Introduction
Out-patient parenteral antimicrobial therapy must be governed by the same standards of antimicrobial stewardship, intravenous catheter care and clinical governance as traditional in-patient, hospital-based care. First described out-patient parenteral antimicrobial therapy (OPAT) has since expanded to many disciplines. By the late 1990s and early 2000s, fever and neutropenia in low risk paediatric patients with cancer were being managed with outpatient therapy in certain centres in the USA in the 1970s, in a cohort of paediatric patients with cystic fibrosis intravascular catheter care and clinical governance as traditional in-patient, hospital-based care. First described.

There is a paucity of randomized controlled trials comparing OPAT with inpatient hospital care, though one from primary care in New Zealand identified that OPAT therapy for cellulitis was safe, effective and preferred by patients. There are 3,688 days of intravenous antimicrobials administered at home using the OPAT document for OPAT (adult and paediatric) in 2010 . After a detailed literature search, the authors could not identify any previous study pertaining to OPAT in paediatrics in Ireland.

Methods
This retrospective study reviews data pertaining to OPAT over a 3 year period at a tertiary respiratory unit at an academic Children's hospital, where children with respiratory paediatricians are reviewed. Data was collected from hospital records and both pharmaceutical companies who supplied the antibiotics. Children attending the respiratory department with a pulmonary exacerbation of cystic fibrosis or recurrent pneumonia were individually assessed by the consultant respiratory paediatrician and CF nurse specialist for suitability for home IV antibiotics. Factors taken into consideration included the clinical condition of the patient, social situation, parental issues and duration of antibiotic course. All patients and parents were well known to the CF team and had a lower respiratory tract infection secondary to a chronic cause. Patients not suitable for OPAT included children who were clinically too unwell for home treatment or whose parents had a history of intravenous drug abuse or failed OPAT education by the CF nurse.

Antibiotic choice depended on known bacterial colonisations, previous drug resistance patterns, pharmacokinetics and known patient allergies. The CF nurse specialists trained parents in administration and storage of medications in addition to hygiene, IV access care, monitoring for all potential side effects and a plan of action in the event of a complication. Parent training on OPAT administration etc. was ~3-5 days, while re-training was usually < 1 day. All antibiotics used were in pre-compounded, sterile devices and administered by the children's parents after completing one on one education regarding same. All patients had 24 hour access to medical assistance either directly or over the phone with the respiratory team (between 8am-5.30pm) or via the in-house medical registrar (between 5.30pm-8am). All first doses of antibiotics were administered in hospital under supervision by the respiratory team. Some patients were initially admitted for a few days until clinically stable and if deemed suitable for OPAT, (by the respiratory and CF consultant and team), continued on the antibiotic treatment at home. Others who were less unwell, received only their first dose of antibiotic in the CF day ward under supervision before returning home to complete the antibiotic course. All patients were clinically reviewed at least weekly, by the respiratory physician and CF nurse specialist in the respiratory day ward.

In addition, antimicrobial drug levels, urea and electrolytes, renal function, liver function and pulmonary function tests were monitored weekly. Early patient, clinical status and multidisciplinary team meeting, and a consultant decision made regarding continuation or discontinuation of therapy.

Results
Between January 2010 and 2013, a total of 361 OPAT courses were administered to 32 children with lower respiratory tract infections. This resulted in 3,688 days of intravenous antibiotics administered at home using the OPAT programme. Regarding diagnosis, 30 (94%) of a total of 32 children treated with OPAT had cystic fibrosis and 2 had recurrent pneumonia: 1 associated with bronchiectasis and the other with an immune deficiency. All children treated with OPAT had pneumonia. Common organisms included Pseudomonas aeruginosa (mucoid and non-mucoid), Staph aureus (methicillin sensitive or methicillin resistant), Haemophilus influenza, Streptococcus pneumonia or a combination of same.

The median age of the children treated was 8.8 years (range 2.75-17.8 years) and 16 (50%) were male. Fourteen different antibiotics and an antifungal were administered (Table 1). Tobramycin was the commonest antimicrobial agent prescribed with 106 courses (29% of total courses) and 1,103 days (30 % of days). Ceftazidime was the second commonest antimicrobial agent prescribed: 70 courses, (19.4%) and 752 days, (20%). On average, children had 24 hours therapy (range 2-112) over the 3 year period, with a mean duration of 10 days therapy (range 2-42 days). At least two antimicrobials were administered simultaneously in all cases. Regarding children on the active lung transplant list, some courses were administered in hospital under supervision by the respiratory team. Some patients were initially admitted for a few days until clinically stable and if deemed suitable for OPAT, (by the respiratory and CF consultant and team), continued on the antibiotic treatment at home. Others who were less unwell, received only their first dose of antibiotic in the CF day ward under supervision before returning home to complete the antibiotic course. All patients were clinically reviewed at least weekly, by the respiratory physician and CF nurse specialist in the respiratory day ward.

