We sought to determine the cost-effectiveness of each UK guideline from an NHS perspective, plus alternatives, using prospective data.

All patients with a new HIV diagnosis attending an ambulatory HIV clinic, plus a sample of those with known HIV were approached; and offered a symptom questionnaire, chest radiograph (CXR), tuberculin skin test (TST), blood interferon gamma release assay (IGRA) and induced sputum for mycobacterial culture (IS). The uptake and results were used to calculate the cost-effectiveness of thirty different testing strategies using univariate, multivariate and probabilistic sensitivity analyses (PSA).

219 subjects, representative of the total clinic population, took part. 73% were male, 28% black African and 95% on antiretroviral therapy (ART). During testing, 2 cases (0.9%) of subclinical TB and 14 (6%) of LTBI were detected. Half the patients with LTBI completed preventive treatment. Over a median of 28 months follow up, no new cases of active TB were identified.

When compared to no testing, only three of the thirty strategies were below the maximum NICE threshold for cost-effectiveness <£30,000/QALY gained. Testing black Africans with just TST or IGRA cost £23,429/QALY and £28,971/QALY respectively, whilst testing black Africans plus those from countries with a TB incidence of >20/100,000 ('middle incidence', MI) cost £25,218/QALY and £32,410/QALY using TST alone or IGRA alone respectively. NICE, BHIVA, or more extensive strategies, were not cost-effective. (Table)

Using PSA, no testing was most likely cost-effective up to £30,000/QALY.

In a contemporary HIV population with very high uptake of ART, neither current UK guideline is cost-effective. Testing black Africans, or black Africans and people from middle TB incidence countries appear at best marginally cost-effective. Future UK guidance needs to reflect changing health demographics, improved outcomes for people in HIV care, and clinical pragmatism.

S89 THE USE OF TUBERCULOSIS CHEMOPROPHYLAXIS IN PATIENTS OF RENAL REPLACEMENT THERAPY

¹N Ahern, ²H Jarvis, ²R Charif, ²OM Kon. ¹Imperial College London, London, UK; ²Imperial College NHS Healthcare Trust, London, UK

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Introduction Individuals with end stage renal disease (ESRD) undergoing renal replacement therapy (RRT) are at increased risk of tuberculosis (TB). Timely identification and treatment of latent TB infection (LTBI) reduces the risk of progression to active disease. Diagnosing LTBI is challenging in ESRD as standard tests, such as the tuberculin skin test (TST) and Interferon Gamma Release Assay (IGRA) are less reliable. Although TB guidelines exist for ESRD they acknowledge a lack of evidence base and are limited in their scope.

This study aimed to establish the current LTBI screening and treatment practice in patients of RRT in a central London teaching hospital with the hypothesis that there would be a varied approach with overall low levels of screening.

Methods New starters on haemodialysis (HD) in the year 2010 were identified from computerised renal databases and information collected on; demographics, renal diagnosis, co-morbidities, dialysis attributes, TB risk factors, screening methods and LTBI treatment. All patients were followed for a period of 5 years to establish the rate of active TB after commencing RRT. Screening

was considered to have taken place if any of the following were performed irrespective of symptoms of active disease; TST, IGRA, radiography specifically to investigate for TB or documented risk stratification.

Results Of the 331 eligible patients only 77 (23.2%) received screening. In those who were screened, 13 (16.9%) were diagnosed with active TB equating to an incidence of 3927/100,000, 37 (48.1%) with latent TB and 27 (35.1%) with neither. Risk factor stratification was the commonest modality of LTBI identification although there were a wide variety of approaches. Chemoprophylactic treatment regimes were non-standardised and often based on clinical experience rather than guidelines. Of those with active infection, disease developed most commonly within the first year of starting HD.

Conclusion High rates of active TB occur mainly within the first year of RRT. There is a lack of a uniform approach to detecting and treating LTBI in this population currently. Risk stratification and the use of immunological tests may offer the most sensitive approach to screening ESRD and within the first year of RRT.

S90 THE NATURE AND DURATION OF SYMPTOMS AND TIME TO STARTING TREATMENT COMPARING OLDER WITH YOUNGER PULMONARY TUBERCULOSIS PATIENTS

¹A Abbara, ²E Hardman, ³SM Collin, ⁴OM Kon, ¹Z Mahomed, ⁵JAL Sullivan, ⁵K Buell, ⁶T Hansel, ¹T Corrah, ¹RN Davidson. ¹London North West Healthcare NHS Trust, London, UK; ²University College Hospital, London, UK; ³University of Bristol, Bristol, UK; ⁴Imperial Healthcare NHS Trust, London, UK; ⁵Imperial College, London, UK; ⁶NHLI, Imperial College, London, UK

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Introduction and objectives In 2013, Public Health England (PHE) reported that 39% of pulmonary tuberculosis (TB) patients >65 years old started treatment >4 months after symptom onset compared to 25% of patients aged 15–44 years. A longer symptomatic period, particular if smear positive, may result in increased transmission and poorer treatment outcomes. We investigated age-related differences in symptom duration and time to starting TB treatment in a large UK cohort of TB patients.

Methods The cohort comprised patients on the London TB register (LTBR) who were treated at Northwick Park Hospital between 2002–2015. Patients aged >65 years were compared with a random sample of patients aged 18–40 years, with respect to symptoms, symptom duration at presenting to secondary care and time to starting treatment after presenting to secondary care.

Results 357 patients over 65 and 517 younger patients were identified. Demographics for the total number of patients are included in Table 1. Data were available for 489 of the younger group and 73 of the older group. 26 of the >65s (35.6%) and 9 (1.8%) of the 65s were diabetic.

Conclusions This study has identified that a potential cause for a delay in diagnosis in the elderly may be related to the decreased frequency of 'classical' TB symptoms in those >65 years of age. Clinicians need to be vigilant despite the lack of these symptoms.

Median duration of symptoms was twice that in older patients versus younger patients (90 days versus 45) with a longer time to starting treatment (7 days versus 2). The total duration (in months) from symptom onset was also higher at 3 months versus 2 months. A higher proportion of older patients (32%) started treatment greater than 4 months from symptom onset compared to 13.1% in younger patients.

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

¹CD Tweed, ¹G Wills, ¹AM Crook, ¹SK Meredith, ¹AJ Nunn, ²CM Mendel, ²SR Murray, ³TD McHugh, ⁴SH Gillespie. ¹MRC Clinical Trials Unit at UCL, London, UK; ²The TB Alliance, New York, USA; ³Division of Infection and Immunity, University College London, London, UK; ⁴University of St Andrews Medical School, St Andrews, UK

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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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