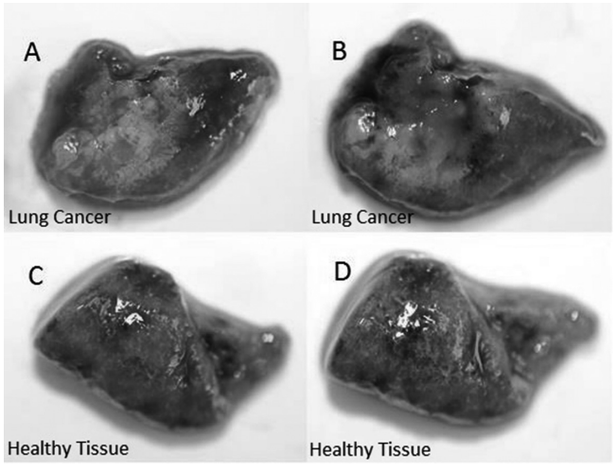
Results 11 patients were included in this study. NSCLC was confirmed in all patients. 7 patients were diagnosed with adenocarcinoma and 4 patients with squamous cell carcinoma. A differential stain for lung cancer versus normal tissue was achieved (Figure 1).



Abstract S35 Figure 1 Lung cancer (a) and healthy tissue (c) prior to MB delivery. Differential staining of lung cancer tissue (b) following MB delivery and wash. Minimal staining of healthy tissue (d) following MB delivery and wash

Conclusion These findings indicate that MB has the potential to differentiate malignant and healthy tissue in an *ex vivo* model. This study supports the utility of MB as a potential diagnostic aid in lung cancer surveillance.

Management of TB

S36 WEEKLY AUDIOGRAMS PRE-EMPTIVELY IDENTIFY AMIKACIN RELATED OTOTOXICITY IN MDR-TB

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Introduction and objectives Updated WHO guidance recommends at least 8 months of aminoglycoside (AG) for MDR-TB but provides no definitions or monitoring strategies for otoxocity. Most UK centres perform 2–4 weekly audiograms; we perform weekly audiograms. We retrospectively investigated whether this strategy pre-emptively identifies ototoxicity before significant hearing loss (HL) is evident.
Methods Patients we treated with amikacin for MDR-TB from 2002–2015, with at ≥4 weekly pure tone audiograms, were included. Audiograms, treatment duration, symptoms, creatinine clearance and outcome were obtained from clinical records. All patients received amikacin at 15 mg/kg per day and had weekly amikacin levels and renal function. Definition of HL was defined as per the ASHA as >20 dB loss of pure tone threshold from baseline at one frequency or >10 dB at two adjacent frequencies.
Results 31 MDR-TB patients fulfilled selection criteria; 15 female, median age 36 years (IQR: 24–43) and median weight 61.5 kg (IQR: 52–65.) 22/31 (70.9%) patients had their first audiogram within 10 days; median 5.5 (IQR:4–7.) The median duration of amikacin treatment was 79.5 days (IQR: 61.75–94) and median total dose of 70.8 g (IQR:44.4–97.75.) 4/31 (12.9%) had moderate-severe baseline hearing loss (HL). A total of 17 (54.8%) patients met the ASHA definition of HL: 7 at 4 kHz, 10 at 6 kHz and 17 at 8 kHZ. The median time to meeting ASHA definition of HL among these patients was 59 days (IQR: 41–84.75). 16/31 (51.6%) patients stopped amikacin earlier than planned and 1 continued; 2 (6.5%) due to symptoms of deafness, 2 (6.5%) due to tinnitus and 12 (38.7%) due to asymptomatic high frequency HL on audiograms. Creatinine clearance and trough amikacin levels remained within range for all patients. Regarding outcomes, 17 (54.8%) completed TB treatment, 5 (16.1%) remain on treatment, 4 (12.9%) transferred, 3 (9.7%) were lost to follow up and 1 (3.2%) died.
Conclusions AGs are important in the treatment strategy of MDR-TB but this must be balanced with the long-term side effects. The ototoxicity of AG is unrelated to elevated drug levels or contributing factors and is a common adverse effect. Weekly audiograms led to earlier detection of pre-symptomatic amikacin ototoxicity and cessation in 38.7% of patients.

