Abstract S90 Table 1

	Younger Patients (18-40)		Older Patients (over 65)	
Total Number	517		357	
Median age (IQR)	29 (26–33)		73 (69–78)	
Gender	189 female, 328 male		151 female, 195 male	
UK Born	39 (7.5%)		39 (10.9%)	
Pulmonary	191 (36.9%)		171 (47.9%)	
Smear Positive	54/191 (28.3%)		14/73 (19.2%)	
Data Available	489 (177pulmonary)		73 (all had pulmonary involvement)	
Symptoms at presentation (all patients)	All patients N = 489	Pulmonary TB N = 177	All patients N = 73	Pulmonary TB N = 73
Cough N (%)	186 (38)	113 (63.8)	38 (52.0)	38 (52.0)
Haemoptysis N (%)	27 (5.5)	22 (12.4)	2 (2.7)	2 (2.7)
Fever N (%)	162 (3.3)	75 (42.4)	18 (24.7)	18 (24.7)
Drenching night sweats N (%)	129 (26.3)	65 (36.7)	12 (16.4)	12 (16.4)
Weight loss N (%)	187 (38.2)	102 (57.6)	43 (58.9)	43 (58.9)
Dyspnoea N (%)	24 (4.9)	15 (8.5)	28 (38.4)	28 (38.4)
Lethargy N (%)	25 (5.1)	7 (4.0)	11 (15)	11 (15)
Reduced Appetite N (%)	28 (5.7)	13 (7.3)	16 (21.9)	16 (21.9)
Neck Lymphadenopathy N (%)	131 (26.8)	7 (4.0)	15 (20.5)	15 (20.5)
Pulmonary TB	Younger Patients (18–40)		Older Patients (over 65)	
Symptom duration at presenting to secondary care in days. Median (IQR)	45 (30–90)		90 (26.25–180)	
Time from secondary care to starting treatment in days. Median (IQR)	2 (1–5.5)		7 (2.25–41.5)	
Pulmonary TB	N = 137		N = 37	
Total time from symptom onset to starting treatment in Months. Median (IQR)	2.0 (1–3)		3.0 (1.5–6.5)	
Proportion starting within 2 months of symptom onset N (%)	82 (59.9)		13 (35.1)	
Proportion starting within 4 months of symptom onset n (%)	119 (86.9)		25 (67.6)	
Proportion starting more than 4 months of symptom onset n (%)	18 (13.1)		12 (32.4)	

Biases in this work including recording bias due to the retrospective nature of symptom recording, the effect of selecting younger patients from more recent years (to improve data availability) and the low proportion of patients over 65 which had symptom and treatment data available.

S91 LIVER FUNCTION TESTS DURING TUBERCULOSIS TREATMENT AND THE IMPLICATIONS ON MONITORING FOR HEPATOTOXICITY

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Introduction and objectives Drug-induced hepatotoxicity is a common complication of tuberculosis treatment.¹ Guidelines based on expert opinion are available, but the natural history of liver enzyme measurements over the course of treatment and the most effective approach to monitoring on treatment remains unclear.

We investigated the pattern of liver enzyme levels in the REMoxTB trial to describe the magnitude and timing of elevations, along with factors that could influence enzyme patterns, and related this to liver function monitoring.

Methods Patients received either standard tuberculosis treatment (2EHRZ/4HR), or a four-month regimen with moxifloxacin substituted for ethambutol (isoniazid arm, 2MHRZ/2MHR) or isoniazid (ethambutol arm, 2EMRZ/2MR). Liver function tests were

performed at weeks 0, 2, 4, 8, 12, 17, and during adverse events. The Chi Square or Fisher's exact test was used for testing proportions among groups, log rank test for comparison of time, and Students t test for comparison of means.

Results 639 patients were allocated to receive standard therapy as controls, 654 to the isoniazid arm, and 635 to the ethambutol arm (see Table 1). 60 patients (9.4%) taking standard therapy developed a peak ALT/AST $\geq 3 \times$ ULN at median time 28 days (IQR 14–56). The mean difference in time to reach peak ALT was 7 days between isoniazid-containing regimens and the ethambutol arm, and a higher proportion of Asian patients elevated ALT/AST $\geq 3 \times$ ULN in isoniazid-containing arms (51.0% vs 26.3%, ($p < 0.001$)). Of the 40/421 (9.5%) HIV positive in Africa, 24/421 elevated ALT/AST $\geq 3 \times$ ULN compared to 25/121 (5.7% vs 20.7%, ($p < 0.001$)) in India elevating ALT/AST $\geq 3 \times$ ULN where 2/121 (1.7%) were HIV-positive.

