitudinal data extracted from ~500 UK practices for chronic respiratory review services, including routine clinical data and linked patient-reported data (collected via questionnaires). The UPLIFT inclusion and exclusion criteria were applied to patients with COPD registered in the OPCRD in 2011/2012.
RESULTS: 11,393 of OPCRD patients had an FEV_1 ⩽70% predicted. The progressive exclusion of ineligible patients is shown in Figure 1. Eligibility criteria were applied as follows (percentage excluded in parentheses): exclusion of non-smokers (11%) and then those with unstable therapy (new respiratory therapy in last 2 months; 2%), spirometry exception codes (since last FEV reading; 1%), myocardial infarction (diagnosis in last 6 months), cardiac arrhythmias (diagnosis in last 12 months; or diagnosis ever with change in anti-arrhythmic therapy in last 12 months) or chronic cardiac failure (inpatient admittance for heart failure in last 12 months) (2%), history of asthma (not yet indicated as resolved; 13%), bronchiectasis (diagnosis any time; 3%) and other chronic respiratory diseases (diagnosis any time). The final population of eligible patients was 5,843 (51%).
CONCLUSION: The RCT population of patients with COPD may be more representative of community-based patients than previously thought. The main reasons for exclusion related to smoking status and unresolved asthma diagnoses, rather than co-morbidities or renal impairment. The remaining published RCTs of long-acting bronchodilator therapy in COPD will be analysed in a similar manner.

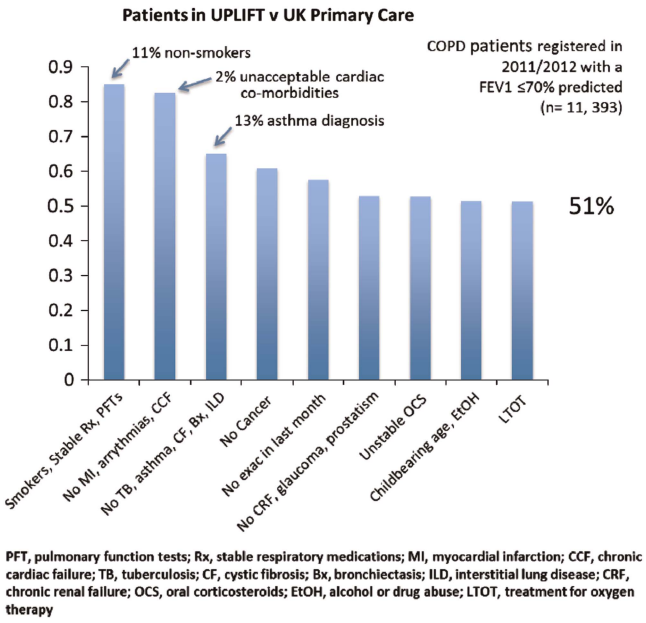

Figure 1. Patients in UPLIFT v UK Primary Care.

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08
Importance of inhaler-device satisfaction and adherence in outcome measures: Real-world observations in US adult asthma patients

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BACKGROUND: It is hypothesised that health-related and patient-reported outcomes in asthma are driven by the degree of patient satisfaction and

adherence with their asthma medication. Evidence of the level of association of satisfaction and adherence impacting outcomes contributes to further understanding and enhancing the management of and impact to asthmatic patients due to their condition.

AIM: To explore the current relationship between patient-reported inhaler satisfaction and adherence amongst adult asthmatics who are currently receiving at least one maintenance inhaler (ICS, LABA, ICS/LABA, LAMA). To then determine if that level of adherence has any influence on subsequent health and patient-reported outcomes via clinical measures including control, impact on sleep, by the standardised measure of health status EuroQuol 5D (EQ-5D-3L) and number of asthma exacerbations in the last 12 months.

METHODS: Real-world evidence via the Respiratory Disease Specific Programme (DSP) identified consulting adult asthmatics who are currently receiving at least one maintenance asthma inhaler. A physician-reported confirmed diagnosis and therapy assessment coupled with the patient-reported measured inhaler satisfaction, adherence and quality of life outcome measures to assess the degree of association. Data were drawn from the USA 2013 Respiratory DSP, a cross-sectional survey of consulting adult asthma patients, 12 years and older. Patients were prescribed at least one maintenance asthma inhaler. Partial Least Squares Path Modelling (PLS-PM) was used to model the relationship between the latent, or hypothetical, grouped variables of inhaler satisfaction, adherence and outcomes. Each hypothetical grouped variable was comprised of the following actual individual variables:

(1) Inhaler Satisfaction: measured by 12 patient-reported satisfaction attributes on a 5-point scale.

(2) Adherence: measured by patient-reported validated Morisky 8-Item Medication Adherence questionnaire.

(3) Outcomes: measured by Asthma Control Test, Jenkins Sleep score, EQ-5D-3L State Valuation and number of asthma exacerbations in the last 12 months.

RESULTS: 246 US adult asthma patients were included in the analysis. The Cronbach's Alpha, a measure of consistency for a group of variables, indicated that the hypothetical variables of inhaler satisfaction, adherence and outcomes were well reflected by the composition of the actual variables in the dataset. Cross-loadings, or correlations, indicated that all actual variables were associated with the correct hypothetical variable. The Cronbach's Alpha and cross-loadings indicated that our model was specified appropriately. Increased adherence was significantly associated with increased inhaler satisfaction ($p = 0.0137$, $R^2 = 2.46\%$) and improved outcomes was significantly associated with increased adherence ($p = 0.0026$, $R^2 = 3.65\%$). The pseudo goodness of fit, which measures the overall prediction performance of the path model, was 11.99%.

CONCLUSION: The degree of patient satisfaction with their asthma inhaler device is observed to have a positive impact on patient-reported adherence, which in turn is associated with improved outcome measures relating to better control, improved sleep, higher quality of life and reduced asthma exacerbations. Whilst this suggests a relationship exists between satisfaction and outcomes amongst US asthma patients, further research is needed to establish if this link is a direct cause or the impact of other variables such as adherence.

09

The GOLD COPD categories are inaccurate in predicting future risk in a UK primary care dataset

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BACKGROUND: The clinical validity of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity assessment system for COPD, which produces categories A, B, C and D, requires full evaluation. Recently the GOLD categories cut-off values have changed.

AIM: To assess the effect of the alternative methods of calculating the categories on their distribution and future risk of exacerbations and the effect of changes in the cut-off values in the GOLD categories on these measures.

METHODS: Data came from a real-life observational cohort study using primary care COPD patients in the Optimal Patient Care database from UK. There were 7,105 patients with COPD who had valid data on MRC, exacerbations and FEV_1% predicted values as well as outcome variables including admissions and future exacerbations. A total of 3015 patients had valid CAT and MRC scores and a valid FEV_1%. Thus we could calculate the categories using all possible allowed methods. The new cut-offs were to change the MRC scale from less symptoms 0-1, and more symptoms 2 or above to less symptoms = 0; more 1 or above. A cut-off using the Clinical COPD Questionnaire (CCQ) score of up to 1.5 less symptoms and 1.5 and above more symptoms.

RESULTS: The distribution between the categories A–D was uneven; using the preferred method of calculation of risk (FEV_1% or number of exacerbations, whichever gives highest risk and symptoms (using CAT)) resulted in the following distribution: A 18%, B 50%, C 4.2% and D 28%. The figures varied substantially according to the way the categories are computed, e.g., the proportion in D varies from 2.8% to 46%. Figure 1 shows the percent of patients with at least one exacerbation in the following year. With the new MRC cut-off value and using the highest risk out of exacerbation or FEV_1%, the proportion having one or more exacerbations in the next year was in A 1.5%, B 3.8% C 4.5% and in D 10.2% and for CCQ A 1.9% B3.8% C 6.5% and in D 10.2%.

CONCLUSION: The GOLD categories vary according to the methods used to calculate them and modifications to the cut-off values are associated with misleading assignment of risk. If adopted, they may lead to inappropriate treatment being given. The optimal method to assess risk is to use the exacerbation frequency.

