254* Sample size estimation for CF clinical trials using rate of lung function decline (RLFD) as an efficacy endpoint

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Loss of lung function is the primary cause of CF mortality, and RLFD is a robust predictor of survival (Statist Med 2002;21:1271−87). RLFD (as FEV_1 % pred/yr) is a more meaningful measure than sustained improvement in lung function, but there is less experience with RLFD as an endpoint. We have used recent epidemiologic data (J Pediatr 2007;151:134−9, Ped Pulm 2007; S30:345) to develop a sample size (N) determination model for RLFD studies in 6−17 yr olds with CF. A mock 500 subject cohort was constructed with distribution of risk variables (age, FEV_1 % pred, PA infection, sex, sputum production, wheeze, and crackles) comparable to the current US CF population. The cohort was randomized into 2 arms stratified by age (32% 6−8 yrs, 30% 9−12 yrs, 38% 13−17 yrs). Subject and group RLFD over 2 yrs were estimated as functions of the presence/absence of risk factors. This was repeated 200 times each for cohorts of 500, 200, 150, 100, 80, 60, 40, and 20 subjects with risk variables randomly redistributed each iteration. Mean RLFD was −2.17 FEV_1 % pred/yr for the cohort. Boundaries within which 90% of confidence intervals for RLFD point estimates fell were plotted against N to determine 80% power thresholds to detect given treatment effects. In this cohort, 33 subjects/arm would be required to assure <80% power to detect a 50% reduction in RLFD, while 18 subjects/arm would be needed to detect a 70% reduction. The power of this method is that it is sensitive to impacts of specific risk factors on RLFD and can be used in conjunction with currently available CF patient registries to estimate sample size requirements for specific subsets of CF patients (e.g. having a specific CFTR mutation or risk factor).

255* Adherence to nebulised therapies for *Pseudomonas* eradication in a paediatric CF population

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Introduction: The UK CF Trust policy for treatment of first/new growths of *Pseudomonas aeruginosa* (PsA) in an asymptomatic child is 3 weeks of oral ciprofloxacin and 3 months of inhaled colistin. Recent use of an adaptive aerosol delivery (AAD) device for inhaled colistin has enabled adherence to be monitored in partnership with families in our clinic. We have investigated the relationship between adherence to 3 months of inhaled antibiotic therapy, PsA clearance (PsA culture-negative cough swabs/sputa for 6 months following start of treatment) and lung function.
Methods: From November 2005, 36 first/new growths of PsA in 33 children were treated with inhaled colistin via an AAD (I-neb, Respironics). Using software provided by the manufacturers, adherence was analysed over the 3 month treatment period. Respiratory cultures were routinely taken after three weeks and three months (and occasionally more frequently). Lung function was performed at the start and the end of eradication.
Results: Adherence data for 23/36 children have been analysed to date. Overall mean (SD) adherence to inhaled treatment was significantly higher in the evenings [86.4(28.9)%] than in the mornings [75.5(24.7)%; p = 0.022]. 17/23 (74%) patients exhibited good adherence (taking >80% of their treatments). Successful PsA eradication was achieved in 17/23. Adherence and lung function were no better in those children that eradicated PsA although numbers were small. No relationship between adherence, PsA clearance and change in lung function was detected.
Conclusions: These data suggest good adherence to inhaled antibiotic treatment for first/new growths of PsA. These preliminary data do not suggest a relationship between adherence to treatment, PsA clearance and lung function.

256 Reported and objective adherence to nebulised therapy in adult patients with cystic fibrosis

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Introduction: Few studies report on adherence in adults with CF, most use self-report, physician report or medical record review which may overestimate true adherence. This prospective study assesses concordance between objective adherence to nebulised therapy [data downloaded from i-neb (Respironics)] and subjective adherence measured by questionnaire administered to patients, CF doctor, pharmacist, physiotherapist, dietitian and nurse.
Methods: i-neb stores data of use of nebulisers (date, time, length of nebulised treatments and details of incomplete treatments). Subjective assessment of adherence was undertaken at clinic and data for 3 months prior to visit downloaded from ineb. Members of the MDT then completed an adherence questionnaire for participants. 2 questions on adherence were given: average number nebs/week and overall % nebulised treatment taken over last 3 months, to assess whether form of questioning affects accuracy.
Results: Adherence is expressed as % prescribed regimen, descriptive data expressed as median (range) and agreement between adherence measures assessed using intra-class correlation coefficient. 68 patients have completed the study to date. Results are summarised in Table 1. No agreement was found between objective adherence and self or MDT report.
Conclusion: Self and MDT reporting of adherence is not accurate. This has implications for studies and clinical practice when assessing and monitoring therapy. True compliance is lower than previously suggested at 36%, this may have QoL and cost implications.

Table 1

| | Average number of nebs/week | | | | | | Overall % nebulisers taken over last 3 months | | | | | | |
	Patient	Pharm	Physio	Dr	Diet	Nurse	Patient	Pharm	Physio	Dr	Diet	Nurse	Objective
Median%	75	57	50	61	62	57	80	50	53	60	60	60	36
Range	133	100	86	100	79	91	100	100	90	100	78	95	112

257* Eradication of recent *Pseudomonas aeruginosa* isolation: TOBI versus colistin/ciprofloxacin

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Early treatment of *Pseudomonas aeruginosa* (*Pa*) (re)infection can postpone chronic infection.
Aim: compare 2 *Pa* antibiotic (AB) eradication regimens.
Method: CF children (0−18 years) with new isolation of *Pa* (sputum or cough swabs) were prospectively randomized to treatment with inhaled TOBI® (300 mg bid for 28 days) *vs* 3 months combination therapy with inhaled Colistineb® (2 milj U bid) + oral ciprofloxacin (10 mg/kg tid) (CC). Monthly airway cultures were taken for 6 months, then 3 monthly. Positive *Pa* culture in the first 6 months was defined as treatment failure. Patients were then switched to the other arm or treated with IV AB if clinically indicated. Secondary outcomes were: *Pa* antibodies (Ab), IgG, lung function, weight and time to *Pa* relapse.
Results: data on 26 patients are available. Median age was 9 years (0−16); median FEV_1 at inclusion 90% predicted. For 7 patients this was the first *Pa* isolation 'ever' (TOBI: 4; CC: 3). For the remaining, median time since previous *Pa* was 23 months (range 6−79). CC treatment failed in 3 out of 10 patients (1 needing IV AB), 2 patients were non-evaluable. For 16 TOBI treated patients 8 failed (2 needing IV), 1 was non-evaluable. Taking into account switches to the other treatment arm, eradication succeeded in 9 of 14 CC and 8 of 17 T (ns).
Pa Ab were raised in 1 patient at baseline and returned negative after successful treatment. At >1 year follow-up 3 patients were chronically *Pa* colonized (1 from the CC group, 2 of the TOBI group); in 1 patient *Pa* Ab levels became +ve.
Conclusion: Success rate of short term eradication in new *Pa* isolation was low. However, use of cough swabs rather then BAL (Gibson 2007) may overestimate lower airway infection. Low patient numbers limit comparison between the 2 regimens yet.