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Title: The changing indications for IGRA testing and impact on TB services in a UK district general hospital

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Body: To assess the impact of interferon gamma release assay (IGRA) testing in a rural UK hospital we retrospectively examined IGRA tests at our laboratory from 2006-2012. Indication and outcome of testing was determined. Of 899 T-SPOT tests, 377 were for investigation of possible active TB. 507 were screening tests for latent TB infection (LTBI). Of these, 329 were prior to monoclonal antibody (mAb) treatment, 101 for contact tracing or new entrants, and 77 as occupational health assessments. Total tests per year did not significantly change between 2008 (179) and 2012 (152). Tests pre-mAb treatment increased (0 in 2006, 55 in 2009, 87 in 2012) leading to increasing referrals to TB services. From 2006-2008, 2 patients received TB chemoprophylaxis (CPX) pre-mAb. This increased to 10 in 2009-2011. Total numbers receiving CPX increased from 7 in 2005 to a peak of 19 in 2010. The mean age of those screened pre-mAb therapy was 54 years compared to 34 for contact and new entrant screening (p= <0.01). There were rises in both pre-mAb screening and resulting CPX usage. The increased sensitivity of T-SPOT compared to skin testing for screening of contacts may have partially offset the overall rise in CPX usage. Screening pre-mAb therapy resulted in a higher proportion of older patients referred for treatment. This raises potential concerns regarding CPX in those at higher risk of hepatotoxicity. We conclude that increasing use of biological agents is resulting in an increase in diagnosis and treatment of LTBI. This has impact both for patients and planning of TB services. The age profile of those requiring chemoprophylaxis may change as result of the changing indications for testing.