

An In-Depth Investigation of Borderline Results  
in QuantiFERON-TB Gold-Plus Testing

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Background

- The QuantiFERON-TB Gold Plus (QFT-Plus; Qiagen, Hilden, Germany) assay is widely used for latent TB infection (LTBI) screening; however, borderline results often show variability during follow-up.
- We investigated the longitudinal variability of borderline TB1 and TB2 results throughout the follow-up period.

Methods

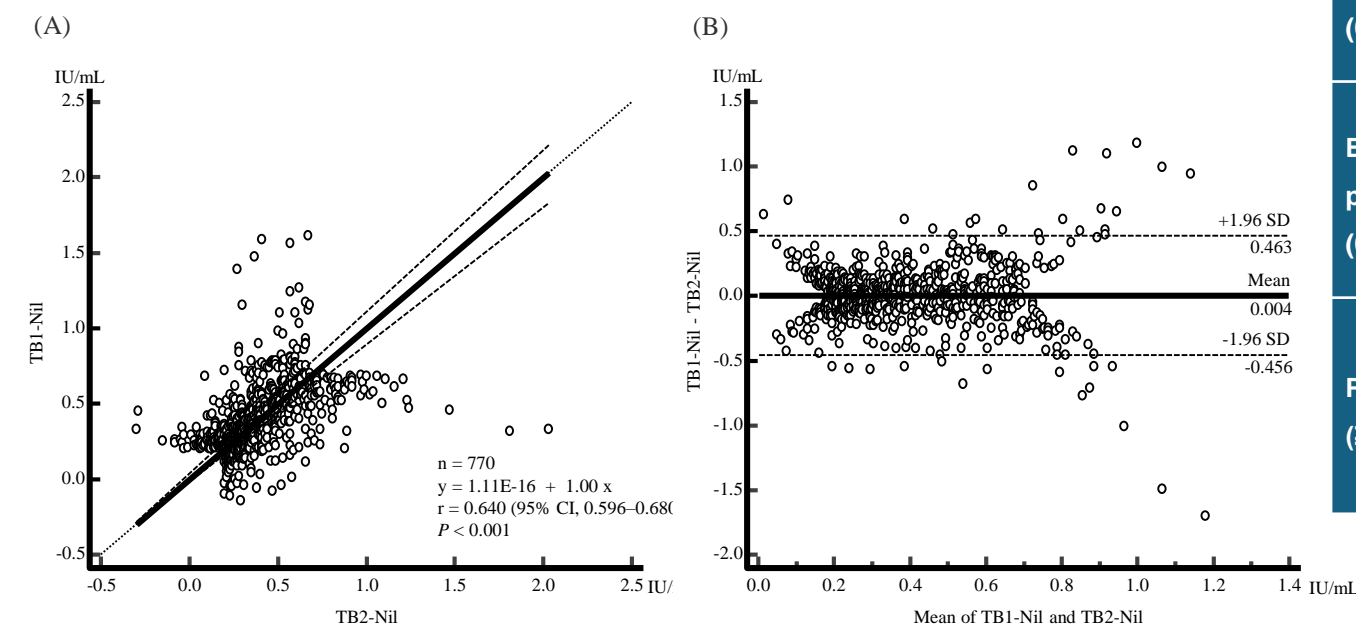
- A total of 770 tests with borderline results (0.2–0.7 IU/mL) in either the TB1 or TB2 tube were retrospectively collected over a five-year period.
- Agreement and correlation between the initial TB1 and TB2 results were analyzed.
- Trends, including reversion and conversion, were assessed separately for TB1 and TB2 tubes, as well as for the overall combined results.

Results

Table 1. Agreement between initial TB1-Nil and TB2-Nil values within the borderline ranges

TB2-Nil (IU/ml)	TB1-Nil (IU/ml)					Kappa (95% CI)
	Negative (< 0.2)	Borderline negative (0.2-0.34)	Borderline positive (0.35-0.69)	Positive (≥ 0.7)	Total	
Negative (< 0.2)	0	99	15	0	114	0.441 (0.401–0.480)
Borderline negative (0.2-0.34)	86	126	61	7	280	
Borderline positive (0.35-0.69)	19	51	180	58	308	
Positive (≥ 0.7)	0	7	60	1	68	
Total	105	283	316	66	770	

Figure 1. Correlation between TB1-Nil and TB2-Nil values within the borderline range in QuantiFERON-TB Gold-Plus test (n=770). (A) Passing Bablok regression. (B) Bland Altman Plot.