[09]

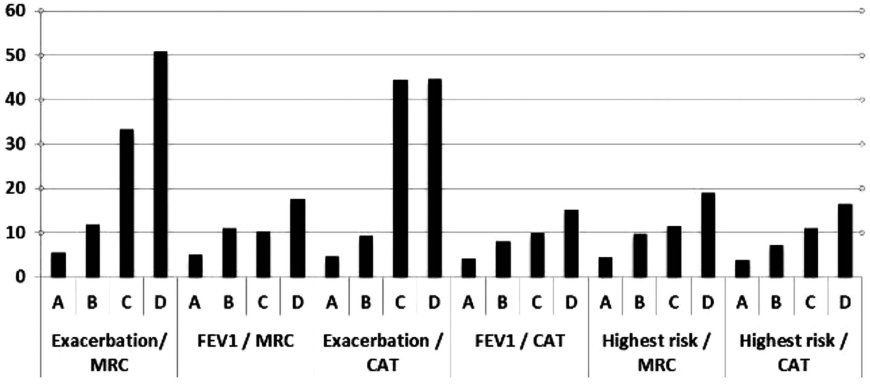

Figure 1. The proportion of patients with 1 or more exacerbations in the follow-up period as seen in the GOLD categories calculated by the alternative methods.

10
Blood eosinophils as a marker of COPD

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BACKGROUND: Raised blood eosinophils are associated with asthma and allergic inflammation. Although it is well known that asthma and chronic obstructive pulmonary disease (COPD) may overlap, there is currently limited data on blood eosinophils in COPD.
AIM: To explore the relevance of blood eosinophils in COPD in a GP database.
METHODS: Patients with COPD were taken from the Optimum Patient Care Research Database. All patients had a read code for COPD, $FEV_1/FVC < 0.7$ and were aged ⩾40 years. We studied two populations: 1) patients with a blood eosinophil measurement performed at steady state, i.e. >4 weeks apart from an exacerbation and 2) patients with repeated eosinophil measurements (median follow up time: 6 years (IQR = 3 to 8)). For population 1 we calculated rate ratios (RR) for the number of exacerbations in the subsequent year using Quasi-Poisson regression, with exacerbations defined as an acute course of oral steroids (OS) and/or antibiotics prescribed at lower respiratory consultation or COPD-related hospital admission/A&E attendance. For population 2 we used a linear mixed effects (LME) model to study stability of eosinophil counts and effects of COPD treatment on it.
RESULTS: Population 1: 10% of 13,780 patients had blood eosinophilia (⩾450/μl), 37% of whom had ⩾1 COPD exacerbations following the eosinophil measurement. For 35% of patients who were non-smokers using inhaled corticosteroids (ICS), blood eosinophilia was associated with a 24% higher exacerbation rate (RR = 1.24 (1.10–1.41)). Eosinophilia was not associated with exacerbations in current smokers (35%) nor in 30% of patients not using ICS or long-acting bronchodilators. Excluding patients with any diagnosis of asthma (42%) did not change this association.
Population 2: The correlation of eosinophil measurements made on the same patient ($n = 23,197$) was moderate ($\rho = 0.56$). 26% of patients had eosinophilia at some stage during follow up, most of them intermittently. Treatment with ICS prior to measurements was associated with lower eosinophil levels (5% in men and 2% in women).
Associations between COPD exacerbations treated with antibiotics (89%) and/or oral steroids (37%) and eosinophil levels were dependent on timing of first prescription relative to eosinophil measurement (figure). Both ICS and OS treatment effects on eosinophil counts were significantly higher in men than in women.
CONCLUSIONS: Blood eosinophilia was associated with an increased exacerbation risk in non-smoking COPD patients treated with ICS. ICS treatment itself had a minor effect on eosinophil counts. Oral steroids greatly reduced eosinophil levels.

11
Real-world effectiveness of a new allergic rhinitis therapy (MP29-02)

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BACKGROUND: In clinical trials MP29-02 (a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP) in an advanced delivery system) provided complete/near complete symptom control in 1 of 6 moderate-to-severe SAR patients[1] and complete relief in 7 of 10 mild-to-moderate PAR patients.[2]
AIM: This study aimed to assess the effectiveness of MP29-02 in routine clinical practice.
METHOD: Results from Germany ($n = 1133$) from a multinational, multicentre, prospective, observational study in adults/adolescents with moderate-to-severe AR for whom MP29-02 was prescribed according to summary of product characteristics are reported. Patients assessed symptom severity using a visual analog score (VAS) from 0 mm (not at all bothersome) to 100 mm (very bothersome), in the AM prior to MP29-02 use, on Days 0, 1, 3, 7 and treatment end. Intended study duration was 14 days. This was flexible to allow for normal clinical practice. Patients had acute AR symptoms on Day 0 and VAS >50 mm. VAS <20 mm was considered controlled.[3] Patients' perceived level of disease control (i.e. well-, partly- and un-controlled) was assessed on Day 3.
RESULTS: MP29-02 (1 spray/nostril bd; daily doses: AZE = 548 μg; FP = 200 μg) provided effective symptom control from Day 1, averaging 21.03 mm by treatment end. 62.7% of patients had VAS <20 mm at that time. Symptoms were well-controlled in those with more- (baseline VAS 75–100 mm) and less-severe symptoms (baseline VAS 50–74 mm). 1 in every 2 patients felt their symptoms were well-controlled after just 3 days treatment.

[10]

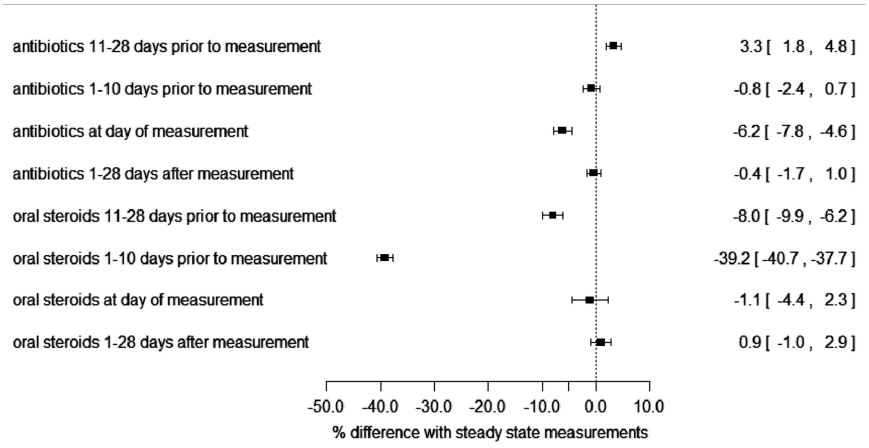

Figure 1. Relative change (in % with steady state measurements as the reference in one LME model) in geometric mean eosinophil levels for measurements at COPD exacerbations for four different categories of timing of the first prescription of antibiotics or oral steroids ($n = 12,425$).

CONCLUSION: MP29-02 provides effective and rapid symptom control in a real-world setting with responder rates higher than those observed in a clinical trial with moderate to severe AR patients, supporting MP29-02's position as the drug of choice for the treatment of AR.

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12
Real life effectiveness of changing fixed-dose combination therapy from Seretide® metered dose inhaler (MDI) to Flutiform® in UK patients with asthma

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BACKGROUND: Data from randomised controlled trials suggest that fluticasone propionate/formoterol (Flutiform®, FP/FOR) is as effective as fluticasone propionate/salmeterol (Seretide®, FP/SAL) for asthma management but achieves more rapid bronchodilation. Real life research is required to assess the acceptability of FP/FOR in primary care asthma patients.
AIM: To investigate the success of changing fixed dose combination therapy from FP/SAL to FP/FOR in patients with asthma.
METHOD: Observational study of UK primary care patients from the Optimum Patient Care Research Database changing fixed-dose combination therapy from FP/SAL via MDI to FP/FOR. Patients aged 12-80 with asthma diagnosis and/or ⩾2 prescriptions for asthma therapy 1 year prior to first FP/FOR prescription. Primary outcome was "change success" defined as ⩾70% of patients with ⩾1 prescription for FP/FOR 6 months following therapy change (not including first prescription). Patient characteristics during year prior to FP/FOR prescription were analysed and compared with patients prescribed FP/SAL prescribed as repeat prescription (Mann-Whitney and $\chi 2$ where appropriate). Oral steroid use in FP/FOR patients was compared 6 months pre- and post-switch using McNemar-Bowker test.
RESULTS: Of 164 patients changing their therapy to FP/FOR, 88.4% had at least 1 further FP/FOR prescription 6 months following the change. 164 FP/FOR patients were compared with 6,228 FP/SAL patients. Overall baseline characteristics were similar although FP/FOR patients were significantly older, more likely to be current smokers and with more lower respiratory tract infection consultations leading to antibiotic prescriptions. 6-month effectiveness analysis before and after FP/FOR switch showed no significant differences in number of oral steroids prescriptions ($p = 0.175$).
CONCLUSION: Change success was achieved with 88.4% of FP/FOR patients receiving a second prescription 6 months following therapy change with no loss of asthma control.