Discussion Monitoring liver function routinely for the first two months of HRZE therapy would have detected approximately 75% of patients with a peak enzyme elevation of $\geq 3 \times$ ULN, and we would recommend this as a standard of care based on these results. However, there is reassurance that over 90% of patients completed therapy without an ALT/AST result $\geq 3 \times$ ULN. HIV positive and Asian patients were at higher risk of liver enzyme elevation and there was a shorter time to peak ALT/AST for those receiving isoniazid.

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Abstract S91 Table 1

		2EHRZ/4HR	2MHRZ/2MHR	2EMRZ/2MR	p value
ALT RESULT	n [◇]	634	649	634	***
	Median peak value as xULN (IQR)	0.83 (0.56–1.35)	0.78 (0.53–1.23)	0.73 (0.51–1.09)	0.046 [†] 0.000 [‡]
	Median time to peak value in arm (days)	28 (14–84)	28 (14–84)	55 (14–84)	0.972 [†] 0.017 [‡]
	No with peak ≥ 3 xULN (%)	41 (6.5%)	35 (5.4%)	25 (3.9%)	0.130
	No with peak ≥ 5 xULN (%)	20 (3.2%)	18 (2.8%)	14 (2.2%)	0.580
	No with peak ≥ 10 xULN (%)	7 (1.1%)	2 (0.3%)	3 (0.5%)	0.204 [§]
AST RESULT	n	639	654	635	***
	Median peak value as xULN (IQR)	1.02 (0.73–1.48)	0.93 (0.68–1.45)	0.90 (0.68–1.28)	0.026 [†] 0.000 [‡]
	Median time to peak value in arm (days)	52 (14–84)	28 (14–84)	55 (13–84)	0.160 [†] 0.917 [‡]
	No with peak ≥ 3 xULN	46 (7.2%)	41 (6.3%)	27 (4.3%)	0.074
	No with peak ≥ 5 xULN	21 (3.3%)	17 (2.6%)	12 (1.9%)	0.292
	No with peak ≥ 10 xULN (%)	8 (1.3%)	5 (0.8%)	5 (0.8%)	0.668 [§]
	No of liver-related withdrawals	11 (1.7%)	7 (1.1%)	4 (0.6%)	0.178

[◇]Some patients not included due to missing ALT results

[†] Isoniazid arm against standard therapy

[‡] Ethambutol arm against standard therapy

[§] Fisher's exact test

Predicting Risk in Pleural Disease

S92 NON-MALIGNANT PLEURAL EFFUSIONS (NMPE): A PROSPECTIVE STUDY INTO 355 CONSECUTIVE UNSELECTED PATIENTS

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Introduction and objectives Non-Malignant Pleural Effusions (NMPE) have an estimated annual incidence of 200,000 in the UK.¹ They are often secondary to underlying organ dysfunction, with congestive heart failure (CHF) the leading cause. CHF itself carries a high mortality risk, with 28% of patients with New York Heart Association (NYHA) class IV dying within a year.² Despite this, information on baseline characteristics, prognostic features and mortality in NMPE is sparse. Our aim is to determine the mortality rates in NMPEs in a prospective observational trial.

Methods We recruited 784 consecutive patients presenting to a pleural service, between 03/2008 and 03/2015, with an undiagnosed pleural effusion. Further analysis was conducted on the 355 patients with NMPE.

Pleural biochemistry, cytology, thoracic USS and chest radiograph were performed. Echocardiogram, CT scans, radiological-guided biopsy and medical thoracoscopy were undertaken as

clinically indicated. Patients were followed-up for a minimum duration of 12 months with final diagnosis decided by independent review by 2 respiratory consultants. Survival data was calculated from study entry to death. Surviving patients were censored on 07/2016.

Results Of the 784 patients, 355 (45%) were diagnosed with a NMPE. These patients had a mean age of 68 (SD17) with 69% of patients male. Patients with CHF (HR 4.7 CI: 2.3–9.5) had a 50% 1-year mortality and a mean age of 79. Renal failure (HR 5.2 CI: 2.1–12.9) and liver failure (HR 4.8 CI: 1.9–11.8) patients had 1-year mortality rates of 31% and 25% respectively (HR c/w inflammatory pleuritis). Bilateral effusions (HR 2.6 CI 1.7–3.9) and transudative effusions (HR 3.1 CI: 2.2–4.3) were associated with a worse prognosis in patients with NMPE, with a 57% and 44% 1-year mortality respectively.

Conclusion This is the largest prospectively collected series in patients with NMPE, demonstrating that those secondary to organ dysfunction have an extremely high 1-year mortality. The presence of a pleural effusion in patients with CHF is a marker of severe disease, almost doubling the mortality risk compared to patients with NYHA class IV CHF.

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