

**Supplementary Table 2.** Disease phenotypes, disease severity and QFT-Plus results in the 102 children with tuberculosis disease. In pTBred, the diagnosis of tuberculosis disease was based on epidemiological, clinical, radiological, and microbiological features according to published criteria.<sup>10</sup> Tuberculosis was further categorized as microbiologically-confirmed or unconfirmed, and as intrathoracic or extrathoracic according to established consensus definitions.<sup>11</sup>

	Site of disease	Number (percentage)*	Severe disease**	Microbiological confirmation**	Positive QFT-Plus result**	Sensitivity (95% CI)
<b>Intrathoracic disease</b>	Ghon focus	13 (20.3)	6 (46.2)	9 (69.2)	12 (92.3)	92.3 (64.0-99.8)
	Ghon complex	22 (34.4)	7 (31.8)	11 (50.0)	16 (72.7)	72.7 (49.8-89.3)
	Adult-type disease	4 (6.3)	4 (100)	4 (100)	4 (100)	100 (39.8-100)
	Pleural	5 (7.8)	0 (0.0)	1 (20.0)	3 (60.0)	60.0 (14.7-94.7)
	Pleural and parenchymal	14 (21.9)	4 (28.6)	8 (57.1)	14 (100)	100 (76.8-100)
	Pericardial	1 (1.5)	1 (100)	0 (0)	1 (100)	100 (2.5-100)
	Not specified	5 (7.8)	Not specified	3 (60.0)	4 (80.0)	80.0 (28.4-99.5)
	<b>Total</b>	64/102 (62.7)	22 (34.4)	36 (56.3)	54 (84.4)	84.4 (73.1-92.2)
<b>Extrathoracic disease</b>	Peripheral lymphadenitis	18 (47.4)	0 (0)	14 (77.8)	15 (83.3)	83.3 (58.6-96.4)
	Abdominal	6 (15.8)	6 (100)	5 (83.3)	6 (100)	100 (54.1-100)
	Osteoarticular	6 (15.8)	6 (100)	4 (66.7)	6 (100)	100 (54.1-100)
	Central nervous system	8 (21.0)	8 (100)	7 (87.5)	8 (100)	100 (63.1-100)
	<b>Total</b>	38/102 (37.3)	20 (52.6)	30 (78.9)	35 (92.1)	92.1 (78.6-98.3)

\* Percentages in this column refer to subgroups according to intrathoracic and extrathoracic disease.

\*\* Percentages in these columns refer to subgroups according to the site of disease.

**Supplementary Table 3.** Characteristics of the 14 patients with final classification of 'not TB' who had positive QFT-Plus results.