13
Relationships between database-recorded objective variables and GINA current control status

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BACKGROUND: Database-recorded measures reflecting asthma symptom control are needed when conducting observational studies using routinely collected electronic patient medical records, as these records usually do not contain measures of daily symptom control.
AIM: To evaluate relationships between objective database-recorded variables and patient-reported Global INitiative for Asthma (GINA) 2012 current control status (changed in GINA 2014 to symptom control).
METHODS: We used anonymous primary care patient data from the Optimum Patient Care Research Database to study patients with asthma ages 18–60 who had 1 year of routinely recorded medical data preceding the date of a patient-completed questionnaire. Patients with other chronic respiratory conditions or receiving maintenance oral steroids were excluded. Questionnaires included Global INitiative for Asthma (GINA) current control status (symptoms and lung function). Objective variables, assessed from the database, included asthma-related hospital attendance, acute oral steroid bursts, antibiotics prescribed with respiratory review, and mean daily dose of short-acting β-agonists (SABA) during 1 year based on prescription records. Those variables showing a significant ($p < 0.05$) association with GINA current control status (dependent variable) in univariable models were entered into a multivariable model and stepwise reduced.
RESULTS: 2468 patients (60% female, 25% current smokers, 14% ex-smokers) of median (IQR) age 46 (38–54) years were included. Acute oral steroid bursts and higher SABA prescribing over 1 year were predictive of GINA uncontrolled status at the end of the year (Table). Absence of antibiotics prescribed with a respiratory review and low (but present) SABA prescribing during the year were predictive of GINA controlled status.

[13]

Table. Multivariable results for ordinal and binary logistic regression: GINA current control status[a] and database-recorded objective variables

Explanatory variable	*Reference (OR = 1.0)*	*Variable*	*Odds Ratio (OR) (95% CI)*	*P value*
Ordinal logistic regression (GINA controlled vs. Partly vs. Uncontrolled)				
Acute oral steroid burst	None	Yes	0.53 (0.41–0.69)	< 0.001
Mean daily SABA dose (μg/day)	⩽ 200	> 200	0.43 (0.37–0.50)	< 0.001
Binary logistic regression (GINA Controlled/partly vs. Uncontrolled)				
Acute oral steroid burst	None	Yes	0.49 (0.38–0.64)	< 0.001
Mean daily SABA dose (μg/day)	⩽ 200	> 200	0.46 (0.39–0.54)	< 0.001
Binary logistic regression (GINA Controlled vs. Partly/Uncontrolled)				
Antibiotic prescription with respiratory review	None	Yes	0.73 (0.56, 0.95)	0.017
Mean daily SABA dose (μg/day)	1–100	0	0.27 (0.18–0.40)	< 0.001
		101–200	0.63 (0.49–0.81)	
		201–400	0.34 (0.25–0.45)	
		> 400	0.15 (0.10–0.23)	

[a]Global INitiative for Asthma control status, 2010–2012 definition; www.ginasthma.org.

CONCLUSIONS: Objective variables relating to current control (mean prescribed SABA dose) and future risk (including acute oral steroid bursts and antibiotics prescribed with respiratory review), collected in patient medical records over the course of a year are predictive of patient-reported GINA 2012 current control status at year-end. Further assessments of their responsiveness to treatment and predictive power for future asthma risk will complement our understanding of how these variables can be used for observational research.

14

Episode pattern and healthcare utilisation in patients with seasonal allergic rhinitis

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BACKGROUND: Allergic rhinitis (AR) occurs in >500 million people worldwide, with the majority suffering from moderate/severe disease. Although its effects are far-reaching they are underestimated.
AIM: This patient survey in the UK aimed to quantify healthcare resource utilisation and establish the symptom pattern experienced by these patients, with a view to informing future economic analyses.
METHODS: 254 mild and 756 moderate/severe patients (total nasal symptom score (TNSS) ⩾8/12, incl. congestion score ⩾2) complete the survey score of ⩾2) recruited through a patient panel completed the survey. The survey included questions on respondent's treatment, episode duration, medication utilisation, GP services and the impact of symptoms on productivity. Descriptive statistics were used to summarise results, enabling estimation of the potential gains from successfully treating SAR symptoms, derived through reduced utilisation of healthcare services and reduced absenteeism.
RESULTS: Moderate/severe patients had a mean severity rating when not taking medication of 5.1/7. They typically experienced 23 symptom episodes/yr, each lasting 12.5 days. 70.5% of patients co-medicated, with the need for a more effective nasal treatment (41.1%) and additional ocular relief (29.1%) the most common reasons. This agrees with the results of a discrete choice experiment (DCE) which was performed in the same cohort where increased efficacy was the main factor driving patient preference for a medication. These patients visited their GP 1.61 times/yr, with 0.57 visits due to dissatisfaction with current treatment. On average, patients were absent from work for 4.1 days/yr due to SAR, with productivity being impacted on 37.7 days/yr. Over half of these moderate/severe patients found productivity was impacted by ⩾40%.
CONCLUSIONS: This survey shows that patients with moderate to severe AR use combination therapy in an attempt to more effectively manage their symptoms. This was confirmed by a separate DCE in the same cohort. Clearly, more effective treatments for AR are urgently needed to control AR symptoms sufficiently to reduce absenteeism and productivity loss associated with AR. The results of the survey provide evidence for the first time that a typical moderate/severe SAR episode lasts for 12.5 days. Therefore, SAR trials of 14 days duration are sufficiently long to detect treatment differences, and represent real-world patient treatment behaviour.

15

Allergic rhinitis medication co-prescribing behaviour of UK general practitioners: a proxy marker of unmet medical need

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BACKGROUND: Allergic rhinitis (AR) places a high burden on its patients, and on GPs who treat them. It is often difficult to control, even with multiple therapies.
AIM: To quantify the unmet medical need in seasonal AR (SAR) and perennial AR (PAR) using co-prescribing behaviour of UK GPs during 2 pollen seasons as a proxy measure.
METHODS: This was a retrospective observational study conducted with data from the Optimum Patient Care Research Database. Diagnoses and prescriptions data for the 2009 and 2010 pollen seasons (1st March to 31st Aug) were assessed for patients with a recorded AR diagnosis who took AR therapy during the study period. Those with SAR had no recorded AR treatment in the six months preceding the first prescription of the study period. Those with PAR suffered from AR outside of the pollen season as indicated by at least one AR therapy prescription in the six months preceding the first prescription of the study period and also had a seasonal exacerbation.
RESULTS: The % of multiple therapy prescriptions increased over both seasons in both SAR and PAR patients. Some 33% of SAR patients started the season on multiple therapy, rising to 45% by season end. A greater shift was seen in PAR patients, starting at 23%, and increasing to over 50% by season end. The percentage of PAR patients receiving dual therapy doubled, and the proportion who received triple therapy tripled over the season. Of patients with a single first prescription, over 20% of SAR patients and over 40% of PAR patients needed an additional GP visit for an add-on prescription. For these patients anti-histamine + intranasal steroid was the most common combination (≈37% of SAR and PAR patients). Adding eye drops to mono- and dual-therapies was also a popular prescription choice for mono-therapy failures (≈42% of SAR patients; ≈30% PAR patients).
CONCLUSION: UK GPs commonly prescribe multiple therapies as the first script of the season for both PAR and SAR patients, with co-prescription becoming more common as the season progresses. 1 in every 5 SAR patients and almost 1 in every 2 PAR patients originally prescribed a single therapy required an additional GP visit for therapy add-on. These results indicate that current therapy options provide insufficient symptom relief for AR patients. There is a clinical need for a more efficient therapy.

