

**Methods** In this 26-week, multicenter, double-blind study, patients  $\geq 40$  years with COPD (forced expiratory volume in 1 second [FEV<sub>1</sub>]  $\geq 40\%$  to  $<80\%$  predicted and no history of exacerbations in the previous year) were randomised (1:1) to QVA149 110/50 g or SFC 50/500 g. In this post hoc analysis, we report the rate of mild, moderate or severe COPD exacerbations during 26 weeks of treatment with QVA149 or SFC.

**Results** Of 522 patients randomised [QVA149 (n = 258), SFC (n = 264); mean age: 63.3 years; mean post-bronchodilator FEV<sub>1</sub>: 60.2% predicted], 82.6% completed. Rate ratio of QVA149 versus SFC [RR] of moderate or severe exacerbations was 0.80 (95% confidence interval [CI]: 0.41–1.56) and for all COPD exacerbations (mild, moderate, and severe), RR was 0.69 (95% CI: 0.44–1.07) (neither statistically significant).

**Conclusion** Risk of exacerbations with once-daily QVA149 was numerically, but not statistically significantly, lower than twice-daily SFC in patients with moderate-to-severe COPD and no previous history of exacerbations. The LABA/LAMA combination QVA149 has the potential to be an alternative to LABA/ICS in preventing COPD exacerbations.

## REFERENCE

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## Pulmonary infection

### P238 ROLE OF NATURALLY-ACQUIRED IGG IN PROTECTION FROM *S. PNEUMONIAE* LUNG INFECTION

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Preventing *Streptococcus pneumoniae* lung infections will have substantial health benefits, yet existing polysaccharide vaccines are not effective against pneumonia. Identifying the mechanisms of naturally-acquired immunity to *S. pneumoniae* lung infections could indicate alternative preventative strategies. Human intravenous immunoglobulin (IVIG) preparations pooled from  $>1000$  donors prevent respiratory infections in patients with hypogammaglobulinaemia. IVIG therefore provides a tool to investigate the naturally-acquired antibody responses to *S. pneumoniae* within a population. We have used mouse models and *in vitro* assays to assess the efficacy of IVIG for preventing *S. pneumoniae* lung infections and to identify the immunodominant target antigens.

In a mouse pneumonia model, IVIG treatment was highly protective against bacteraemia (17% septicaemia v. 100% in controls,  $P = 0.015$ ) and partially protected against lung infection (lung CFU log<sub>10</sub> 3.7 for IVIG v. 6.3 for controls,  $P = 0.041$ ) but not against nasopharyngeal colonisation. Depletion of phagocyte subsets demonstrated that IVIG-mediated protection required neutrophils and macrophages for lungs and blood respectively. Flow-cytometry assays demonstrated that IgG within IVIG preparations opsonised *S. pneumoniae* effectively. Importantly, IgG opsonisation was reduced by pre-treatment of bacteria with pronase to remove bacterial surface proteins but not by depletion of anti-capsular antibody. Furthermore, *in vitro* assays demonstrated that IVIG facilitated phagocytosis, growth impairment and bacterial agglutination of capsule-deficient *S. pneumoniae* mutants, in mice IVIG depleted of anti-capsular antibody remained protective against lung infection and septicaemia. These results

demonstrate that surface proteins rather than the capsule are targets for naturally-acquired adaptive immunity to *S. pneumoniae*. The potential *S. pneumoniae* protein antigen targets in IVIG were assessed using a semi-quantitative assay against 18 recombinant pneumococcal proteins. The results demonstrated significant IgG responses to the conserved pneumococcal protein antigens PhtD, PspC, PspA and PsaA. Interestingly, antibody titres to some of these antigens were reduced in sera from elderly compared to younger subjects, potentially identifying people at higher risk of *S. pneumoniae* infection. Our data demonstrate that the accepted paradigm that naturally-acquired immunity to *S. pneumoniae* depends on anti-capsular antigen is inaccurate, and instead antibody to proteins is dominant. These data will allow better evaluation of those at risk of *S. pneumoniae* infection and improved vaccine design.

### P239 A ROLE FOR POLYCYSTINS IN AIRWAY MUCOCILIARY CLEARANCE?

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Polycystins 1 and 2 are the gene products of the mutated genes PKD1 and PKD2 in autosomal dominant polycystic kidney disease (ADPKD). They are localised to primary cilia in the kidney and thought to detect fluid flow. Recently patients with ADPKD have been shown to have an increased incidence of radiological findings of bronchiectasis, an abnormal dilatation of the bronchioles involving impaired mucociliary clearance (Driscoll *et al* 2009). We hypothesise that proteins from the polycystin pathway are present in respiratory epithelium and that this pathway is defective in bronchiectasis.

We demonstrate using immunofluorescent antibodies that the extracellular portion of polycystin 1 and the n terminal tail of polycystin 2 consistently localise to cilia of nasal epithelial cells from healthy individuals and that blocking polycystin 1 with antibodies can alter ciliary beat. Contrary to our hypothesis there were no differences in the distribution of these proteins in a group of patients with bronchiectasis (n = 13)

In conclusion we have shown that polycystins 1 and 2 are present in the motile cilia of the airways and may be involved in ciliary beat frequency regulation. We did not find any evidence of disruption of the polycystin proteins in a small population of patients with bronchiectasis.

### P240 DOES A RELATIONSHIP EXIST BETWEEN SERUM ALBUMIN AND LACTATE WITH THE LENGTH OF STAY IN PATIENTS ADMITTED WITH COMMUNITY ACQUIRED PNEUMONIA?

