# 479. Cystic fibrosis: detection and monitoring of early lung disease

**4655**

**Late-breaking abstract: VX-770, an investigational CFTR potentiator, in subjects with CF and the G551D mutation**

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**Background:** Restoring dysfunctional CFTR mediated ion transport is a potential treatment for CF. VX-770, a CFTR potentiator, is designed to increase CFTR ion transport activity.
**Aims and objectives:** This Phase 3 study evaluated the efficacy and safety of VX-770 in subjects with CF who have the G551D mutation on at least one *CFTR* allele.
**Methods:** A randomized, double-blind, placebo-controlled trial of subjects ≥12 years of age who received oral VX-770 150 mg q12h (n=83) or placebo (n=78) for up to 48 weeks.
**Results:** The mean absolute change from baseline through Week 24 in % predicted $FEV_1$ (primary endpoint), improved by 10.4% in the VX-770 group, while the placebo group decreased by 0.2% (P<0.0001). This reflected a mean increase of 361 mL (P<0.0001) and a mean relative change from baseline of 16.9% of predicted $FEV_1$ (P<0.0001) in the VX-770 group compared to placebo. Improvement in $FEV_1$ with VX-770 was evident at Day 15 and maintained through Week 48, at which time the VX-770 group showed an improvement of 10.1% (366 mL change) while the placebo group had a decrease of 0.4% (7 mL change). A 55% reduction in the risk of pulmonary exacerbations (P=0.0012) was observed through 48 weeks with VX-770 treatment. The reduction from baseline in sweat chloride, a biomarker of CFTR activity, was –48.1 mmol/L through Week 48 in the VX-770 group compared to placebo (P<0.0001). The safety profile of VX-770 was comparable to placebo.
**Conclusions:** VX-770 demonstrated a clinically relevant and statistically significant improvement in pulmonary function and reduction in pulmonary exacerbations and sweat chloride up to 48 weeks of treatment. The safety profile was similar to placebo.
Supported by Vertex

**4656**

**Improvement in lung function during the 1st year of life in infants diagnosed with CF through newborn screening (NBS)**

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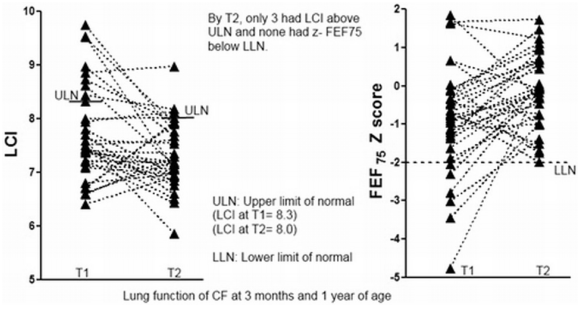
Despite early diagnosis and specialist treatment, NBS CF infants showed reduced lung function (LF) within the 1st year of life [1]. We have reported a significantly elevated lung clearance index (LCI) and reduced forced expiratory volume and flow ($FEV_{0.5}$ and $FEF_{75}$ z-scores) in CF vs healthy controls (HC) by age 3 months [2].
**Hypothesis:** These reductions in LF persist to 1 year of age.
**Methods:** Multiple breath washout and raised volume techniques were performed in CF infants from 6 tertiary CF centres in London, UK and prospectively recruited HC.
**Results:** 35 CF and 18 HC infants have completed paired measurements at 3 months (T1) and 1y (T2). Significant improvements in the CF group were seen in anthropometry, LCI, $FEV_{0.5}$ and $FEF_{75}$ z-scores by T2, with no significant differences from HC at this stage, except for a slightly elevated LCI.

Table 1. Lung function results (mean [SD])

| | CF (n=35) | | HC (n=18) | |
|---|---|---|---|---|
| | T1 | T2 | T1 | T2 |
| LCI | 7.7 (0.9) | 7.3 (0.6)* | 7.3 (0.5) | 6.9 (0.5)* |
| Z-$FEV_{0.5}$ | –1.1 (1.1) | –0.3 (1.4)** | –0.2 (0.7) | –0.4 (1.0) |
| Z-$FEF_{75}$ | –0.8 (1.4) | –0.1 (1.0)* | –0.2 (0.8) | –0.2 (1.0) |

*p<0.05; **p<0.005 (paired t test: T2-T1).

**Conclusions:** CF infants improved their LF within the 1st year of life with our standard respiratory and nutritional management. Furthermore, most NBS CF babies may do so well in the 1st year of life on standard therapy that novel treatments could be deferred.