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Assessing allergic rhinitis symptom control: results from a digital survey conducted during EAACI 2013

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BACKGROUND: Allergic rhinitis (AR) is poorly controlled in many patients, who continue to experience nasal and ocular symptoms[1] even on multiple therapies.[2] However, exactly what is meant by `control'? A simple way to assess AR control is needed; a common language for physicians and patients to more effectively manage this disease.
AIM: To assess how physicians (i) measure AR control, (ii) perceive the control status of patients and (iii) regard the usefulness of a simple visual analogue scale (VAS) to gauge control.
METHODS: 307 EAACI 2013 delegates completed an iPAD survey. Delegates were asked to (i) indicate how many AR patients they saw per week during the season, (ii) assess the proportion of patients they considered to be well-, partly- and un-controlled, (iii) communicate how they gauged control (>1 answer permitted) and (iv) assess how useful they would find a VAS as a method of gauging control.
RESULTS: Respondents reported seeing 46.8 (s.d. 68.5) AR patients/week on average during the season. They considered that AR was controlled, partly controlled and uncontrolled in 38.7% (s.d. 24.0), 34.2% (s.d. 20.2) and 20.0% (s.d. 16.34) of patients, respectively. Delegates reported assessing disease control in many different ways, including symptom severity (74%), frequency of day- and night-time symptoms (67%), activity impairment (57%), respiratory function monitoring (40%) and incidence of exacerbations (50%). 91% of delegates felt that a VAS was a useful tool to assess disease control.
CONCLUSION: Physicians assessed AR control in many different ways and considered that over 50% of their patients had sub-optimally controlled disease. Almost all physicians considered the VAS a useful tool to assess AR

control. Such a tool would enable control assessment in a simple and consistent way and should improve the way this disease is perceived and managed.

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17

Assessment of potentially important device errors made by patients with asthma in the global iHARP review service

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AIM: The global iHARP asthma review service addresses a key strand of the IPCRG's position on establishing reasons for poor asthma control. This is a preliminary study to determine the frequency of potentially important device errors made by patients with asthma in real-life primary care clinical practice.

METHODS: Retrospective, observational study using iHARP database including patient records and questionnaires. Patients from 8 countries with asthma at GINA step 3-4 were recruited. The iHARP steering committee defined generic (error common across all devices) and device-specific errors that might potentially limit drug uptake. Errors were recorded by trained nurses (doctors recorded errors in Spain) from 2011-2013. The frequency and inhalation stages of errors were categorised for patients using dry powder inhaler (DPI) Diskus, DPI Turbohaler, metered dose inhaler (MDI) and MDI with spacer devices. Variables were adjusted for potential collinearity.

RESULTS: Of 3654 patients (34% male; median age [IQR] 53 [41, 63]) 59.3% were from UK, 12.4% Netherlands, 11.3% Italy, 10.3% Spain, 4.5% Australia, 1.6% Sweden, 0.4% France and 0.2% Norway. The proportion of patients making $\geqslant 1$ potentially important generic and device-specific errors overall was 89%, and by device type was: 95% DPI Diskus; 87% DPI Turbohaler; 92% MDI; 87% MDI with spacer (similar for MDI and MDI with spacer). Table 1 shows the frequency of potentially important generic and device-specific errors as a percentage of errors made.

CONCLUSION: Patients with asthma routinely make potentially important device errors with all asthma devices across countries. Inhalation errors are most frequent. Spacers are not a panacea. Future analysis of errors vs. asthma control might help validate which errors are important.

18

Characterising patients with asthma using Diskus at risk of making serious errors in primary care

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BACKGROUND: Correct inhalation technique is crucial for asthma therapy delivery. Incorrect technique could influence patient outcomes.

AIM: To characterise patients with asthma using Diskus at risk of making serious errors in real-life international primary care clinical practice.

METHODS: A retrospective, cross-sectional analysis using the international iHARP database composed of electronic patient records and patient-reported questionnaires. Characteristics of patients using Diskus with no other chronic respiratory disease aged $\geqslant 18$ years with no serious errors were compared against those making $\geqslant 1$ serious error using Mann-Whitney test and χ^2 test for numerical and categorical variables, respectively. Serious errors were defined by the iHARP steering committee and observed by a qualified nurse (doctors observed patients in Spain) between June 2011 and November 2013.

RESULTS: Of 3681 patients with asthma, 624(17%) were using Diskus. Of these 624 patients 37% were from the UK, 24% Italy, 16% Spain, 13% the Netherlands, 6% Australia, 1% France, 1% Sweden and 1% Norway. 67% were female and median age was 52 (Interquartile range [IQR] 41-63). 55% of Diskus patients made $\geqslant 1$ serious error. Most frequent errors were `Does not breathe out slowly to residual volume' (33%), `No breath-hold, or breath-hold for < 3 seconds' (25%) and `Inhalation is not forceful from the start' (21%). 57% of patients in the $\geqslant 1$ serious error group did not have their inhaler technique checked in the last 12 months compared to 47% in the no error group (Table 1; $p = 0.012$). 70% of patients in the $\geqslant 1$ serious error group thought their inhaler technique was above average, which was significantly different from the no error group (80%) (Table 1; $p = 0.017$). Female patients (61%), obese (BMI > 30) patients (30%) and current smokers patients (13%) made significantly more serious errors (Table 1; $p = 0.032$, $p = 0.036$ and $p = 0.002$, respectively). Making serious errors was not significantly associated with age, Charlson Comorbidity Index score, lung function, duration of asthma diagnosis and adherence to ICS therapy.

CONCLUSION: Inhaler technique remains poor which could potentially influence asthma outcomes. Patients who are obese, female or are current smokers are particularly at risk of making Diskus errors. Patients who had not had their inhaler technique checked during the last 12 months made more serious errors, which highlights the importance of regular monitoring.

[17]

Table 1. Frequency of potentially important generic and device-specific errors categorised by stage as percentage of errors made

Potentially important device errors (categorised by stage)	*Overall (n = 3654)*	*By device type*			
		DPI Diskus (n = 627)	*DPI Turbohaler (n = 1715)*	*MDI (n = 998)*	*MDI with spacer (n = 314)*
Preparation errors, *n* (%)	2066 (21)	306 (23)	894 (21)	609 (20)	257 (23)
Positioning errors, *n* (%)	2302 (24)	327 (25)	1402 (34)	468 (16)	105 (9)
Inhalation errors, *n* (%)	3921 (41)	513 (39)	1587 (38)	1416 (47)	405 (36)
Completion errors, *n* (%)	43 (1)	12 (1)	19 (1)	12 (1)	0 (0)
Lack of device-related general knowledge, *n* (%)	1264 (13)	155 (12)	264 (6)	487 (16)	358 (32)
Total errors, *n* (%)	9596 (100)	1313 (100)	4166 (100)	2992 (100)	1125 (100)

[18]

Table 1. Demographics for patients with asthma using Diskus

Demographic	*No errors (n = 282)*	*≥ 1 error (n = 341)*	*Total (n = 623)*	*P-value*
Gender				
Female, *n* (%)	176 (62)	221 (65)	380 (61)	**0.032**
Age				
Median (IQR)	52 (39–63)	52 (42–62)	52 (41–63)	0.837
Smoking status				
Non-smoker, *n* (%)	163 (58)	193 (56)	356 (57)	**0.002**
Current smoker, *n* (%)	28 (10)	50 (15)	78 (13)	
Former smoker, *n* (%)	91 (32)	98 (29)	189 (30)	
BMI				
BMI, mean (SD)	27 (5)	28 (6)	28 (6)	**0.008**
Underweight (BMI < 18.5), *n* (%)	4 (1)	4 (1)	8 (1)	**0.036**
Normal BMI (18.5–24.99), *n* (%)	107 (38)	107 (32)	214 (35)	
Overweight (BMI 25–29.99), *n* (%)	102 (36)	110 (32)	212 (34)	
Obese (BMI >30), *n* (%)	69 (25)	120 (35)	189 (30)	
Technique check				
Not checked in last 12 months, *n* (%)	132 (47)	194 (57)	326 (52)	**0.012**
Patients subjective inhaler technique				
Unknown, *n* (% of total)	12 (4)	23 (7)	35 (6)	**0.017**
Very poor, *n* (%)	8 (3)	5 (2)	13 (2)	
Poor, *n* (%)	3 (1)	8 (3)	11 (2)	
Fair, *n* %)	11 (4)	33 (10)	44 (8)	
Average, *n* (%)	32 (12)	46 (15)	78 (13)	
Good, *n* (%)	108 (40)	110 (34)	218 (37)	
Excellent, *n* (%)	108 (40)	116 (36)	224 (38)	
Total, *n* (%)	282 (100)	341 (100)	623 (100)	—

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Dynamics of treatment within a year in patients diagnosed with either allergic, non-allergic rhinitis or hay fever over the period 1992–2012

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BACKGROUND: Treatment of rhinitis has changed over the past 20 years, not least due to the changing face of this disease, but also due to the introduction of new medications and, with passing time their availability without a prescription over the counter.

