levels of ICS adherence. A similar spike in salbutamol occurred in March 2020, however, an overall reduction in salbutamol prescriptions was seen in 2020 ($P=0.039$). National figures highlighted a progressive increase in prescription of peak flow meters over 2020.

Conclusion A marked spike in national ICS prescriptions occurred in March 2020. This increase appears to reflect improved adherence in patients with low levels of adherence rather than a hoarding effect or large-scale initiation in ICS-naïve patients. Despite a comparable spike in salbutamol prescriptions, 2020 saw an overall reduction in salbutamol prescriptions. Prescription of peak flow meters steadily increased over 2020 in keeping with the need for more remote monitoring.

Beyond acid-fast: diagnosis and treatment of TB in the 21st Century

S37 DUAL STEP INTERFERON-GAMMA RELEASE ASSAY TESTING CAN IMPROVE TUBERCULOSIS (TB) RISK STRATIFICATION IN CONTACTS OF PULMONARY TB: A PROSPECTIVE ADULT HOUSEHOLD CONTACT COHORT STUDY

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Introduction Studies report modest and variable predictive value of an interferon-gamma release assay (IGRA) test performed 8–12 weeks after index notification, to identify latent tuberculosis (TB) infection at risk of progressing to active TB. There is limited data evaluating predictive value of changes in the IGRA response with serial testing following recent exposure in a low-TB burden setting.

Objectives To quantify the risk of progression to active TB using the serial IGRA response between baseline and 3 months in pulmonary TB contacts.

Methods We performed an ethically approved prospective cohort study of pulmonary TB contacts between September 2015 and May 2018. Participants were recruited immediately after index case notification and had IGRA (QuantIFERON-TB Gold, QFT) test at baseline and 3 months. QFT+ve contacts did not receive chemoprophylaxis, but were followed prospectively up to 4 years with three monthly review during the first 2 years. In contacts developing TB (progressors), whole genome sequencing (WGS) was performed to inform case linkage. We defined changes in serial IGRA response as conversion (QFT negative to positive); or in contacts QFT+ve at baseline, as $> 0.27\text{IU/L}$ change in the QFT response, representing >2 standard deviations of the mean serial QFT variability observed in a control group without recent TB exposure.

Results 297 contacts were followed for a median of 1437 days (IQR 1159–1460). 124 contacts (41.8%) were QFT+ve at 3 months, of which 19 seroconverted from baseline. 20 progression events occurred and 6 diagnoses (30%) were made within 3 months of index notification including two QFT-ve cases. The remaining 14 cases were QFT+ve at baseline, and diagnosed after a median of 285 days. All 9 culture confirmed progressors were WGS matched to their index. For

Abstract S27 Table 1 Two –year incident tuberculosis risks in untreated adults pulmonary TB contacts

	2- year risk (95% CI)
QFT positive (at 3 month)	10.8 (4.8 – 16.5)
Quantitative QFT (at 3 month)	
<1	12.3 (0 – 24.5)
1–4	7.5 (0 – 17.0)
>4	11.7 (0.0 – 19.5)
Serial QFT	
Seroconversion	33.6 (7.5 – 52.3)
If QFT positive at baseline	
Significant increase	6.3 (0 – 14.5)
Significant decrease	2.9 (0 – 8.5)
No significant change	8.8 (0 – 35.8)

QFT+ve contacts, 2-year risk of incident TB was 10.8%, with no significant difference according to index smear status or quantitative QFT value (Table). Serial QFT identified greatest risk in seroconverters (2-year risk =33.6%) but no increased risk in QFT+ve contacts with a significant change after 3 months (table 1).

Conclusions Our data suggests serial QFT testing at baseline and 3 months after index notification improves risk stratification in pulmonary TB contacts.

Please refer to page A188 for declarations of interest related to this abstract.

S38 EVALUATION OF MYCOBACTERIUM TUBERCULOSIS-SPECIFIC IFN- γ , TNF- α , CXCL10, IL2, CCL2, CCL7 AND CCL4 LEVELS FOR ACTIVE TUBERCULOSIS DIAGNOSIS

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Background Novel diagnostic tests for active tuberculosis (ATB) are urgently needed. We aimed to efficiently and robustly assess whether seven previously identified, promising biomarkers (IFN- γ , TNF- α , CXCL10, IL2, CCL2, CCL7 and CCL4) could distinguish patients with ATB within a cohort of patients presenting with the full clinical spectrum of suspected TB in routine practice.

Methods We designed a nested case-control study ($n=92$) within the IDEA study.¹ Uniquely, we enriched our ATB population to include ~50% patients in whom current IGRAs fail (and unmet clinical need is greatest), to assess whether any biomarker offered superior diagnostic accuracy to IFN- γ . We utilised stored supernatants from QFT-GIT tests performed in the IDEA study and compared *Mycobacterium tuberculosis*-specific biomarker levels in patients with ATB and non-tuberculosis respiratory diseases using Meso Scale Discovery U-PLEX assays. We analysed group differences using Kruskal-Wallis tests.

Results In phase I, we analysed IFN- γ , TNF- α , CXCL10, IL2, CCL2, CCL7 and CCL4 levels in 32 patients. MSD-measured biomarkers (except CCL4) detected higher numbers of true positives (TP) compared to QFT-GIT, however, all biomarkers