臺北市立萬芳醫院 - 委託財團法人臺北醫學大學辦理
Taipei Municipal Wan Fang Hospital (Managed by Taipei Medical University)

Journal Club

IGRAs結果與LTBI轉變為ACTIVE TB的相關性

2022.08.22 (W1) 13:00~14:00

醫學檢驗科 曹頌慈

EP2.0簽到QR code

BMC Infectious Diseases

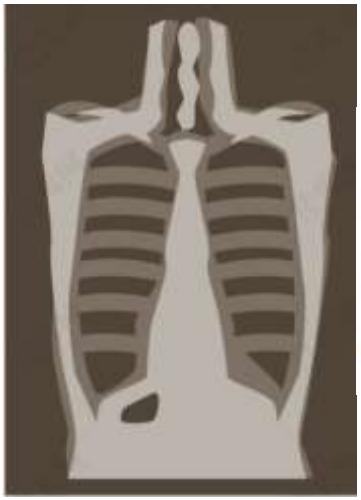
Published: 22 May 2021 *BMC Infectious Diseases* **21**, Article number: 467 (2021)

Jorge R. Ledesma, Jianing Ma, Peng Zheng, Jennifer M. Ross, Theo Vos & Hmwe H. Kyu

Interferon-gamma release assay levels and risk of progression to active tuberculosis: a systematic review and dose-response meta-regression analysis

- In 2020, an estimated 9.9 million people fell ill with TB worldwide
- 5.5 million
  3.3 million
  1.1 million
- 80 thousand (8% of the total)

World Health Organization (WHO). Advocacy package (who.int)



END TB

World Health Organization

Mycobacterium tuberculosis complex (tuberculosis)

5-15%

Active TB

Latent Tuberculosis Infection (LTBI）

- T-cell-based interferon gamma release assays (IGRAs)
  - QuantiFERON TB Gold in tube (QFT-GIT) 第三代
    QuantiFERON-TB Gold Plus (QFT-Plus) 第四代
  - T-SPOT.TB

  - 優點:特異性高、接種BCG疫苗不影響檢驗結果
  - 缺點:費用昂貴、再現性不佳

丙型干擾素釋放試驗(Interferon-gamma release assay, IGRA)

- 國內IGRA檢驗使用QuantiFERON-TB，自

IGRA結果判讀

臺北市立萬芳醫院-委託財團法人臺北醫學大學辦理-醫學檢驗科報告單

臺北市文山區興隆路三段111號

組別：細菌組　檢體：Blood　出生日期：[redacted]

病歷號碼：[redacted]　姓名：[redacted]　別：男　年齡：44歲

診別：門診　科別：風溼免疫　開單醫師：陳璇方

檢驗單號：[redacted]　試管編號：[redacted]　報告單號：[redacted]

開單日期：111/05/12　16:18　簽收日期：111/06/27　13:40　採檢日期：111/06/27　13:40

報告日期：111/07/01　13:48

檢驗名稱	檢驗結果值	單位[參考值]{備註}
IGRA((須通報)丙型干擾素釋放試驗IGRA檢驗)(positive)	[]	
Nil control()	0.05	IU/mL[]
TB Antigen()	.	IU/mL[]
TB 1 Antigen(TB1抗原)	0.46	IU/mL[]
TB 2 Antigen(TB2 抗原)	0.31	IU/mL[]
Mitogen control()	>10	IU/mL[]

檢驗師：風純琪 Null覆核檢驗師：廖啟智 檢字第010359號

LTBI治療

疾

https://www.cdc.gov.tw/Uploads/5eb26623-b179-4e8b-b860-98810501b821.pdf

thebmj | BMJ 2020;368:m549 | doi: 10.1136/bmj.m549

Absolute risk of tuberculosis among untreated populations with a positive tuberculin skin test or interferon-gamma release assay result: systematic review and meta-analysis