AIM: The aim was to evaluate the dynamics of prescriptions of various treatment regimens for rhinitis patients over the past 20 years from 1992 to 2012.

METHODS: This was a retrospective database study using the Optimum Patient Care Research Database which holds patient data from 392 practices across the UK. Patients included in the analysis had a recorded diagnosis of allergic rhinitis, non-allergic rhinitis or hay-fever with a rhinitis related prescription. The number of therapies and the number of prescriptions were calculated annually. Types of therapies were categorised based on the annual prescriptions, as single therapies and their combinations. The therapies included were as follows: oral/injected antihistamines (AH), intranasal steroids (INS), eye drops (ED), nasal sprays including nasal antihistamines, systemic corticosteroids, immunotherapy and leukotriene receptor antagonists. Patients were classified based on presence of asthma diagnosis.

RESULTS: The % of non-asthma patients prescribed ⩾2 therapies annually increased from 15.4% in 1992 ($n = 270$) to 44.8% in 2012 ($n = 3,855$), driven predominantly by increased prescriptions of intranasal steroids (INS)+ antihistamine (AH), INS +AH + eye drops (ED) and AH +ED. The % of patients on dual therapy doubled in 2 decades from 14.1% to 32.9%, with the proportion on triple therapy increasing by more than x8 from 1.3% in 1992 to 11.1% in 2012. The trends follow a similar pattern for asthma patients, the % prescribed ⩾2 therapies annually increased from 19.6% in 1992 ($n = 721$) to 44.6% in 2012 ($n = 3316$).

CONCLUSIONS: These data highlight that (i) INS alone provide insufficient symptom relief for many patients (ii) rhinitis is becoming more difficult to treat with more patients being prescribed non-guideline recommended medication combinations (ARIA 2010); and that (iii) ocular symptoms drive co-prescribing behaviour for many patients. There is a need to simplify rhinitis treatment with a new single medication option which more effectively relieves both nasal and ocular symptoms.

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Evaluation of cardiovascular disease risk following exposure to nicotine replacement therapy compared to smoking cessation advice in a real-life UK primary care population

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BACKGROUND: Nicotine is known to affect cardiovascular function. There have been anecdotal reports of increased cardiovascular events among smokers prescribed nicotine replacement therapy (NRT).

AIM: To assess cardiovascular disease event rates and survival among smokers who attempted smoking cessation using NRT or smoking cessation advice only.

Table 1. Comparison of cardiac events and mortality for NRT group relative to advice group at 4 and 52 weeks

Outcome period	*Adjusted HR/OR (95% CI) for NRT Group relative to Advice group (1.00)*			
	Time to 1st ischaemic heart disease diagnosis (HR)	*Time to 1st cerebrovascular disease diagnosis (HR)*	*Consultations in primary/secondary care for ischaemic heart disease/cerebrovascular disease (OR)*	*Survival time (All-cause mortality) (HR)*
4 weeks	1.00 (0.64, 1.55)	0.97 (0.31, 2.99)	—	—
52 weeks	1.08 (0.91, 1.29)	1.30 (0.90, 1.88)	1.20 (1.04, 1.38)	1.62 (1.23, 2.13)

METHODS: A matched retrospective cohort study using primary care data collected by the Clinical Practice Research Datalink. Smokers aged 18 to 75 who were prescribed NRT or smoking cessation advice only (unexposed group), as their first smoking cessation attempt, were included. Patients prescribed other pharmacological interventions for smoking cessation up to 12 months following their index cessation attempt were excluded. NRT users were matched to unexposed patients on gender, age, hypertension, cardiovascular disease, cerebrovascular disease, ischaemic heart disease, diabetes and chronic obstructive pulmonary disease. Outcomes were analysed at 4 and 52 weeks following smoking cessation attempt. Time to first ischaemic heart disease or first cerebrovascular disease diagnosis and all-cause mortality were analysed using Cox's Proportional Hazards models. The odds of consultations for ischaemic heart disease or cerebrovascular disease were analysed using conditional logistic regression models. Models were adjusted for baseline (one year prior to cessation attempt) confounders where necessary.
RESULTS: Median age of the study population (49,779 patients: NRT = 16,593 and cessation advice only = 33,186) was 45 years [IQR 38-55], 48.7% were males. Time to first ischaemic heart disease or cerebrovascular disease, assessed at 4 or 52 weeks, was similar among NRT users and the unexposed. The odds of NRT patients having one or more primary or secondary care consultations for ischaemic heart disease or cerebrovascular disease were significantly higher relative to the unexposed. Survival rates were significantly lower for NRT patients at 52 weeks, after adjustment for baseline confounders.
CONCLUSIONS: Rates of ischaemic heart disease and cerebrovascular disease at 4 and 52 weeks were similar among NRT users and patients provided with smoking cessation advice only. All-cause mortality rates and consultations for ischaemic heart disease and cerebrovascular disease were observed to be significantly higher for patients prescribed NRT.

21
Identifying factors, including biomarkers, associated with future asthma exacerbation and hospitalisation risk from routine UK primary care clinical records

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BACKGROUND: Primary care physicians are increasingly interested in stratifying patients to help prescribe individualised therapies. Factors

[21]

Table 1. Baseline factors associated with ⩾2 severe exacerbations in outcome

		Patient distribution, n (%)	*Odds ratio (95% CI)*	*P-value*
☒Biomarker: blood eosinophil count (Reference category: ≤ 400/μl)	> 400/μl	1,831 (22)	1.48 (1.39–1.58)	< 0.001
Acute courses of oral corticosteroids (Reference category: No course)	1 course	1,598 (19)	3.75 (3.51–4.02)	< 0.001
	2 courses	1,053 (13)	7.31 (6.73–7.95)	< 0.001
	≥ 3 courses	2,832 (34)	25.69 (23.90–27.62)	< 0.001
GINA management step (Reference category: 2)	0	522 (6)	1.58 (1.42–1.76)	< 0.001
	1	568 (7)	1.18 (1.06–1.30)	0.002
	3	1,071 (13)	1.28 (1.17–1.38)	< 0.001
	4	3,679 (44)	1.88 (1.77–2.01)	< 0.001
	5	367 (4)	3.12 (2.64–3.68)	< 0.001
GP consultations for lower respiratory tract infections resulting in antibiotic prescription (Reference category: No consultation)	1 consultation	1,674 (20)	1.18 (1.10–1.26)	< 0.001
	≥ 2 consultations	1,058 (13)	1.28 (1.17–1.40)	< 0.001
Paracetamol prescription (Reference category: No prescription)	≥ 1 prescription	3,878 (46)	1.23 (1.17–1.30)	< 0.001
Sex (Reference category: Male)	Female	6,092 (72)	1.21 (1.14–1.28)	< 0.001
Asthma-related hospital outpatient visit (Reference category: No visit)	≥ 1 visit	836 (10)	1.20 (1.09–1.32)	< 0.001
BMI (Reference category: Normal [18.50–24.99 kg/m^2])	Underweight (< 18.50 kg/m^2)	221 (3)	1.11 (0.94–1.30)	0.220
	Overweight (25.00–29.99 kg/m^2)	2,092 (26)	1.08 (1.01–1.16)	0.028
	Obese (≥30 kg/m^2)	3,822 (47)	1.17 (1.10–1.25)	< 0.001
Smoking status (Reference category: Non-smoker)	Current smoker	1,600 (19)	1.15 (1.07–1.23)	< 0.001
	Former smoker	2,201 (26)	0.93 (0.88–0.99)	0.028
Gastro-oesophageal reflux disease (Reference category: No diagnosis)	Diagnosis	1,689 (20)	1.12 (1.05–1.20)	0.001
Diabetes (type 1 or 2) (Reference category: No diagnosis and/or therapy)	Diagnosis and/or therapy	2,711 (32)	1.11 (1.05–1.18)	< 0.001
Rhinitis (Reference category: No diagnosis and/or therapy)	Diagnosis and/or therapy	4,176 (50)	1.10 (1.05–1.16)	< 0.001
Anxiety and/or depression (Reference category: No diagnosis)	Diagnosis	3,894 (46)	1.09 (1.03–1.15)	0.001
Eczema (Reference category: No diagnosis)	Diagnosis	3,032 (36)	1.08 (1.03–1.14)	0.003
Age	Per year of age	8,429 (100)	1.007 (1.005–1.008)	< 0.001