S37 THE RESPONSE OF OBJECTIVELY-MEASURED COUGH TO TREATMENT IN TUBERCULOSIS: AN EXPLORATORY STUDY

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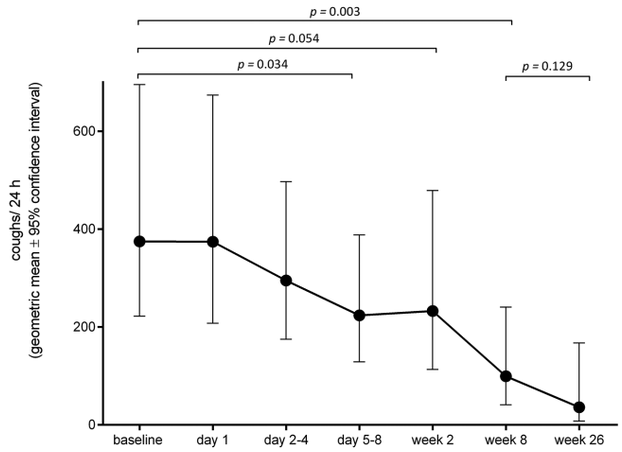
Introduction and objective Cough is predominant in pulmonary tuberculosis and transmits infection, yet it is unclear how rapidly it responds to treatment. We explored changes in objectively-measured cough frequency during TB therapy with respect to other markers of disease.
Method Before or on commencing anti-tuberculous treatment, consecutive patients with pulmonary tuberculosis wore the Leicester Cough Monitor for 24 h, a device comprising a small digital audio recorder and microphone with software for cough detection. Those with a baseline cough frequency greater than the upper limit of normal (*c.* 100 coughs/24 h [c/24h]) were asked to undergo repeat monitoring during initial hospitalisation (if applicable), and later to coincide with routine clinic attendance or directly observed therapy (DOT).
Results Median baseline cough frequency was 203 (IQR 75–470) c/24 h in all participants (n = 44), and >100 c/24 h in 32 (73%). 22 patients were willing and available to undergo serial cough monitoring (12 current smokers, 18 sputum smear positive disease [12 also with visible lung cavities], and one with HIV). Three had isoniazid-resistant disease; the remainder were fully drug-sensitive. All were eventually treated successfully. None had other respiratory diagnoses.

Cough frequency in the majority declined consistently during therapy with substantial improvements by one week (Figure 1). At 2 and/or 8 weeks, five patients had a higher cough frequency than at baseline. Amongst these slow responders there was initial extensive radiographic change (n = 1), poor drug adherence with ongoing weight loss (n = 1), a paradoxical reaction to treatment with the development of a paraspinal abscess (n = 1), and, in the patient with HIV, persistent sputum smear positivity at 8 weeks with minimal radiographic improvement despite DOT and normal plasma rifampicin levels. One other patient

had a highly variable cough frequency during the first 8 weeks of treatment. There was no evidence for an effect of isoniazid resistance, cavitary disease, smear status or smoking on early rates of cough resolution, although there was a trend towards relatively higher cough frequencies in smokers than non-smokers at the end of treatment ($p = 0.100$).



Abstract S37 Figure 1 Objectively-measured cough frequency during treatment of pulmonary tuberculosis

Conclusions Objective cough frequency measurement is feasible in tuberculosis and could provide a novel biomarker of treatment response.

S38 PREDICTIVE ACCURACY AND CLINICAL IMPACT OF XPERT MTB/RIF FOR THE DIAGNOSIS OF SPUTUM SMEAR-NEGATIVE PULMONARY TUBERCULOSIS USING BRONCHOALVEOLAR LAVAGE FLUID

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Introduction Sputum smear-negative pulmonary tuberculosis (TB) is increasingly prevalent with bronchoalveolar lavage (BAL) frequently used for diagnostic sampling. Direct molecular testing has reported higher sensitivities compared to smear microscopy. This study aims to assess the predictive accuracy and clinical impact of Xpert MTB/RIF; a PCR-based cartridge assay used to identify M.tb in BAL fluid samples.