Pt	Age (years)	Sex	BCG status	Risk factors for TB	Reason for TB testing	QFT-Plus result <sup>a</sup>	TST (mm)	Other investigations	Final diagnosis <sup>b</sup>
1	12.0	M	nk	Born in Morocco; travel to Morocco and drinking unprocessed milk	Cervical and axillary lymphadenitis	not available	20	Necrotizing granulomatous pattern in node biopsy. PCR positive for <i>Mycobacterium mucogenicum</i> , negative cultures. Normal chest X-ray.	<i>Mycobacterium mucogenicum</i> lymphadenitis + incidentally diagnosed LTBI
2	16.0	M	nk	Born in Morocco	Hemoptysis	3.40/5.05	15	Normal pulmonary CT scan and bronchoscopy.	Self-limiting hemoptysis + incidentally diagnosed LTBI
3	10.3	F	Yes	None	Persistent fever and cough	0.22/0.55	15	Pulmonary CT scan showed unspecific, small nodular lesion in left upper lobe.	Self-limiting fever with incidental pulmonary node + incidentally diagnosed LTBI
4	11.2	F	No	Prolonged stay in Morocco	Cervical lymphadenitis	6.62/6.62	23	Anterior mediastinal mass in pulmonary CT scan. Biopsy consistent with Hodgkin's lymphoma.	Hodgkin's lymphoma + incidentally diagnosed LTBI
5	16.7	M	nk	Born in Ivory Coast	Prolonged low-grade fever	6.10/6.82	ND	Normal chest x-ray.	Self-limiting fever + incidentally diagnosed LTBI
6	17.4	M	Yes	Born in Guinea	Cough, low-grade fever and asthenia	0.27/0.75	ND	Normal chest x-ray and pulmonary CT scan.	Self-limiting respiratory tract infection + incidentally diagnosed LTBI
7	13.6	M	No	Close contact with smear-positive TB case	Traumatic elbow arthritis	3.15/4.85	22	Normal chest X-ray; arthritis cured with non-steroidal anti-inflammatory drugs	Traumatic elbow arthritis + incidentally diagnosed LTBI
8	15.7	M	Yes	Close contact with smear-positive index case	Bilateral progressive panuveitis	3.67/4.04	ND	Also positive T-SPOT.TB assay. No response to antituberculous treatment; good response to corticosteroids. Normal chest x-ray.	Autoimmune uveitis + incidentally diagnosed LTBI
9	13.6	M	No	None	Sacroiliitis	6.01/4.68	25	Sacroiliitis resolved with non-steroidal anti-inflammatory drugs alone. Normal chest x-ray.	Idiopathic sacroiliitis + incidentally diagnosed LTBI
10	11.7	F	No	Annual travel to Morocco	Avascular peripheral retinopathy	0.52/0	0	Repeat QFT-Plus 1 month later: negative. No etiology identified.	Avascular peripheral retinopathy of unknown origin + false positive QFT-Plus result
11	8.7	F	No	None	Limp and fever	0.30/0.64	0	Repeat QFT-Plus 2 weeks later: negative. MRI identified a benign bone tumour in the left acetabulum. Normal chest x-ray.	Benign bone tumor + false positive QFT-Plus result
12	1.0	F	No	None	Cervical lymphadenitis	1.27/0.01	0	Repeat QFT-Plus 1 month later: negative. Ultrasound scan consistent with reactive lymphadenitis. Normal chest x-ray.	Self-limiting cervical lymphadenitis + false positive QFT-Plus result
13	0.8	M	No	None	Recurrent pneumonia	not available	0	Pulmonary CT scan and fbronchoscopy showed left main bronchus stenosis. Normal immune work-up. BAL cultures identified <i>Pseudomonas</i> , <i>Haemophilus</i> , <i>Klebsiella</i> and <i>Moraxella</i> (mycobacterial cultures negative).	Recurrent pneumonias due to airway malformation + false positive QFT-Plus result
14	1.3	F	No	None	Fever without a focus	0.23/0.38	ND	Repeat QFT-Plus 2 weeks later: negative. Amastigotes on microscopy and positive PCR for <i>Leishmania</i> on bone marrow. Normal chest x-ray.	Visceral leishmaniasis + false positive QFT-Plus result

<sup>a</sup>TB1 minus nil / TB2 minus nil, in IU/mL

<sup>b</sup>Interpretation of tuberculosis immunodiagnostic test results (as LTBI or false-positive test result) was done by the treating physician.

Abbreviations: BAL, bronchoalveolar lavage; BCG, bacillus Calmette-Guérin vaccine; CT, computerized tomography; F, female; M, male; MRI, magnetic resonance imaging; ND, not done; NK, not known; PCR, polymerase chain reaction; Pt, patient number; QFT-Plus, QuantiFERON-Plus; TB, tuberculosis; TST, tuberculin skin test.

**Supplementary Table 4.** Disease phenotype, QFT-Plus results and final diagnoses in 182 children with final classification of ‘not TB’.