Table 2. Baseline factors associated with ⩾1 hospitalisation in outcome

		Patient distribution, n (%)	*Odds ratio (95% CI)*	*P-value*
Biomarker: blood eosinophil count (Reference category: ≤ 400/μl)	>400/μl	204 (20)	1.27 (1.08, 1.50)	0.005
Prior asthma-related hospitalizations (Reference category: No hospitalisation)	≥ 1 hospitalisation	152 (15)	6.54 (5.32, 8.04)	< 0.001
Acute courses of oral corticosteroids (Reference category: No course)	1 course	169 (17)	1.74 (1.44, 2.09)	< 0.001
	2 courses	102 (10)	2.66 (2.10, 3.36)	< 0.001
	≥ 3 courses	164 (16)	3.13 (2.54, 3.86)	< 0.001
Anaphylaxis at any time (Reference category: No episode)	≥ 1 episode	17 (2)	2.20 (1.29, 3.76)	0.004
GINA management step (Reference category: 1–2)	0	92 (9)	1.77 (1.39, 2.24)	< 0.001
	3	126 (12)	1.11 (0.90, 1.37)	0.352
	4–5	397 (39)	1.58 (1.36, 1.85)	< 0.001
BMI (Reference category: Normal [18.50–24.99 kg/m^2])	Underweight (< 18.50 kg/m^2)	50 (5)	1.63 (1.19, 2.23)	0.002
	Overweight (25–29.99 kg/m^2)	221 (23)	0.80 (0.67, 0.96)	0.018
	Obese (≥30 kg/m^2)	420 (43)	0.89 (0.76, 1.05)	0.170
Diabetes (type 1 or 2) (Reference category: No diagnosis and/or therapy)	Diagnosis and/or therapy	392 (39)	1.46 (1.27, 1.68)	< 0.001
GP consultations for lower respiratory tract infections resulting in antibiotic prescription (Reference category: No consultation and prescription)	1 consultation and prescription	205 (20)	1.37 (1.16, 1.62)	< 0.001
	≥ 2 consultations and prescriptions	100 (10)	1.22 (0.96, 1.55)	0.098
Smoking status (Reference category: Non-smoker)	Current smoker	211 (21)	1.28 (1.08, 1.52)	0.006
	Former smoker	287 (28)	1.10 (0.94, 1.28)	0.239
Ischaemic heart disease (Reference category: No diagnosis)	Diagnosis	104 (10)	1.28 (1.02, 1.60)	0.035
Paracetamol prescription (Reference category: No prescription)	≥ 1 prescription	432 (43)	1.23 (1.07, 1.41)	0.004
Anxiety and/or depression (Reference category: No diagnosis)	Diagnosis	496 (49)	1.21 (1.06, 1.38)	0.005
Age (Reference category: 12–60 years)	61–80 years	367 (36)	1.21 (1.04. 1.40)	0.012
Rhinitis (Reference category: No diagnosis and/or therapy)	Diagnosis and/or therapy	439 (43)	0.81 (0.71, 0.92)	0.002

associated with future asthma exacerbation and hospitalisation risk could be incorporated into a tool for therapeutic decision making.

AIM: To identify factors associated with future asthma exacerbation and hospitalisation risk in a real life setting from UK primary care clinical records.

METHODS: Retrospective, observational study using Clinical Practice Research Datalink and Optimum Patient Care Research Database. Patients aged 12-80 years with asthma and no other chronic respiratory disease. Subset of patients with UK Hospital Episode Statistics (HES) data included for hospitalisation analysis. The study period was 1 year before (baseline) and 1 year after (outcome) date of last blood eosinophil count. Outcomes: Hospitalisations (asthma-related inpatient admission or A&E visit) and ATS/ERS defined severe exacerbations (hospitalisation or acute course of oral corticosteroids). Baseline characteristics: biomarkers; demographics; co-morbidities and markers of disease severity. Univariable logistic regression was used to identify baseline characteristics associated with ⩾2 severe exacerbations or ⩾1 hospitalisation in outcome ($p < 0.05$). The characteristics were then included in multivariable models and reduced to lists of non-collinear factors.

RESULTS: Of 130,547 patients (34% male; mean age [standard deviation] 49 [17] years), 6% had ⩾2 severe exacerbations in outcome. 44% of patients with ⩾2 severe exacerbations in outcome had ⩾2 severe exacerbations in baseline. Table 1 shows baseline factors associated with ⩾2 severe exacerbations in outcome (multivariable results).

Of 61,861 patients with HES data (34% male; mean age [standard deviation] 49 [17] years), 2% had ⩾1 hospitalisation in outcome. 15% of patients with ⩾1 hospitalisation in outcome had ⩾1 hospitalisation in baseline. Table 2 shows baseline factors associated with ⩾1 hospitalisation in outcome (multivariable results).

CONCLUSION: Key risk factors associated with both future severe exacerbations and hospitalisations identified through multivariable analysis include: elevated blood eosinophils; acute courses of oral corticosteroids, higher GINA management step, diabetes, anxiety and/or depression, GP consultations for lower respiratory tract infections with antibiotics, paracetamol prescriptions, current smoker and increasing age.

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Intranasal corticosteroid treatment failure in allergic rhinitis: assessment of unmet need by measuring shift to multiple therapies

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BACKGROUND: Intranasal corticosteroids (INS) are the most effective allergic rhinitis (AR) treatment.[1] However, they provide insufficient symptom relief for some patients. An INS efficacy threshold of 60% reduction in overall nasal symptom score has been identified, above which INS fail to differentiate from placebo.[2] The burden of this pharmacologic insufficiency has not been fully elucidated. In this study, we numerically describe INS treatment failure in AR patients in real-life, and show how those patients with insufficient symptom control are currently managed.

AIM: In this study, we aim to numerically describe INS treatment failure in AR patients in real-life, and show how those patients with insufficient symptom control are currently managed.

METHODS: This was a retrospective database study using the Optimum Patient Care Research Database which holds patient data from 354 practices across the UK. Patients included in the analysis had a recorded AR diagnosis and ⩾1 AR therapy prescription during 1st March 2010 to 31st August 2010. Here we focus on those AR patients for whom an INS was the first prescription.

RESULTS: In all, 2197 AR patients were included. INS proved insufficient for 36.1% of these patients; 32.4% ($n = 712$) required an add-on therapy and 3.7% ($n = 82$) changed INS AND received additional therapy. Of those 712 patients who received an add-on to their INS, 75.7% received one, 22.2% received two and 2.1% received 3 add-ons. The most common single medications added on to existing INS therapy were antihistamines (AH; 77.6% of patients), eye drops (9.5%), systemic corticosteroids (9.3%) and leukotriene receptor antagonists (2.8%).

CONCLUSION: INS provide insufficient symptom control in about one third of AR patients who visit their doctor. Combined use of INS and oral AH, the most common multiple therapy regimen prescribed by doctors, is not recommended by ARIA due to lack of clinical data or proven non-superiority over INS monotherapy.[1] There is a need for a faster, more effective AR therapy with proven superiority over current gold standard therapy in direct comparison head to head studies.