Methods A retrospective evaluation of adult patients (n = 293) with suspected pulmonary TB who underwent BAL in a tertiary centre in London between January 2011 and December 2014 were collected. MTB/RIF, smear microscopy, and liquid culture were performed on all sets of BAL fluid. The impact of MTB/RIF on time to TB diagnosis and anti-TB treatment initiation were recorded as markers of clinical impact.

Results 57/293 (19.5%) patients had BAL culture-positive TB for which a significantly higher proportion had positive MTB/RIF results compared to smear microscopy (77.2%, 95% CI 63.8%–86.8% vs. 38.6%, 95% CI 26.3%–52.4%; $p < 0.001$). The specificity of MTB/RIF was 95.7% (92.1%–97.8%) with a negative predictive value (NPV) of 94.6% (90.7%–97.0%). 22/57 (38.6%) culture-positive patients had negative smear microscopy results but positive MTB/RIF results.

90/293 (30.7%) patients were clinically-diagnosed and treated for pulmonary TB. In this subgroup, MTB/RIF again outperformed smear microscopy in terms of sensitivity (54.2%; 95% CI 43.7%–64.3% vs. 27.1%, 95% CI 18.8%–37.3%; $p < 0.001$). The specificity of MTB/RIF was 81.6% (80.0%–86.2%).

The use of MTB/RIF provided a significant advantage in time to TB diagnosis in culture-positive patients as compared to smear microscopy (1 days; IQR 0–2 days versus 10 days; IQR 0–15 days; $p < 0.05$). In a specific cohort of smear-negative culture-confirmed TB patients, MTB/RIF reduced the time to TB diagnosis from an average of 14 days (95% CI 12–16 days) to 1 day (95% CI 0–2 days; $p < 0.05$).

There was no statistical difference in time to anti-TB treatment initiation between those who were either smear microscopy positive and/or MTB/RIF positive in culture-positive patients (1 day; IQR 0–3 days versus 1 day; IQR 0–2 days; $p = 0.164$).

Conclusion MTB/RIF used in BAL samples had a higher and more rapid diagnostic accuracy compared to smear microscopy and could replace routine smear microscopy in pulmonary TB diagnosis.

S39 PRELIMINARY RESULTS OF A LATENT TUBERCULOSIS SCREENING AND TREATMENT PROJECT AND THE ROLE OF TB SERVICES IN SECONDARY CARE

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Introduction Since July 2014, the London Borough of Newham has offered latent tuberculosis (TB) screening to all recent migrants (residing in the UK less than 5 years), aged 16–50 years, from countries with a TB incidence of greater than 150/100 000 cases/year. All migrants are offered an interferon gamma-release assay (IGRA) when registering with a general practitioner. Active TB is excluded by the GP using chest radiography, blood tests and clinical examination. All IGRA positive patients are tested for HIV, Hepatitis B and C. All patients without underlying liver disease, Hepatitis B, C or HIV infection and those who are not immunosuppressed are offered treatment for LTBI with Rifampicin and Isoniazid for 3 months in primary care. Patients with positive results not meeting the above exclusion criteria are referred to the local secondary care service using a standardised referral protocol.

We conducted a retrospective study reviewing records of all patients referred to secondary care from the LTBI screening programme.

Results From July 2014 to March 2015, a total of 5683 patients were offered screening. 3272 proceeded to IGRA testing of which 866 were positive. Of these patients, 138 were referred to the TB clinic. The most common reasons for referral were symptoms suggestive of active TB (26%), abnormal liver function tests (19%) before and after initiation of treatment, an abnormal chest radiograph (CXR) (10%), Pregnancy or breastfeeding (9%), Hepatitis B or C infection (7%) or previously treated latent or active TB (7%). Of those referred, 11 patients were found to have active disease. 6 patients had mediastinal lymph-node TB, 4 pulmonary and one patient had TB of the knee.

Conclusion Screening for latent tuberculosis in primary care has identified a significant of number of cases of active Tuberculosis, particularly mediastinal TB.