BMJ 2020 ; 368 doi: https://doi.org/10.1136/bmj.m549 (Published 10 March 2020)
Cite this as: BMJ 2020;368:m549

Table 1 Risk of tuberculosis (TB) among exposed populations

Population and definition of positive test result	Among test positive participants					
	No of cohorts	No of participants	Total (mean) person years follow-up	Active TB events (%)*	TB rate per 1000 person years (95% CI)†	I^2 (%)
General population‡						
TST ≥10 mm	3	33 811	249 093 (7.4)	55 (0.2)	0.3 (0.1 to 1.1)	96
Close and casual contacts (together)§						
All age groups:						
All IGRA positive	9	2199	6667 (3.0)	89 (4.0)	13.3 (10.8 to 16.4)	0
TST ≥5 mm	4	7861	32 708 (4.2)	227 (2.8)	8.4 (4.3 to 16.5)	95
TST ≥10 mm	5	5728	22 561 (3.9)	97 (2.6)	9.4 (4.0 to 21.8)	93

A recent meta-analysis of cohort studies indicated that TB contacts with a positive IGRA result have a 10.8-fold higher rate of progression to active TB

Absolute risk of tuberculosis among untreated populations with a positive tuberculin skin test or interferon-gamma release assay result: systematic review and meta-analysis | The BMJ

> Am J Respir Crit Care Med. 2015 May 15;191(10):1176-84. doi: 10.1164/rccm.201502-0232OC.

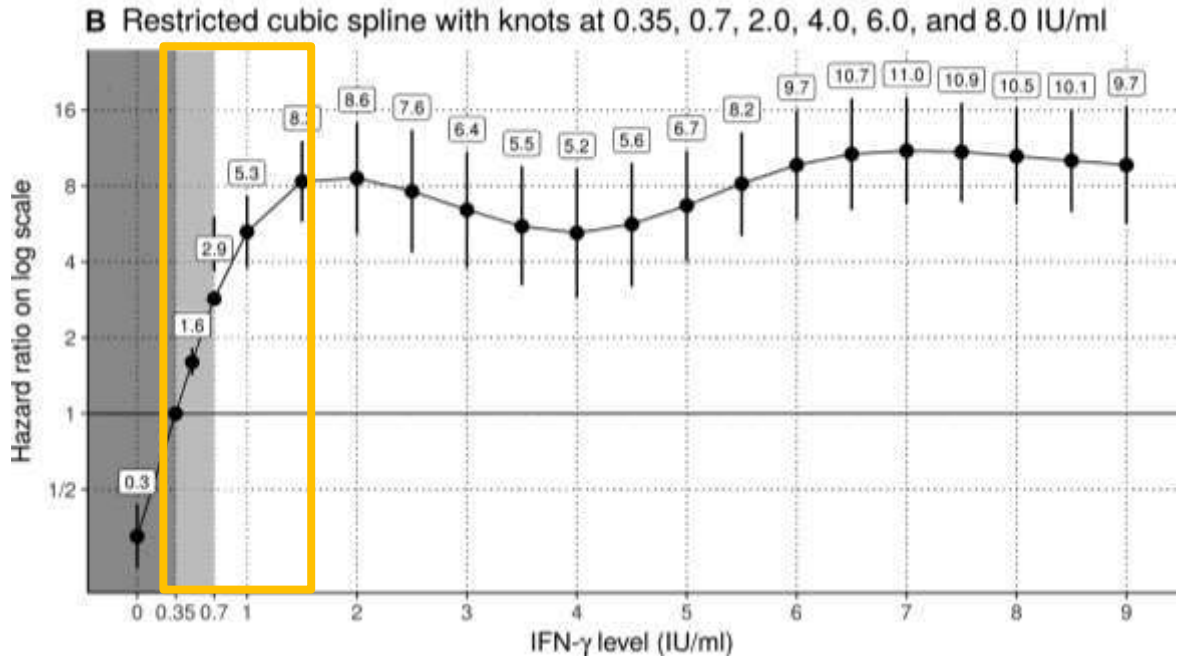
Risk Assessment of Tuberculosis in Contacts by IFN-γ Release Assays. A Tuberculosis Network European Trials Group Study