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23

Real-life prescribing and outcomes of long-acting muscarinic antagonist (LAMA) therapy for adult patients with asthma in UK clinical practice

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BACKGROUND: Long-acting muscarinic antagonists (LAMAs) are not currently licensed for use in asthma; however, emerging evidence suggests that adding LAMAs to inhaled corticosteroids (ICS), alone or in conjunction with long acting β-agonists (LABAs), may improve bronchodilation and asthma control.
AIM: To characterise patients with asthma in UK general practice who were prescribed LAMA and to examine impact on asthma outcome measures.
METHODS: Retrospective study using data from the Optimum Patient Care Research Database. Patients were aged ⩾18 years with a READ code (UK standardized code for general practice) for asthma, ⩾1 prescription for tiotropium and ⩾2 years of continuous practice data (1 year before and 1 year after first tiotropium prescription). Patients with a READ code for COPD were excluded. Peak expiratory flow rate, FEV_1, and FEV_1/FVC ratio were used to characterize lung function. Endpoints examined the year before and after initiating LAMA included severe exacerbations (acute course of oral corticosteroids or asthma-related inpatient admission or emergency department attendance) and risk-domain asthma control (no severe exacerbation or antibiotics prescribed for respiratory tract infection).
RESULTS: The database contained 2,042 patients meeting study inclusion criteria. Mean (s.d.) age was 63 (14) including 17% current smokers and 37% ex-smokers. The majority of patients were at British Thoracic Society treatment steps 3 (22%) and 4 (50%), with 10% at step 1 and 12% at step 2 (6% had received no prior therapy). There were no significant differences between baseline and outcome year lung function results. Comparison of baseline and outcome severe exacerbations and asthma control (see Table 1).

Comparison of baseline and outcome severe exacerbations and asthma control

	BASELINE YEAR (N = 2042)	*OUTCOME YEAR (N = 2042)*	*P-value*
Severe exacerbations, mean (s.d.)	0.68 (1.20)	0.46 (1.00)	< 0.001[a]
0, *n* (%)	1290 (63.2)	1499 (73.4)	
1, *n* (%)	415 (20.3)	330 (16.2)	< 0.001[b]
2, *n* (%)	180 (8.8)	116 (5.7)	
⩾3, *n* (%)	157 (7.7)	97 (4.8)	
Risk-domain asthma control, *n* (%)	846 (41.4)	1071 (52.4)	
Uncontrolled *n* (%)	1196 (58.6)	971 (47.6)	< 0.001[c]

[a]Wilcoxon signed rank test.
[b]Marginal homogeneity test.
[c]McNemar Test.

CONCLUSIONS: These findings suggest that LAMAs are being prescribed off-label to treat asthma in the UK and that LAMA therapy may be associated with reduced exacerbations and improved asthma control. Pragmatic trials and matched cohort analysis are needed to further evaluate the effect of LAMA on asthma control for the real-life population of patients seen in primary care.

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Real-life prescribing predictors in newly diagnosed COPD patients

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BACKGROUND: Real-life general practice (GP) prescribing patterns may differ from Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations for optimal COPD management.
AIM: To identify the main factors affecting GP prescribing choices for first COPD therapy.
METHODS: Retrospective study using the Optimum Patient Care Research Database, which includes primary care respiratory data from 387 UK practices linked with patient-reported questionnaires. Patients included were aged ⩾40 years and had a COPD diagnosis between 1997–2010 supported by FEV_1/FVC0.7, and with 1 year pre- and ⩾2 years post-diagnosis data. First therapy was defined as drugs prescribed during 1 year before and at COPD diagnosis, grouped into short-acting (short-acting β_2-agonists and/or muscarinic antagonists) and maintenance therapy (long-acting β_2-agonists and/or muscarinic antagonists and/or inhaled corticosteroids and/or leukotriene receptor antagonists and/or theophylline). Factors significantly ($p < 0.05$)

Table 1

		Patient distribution	*(1) Odds of being prescribed any therapy (No therapy = 1.00)*	*(2) Odds of being prescribed maintenance therapy (Short-acting/No therapy = 1.00)*
		n (%)	*OR[a] (95% CI)*	*OR (95% CI)*
Co-morbid asthma[b]	Yes	3,263 (20)	3.89 (3.43; 4.41)	5.53 (5.02; 6.08)
Exacerbations rates[c] (reference category: 0)	1	3,857 (24)	2.33 (2.12; 2.56)	1.63 (1.50; 1.76)
	2	1,405 (9)	3.60 (3.04; 4.27)	2.56 (2.26; 2.90)
	3+	1,215 (8)	4.62 (3.75; 5.69)	3.86 (3.34; 4.46)
mMRC score[d] (reference category: 1)	2	7,137 (44)	1.18 (1.05; 1.32)	1.20 (1.09; 1.33)
	3	4,003 (25)	1.22 (1.08; 1.38)	1.33 (1.19; 1.48)
	4	2,232 (14)	1.25 (1.09; 1.44)	1.37 (1.20; 1.55)
	5	579 (4)	1.38 (1.10; 1.72)	1.69 (1.39; 2.06)
Lung function grade[e] (reference category: 1)	2	8,964 (55)	1.15 (1.03; 1.28)	1.03 (0.94; 1.14)
	3	4,163 (26)	1.26 (1.12; 1.43)	1.18 (1.06; 1.32)
	4	784 (5)	1.29 (1.06; 1.57)	1.32 (1.11; 1.57)
Total		16,185 (100)	11,918 (74)	8,082 (50)

[a]Adjusted for BMI and gender. Missing data for BMI for 100 patients (1%).
[b]Recorded ever.
[c]Calculated during 1 year prior to and at COPD diagnosis.
[d]Recorded closest to initial date of COPD diagnosis.
[e]Recorded closest to initial date of COPD diagnosis. Grade 1 was defined as FEV_1% predicted > 80; grade 2 as FEV_1% predicted ⩾ 50 to < 80; grade 3 as FEV_1% predicted ⩾30 to < 50; grade 4 as FEV_1% predicted < 30.

affecting the odds of being prescribed (1) any first COPD therapy vs. no therapy and (2) first maintenance vs. short-acting or no therapy, were identified with univariable logistic regression and included in a best fitting multivariable model of non-collinear predictors. Potential predictors were routine clinical data, patient demographics, comorbidities, annual exacerbation rates (COPD-related hospital admissions, A&E visit, acute course of oral steroids, or antibiotic prescribing for lower respiratory related tract infections), modified Medical Research Council (mMRC) score and lung function data.
RESULTS: Of 20,154 patients included, 72% were prescribed any first COPD therapy and 49% overall were prescribed first maintenance therapy. Table 1 shows factors significantly predictive of the odds of being prescribed (1) any first therapy and (2) first maintenance therapy. The analysis has been undertaken on the subset of 16,185 (80%) patients with mMRC data available.
CONCLUSIONS: Data suggest that the main factors affecting the choice of initial COPD therapy may be presence of co-morbid asthma and exacerbation rates, followed by symptoms (mMRC score) and lung function grade (weaker predictors). The presence of co-morbid asthma, increased exacerbation rates and symptoms (mMRC score) and decreased lung function increase the odds of receiving any first therapy and first maintenance therapy for COPD.

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Long-term outcomes of inhaled controller therapies added to systemic corticosteroids after asthma-related hospital discharge

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BACKGROUND: Much of the evidence on early use of inhaled controllers after severe asthma exacerbations is about their short-term benefits.
AIM: To investigate the longer-term outcomes associated with the use of various inhaled controllers after severe asthma exacerbations in the real-world setting.
METHODS: We used administrative health data from British Columbia, Canada (2001-2012) to evaluate 365-day readmission rate (primary outcome), long-term adherence to controller medications, and use of reliever medications associated with different inhaled controller treatments as an add-on to systemic corticosteroids (SCS) following discharge from an asthma-related admission in adolescents and adults. Exposure was assessed in the 60 days after discharge, and categorized as monotherapy with SCS (SCS-only) versus SCS plus inhaled controller therapy (SCS+inhaler); the latter was further divided into SCS+inhaled corticosteroid (SCS+ICS) and SCS+ICS and long-acting beta agonists (SCS+ICS/LABA). Generalized linear models, adjusted for generalized propensity scores, were used for inference.
RESULTS: The final cohort included 2, 272 post-discharge periods (43.0% SCS-only, 26.9% SCS+ICS, and 30.1% SCS+ICS/LABA). Readmission rate was significantly lower in the SCS+inhaler versus SCS-only (RR = 0.74 [95%CI 0.59–0.93]), but similar between SCS+ICS and SCS+ICS/LABA (RR = 0.78 [95%CI 0.59–1.04]). Long-term adherence, defined as medication possession ratio, to controller medications was 83% higher in SCS+inhaler than SCS-only, and 64% higher in SCS+ICS/LABA than in SCS+ICS. The use of reliever medications was similar across exposure groups.
CONCLUSION: Early initiation of inhaled controllers might confer long-term benefit, likely due to higher adherence, after severe asthma exacerbations. Combination therapy with ICS/LABA seems to be as safe as monotherapy with ICS, with the added benefit of better long-term adherence.