**References:**
[1] Linnane. AJRCCM 2008.
[2] Thia. Ped Pulm 2010.

**4657**

**Infection and inflammation does not effect ventilation distribution in infants with cystic fibrosis (CF)**

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**Introduction:** Preschool and school aged children with CF have been reported to show an elevated lung clearance index (LCI), which further increases in the presence of *Pseudomonas aeruginosa* infection. In contrast, increased LCI is less prevalent in infants with CF. The aim of this study was to assess the impact of pulmonary infection and the presence of free neutrophil elastase (NE) as a marker of airway inflammation, on ventilation distribution in infants and children ≤ 2 years with CF.
**Methods:** Multiple breath washout (MBW) using 5% $SF_6$ and an ultrasonic flowmeter (Ecomedics, Switzerland) was performed 1-3 days prior to bronchoalveolar lavage (BAL) in 85 children. LCI and the 1st and 2nd moment ratio (M1/M0 and M2/M0) were determined from the washout. Generalised estimating equations with exchangeable working correlation structure were used to estimate linear regression coefficients. Adjustments were made for sex, height and functional residual capacity.
**Results:** The presence of a pulmonary infection (n=13; $\geq 10^5$ cfu.ml $^{-1}$) had no impact on LCI (p=0.353), but did result in increased M1/M0 (p=0.027) and M2/M0 (p=0.052) when compared to un-infected infants (n=36). Children with *P. aeruginosa* (n=4) colonisation showed no altered MBW outcomes when compared to the un-infected group. Similarly, the presence of NE (n=14) was not associated with altered MBW outcomes.
**Conclusion:** LCI in this group of children was not a sensitive measure of CF lung disease as indicated by free NE or endobronchial infection. Moment ratios appear to be more sensitive to lung disease associated with infection than LCI.

**4658**

**Comparison of cystic fibrosis structural lung disease detected by inspiratory and expiratory chest CT scans in infants and preschool children**

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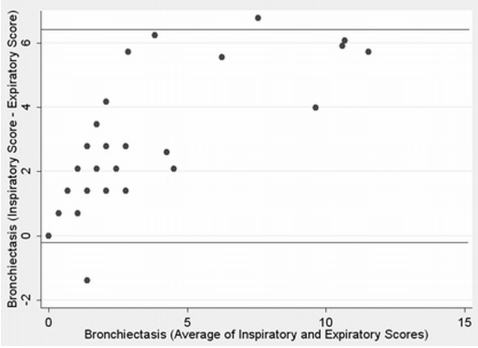
**Introduction:** Chest computed tomography (CT) reveals early cystic fibrosis (CF) structural lung disease. Typically, bronchiectasis (Bx) is assessed on inspiration and gas trapping on expiration, but in older children expiratory scans reliably detect both, reducing radiation exposure.
**Objective:** To compare the presence and extent of CF structural lung disease detected on volumetric inspiratory and expiratory scans in young children.
**Methods:** 38 children with CF age 1-5 years underwent inspiratory and expiratory volumetric chest CT. De-identified scans were assessed in random order by 2 observers using the Brody II score. Intraclass correlation coefficients (ICC) and Bland-Altman plots using mean scores determined agreement between expiratory and inspiratory scans.
**Results:** There was substantial agreement between mean Brody II component scores from inspiratory and expiratory scans (ICC range 0.637 to 0.866). For Bx, the ICC was 0.864, however, there was a systematic bias evident on Bland-Altman plot as shown, with consistently higher scores on inspiration. Further, analysis of binary outcomes (presence/absence of Bx) indicated that Bx was not demonstrated

on the expiratory scan in 40% of subjects when demonstrated on the inspiratory scan.




**Conclusions:** In early CF Bx, the presence and extent of Bx is underestimated with expiratory scans alone compared with inspiratory scans.

**4659**

**Magnetic resonance imaging (MRI) as a non-invasive, radiation-free imaging modality to study the onset and progression of lung disease in infants and young children with cystic fibrosis**

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Little is known about the onset and spontaneous progression and routine lung function testing is not available for monitoring of early CF lung disease. The aim of the present study was to validate pulmonary MRI to study the onset and progression of lung disease in infants and young children with CF.
In 34 CF patients (age: 2.5±0.4; 17f, 17m) MRI (1.5T) was performed in free breathing. For morphological imaging a T2w-(HASTE PACE) and a T1w T1-TSE sequences pre and post contrast media in coronal and transversal orientation were used. Functional imaging was performed using a 3D-FLASH-sequence with a temporal resolution of 1.5s after iv injection of Gadolinium-DTPA. Two independent radiologists analyzed the images with a dedicated MRI score (range 0-72).
Morphological and functional abnormalities in the CF lung were detected by MRI in the first year of life (MRI score 6.3±1.1; n=6) and the score increased significantly to 16.2±1.7 ($p< 0.05$; n=5) at the age of 4 years. Perfusion defects were reversible in follow up scans in a substantial number of patients. Further, MRI scores were reduced after antibiotic therapy for pulmonary exacerbations (pre treatment: 20.2±7.7vs post treatment 13.0±4.9; $p<0.05$).
Our study indicates that MRI of the lung is sensitive to detect abnormal morphology, function and response to therapy in early CF lung disease. These results suggest that MRI may be suitable for non-invasive diagnostic monitoring of disease severity and may serve as a novel endpoint for clinical trials in early CF lung disease. Supported by Mukoviszidose e.V.

