Conclusions 1. Results of this analysis do not support the use of FVC as a surrogate end-point for mortality or hospitalisation in IPF, sarcoidosis or bronchiectasis trials. 2. Reporting of FVC in clinical trials is highly variable making synthesis of results for meta-analysis difficult. We suggest all trials make available baseline, final and change in FVC, both unadjusted and percent predicted, and as relative (% change), at least in an online appendix.

S15 FVC OR TLCO? IMPACT ON TREATMENT FOLLOWING NICE (NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE) APPROVAL OF PIRFENIDONE

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Introduction Idiopathic Pulmonary Fibrosis (IPF) is a progressive, fatal lung disease with median survival of 3 years (1). NICE has recently approved Pirfenidone, which is the first licensed treatment for IPF. Pirfenidone is licensed for mild to moderate IPF, and the current NICE recommendation is that all patients with FVC (Forced Vital capacity) between 50–80% predicted should be considered for therapy. However, there is no agreed classification of disease severity in IPF. In clinical practice a combination of both FVC and DL_{CO} (diffusion of lung carbon monoxide) is used to monitor disease progression. We explore the practical impact of using FVC on Pirfenidone prescribing.
Methods 218 incident cases of IPF have been enrolled in a prospective cohort study PROFILE in Central England from September 2009 to June 2013. All patients had a diagnosis of definite or probable IPF based on the ATS consensus 2000. The patients were stratified according to both FVC and DLco. Lung function defects were considered mild (FVC>80%, DL_{CO}>60%), moderate (FVC 50–80%, DL_{CO} 40–60%) and severe (FVC<50%, DL_{CO} <40%).
Results The median age was 72 years with majority cohort males (77% males' vs 23%females). 181(84%) cases met diagnostic criteria for definite IPF. There was only a moderate correlation between FVC and T_LCO with correlation coefficient = 0.54 and $p < 0.001$. A total of 79 patients (44%) would be eligible for treatment based on FVC criteria. However, this includes 46 patients (25%) who might be considered to have severe disease based on DLco criteria. (Table 1)
Conclusion Over half our patients eligible for Pirfenidone, based on current NICE criteria, will have severely reduced DL_{CO}. This highlights the need for an agreed classification of IPF disease severity. Follow up of PROFILE study patients may help guide a classification system.

REFERENCES

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Abstract S15 Table 1. PROFILE cohort September 2009 to June 2013 Nottingham & Central England NHS Trust

	FVC at diagnosis			
DL_{CO}(↓)	*Mild (>80%)*	*Moderate (50–80%)*	*Severe (<50%)*	Total (n)
Mild (>60%)	34	4	0	38
Moderate (40–60%)	40	29	1	70
Severe (<40%)	22	46	5	73
Total (n)	96	79	6	181

S16 OUTCOMES IN IDIOPATHIC PULMONARY FIBROSIS: A META-ANALYSIS FROM PLACEBO CONTROLLED TRIALS

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Background Much of the data regarding the natural history of Idiopathic pulmonary fibrosis (IPF) pre-dates current clinical criteria. Despite high mortality debate has been sparked recently regarding the appropriateness of mortality as an endpoint for clinical trials. Additionally, respiratory infections are seen to have a role in the natural history of IPF. We aimed to evaluate the frequency of mortality and respiratory infections in the placebo arms of IPF trials.
Methods We identified randomised, placebo-controlled trials of IPF though a systematic review of MEDLINE, EMBASE, AMED and Cochrane central. Outcomes were mortality and lower respiratory tract infection (LRTI). We standardised event rates and compared differences using incidence rate ratios between subgroups of trials, according to disease severity inclusion or use of low-dose corticosteroids).
Results Thirteentrials were included, involving 1631 patients (2067.7 patient-years of follow-up). Standardised mortality was 91.9 deaths per 1,000 patient-years (range 18.8 to 224.5 per 1,000 years), though rates were higher in trials permitting low-dose immunosuppression and lower in trials excluding severe disease (table 1). Rates of respiratory tract infections were higher in trials including severe disease and in trials including patients receiving immunosuppression (table 1)
Conclusion Mortality rate was heterogenous and dependent on entry criteria, with rates in studies excluding severe disease half that of unselected studies. Rates of infection in IPF are high, even without concurrent use of immunosuppression. Given low mortality rates, consideration should be given to alternative primary outcomes to mortality in future IPF trials of patients with mild-moderate disease.

Abstract S16 Table 1.

	Rate per 1,000 patient-years follow-up		*Incidence rate ratio (95% C.I.)*	
	Standardised Mortality Rate	Standardised LRTI Rate	Mortality	LRTIs
All trials	91.9	172.5	-	-
Permitting low-dose (< 20mg/day) steroids	95.8	227.1		
No steroids	72.9	63.4	1.31 (0.93–1.88)	3.58 (2.16–5.13)
Severe disease (FVC<55%) included	188.6	257.8		
Severe disease excluded	78.6	153.9	0.42 (0.30–0.59)	0.60 (0.45–0.81)

S17 A PROTHROMBOTIC STATE IS ASSOCIATED WITH INCREASED MORTALITY IN IDIOPATHIC PULMONARY FIBROSIS

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