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

Abstract S38 Table 1 Biomarker performance of *Mtb*-specific IFN- γ , CXCL10 and CCL2 for ATB diagnosis

Biomarker	Active TB		OD		Sensitivity (95% CI)	Specificity (95% CI)
	True-positive	False-negative	True-negative	False-positive		
QFT-GIT	26	31	28	7	45.6 (32.4 – 59.3)	80.0 (63.1 – 91.6)
IFN- γ	41	13	14	19	75.9 (62.4 – 86.5)	42.4 (25.5 – 60.8)
CXCL10	43	12	14	20	78.2 (65.0 – 88.2)	41.2 (24.7 – 59.3)
CCL2	26	28	15	19	48.1 (34.3 – 62.2)	44.1 (27.2 – 62.1)
IFN- γ +CXCL10	44	10	9	24	81.5 (69.2–89.6)	27.3
IFN- γ +CCL2	43	11	6	27	79.6 (67.1 – 88.2)	18.2
CXCL10+CCL2	44	11	7	27	80	20.6
IFN- γ +CXCL10 + CCL2	45	9	4	29	83.3	12.1

Diagnostic performance for a) QFT-GIT (commercially available IGRA test), b) IFN- γ , c) CXCL10, d) CCL2, e) IFN- γ + CXCL10 combined test, f) IFN- γ + CCL2 combined test, g) CXCL10 + CCL2 combined test, h) IFN- γ + CXCL10 + CCL2 combined test, in patients with ATB and OD (n=92). Combined test algorithm: AND/OR inclusion criteria.

lost specificity (42.9% increase in false positive (FP) results). TNF- α , IL2 and CCL7 had very low raw biomarker concentrations.

In Phase II, based on above results, we analysed IFN- γ , CXCL10 and CCL2 in a further 60 patients (table 1). CXCL10 achieved the highest increase in TP results for ATB diagnosis, with 43 TP compared with 26 TP results for QFT-GIT. MSD-measured IFN- γ detected 41 TP results, while CCL2 only detected 26 TP. All three biomarkers demonstrated >35% loss of specificity compared to QFT-GIT. The QFT-GIT sensitivity and specificity values in our study population were 45.6% and 80% respectively. A 'triple-test' combining IFN- γ , CXCL10 and CCL2 results achieved sensitivity 83.3% and specificity 12.1%.

Conclusion Our study provides a unique and novel gating method for efficiently assessing the diagnostic performance of candidate biomarkers for ATB diagnosis. Our study population was purposely engineered to compare candidate biomarkers to QFT-GIT in a clinically-relevant manner and we hope our study design will aid future, targeted efforts for high-quality biomarker follow-up studies.

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

S39

IS THE TREATMENT OF LATENT TUBERCULOSIS INFECTION AMONGST RECENT MIGRANTS SAFE AND EFFECTIVE IN PRIMARY CARE?

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Introduction The control of latent tuberculosis infection (LTBI) is a key priority in national and global strategies to eliminate tuberculosis (TB). We tested whether a novel community model of care delivered by general practitioners (family physicians) and community pharmacists to treat LTBI amongst recent migrants was effective and safe. Criteria for LTBI testing followed national guidelines.

Methods The CATAPuLT trial (Completion and Acceptability of Treatment Across Primary Care and the community for Latent Tuberculosis) was a pragmatic cluster-randomised, parallel group, superiority trial conducted in 34 general practices in London, UK, comparing LTBI treatment in recent migrants in primary care to secondary care. The primary outcome was treatment completion. Secondary outcomes included treatment adherence, treatment acceptance, adverse events, patient satisfaction, the incidence of active TB and a comparison of costs per case completing treatment.

Results Between September 2016 and May 2019, 7495 patients were offered testing for LTBI, 3624 were tested and 807 returned positive interferon-gamma release assay (IGRA) results. In the primary care arm, 224 were offered and 146 patients accepted treatment. In the secondary care arm, 138 were offered and 130 patients accepted treatment. In primary care, 82.6% of patients accepting LTBI treatment completed it, compared to 86.0% in secondary care. There was no significant difference in treatment completion between the two arms (aOR:0.64, 95%CI:0.31–1.29). There was also no difference in treatment adherence (aOR:0.64, 95%CI:0.32–1.28), drug induced liver injury (DILI) (0.7% vs 2.3%, aOR:0.29, 95%CI:0.03–2.84) or patient satisfaction (aOR:1.80, 95%CI:0.84–3.86). Treatment acceptance was lower in primary care (65.2% vs 94.2%, aOR:0.10, 95%CI:0.03–0.31). The cost per patient completing treatment was lower in primary care with an incremental saving of £315.26.

Conclusions The treatment of LTBI in recent migrants within primary care is effective and safe with lower costs when compared to treatment within secondary care.