Site of disease	Symptom/sign that prompted testing for TB	QFT-Plus result (%)			Final diagnosis (no. of indeterminate QFT-Plus results)
		Negative	Positive	Indeterminate	
<b>Thoracic</b>	Clinical signs of pneumonia and/or radiological infiltrates, n=58	45 (77.6)	2 (3.5)	11 (18.9)	CAP resolving with antibiotics (no organism identified), n=30 (2) Bacteriologically-confirmed CAP, n=8 (3) Self-limiting CAP, n=8 (1) Aspergillosis in patients with medullar aplasia, n=2 (2) Self-limiting hilar lymphadenopathy, n=3 Pneumonia and meningitis caused by <i>S. pneumoniae</i> , n=1 (1) <i>Empyema</i> caused by <i>S. aureus</i> , n=1 (1) Cystic adenomatoid malformation, n=1 (1) Pulmonary echinococcosis, n=1 Sarcoidosis, n=1 Endotracheal sarcoma, n=1 Bronchial stenosis, n=1
	Prolonged cough, n=7	6 (85.7)	1 (14.3)	0 (0.0)	Self-limiting cough, n=3 Asthma, n=3 Chronic idiopathic cough, n=1
	Pericardial effusion, n=3	3 (100)	0 (0.0)	0 (0.0)	Viral pericarditis/myocarditis, n=3
	Hemoptysis, n=3	2 (66.7)	1 (33.3)	0 (0.0)	Self-limiting hemoptysis, n=2 Autoimmune hepatitis and alveolar hemorrhage, n=1
	Chest pain, n=1	1 (100.0)	0 (0.0)	0 (0.0)	Sickle cell disease, n=1
	Dysphonia n=1	1 (100)	0 (0.0)	0 (0.0)	Laryngeal papillomatosis, n=1
	<b>Total n=73</b>	<b>58 (79.5)</b>	<b>4 (5.5)</b>	<b>11 (15.0)</b>	
<b>Extrathoracic</b>	Cervical mass, n=65	58 (89.2)	3 (4.6)	4 (6.2)	Self-limiting cervical lymphadenitis, n=30 (2) Lymphadenitis that resolved with antibiotics, n=5 (1) Probable NTM lymphadenitis, n=12 Microbiologically-confirmed bacterial lymphadenitis, n=6 (1) Confirmed NTM lymphadenitis, n=5 Hodgkin’s lymphoma, n=3

					Epstein-Barr virus infection, n=1 Castleman's disease, n=1 Mastoiditis, n=1 Odontogenic cyst, n=1
	Fever or constitutional syndrome, n=23	20 (87.0)	2 (8.7)	1 (4.3)	Self-limiting fever, n=15 PFAPA syndrome, n=2 Abdominal lymphatic malformation, n=1 (1) Visceral leishmaniosis, n=1 Newly diagnosed type 1 diabetes, n=1 SAPHO syndrome, n=1 Acute hepatic failure, n=1 Renal abscess, n=1
	Osteoarticular disease, n=8	5 (62.5)	3 (37.2)	0 (0.0)	Self-limiting arthritis, n= 4 Discitis resolving without antibiotics, n=1 Benign bone tumor, n=1 Psoriatic arthritis, n=1 Traumatic arthritis, n=1
	Skin lesions, n=4	4 (100)	0 (0.0)	0 (0.0)	Biopsy-proven panniculitis, n=2 Erythema nodosum, n=2
	Ocular disease, n=3	1 (33.3)	2 (66.7)	0 (0.0)	Autoimmune uveitis, n=1 Erdheim-Chester disease (histiocytosis), n=1 Idiopathic avascular retina, n=1
	Gastrointestinal symptoms, n=2	2 (100)	0 (0.0)	0 (0.0)	Acute pancreatitis, n=1 Self-limiting diarrhea, n=1
	Axillary lymphadenitis, n=1	1 (100)	0 (0.0)	0 (0.0)	BCGitis, n=1
	Pancytopenia, n=1	1 (100)	0 (0.0)	0 (0.0)	Medullar aplasia, n=1
	Ataxia n=1	1 (100)	0 (0.0)	0 (0.0)	Acute disseminated encephalomyelitis, n=1
	Chronic otorrhoea n=1	0 (0.0)	0 (0.0)	1 (100)	Bacterial otitis externa, n=1 (1)
	<b>Total n=109</b>	<b>93 (85.3)</b>	<b>10 (9.2)</b>	<b>6 (5.5)</b>	

Abbreviations: CAP, community-acquired pneumonia; n, number; NTM, non-tuberculous mycobacteria