Spectrum of latent tuberculosis — existing tests cannot resolve the underlying phenotypes: authors' reply

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We agree with the comments in response to our Review (The spectrum of latent tuberculosis: rethinking the biology and intervention strategies. *Nature Rev. Microbiol.* 7, 845–855 (2009))¹ from Pai (Spectrum of latent tuberculosis — existing tests cannot resolve the underlying phenotypes. *Nature Rev. Microbiol.* 8, 19 Jan 2010 (doi:10.1038/nrmicro2236-c1))² stating that current diagnostic tests do not address the challenge of identifying subgroups of individuals in the latent tuberculosis (TB) spectrum who would benefit most from preventive therapy. Indeed, we hope that the framework set out in our Review will help to target efforts towards the development of improved diagnostic tools. The strategy of serial IGRA testing as proposed by Pai

is likely to be one element in progressing towards this goal, although broadening the range of cytokines beyond a reliance solely on interferon- γ may well be important. A key limitation to the time-dependent approach that is illustrated by Pai is that accurate information about the time of initial exposure is unavailable in most endemic settings. Parallel studies based on experimental challenge in the non-human primate model may be helpful in establishing a clear time course for the correlation of immune markers with microbiological and clinical changes.

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Competing interests statement

The authors declare no competing financial interests.