specificity for muscle wasting, (with 55% sensitivity). Other microRNAs did not show significant differences between the groups.

Conclusion Mir-181 has been shown to be involved in both regulation of inflammation and muscle regeneration and differentiation. Mir-181 provides a potential biomarker of developing muscle wasting and with further development in the future may prove to be useful in directing treatment.

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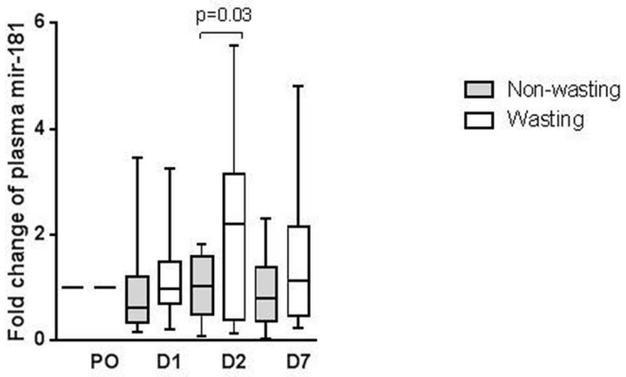

Abstract S55 Figure 1. Relative plasma mir-181 concentration in non-wasting (n = 19) and wasting patients(those with >9.24% muscle loss: n = 23) pre-operatively (PO), on day1 (D1), day 2 (D2) and on day 7 (D7). Data presented as box and whisker plots with median, interquartile ranges and 5–95% percentiles. P= 0.03 at day 2 for comparison between groups with Kolmogorov-Smirnov test.

TB: predicting disease occurrence and severity

S56 DOES TIME SINCE ARRIVAL AFFECT SITE OF TB DISEASE IN UK MIGRANTS?

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Background In contrast to global tuberculosis (TB) epidemiology, the UK and many low incidence countries have a high proportion of cases with extra-pulmonary tuberculosis (ETB). Almost 70% of reported cases in the UK are non-UK born, and many of these develop TB within the first five years after entry to the UK. The aim of the study was to analyse whether time since entry to the UK was associated with site of disease among migrants.

Methods All TB cases (n = 95,427) reported to national enhanced TB surveillance system in the UK from 2000–2011 were included. In univariable analysis we explored associations between site of disease and place of birth, ethnic group, gender, age and previous TB diagnosis, using proportions and unadjusted odds ratios. Logistic regression was used to assess the association between site of disease and time since entry to the UK, adjusted for significant confounders.

Results A total of 86,754 cases had complete information for site of disease and place of birth. Of these, 46,284 (53%) cases had ETB increasing from 47% in 2000 to 58% in 2011. ETB was more common amongst the non-UK born (61%) compared with UK-born TB cases (36%). Cases who entered the UK more than one year ago were almost 3 times more likely to have ETB compared to UK born cases after adjusting for sex, age, ethnicity and previous TB diagnosis (aOR 2.98, 95% CI 2.89–3.07). Females (OR 1.22 95% CI 1.18–1.26), adults aged 30–60 years and individuals of black African/Indian subcontinent ethnicities were significantly more likely to have ETB.

Conclusions ETB was associated with being non-UK born, having entered the UK more than a year before diagnosis, female gender, age 30–60 years, and ethnic group. Conveying our findings to healthcare workers in the UK may improve awareness of ETB in specific populations, which could help lead to earlier diagnosis.

S57 DIABETES AND LATENT TUBERCULOSIS INFECTION: NESTED CASE-CONTROL STUDY WITHIN THE PREDICT COHORT

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Background Diabetes is associated with an increased risk of tuberculosis disease, but it is unclear whether a similar association exists between diabetes and latent tuberculosis infection (LTBI).

Methods The ongoing UK PREDICT (Prognostic Evaluation of Diagnostic IGRAs Consortium) cohort study aims to recruit 10,000 participants to assess the predictive values of interferon gamma release assays (IGRAs) for the development of active TB in recent entrants to the UK and contacts of active TB cases. We used a nested case-control design within the first 5000 recruits in this cohort, to investigate the association between diabetes and LTBI. Participants in PREDICT provide demographic, medical and social information, including any history of diabetes. LTBI is detected using the two commercially available IGRAs, Quantiferon Gold In-Tube and TSpot.*TB*. Cases were individuals who tested positive on either or both IGRAs; controls were negative on both assays (or negative on one and indeterminate on the other). Logistic regression was used to estimate odds ratios and adjust for potential confounders. Assuming a 5% diabetes prevalence, 1084 cases and 3252 controls would allow the detection of a 1.5-fold increase of LTBI with 80% power and 5% error.

Results Overall, 1388/4730 (29%) had a positive IGRA. 286/4730 (6%) reported a history of diabetes. Amongst diabetic participants, 168 used insulin and/or oral hypoglycaemic medications and 25 reported control through diet alone (1 participant was being monitored only and for 92 the level of control was unknown). Univariate analysis found an association between diabetes and LTBI (OR = 1.45 [95% CI 1.13–1.86], p = 0.003). After adjustment for age, this association was no longer apparent (OR = 1.15 [95% CI 0.88–1.50], p = 0.30). Adjustment for other variables in addition to age (sex, ethnicity, birthplace outside the UK, previous contact with a TB case, or previous TB diagnosis) did not substantially change the estimated age-adjusted

OR relating diabetes to LTBI. Similar results were obtained when the analysis was restricted to contacts.

Conclusions In the current PREDICT cohort, diabetes does not appear to be associated with LTBI after adjustment for age. The relationship between diabetes and TB disease observed elsewhere may reflect an increased risk of disease rather than infection.