Regarding adverse events there were 3 (2%) portocath infections: one cultured Candida albicans, one Enterococcus and one Streptococcus maltophilia. All three were surgically removed after failure to respond to antimicrobial therapy while awaiting surgery. There was one (0.6%) re-admission: a child who had a deterioration in pulmonary status and chest radiograph findings. She was noncompliant with chest physiotherapy at home and subsequently was the patient who cultured Candida albicans from her portocath. All children attended for weekly review, laboratory monitoring and lung function testing where age appropriate. All children had follow up review in the day ward with lung function testing.
The benefits of OPAT include institutional, organisational and patient. Our results concur with those internationally, that OPAT reduces the demand for hospital bed use (361 OPAT courses with a mean duration of 11 days). Savings are achieved through avoidance of non-essential admissions, early discharge with minimal re-admissions resulting in a substantial capacity gain for each institution. The cost savings of OPAT have been consistently demonstrated; in the UK, OPAT has been delivered at 41% of equivalent in patient cost, in Canada at 57% and in Singapore at 61%. Patient benefits include reduced risk of health care associated infections and higher levels of satisfaction with OPAT (in appropriate conditions) than with inpatient hospital care. Success of OPAT is dependant on appropriate patient selection, weekly follow up of patient clinical status, blood tests, 24 hour access to medical advice and overall adherence to national practice guidelines. Multiple reasons exist as to why CF is suited to OPAT due to the chronicity of this condition, children often require multiple courses of antibiotics per annum resulting in repeated training and experience of parents in OPAT, children and families are well known to the respiratory team because of 3 month clinical reviews and children are accustomed to regular phlebotomy and investigations. Additionally, many of these children have permanent indwelling IV access (portocaths) in place (72% in this study).

Our findings are similar to those internationally in that we identified OPAT to be safe and effective. Our findings differ in type of infection treated, commonest antibiotic prescribed and duration of therapy. The latter two are directly related to the fact that OPAT is run by the respiratory team for respiratory patients only, so all our patients had pneumonia whereas in other studies bone and joint or soft tissue infections predominant. Tobramycin and ceftazidime were the most common antibiotics prescribed in our study, (treatment for Pseudomonas aeruginosa pneumonia in CF) whereas ceftriaxone and cefazolin were the most commonly prescribed antibiotics in a recent paediatric OPAT paper where bone and joint (21%) and bloodstream (5%) infections predominated. The most common duration of treatment varied between 12 days for paediatric OPAT in the USA to 24 days for infective endocarditis in adults in Australia recently 23. Our study had a mean duration of 11 days of OPAT because children with CF are traditionally given -14 days IV antibiotic treatment if > 5years of age which may extend up to 4-6 weeks if severe infection and lung disease. Children with CF generally culture multiple organisms in their sputum. Antibiotic choice is based on recent sputum sensitivities. While the combination of Tobramycin plus ceftazidime was the commonest prescribed for Pseudomonas aeruginosa alone, Flucloxacillin plus cefuroxime was the commonest combination for children culturing Staph aureus plus Haemophilus influenza. Prophylactic nebulised colomycin and/or nebulized tobramycin is used in children chronically colonised with Pseudomonas aeruginosa. Prophylactic azithromycin may be added if symptoms persist despite nebulised antibiotic therapy. At our institution, no antibiotic prophylaxis is given to children who culture Staph aureus alone, consistent with the North American model of care. Telzoplanin was favoured over Vancomycin due to the side effect profile and need for drug levels in the latter.

Attendance for weekly review compares favourably to other studies: 100% in our study, versus 88% when OPAT was managed by others 22. However, services in Ireland (OPAT, inpatient and outpatient) are not reviewed in a recent paediatric USA OPAT study at an academic childrens hospital. Complications included 1 (0.3%) re-admission and 3 (2%) portocath infections which compares with 11% treatment failure and 29% catheter or antibiotic associated complications in a recent paediatric OPAT study 23. There were 3-4 patients (11%) under regular review by the transplant team regarding same. The one child with CF who received most OPAT courses (n=112), had a portocath infection (Stenotrophomonas maltophilia) and has since received a double upper lobe lung transplant.

In our current climate of health care budget cuts, pressure on inpatient bed availability and risk of nosocomial infections, OPAT is an important and effective tool. Future plans for OPAT nationally include, implementation of national OPAT practice standards, establishing a national registry, regular audit of all OPAT programmes to ensure standards are maintained and expansion to more hospitals and disease states. Continued monitoring of failures, adverse effects and effectiveness is important in this expanding area. This study is the first, identified by the authors to review OPAT in Paediatrics in Ireland.

Correspondence: DM Slattery Department of Paediatric Medicine, Children’s University Hospital, Temple St, Dublin 1 Email: michaelkennedy@eircom.net

References