**4660**

**What is the significance of aspergillus fumigatus in BAL in children with cystic fibrosis**

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**Background:** *Aspergilllus fumigatus* (*AF*) is frequently found in the airways of children with cystic fibrosis (CF) and recent evidence suggests this may be clinically important. (Chest 2006;130:222, Ped Pulm 2007;42:785)
**Aims:** In this retrospective study, we hypothesised that children with CF who have *AF* seen on direct staining of bronchoalveolar lavage (BAL) will have a worse clinical state than both those who only culture *AF* (positive controls) and those with no isolation (negative controls). Primary outcome was $FEV_1$; secondary outcomes included BMI, IgE, IV antibiotics, steroids and antifungals.
**Results:** In the year prior to bronchoscopy (FOB), the groups were similar in terms of weight centile, IV antibiotics received and $FEV_1$. One year post FOB, the groups with *AF* in their BAL, on cytology or microscopy, had a lower $FEV_1$ despite receiving more IV antibiotics and more antifungal therapy.

Patient groups

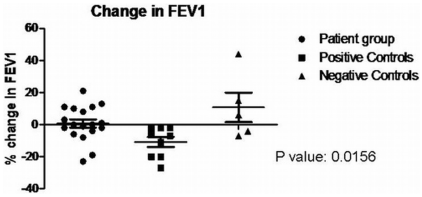
| | Age range | Mean (y) | Male n (%) |
|---|---|---|---|
| Pt group | 4m-14y | 8.68 | 6 (23%) |
| +ve controls | 3m-14y10m | 8.77 | 6 (46%) |
| –ve controls | 4m-15y10m | 7.8 | 8 (62%) |

Lung function

| | 1 year pre | BAL | 12 months post | 24 months post |
|---|---|---|---|---|
| Pt group | 75 | 63 | 75 | 72 |
| +ve controls | 75 | 65 | 64 | 68 |
| -ve controls | 74 | 60 | 83 | 83 |

FEV1 (% predicted).

The group without *AF* had a greater increase in $FEV_1$.




**Conclusion:** The results add to the growing evidence that *AF* in the airways of children with CF is associated with a worse clinical state, whether identified on direct smear or culture.

**4661**

**Newborn screening for cystic fibrosis improves lung function and growth at time of transfer to adult care**

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**Introduction:** Newborn screening (NBS) for Cystic Fibrosis (CF) is associated with improved early nutritional outcomes and improved spirometry in children.
**Aim:** To determine whether the early diagnosis and treatment of CF with NBS in NSW in 1981 led to better clinical status and survival at transfer to adult care.
**Methods:** Retrospective observational study compromising 2 cohorts: diagnosed symptomatically in the 3 years before newborn screening was introduced ("non-screened") and diagnosed in the first 3 years of NBS ("screened"). Patients were followed up until transfer to adult care, before age 19 years. ANOVA was used for clinical outcomes & survival was compared using a Cox proportional hazard model.
**Results:** Compared with non-screened patients (n=55), screened patients (n=56) were less likely to have pseud. aeruginosa in sputum at diagnosis (p=0.001), older when they acquired pseudomonas (p=0.001) & had better lung function when transferred to adult care: higher FEV1%, (mean difference = 17.2%; P = 0.012), FVC% (16.7%; P = 0.013), FEF50% (20.6%; P = 0.021) and a non-significantly higher BMI (0.95 kg/m$^2$; P = 0.143). There was a non-significant 41% mortality risk reduction in screened patients as compared to non-screened patients (Hazard Ratio (95% CI): 0.59 (0.24-1.43); p =0.25) Each 1% increase in FEV1% was associated with a 3% decrease in risk of death (p=0.002) and each 1 unit BMI increase was associated with an 46% decrease in risk of death ($p<0.001$).
**Conclusion:** NBS for CF leads to better lung function and nutritional state at time of transfer to adult care in screened patients. Both outcome measurements are good predictors for long term-survival.