S58 TB CO-INFECTION IS ASSOCIATED WITH POOR SURVIVAL AMONG HIV INFECTED PATIENTS IN ENGLAND AND WALES

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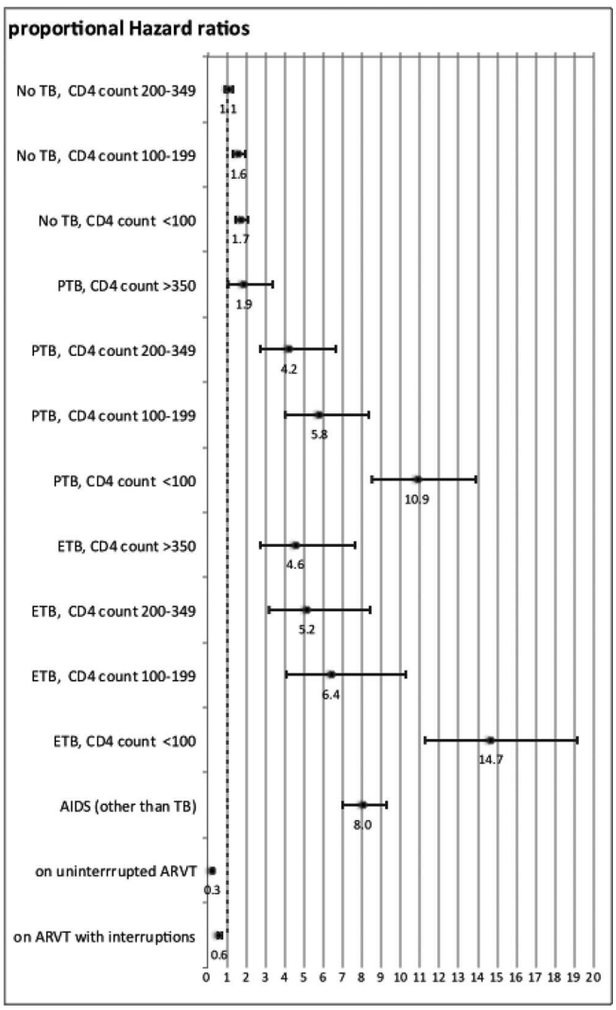

Abstract S58 Figure 1 Multivariable Cox regression model for all cause mortality in persons living with HIV diagnosed in the UK, 2000–2009. Cox regression model for all-cause mortality. There was significant interaction of TB co-infection, CD4 count at diagnosis and site of TB disease–the strata are therefore displayed separately. Dots denote point estimates for hazard ratios for all cause mortality; bars denote 95% confidence intervals. The model was also adjusted for age, sex, region of birth, and probable route of exposure (not displayed here, as effect sizes are moderate and to keep fewer categories). Abbreviations: PTB–pulmonary TB, ETB–extrapulmonary TB, ARVT–Antiretroviral Therapy. The baseline patient is characterised, as a 25–34 year-old UK-born MSM who has never been on ARV, is not TB co-infected and has a CD4 count of 350 or above.

Introduction Tuberculosis (TB) rates in the UK are amongst the highest in Western Europe and HIV-TB co-infection (HIV-TB) contributes significantly to the burden of TB in the UK. Globally, HIV-TB is associated with significant morbidity and mortality, in particular where there is delayed diagnosis. Analysis of setting-specific survival can inform local healthcare policy. Here we report the outcome of individuals diagnosed with HIV in the UK, with particular emphasis on TB co-infection.

Methodology We examined deaths among a retrospective national cohort of adults (15 years +) diagnosed with HIV infection between 2000–2008 linked to the national TB databases and death records from the Office of National Statistics to mid-2010. Hazard ratios (HR) estimates using uni- and multi-variable Cox regression modelling were calculated to compare all-cause and AIDS-specific mortality by key demographic and clinical markers.

Results A total of 1,880 (4.3%) deaths were observed among 44,050 HIV-diagnosed adults during 149,663 person-years of follow-up. 3,188 (7.2%) adults developed TB and HIV-TB cases accounted for 341 (18.1%) of all deaths of whom 270 (79.2%) were late presenters (CD4<200 at HIV diagnosis). One year mortality after HIV diagnosis was 45% overall and greater among HIV-TB cases (54%) and those with low CD4 counts at diagnosis (69% for CD4<50). TB co-infection and a low CD4 count at HIV diagnosis significantly increased the hazard of all-cause mortality. In the fully adjusted model, the highest HR was among adults with extrapulmonary TB and pulmonary TB cases with CD4 count <100 at diagnosis (figure1). The Cox model of AIDS-specific mortality showed similar findings, albeit with increased effect size. Increasing age, female sex, UK country of birth, heterosexual route of exposure to HIV and other AIDS conditions were also associated with poor survival. Antiretroviral therapy (ART) was protective, even if interrupted.

Discussion Despite the availability of effective ART and TB screening and treatment, we observed high death rates among a large national HIV cohort associated with late diagnosis and TB infection. The findings highlight the on-going need for expanded HIV testing and increased TB case finding among HIV diagnosed adults to ensure appropriate and early treatment initiation for both conditions.

S59 DRAMATIC DECLINE IN PLASMA SMALL RNA CONCENTRATION IN HIV-INFECTED AND UNINFECTED INDIVIDUALS RECEIVING ANTI-TUBERCULOSIS THERAPY: A PUTATIVE BIOMARKER OF TREATMENT RESPONSE

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Non-coding RNA molecules, particularly miRNA, regulate translation of mRNA and have been found to target expression of genes important in immune response, such as IFN- . Differences in blood transcriptome signatures and differential miRNA expression have been reported to discriminate between uninfected, active and latent tuberculosis. We analysed the ability of small RNA molecules (0–150 nucleotides) in blood plasma to act as biomarkers of tuberculosis treatment response. Total blood