- Agreement and correlation between initial borderline TB1 and TB2 results were weak and moderate (Cohen’s  $\kappa$  = 0.441 [95% CI, 0.401–0.480]; Spearman rank correlation coefficient = 0.640 [95% CI, 0.596–0.680],  $P$  < 0.001) (Table 1 and Figure 1).
- Variability, including reversion and conversion, was highest in TB2 during the first follow-up (33.8%, 47/139) and decreased with subsequent tests (Table 2).
- Result variability was observed in 30.2% (13/43) of individuals with  $\geq 2$  follow-up tests, excluding those who received LTBI treatment (Table 3).
- Initial borderline results in both TB1 and TB2 tended to show higher rates of reversion and conversion.

Table 2. Follow-up intervals and QuantiFERON-TB Gold-Plus results in individuals with repeat testing

	First follow-up test interval (median = 13 mon, range = 0-59 mon, IQR = 11-16 mon), N=139					
	≤ 6mo (N=18)		7-12mo (N=43)		> 12mo (N=78)	
	TB1(%)	TB2(%)	TB1(%)	TB2(%)	TB1(%)	TB2(%)
Conversion	1(5.6)	4(22.2)	5(11.6)	5(11.6)	8(10.3)	10(12.8)
Reversion	6(33.3)	6(33.3)	1(2.3)	8(18.6)	10(12.8)	14(17.9)
	Second follow-up test interval (median = 13 mon, range = 2-44 mon, IQR = 11-14 mon), N=68					
	≤ 6mo (N=4)		7-12mo (N=28)		> 12mo (N=36)	
	TB1(%)	TB2(%)	TB1(%)	TB2(%)	TB1(%)	TB2(%)
Conversion	0(0.0)	2(50.0)	1(3.6)	1(3.6)	4(11.1)	4(11.1)
Reversion	2(50.0)	1(25.0)	0(0.0)	1(3.6)	4(11.1)	2(5.6)
	Third follow-up test interval (median = 12 mon, range = 8-19 mon, IQR = 11-14 mon), N=34					
	≤ 6mo (N=0)		7-12mo (N=22)		> 12mo (N=12)	
	TB1(%)	TB2(%)	TB1(%)	TB2(%)	TB1(%)	TB2(%)
Conversion	0(0.0)	0(0.0)	2(9.1)	1(4.5)	0(0.0)	1(8.3)
Reversion	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(8.3)
	Forth follow-up test interval (median = 11 mon, range = 8-17 mon, IQR = 10-13 mon), N=20					
	≤ 6mo (N=0)		7-12mo (N=13)		> 12mo (N=7)	
	TB1(%)	TB2(%)	TB1(%)	TB2(%)	TB1(%)	TB2(%)
Conversion	0(0.0)	0(0.0)	1(7.7)	1(7.7)	1(14.3)	1(14.3)
Reversion	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(14.3)	0(0.0)

Abbreviations: LTBI, latent TB infection

Table 3. Trends in follow-up results based on initial borderline TB1 and TB2 tube values from the QuantiFERON-TB Gold-Plus assay in individuals with  $\geq 2$  follow-up tests, excluding those who received LTBI treatment (N = 43)

TB1-Nil (IU/ml)	TB2-Nil (IU/ml)	N	Consistent (%)	Reversion (%)	Conversion (%)
Negative (< 0.2)	Negative (< 0.2)	0	0	0	0
	Borderline negative (0.2-0.34)	3	3 (100.0)	0	0
	Borderline positive (0.35-0.69)	1	0	1 (100.0)	0
	Positive (≥ 0.7)	0	0	0	0
Borderline negative (0.2-0.34)	Negative (< 0.2)	16	15 (93.75)	0	1 (6.25)
	Borderline negative (0.2-0.34)	11	7 (63.6)	0	4 (36.4)
	Borderline positive (0.35-0.69)	2	0	2 (100)	0
	Positive (≥ 0.7)	0	0	0	0
Borderline positive (0.35-0.69)	Negative (< 0.2)	0	0	0	0
	Borderline negative (0.2-0.34)	0	0	0	0
	Borderline positive (0.35-0.69)	7	4 (57.1)	3 (42.9)	0
	Positive (≥ 0.7)	2	1 (50.0)	1 (50.0)	0
Positive (≥ 0.7)	Negative (< 0.2)	0	0	0	0
	Borderline negative (0.2-0.34)	0	0	0	0
	Borderline positive (0.35-0.69)	1	0	1 (100.0)	0
	Positive (≥ 0.7)	0	0	0	0

Results after latent TB infection treatment were excluded.  
Consistent results include consistent positive and consistent negative. Reversion results include consistent reversion and transient reversion. Conversion results include consistent conversion and transient reversion.  
Abbreviations: LTBI, latent TB infection

Conclusion

- Careful interpretation is required for patients with borderline results in both TB1 and TB2.
- Follow-up testing is recommended, as variability decreases over time.

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