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Title: Outcomes of early interferon-gamma release assay (IGRA) testing in recent contacts of smear positive pulmonary tuberculosis (TB)

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Body: Introduction Interpretation of single point IGRA testing with QuantiFERON-TB Gold In Tube (QFT) to identify recently acquired latent M.tuberculosis infection (LTBI) in contacts of active TB may be confounded by previous exposure (false positive) or testing too soon after exposure, prior to development of adaptive immunity (false negative). Aim To determine the relationship between exposure duration & quantitative QFT in household contacts of smear positive pulmonary TB with heterogeneous risk of remote LTBI. We hypothesise a closer association of QFT with exposure time in contacts at low risk of remote LTBI. To estimate the exposure duration needed prior to testing for QFT to reliably identify LTBI. Method 136 QFT tested contacts of 14 smear positive pulmonary TB cases were studied. Quantitative QFT & index symptom duration (days) were recorded. Risk of remote LTBI was scored by age & country of birth and contacts were categorised into low, moderate and high risk subgroups. Result There was a weak correlation between QFT value in contacts and their exposure duration ($R^2 = 0.06$; $p = 0.01$). Subgroup analysis identified this correlation to be significant in contacts at low risk of remote LTBI [UK born, <25 years ($R^2 = 0.31$; $p < 0.001$)]. In this subgroup positive QFT results were obtained for contacts that were tested >120 days after onset of index symptoms. In contrast, 3 of 33 at moderate risk and 15 of 32 at high risk of remote LTBI were QFT positive with earlier (<120 days) testing. Conclusion Adaptive immunity to recently acquired LTBI is detectable with QFT testing if delayed 120 days after onset of index symptoms in close contacts at low risk of previous LTBI.