## 482. How to improve lung cancer care

**4670**

**Time to diagnostic procedures and treatment in outpatients diagnosed of lung cancer (LC) included in our rapid diagnose protocol (RPD)**

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**Aim:** To determine the time to diagnose procedures and treatment in outpatients diagnosed of LC in Navarra (Spain) included in a RDP.
**Method:** Retrospective analysis of outpatients diagnosed of LC in our RDP from January 2006 to October 2010. The reference date was the day they were sent to our service. We analyzed time to CT, to bronchoscopy, to endobronchial ultrasound transbronchial needle aspiration (RT-EBUS), to transparietal fine needle aspiration (TFNA) and to Positron emission Tomography (PET), time to treatment and the hospitalization average.
**Results:** 70 patients were diagnosed of LC in our RDP; 80% were men, the mean age was 63.9; 68.5% were remitted from primary care (PC). The mean time to

the last diagnostic procedure was 22,5 days from PC and 16,4 from first visit in our RDP (RDPfv).The table reflects time from PC*(or other remission service) or RDPfv to each procedure.

Table 1

| | Patients | Mean |
|---|---|---|
| PC*-RDPfv | 70 | 6 |
| RDPfv-CT | 70 | 6.8 |
| RDPfv- Bronch. | 51 | 9.7 |
| RDPfv-TFNA | 20 | 19.4 |
| RDPfv-2TFNA | 4 | 22.2 |
| RDPfv-3TFNA | 1 | 21 |
| RDPfv-PET | 33 | 17.4 |
| RDPfv-EBUS | 9 | 19.7 |

We use PET since 2006 and EBUS since October 2008. 75% of patients didn't need hospitalization. The mean days, when needed, was 3.1 (1-8). Patients required surgical treatment in 22,8%, oncologic in 68.5% and Palliative Care as first choice in 8,5%. Globally, time from PC* to treatment was 37,4 days (5-103) and from RDPfv to treatment was 31,4days (0-90).
**Conclussions:** With our RDP we have achieved a lower time delay to diagnosis and treatment (no difference between kind of treatment)of LC comparing with most of the existing recommendations.
We haven't need hospitalization in most cases and the mean of days was low.

**4671**
**Self reporting of symptoms and delays in patients presenting to a rapid access lung cancer clinic (RALCC)**
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**Introduction:** The RALCC at our hospital is aimed at expediting the diagnosis of suspected thoracic malignancies.
**Methods:** A self-reported questionnaire to consecutive patients on their first visit. Patient's perception of why they were attending, symptoms, duration before seeking medical attention, time to referral and risks for lung cancer recorded.
**Results:** 154 patients, 81 male, 73 female, mean age 63 years (21-86). GP's made most referrals 87% and 68% perceived abnormal radiology as reason for attendance. Majority were symptomatic 88.6% with 57% reporting ≥3 symptoms. Cough was most common presenting symptom 61%, fatigue 52%, dyspnoea 45%, chest infection 45%, chest pain 40%, weight loss 32% and haemoptysis 25%. Haemoptysis had the least delay in presenting to a health care provider (mean 30 days, range 2-120) whereas for cough, dyspnoea and chest pain mean dealy was 4.5 months. Average delay in seeking medical attention and referral to RALLC was 14 weeks. 72% were current or ex-smokers and 21% reported at least one first degree relative with lung cancer.
**Conclusions: s**ignificant delays exist between symptom onset and presentation to a health care provider and depends on symptom type. The bulk of the delay was before patients sought medical attention but there was still a sizeable delay between presentation and referral toRALCC. One in 5 patients had a first degree relative with lung cancer indicating that this may have been a factor in the decision to refer. Our study highlights the need for increased public awareness regarding the presenting symptoms of lung cancer and there exists the opportunity to reduce delays in diagnosis resulting in better outcomes.

**4672**
**Managing patient pathways to achieve lung cancer waiting time targets: Mixed method study**
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**Background:** England's NHS introduced a 62-day target, from referral to treatment, to make lung cancer patient pathways more efficient. This study aims to understand pathway delays that lead to breaches of the target when patients need care in both secondary and tertiary setting so more than one institution is involved.
**Methods:** Mixed method cross case analysis. Qualitative methods include pathway mapping and semi-structured interviews. Quantitative analysis of patient pathway times from cancer services records.
**Setting:** Two tertiary referral hospitals in London
**Participants:** Database records of 53 patients were analysed. 19 sets of patient notes were used for pathway mapping. 17 doctors, 4 nurses, 8 managers and administrators were interviewed.
**Results:** The majority of the patient pathway (68.4%) is spent in secondary centres. There is more variability in the processes of secondary centres but tertiary centres do not have perfect processes either.
Three themes emerged from discussions: information flows, pathway performance, and the role of the multidisciplinary approach.
**Conclusions:** The actions of secondary centres have a greater influence on whether a patient breaches the 62-day target, compared to tertiary centres. Nevertheless variability exists in both, with potential for improvement.