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**Introduction** Previous studies have shown that high lactate and CURB65 scores are associated with increased mortality and morbidity in patients with community acquired pneumonia (CAP). We attempted to investigate a simple way to identify those patients who are likely to have prolonged hospital admission from CAP by using different biomarker.

**Method** We included first 50 patients who were diagnosed to have CAP by respiratory physicians on admission at Russell's

Hall hospital, Dudley in December 2012. We calculated CURB scores and measured their lactate level, serum albumin and white cells count on admission. We also monitored their albumin levels throughout the admission. We then examined the association between these factors and LOS using Spearman's rank correlation coefficient (RS).

**Results** There was no mortality from CAP in our study population. Mean length of stay was 7 days (1–41). There was positive correlation between CURB65 and LOS ( $R_s = 0.41$ ,  $p = 0.003$ ). We did not observe any statistically significant correlation between the lactate level, albumin level or white cell count on admission and the LOS. Interestingly, we noticed that there was a statistically significant negative correlation with the day 3–5 albumin level with LOS ( $R_s = -0.522$ ,  $p = 0.000627$ ).

**Conclusions** Our study suggests that low albumin on day 3–5 increases hospital LOS therefore it could be postulated that early nutritional intervention to keep higher level of albumin might decrease length of stay. We also believe that combining admission CURB65 and day 3 albumin will give us better tool to predict LOS but prospective study is needed to evaluate these findings further.

#### P241 'CURE-CAP': A COMPREHENSIVE ADMISSION & DISCHARGE PNEUMONIA CARE BUNDLE

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**Introduction** The annual incidence of Community acquired pneumonia (CAP) is 5–11/1000. Between 22% and 42% require admission to hospital. Wide variation exists in the management of CAP despite guidelines issued by the British Thoracic Society (BTS). Care bundles have been shown to improve outcomes through standardisation of care in other diseases as well as in CAP. A BTS/NHS Improvement initiative is due to launch a pneumonia admission bundle. However, it does not address the issue of standards around comprehensive discharge care.

**Objectives** To design and implement a care bundle for the management of CAP, that incorporates admission and discharge standards and to assess improvements post-implementation.

**Methods** We formulated a CAP bundle including a triage tool, with the acronym 'CURE-CAP', focussing on seven key standards (Fig. 1). Data was collected retrospectively on consecutive patients admitted to our GP Assessment Unit with a primary diagnosis of CAP with a 3-month period of implementation in between. Compliance to standards before and after implementation of the bundle was then measured.

**Results** The pre-implementation cohort had 43 patients (17 (40%) male; median (range) age 74 (36–101)) and post-implementation cohort had 30 (8 (27%) male; median (range) age 82 (36–93)). Chest x-ray was performed within 4 hrs in 30/43 (70%) in the pre-implementation cohort, increasing to 30/30 (100%) post-implementation. Time from admission to x-ray improved as well (median (range) 2:49 (0:30–18:27) to 1:00 (0:21–2:42)). Urgent oxygen assessment was performed in 100% cases in both cohorts. Recording of the CURB-65 severity score improved from 35/43 (81%) to 28/30 (93%). Early antibiotic administration (within 4 hrs) increased from 12/43 (28%) to 20/30 (68%) with appropriate (severity based) antibiotics selection improving from 29/43 (67%) to 28/30 (93%). The bundle led to total compliance with all discharge standards including appropriate smoking cessation counselling (5/7 (71%) to 4/4 (100%)),

patient information leaflet provision (0% to 100%) and appropriate follow-up arranged (16/43 (37%) to 30/30 (100%)).

**Conclusions** We have successfully designed a CAP admission and discharge care bundle and shown improvements across all measured standards post implementation. A further study is planned to measure effects on direct patient outcomes.

Abstract P241 Figure 1. CAP Bundle

#### P242 WHAT IS THE PRE-ADMISSION NHS-CONSULTATION BEHAVIOUR OF ADULTS WITH COMMUNITY-ACQUIRED PNEUMONIA?

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**Introduction** Under 75 mortality from respiratory disease is highlighted as a target in the NHS Outcomes Framework. Community-acquired pneumonia (CAP) cases are likely to form a considerable proportion of such deaths. Most CAP deaths occur in hospital, but it is not known whether initiatives to reduce such deaths should be primarily targeted at hospital or alternatively at pre-hospital care. To help address this we set out to identify the pre-admission NHS contact behaviour of adults admitted for CAP. **Methods** Adult admissions for CAP to one NHS Trust were prospectively identified between 14<sup>th</sup> May and 25<sup>th</sup> June 2013. For each case the diagnosis was validated by chest radiograph examination. After written informed consent a structured interview was conducted with each patient. Anonymous data was collected in an Excel spread-sheet and analysed with IBM SPSS 20.

**Results** Of 83 possible pneumonia cases, 64 were confirmed to have radiographic pneumonia and 44 included in the study (Exclusions: declined - 4; language barrier - 4; immune compromise-5; unable to provide history due to illness or confusion-7). Median age was 73 years and CURB65 distribution was 0–1 (36%), 2 (30%), 3–5 (34%) - similar to the BTS audit population. Only 17 (38%) had had some form of pre-admission NHS contact for this illness, the majority presenting directly to hospital. Pre-admission NHS contacts included GP contact (17, including 9 consultations, 5 telephone contacts, 2 home visits, 1 out-of-hours service), 1 walk-in centre and 1 A & E attendance. 1 case had 3 pre admission NHS contacts. There were no contacts with NHS Direct / 111. Those with sputum production, higher CURB65 scores and longer illness duration were significantly more likely to have had pre-admission NHS contact (Table).