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Longitudinal objective assessment of inhaler implementation adherence after a Hospital exacerbation of COPD

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INTRODUCTION: Poor adherence to inhaler therapy is associated with increased health care use. However there are several potential drivers to poor adherence in COPD. We used a novel audio recording device attached to an inhaler to assess adherence rates and associated patterns of inhaler use in a cohort of patients with COPD.
METHODS: This was a pilot prospective 1 month observational study of patients discharged from Hospital following an exacerbation of COPD. They were given an INCA adapted salmeterol/fluticasone inhaler and asked to use it as directed. The device was analysed at the end of one month.
RESULTS: Thirty-eight patients were included for analysis after averagely 25 days follow-up. The mean FEV_1 was 1.3L. Overall, adherence, assessed by

[26]

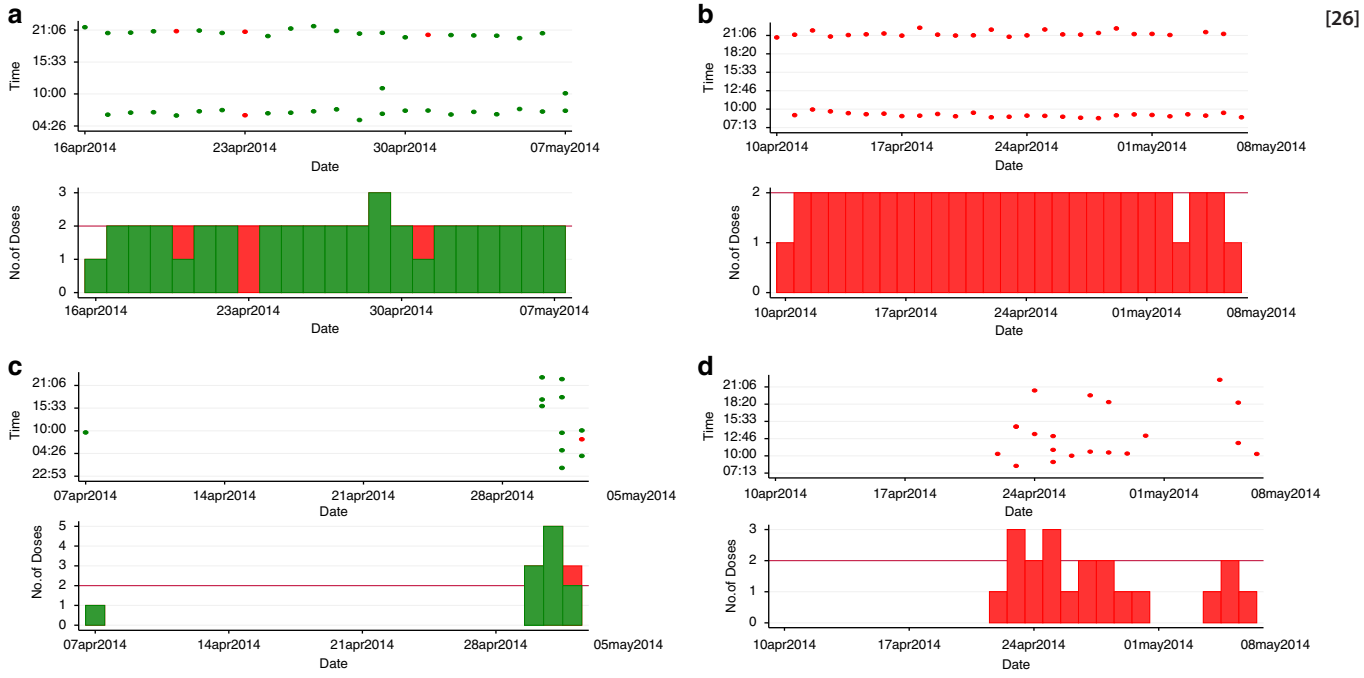

Figure 1. Patterns of inhaler use by patients following an exacerbation of COPD. The graphs show calendar plots (time of day and days of the week) with time of use and technique of inhaler use shown, good technique in green, significant, objectively assessed incorrect technique in red. Four patterns were observed: (**a**) good technique and regular adherence in a quarter of patients. Poor technique but regular time of use was observed in a further quarter of patients (**b**), two other patterns, irregular use (**c**) or (**d**) irregular technique and irregular technique was seen in the remainder of the patients.

attempts to take their inhaler showed an adherence rate of 0.71, when errors were accounted for the actual adherence rate for this cohort of patients was low only 0.31. Poor inspiratory flow rate was the commonest error of inhaler use in this study. Four patterns, equally distributed in frequency were detected, overall good adherence both in time and technique, poor technique good time of use, erratic symptom driven and irregular adherence (Figure 1).

CONCLUSION: The implementation adherence rate of the study patients is very poor with multiple patterns of inhaler use. Clinical effectiveness studies could be used to tailor management of COPD patients in future, for example using nebulisers in place of inhalers in patients unable to use inhalers.

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Step up therapy–prescribing practice and its implications

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BACKGROUND: When inhaled corticosteroids (ICS) fail to control symptoms in children, guidelines recommend the addition of long acting beta agonist (LABA), with other treatment options being available if symptoms persist.

AIMS: Our aims were to determine the proportion of initial "step up" episodes where LABA were prescribed and to describe characteristics of individuals not stepped up with LABA.

METHODS: Between 1999 and 2011, initial step up episodes were identified in children aged 5-12 years with asthma and in receipt of ICS. Data sources were Clinical Practice Research Datalink and Optimum Patient Care Research Database.

RESULTS: Initial step up episodes were identified in 10,793 children. ICS dose was increased in 6252 children (58%), LABA was introduced in 3436 (32%, including 1107 where fixed dose combination inhaler (FDC) replaced the ICS inhaler), and Leukotriene Receptor Antagonist (LTRA) was added in 1105 (10%).

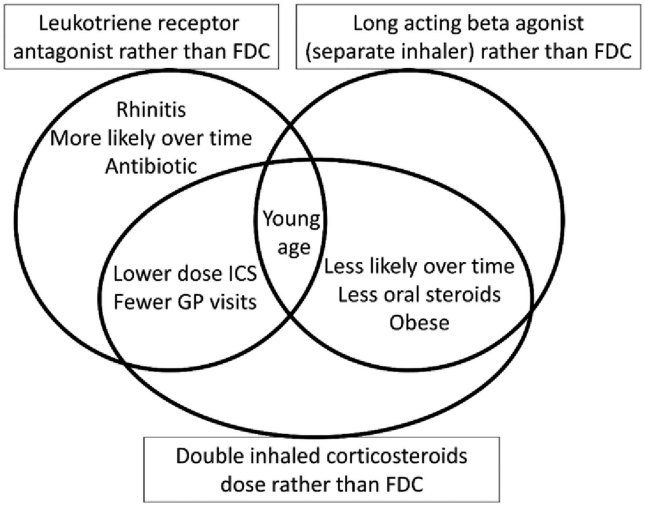

Figure 1. Venn diagram summarising the characteristics of children aged 5-12 with asthma where treatment other than change to fixed dose combination inhaler (FDC) was commenced.

Compared to children stepped up to LABA, others were younger and prescribed lower doses of ICS and reliever medication (Figure 1). ICS dose increase was more likely in obese children and LTRA prescribing was more likely in children with rhinitis and in receipt of antibiotics. Compared to FDC, step up to separate LABA inhaler was more likely in younger, obese children who were prescribed less oral steroids.

CONCLUSION: Only one third of initial step up episodes in children with asthma treated with ICS are to add LABA. Different characteristics of children prescribed therapies other than LABA suggest that prescribers tailor treatment in some clinical settings.