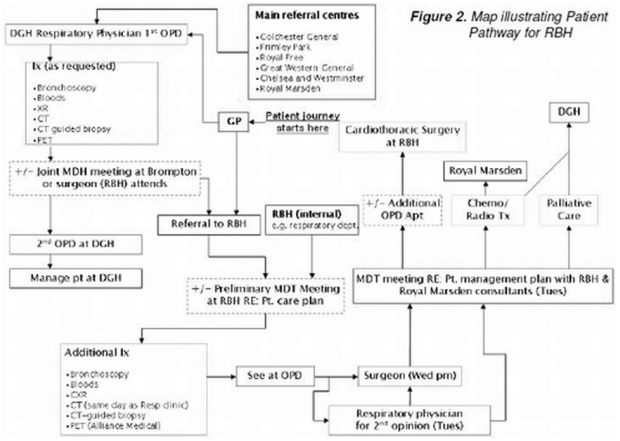

*Figure 2. Map illustrating Patient Pathway for RBH*

**Abstract 4672** – Figure

**4673**
**Lung cancer multi-disciplinary team (MDT) decisions audit**
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**Background:** Lung cancer resection and survival rates in the UK vary; the reasons for this are unclear.
**Aims:** To compare lung cancer MDT decision outcomes in 4 hospitals in one cancer network.
**Methods:** Each lung cancer MDT randomly selected 5 of their MDT cases and submitted them to the other MDTs for assessment. MDT decision outcomes for each case, including each MDT's own previously discussed MDT cases were collated. Mean percentage agreement of MDT outcomes was calculated for TNM staging and referrals for PET scan, curative surgery, radical radiotherapy and palliative chemotherapy.
**Results:** 3 hospital MDTs discussed 15 cases as well as having previously discussed their own 5 cases. 1 hospital submitted their 5 previously discussed cases but failed to discuss the other cases submitted to them. There were 17 non-small cell lung cancer cases, 2 indeterminate cases and 1 small cell lung cancer case. The number of cases referred for curative surgery varied between 6 to 7 cases per MDT. Percentage agreement was 83% for T staging, 91% for N staging, 98% for M Staging, 87% for referral for PET scan, 98% for curative surgery referral, 95% for radical radiotherapy referral and 93% for palliative chemotherapy referral.
**Discussion:** There was good agreement for staging and very high agreement for treatment referral. In this pilot study the high agreement for potentially curative treatment does not support the view that some MDTs are not referring patients for potentially curative treatment. As numbers are small we propose this issue be addressed by a national web-based quality assurance programme where each MDT assesses and reports sample cases each month and is given formative feedback.

**4674**
**Histological typing of lung cancer in bioptically obtained specimens under the aspect of therapeutical approaches – A multi-center study**
Annette Fisseler-Eckhoff[1], Rica Zinsky[1], Florian Laenger[2], Phillip Schnabel[3], Iver Petersen[4], Klaus Junker[5]. *[1]Dr. Horst-Schmidt Kliniken, Institute of Pathology and Cytology, Wiesbaden, Germany; [2]Medizinische Hochschule Hannover, Institute of Pathology, Hannover, Germany; [3]Universitaetsklinikum Heidelberg, Institute of Pathology, Heidelberg, Germany; [4]Universitaetsklinikum Jena, Institute of Pathology, Jena, Germany; [5]Klinikum Bremen Mitte, Institute of Pathology, Bremen, Germany*

The insufficiency of classifing lung cancer as SCLC or NSCLC clinical arose with the approval of the antifolate pemetrexed, which has a lower antitumorous effectivity in Squamous Cell Carcinoma. Often only biopsy specimens are available to exclude a squamous differentiation before chemotherapy decision.
The restrictive nature of subtyping lung cancer in biopsies demanded a skilled and experienced pathologist. This interlaboratory comparison should discover the accordance of subtyping of lung cancer biopsies evaluated in 5 different pathological institutes in germany. Is it possible to improve the accuracy histological typing by additional immunhistochemistry (IHC) panel?
60 biopsy specimens with Hematoxylin-eosin (HE) stain and immunhistological stained slides of at least Ck7, Ck5/6, p63, TTF1 were assembled and analysed from the pathologists. An estimation of predominantly-non-squamous yes/no and the histological subtype was done after examination the HE slide and again after the examination of the IHC. These two results were compared.
All 60 cases were analysed by all 5 participants. In average the agreement of

predominantly-non-squamous with inspecting the HE slide was 50% and arose after IHC to 87%. The accordance of histological subtype arose from 58% after HE slide to 88% after IHC.
Histological subtyping of lung cancer biopsies can be done reliably with the help of an immunhistochemical panel of CK5/6, CK7, TTF1 and p63. Thus, we recommend the use of IHC to ensure diagnosis of lung cancer biopsies especially for patients coming into consideration for pemetrexed chemotherapy.