Jean-Pierre Zellweger [1], Giovanni Sotgiu, Michael Block, Simone Dore, Neus Altet, Rebecca Blunschi, Matthias Bogyi, Graham Bothamley, Christina Bothe, Luigi Codecasa, Patrizia Costa, Jose Dominguez, Raquel Duarte, Andreas Flee, Isabelle Fresard, José-María García-García, Delia Goletti, Petra Halm, Doris Hellwig, Eveline Henninger, Helga Heykes-Uden, Liane Horn, Katarzyna Kruczak, Irene Latorre, Geneviève Pache, Heidrun Rath, Felix C Ringshausen, Asunción Seminario Ruiz, Ivan Solovic, Maria-Luiza de Souza-Galvão, Ursula Widmer, Peter Witte, Christoph Lange, TBNET

Collaborators, Affiliations + expand

PMID: 25763458 DOI: 10.1164/rccm.201502-0232OC

結核發病風險(培養)



In addition, recent individual studies have suggested a need to further examine the entire distribution of IGRA values for risk analyses of subsequent active TB

https://doi.org/10.1164/rccm.201502-0232OC

Research | Open Access | Published: 28 January 2013

Screening for tuberculosis and the use of a borderline zone for the interpretation of the interferon-γ release assay (IGRA) in Portuguese healthcare workers

Albert Nienhaus ✉ & José Torres Costa

Journal of Occupational Medicine and Toxicology **8**, Article number: 1 (2013) | Cite this article

First QFT	Second QFT						Total	
	<0.2 IU/mL		0.2– <0.7 IU/mL		≥0.7 IU/mL			
	n	%	n	%	n	%	n	%
<0.2 IU/mL	588	82.0	73	10.2	56	7.8	717	59.8
0.2– < 0.35 IU/mL	24	35.3	18	26.5	26	38.2	68	5.7
0.35– < 0.7 IU/mL	48	45.7	21	20.0	36	34.3	105	8.8
≥0.7 IU/mL	45	14.6	46	14.9	218	70.6	309	25.8
All	705	58.8	158	13.2	336	28.0	1199	100.0

Table 2 Conversion and reversion rates depending on the use of a borderline zone and the INF-γ concentration of the first QFT

First QFT	Second QFT			
	Negative		Positive	
	n	%	n	%
Negative	657	83.7	128	16.3
Positive	120	29.0	294	71.0
All	777	64.8	422	35.2

Some researchers have called for a need to report a **borderline zone**, an intermediate area between a negative and positive IGRA test, to improve the diagnostic accuracy of potential development of active TB

Table 3 Results of the first and second QFT (negative: <0.35 IU/mL, positive: ≥0.35 IU/mL)

Nienhaus A, Costa JT. Screening for tuberculosis and the use of a borderline zone for the interpretation of the interferon-γ release assay (IGRA) in Portuguese healthcare workers. J Occup Med Toxicol. 2013;8(1):1 Available http://occup-med.biomedcentral.com/articles/10.1186/1745-6673-8-1

步驟 1：系統性文獻回顧探討的問題為何？(PICO)

- P(Patient/Problem)
  INF-γ數值與LTBI轉變為ACTIVE TB是否具有相關性
- I(Intervention)
  貝式迴歸分析
- C(Comparison)
  定性報告
- O(Outcomes)
  分析INF-γ，評估各族群中LTBI轉變為Active TB的風險

- Literature search
- Study selection
- Data extraction
- Assessment of quality of included studies