**4675**
**The lung cancer patient in the emergency department**
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**Introduction:** – Currently, there are very few data in the literature on the causes of emergency department consultation for lung cancer patients, leading us to review the records of patients with lung cancer who presented at the emergency room of our cancer institute in order to determine the importance of emergencies and the main causes.
**Methods:** – We conducted a retrospective study including all patients with lung cancer consulting at the emergency department over a three years period (1st January 2008 and 31st December 2010).
**Results:** – Among 6575 consultations, 548 (8.3%) were selected, corresponding to 269 patients with lung cancer (out of 626 patients with lung cancer treated in our institution during the same period). Their main characteristics were: men/women 169/100, median age 61 years, non small cell lung cancer/small cell lung cancer 234/35, stage I/II/III/IV 7/3/42/217. The main reasons of consultation were respiratory symptoms (22.3%), fever (19.9%), pain (16.3%) and digestive symptoms (13.5%). Symptoms were due directly to cancer in 32.3%, to a cancer complication in 14.4% and to anticancer treatment in 20.3% of the cases.
The majority of the consultations lead to hospital admission: 54.5% were admitted in normal ward and 8.2% in the Intensive Care Unit. Median duration of hospitalisation was 9 days. Over the 344 hospitalisations, 61 deaths occurred (17.7%).
**Conclusion:** – Our study shows that lung cancer patients represent only 8% of the patients consulting in the emergency department. About half of the lung cancer patients have at least one consultation in emergency during their disease mainly for pain and respiratory problems.

**4676**
**Relapse after radical surgery for non-small cell lung cancer 2005-2009 – A retrospective quality management analysis**
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National guidelines for post-therapy lung cancer care are about to be introduced in Denmark. At our hospital, "usual care" after radical surgery for non-small cell lung cancer (NSCLC) has previously been to suggest the patient to have a chest x-ray once a year. To prepare improved post-therapy care we have made a retrospective analysis of the 986 consecutive patients from the primary uptake area reported by our diagnostic unit to the Danish Lung Cancer Registry in the 5-year period 2005–2009. Of the 792 patients with NSCLC 227 (28.7%) were treated with curative intent. Out of these 153 (19.2% of all with NSCLC) had intended radical resection of the primary tumor and if needed chemotherapy, radiotherapy, and/or resection of a single secondary tumor to assure a radical primary treatment. Median age for the 75 women and 78 men was 66 years (range 37 to 85 years). Clinical stages I, II, IIIa, and IIIB+IV were found in 122, 19, 5, and 7 patients. Two patients died at day 14 and day 31 after surgery. Among the 151 remaining patients, we have until February 22, 2011 recorded a relapse in 62 patients and a new lung cancer in three patients. In one patient, the cancer was found at post mortem examination, in 48 patients clinical symptoms lead to the diagnosis while a scheduled control by chest x-ray, CT, PET-CT, bronchoscopy, or blood tests lead to the diagnosis in 16 cases. Twenty-eight patients (18.5%) had a relapse within one year from surgery. Median time to relapse after a scheduled test was 288 days against 478 days in patients diagnosed after symptoms. Scheduled post-therapy control for all NSCLC patients may considerably shorten the time to detection of a relapse.

## 483. The impact of the organisation of care on costs: the role of the physician in home care

**4677**
**An evaluation of the safety, efficacy and cost-effectiveness for patients with acute respiratory illness, of a community-based intravenous medication service: The first 26 months**
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**Background:** Patients with acute respiratory illnesses such as acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and pneumonia occupy significant proportion of acute hospital beds. There is therefore an increasing focus on intermediate care initiatives to facilitate early supported discharge (ESD) and admission avoidance (AA) in such patients. Since 10.11.08, our hospital in partnership with Community Intervention Team (C.I.T.) provided service for administration of intravenous (IV) medications, facilitating ESD/AA.
**Aim:** To evaluate the AMNCH/C.I.T. IV service, in terms of safety, readmission rates, adverse events, bed-days saved, patient satisfaction and cost-effectiveness.
**Results:** Up to 31.1.11, of 285 patients referred to this service, 32% had a primary diagnosis of acute respiratory illness. 44 patients were male, 48 female. Mean age was 58.5 years (range 18-95). ESD and AA was facilitated in 67% and 33% respectively. Respiratory diagnoses were: pneumonia (n = 63), AECOPD (n = 7), exacerbation of asthma (n = 4), exacerbation of bronchiectasis (n = 5) and non-pneumonic respiratory infection (n = 13). IV treatment saved a minimum of 486 bed-days. Average length-of-stay in the service was 5.3 days. Readmission rate was 3.2%. No adverse incidents were reported. Patient satisfaction was 100%. We estimate that home treatment of these patients saved €457,300 for AMNCH compared to equivalent treatment in hospital.
**Conclusion:** We conclude that the service continues to be a safe, effective, inexpensive modality for ESD/AA in patients, with significant bed-days and cost-savings for AMNCH.

**4678**
**Potential economic savings of administration of home intravenous antibiotic therapy to patients with acute respiratory infections in Ireland**
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**Introduction:** Acute respiratory infections (ARI) account for a significant proportion of prolonged hospital stays. Intermediate care initiatives supporting home intravenous antibiotics (HIVA) aim to facilitate early discharge and avoid unnecessary admissions. Numerous studies have demonstrated the efficacy of HIVA for acute infections. International studies have shown increased patient satisfaction, improved quality of life, fewer investigations, less cross-infections, decreased social disruptions and increased cost-effectiveness.
**Objective:** The purpose of this study was to analyse the potential cost-effectiveness of HIVA in patients with ARI in Ireland.
**Methods:** Using the Health Service Executive (HSE) Casemix and assuming a 60% uptake of ARI patients satisfying HIVA criteria with a length of stay (LOS) of 1-3 days, cost-estimates relating to cost/bed and LOS were used to calculate cost/bed-day savings if HIVA is introduced.
**Results:** The approx. annual admission rate for ARI conditions such as pneumonia, COPD, asthma, CF and bronchiectasis is 26,700 patients/yr with an average cost per admission of €70,600. Based on an average LOS of 9.2 days at a cost/bed day of €1,920, the cost/ARI admission is €17,664. This equates to €473m. An LOS of 1-3 days would result in cost-estimates of €51.4-154.2m, a gross difference of €318.8m. Accounting for expenses such as capacity, staff, training, equipment, travel and others, we estimate bed-day savings of €200-220m/yr.
**Conclusion:** HIVA administration is a safe, cost-effective alternative in suitable patients with ARI, potentially providing significant savings to the health service in Ireland.

**4679**
**A prospective re-audit of admissions and discharge delays occurring in patients admitted to a district general hospital's respiratory ward in the United Kingdom**
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**Introduction:** The National Confidential Enquiry into Patient Outcome and Death recommends that following initial assessment and treatment, patients should be transferred to a ward which is appropriate for their clinical condition.
**Objective:** To assess delays prior to discharge for patients (respiratory vs non-respiratory) whom are medically fit for discharge, following a reduction in respiratory beds from 62 to 46 as recommended by Sarker et al 2010.
**Methods:** A prospective 2-week audit was conducted on respiratory wards and in-

A summary table comparing the current re-audit to the previous initial audit

| | | Chadwick et al | Sarkar et al |
|---|---|---|---|
| Total number of patients | | 109 | 141 |
| Number of patients | Primary respiratory diagnosis | 70 | 96 |
| | Primary non-respiratory diagnosis | 38 | 45 |
| Mean age of patients(yrs) | Respiratory group | 62 | 68 |
| | Non-respiratory group | 72 | 67 |
| Number of male vs female patients | Respiratory group | 31 vs 78 | 40 vs 101 |
| | Non-respiratory group | 22 vs 87 | 25 vs 116 |
| Average length of stay for all patients(days) | | 14 | 13 |
| Total number of patients with delayed discharge | | 14 | 75 |
| Average delay in days | Respiratory group | 10 | 8 |
| | Non-respiratory group | 11 | 15 |

cluded patients admitted under three respiratory consultants. Information collated: date of admission and of discharge, age, primary medical diagnosis and reason for delay.
**Results:**
**Conclusions:** A reduction in respiratory beds lead to a reduction in patients with delayed discharge regardless of the underlying medical diagnosis. All delays were still attributable to social reasons. Efficient triage and transfer to appropriate wards on admission will further reduce the number of delayed discharges.

**4680**
**The attitude of physicians for asthma treatment and results in the inhaler market between 2004-2009 in Turkey**
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We evaluated the effects Turkey Conversion Programme in Health in 2004 on drug market used for treatment of asthma.
We analyzed the data from IMS the programme following the drug market and the data from the Social Security Institution (SSI) for comparative studies.
In 2004 SSI paid nearly 4.0 billion Euro for drugs which increased to 8,5 billion (110%).Inhaler dust asthma drugs was 88.9 million and increased to 280.6 million (3.16 fold). Drug prescribed was 6.037.172 and increased to 20.848.085 boxes (3.45 fold).In the market of subgroup for inhaler dust asthma drugs distribution was; the rescue drugs 31.5%, combined drugs 17.7%, nebules 10.5%.The rates in 2009 were 20.2%, 29.6% and 18% respectively. Economically distribution was; 48.4% for combined drugs, 6.3% for nebules and 6.3% for rescue drugs.Rates for 2009 were 58.4%, 9.2% and 4.1%.The number of rescue drugs increased from 1.901.938 boxes to 4.220.664 (2.22 folds). The financial increase was 4.62 fold from 5.570.177 to 25.739.326.The number for nebules was 631.184 and increased to 3.762.806 (5.96 fold) the cost for them was 5.570.177 increased to 25.739.326 (4.62 fold).The combined drug subgroup the number of prescriptions were 1.066.486 increased to 6.178.315 (5.79 fold).The cost was 43.006.559 and increased to 163.814.343.
There has been an increase in the costs for inhaler drugs used for asthma treatment.Our analyses showed that this increase mostly caused by increase in the number of prescribed combined drugs. This increase we believe decreased the need for rescue drugs but had no effect on the nebules that has been used

**4681**
**Stepping up the controller medication in asthma patients: Impact of various treatment options on costs**
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**Introduction:** To compare asthma-related costs among adults who step-up their controller medication.
**Methods:** A population-based study was conducted using the administrative health data of British Columbia, Canada (1997 to 2007). Hospitalization, physician visits, and prescription records were used to identify asthma patients (age 14-65) and calculate direct costs. Four cohorts were constructed as those who: increased the dose of inhaled corticosteroids (ICS+ group), switched to ICS/long-acting beta-agonist (LABA) in a single formulation (ICS/LABA group), added LABA in separate formulations (ICS+LABA group), or added leukotriene receptor antagonist (ICS+LRA group). The outcome was the direct cost of asthma (2008 CAD) in the year after the step-up, adjusted for multiple demographic, resource use, and comorbidty variables from the previous year.
**Results:** 32,640 patients (average age 42.3; 60.3% female) were included (7,115 ICS+, 19,457 ICS/LABA, 4,086 ICS+LABA, and 1,982 ICS/LRA). The average costs of asthma for the year after the index date for the ICS+ group was $509. Compared to ICS+, all other groups had significantly positive incremental costs: +$358.0 for ICS/LABA, +$504.3 for ICS+LABA, and +$541.6 for ICS/LRA (all P-values$<$0.01). Higher age, higher resource use, and higher cumulative dose of rescue medication in the year prior to the step-up date were predictors of higher costs after the step-up date (all p$<$0.01).
**Conclusions:** Based on relatively large sample and adjusted for several potential confounders, increasing ICS dose as a step-up approach was associated with the lower costs compared to addition of a second class of controller medication.

**4682**
**The cost and diagnostic efficacy of microbiological evaluation of exudative pleural effusion**
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**Purpose:** To evaluate the cost and diagnostic efficacy of microbiological studies of pleural fluids.
**Method:** Hospitalized patients with exudative pleural effusion were prospectively evaluated. The fluid samples were examined for Gram stain, acid-fast bacilli smear together with specific bacterial, fungal and mycobacterial cultures.
**Results:** Bacteriologic and EZN stains of the pleural fluids were negative in 89 cases included whereas fluid cultures were positive in 9 (10,1%) cases [3 (12,5%) of the 24 with tuberculous pleurisy and 6 (28,5%) of the 21 with empyema or other parapneumonic pleural effusion]. The cultures of the malignant, nonspecific and paramalignant fluids were negative. In cases with empyema or other parapneumonic pleural effusion and tuberculous pleurisy, no significant difference was determined between culture-positive and culture-negative cases regarding age, gender, fever or fluid LDH and glucose levels; positive cultures were more frequent in the presence of fluid purulence (55.6% versus 8.3%, p=0.046). In 5 (83.3%) of the 6 culture-positive and in 6 (40%) of the 15 culture-negative cases with empyema or other parapneumonic effusion, change in antibiotic treatment was necessary. The costs of the microbiological studies was 39.4 Euro for each case and 1735 Euro and 1419 Euro for cases with noninfectious and infectious fluids, respectively.
**Conclusion:** Diagnostic yield of the routine microbiological studies of pleural fluids was determined low. It was concluded that requesting microbiological studies of pleural fluids in cases strongly considered to have infection on clinical basis and/or in cases with purulent fluid would be more beneficial regarding diagnostic yield and cost.