  (Newcastle-Ottawa quality assessment scale , NOS)
- Data analysis

  (Bayesian meta-regression Method)
- Sensitivity analyses and subgroup analyses

步驟 2：系統性文獻回顧的品質如何？(FAITH)
F - 研究是否找到 (Find) 所有的相關證據？

良好的文獻搜尋至少應包括二個主要的資料庫(如：Medline, Cochrane 考科藍實證醫學資料庫, EMBASE 等)，並且加上文獻引用檢索(參考文獻中相關研究、Web of Science, Scopus 或 Google Scholar)、試驗登錄資料等。文獻搜尋應不只限於英文，並且應同時使用 MeSH 字串及一般檢索詞彙(text words)。

In this systematic review and meta-regression analysis we followed the PRISMA and MOOSE checklists. We searched PubMed and Embase from 1 January 2001 to 10 May 2020 for studies that reported the risk of progression from latent to active TB based on baseline IGRA values. The full search strategy is available in the supplementary material. In addition, we made no restrictions in study language. The reference lists of eligible full texts and identified systematic reviews were reviewed for additional relevant studies.

Study type	Search Terms
Retrospective or prospective cohort studies	PubMed search terms: ("Interferon-gamma Release Tests"[MeSH] OR "IGRA"[tiab] OR "interferon-gamma release assay*"[tiab] OR "Quantiferon*"[tiab] OR "QFT"[tiab] OR "Interferon-gamma release test*"[tiab]) AND ("reactivation"[tiab] OR "reactivity"[tiab] OR "activation"[tiab] OR "predictive"[tiab] OR "risk"[tiab]) AND ("tuberculosis"[MeSH] OR "tuberculosis"[tiab]) AND ("prospective"[tiab] OR "cohort"[tiab] OR "follow up"[tiab]) ("2001/01/01"[PDAT] : "2020/05/10"[PDAT]) Embase search terms: ('Interferon-gamma Release Tests'/de OR 'IGRA':ab,ti OR 'interferon-gamma release assay*':ab,ti OR 'Quantiferon*':ab,ti OR 'QFT':ab,ti OR 'Interferon-gamma release test*':ab,ti) AND ('reactivation':ab,ti OR 'reactivity':ab,ti OR 'activation':ab,ti OR 'predictive':ab,ti OR 'risk':ab,ti) AND ('tuberculosis'/de OR 'tuberculosis':ab,ti) AND ('prospective':ab,ti OR 'cohort':ab,ti OR 'follow up':ab,ti) AND [1-1-2001]/sd NOT [5-10-2020]/sd

步驟 2：系統性文獻回顧的品質如何？(FAITH)
F – 研究是否找到 (Find) 所有的相關證據？

Study selection

Retrospective or prospective cohort studies and clinical trials that assessed QuantiFERON-TB Gold in tube (QFT-GIT) or QuantiFERON-TB Gold Plus (QFT-Plus) results, defined as the difference of interferon-gamma level between the TB antigen tube and negative control tube, as the exposure variable and progression to active tuberculosis as an outcome, were eligible for inclusion. The study participants were adults or children who were free of active TB disease at baseline. We excluded studies that contained a sample with a confounding disease (e.g. lung cancer, rheumatic diseases, inflammatory bowel diseases), that did not test all individuals with QuantiFERON-TB, or did not follow-up all individuals for progression to active TB disease. We further excluded studies that only focused on QuantiFERON-TB conversion or had participants with previous positive QuantiFERON-TB tests.

評讀結果：■是　否　不清楚

步驟 2：系統性文獻回顧的品質如何？(FAITH)
A - 文獻是否經過嚴格評讀 (Appraisal)？

應根據不同臨床問題的文章類型，選擇適合的評讀工具，並說明每篇研究的品質(如針對治療型的臨床問題，選用隨機分配、盲法、及完整追蹤的研究類型)。

Data extraction

Data were extracted using a standardized data extraction form developed a priori. The following variables were extracted from each study: study design, location, follow-up duration, sample attrition rate, baseline age-sex distribution, TB preventive treatment use, sample size by baseline QuantiFERON-TB results (IU/ml categories), number of cases progressing to active TB by IU/ml categories, and method for diagnosing active TB. Information on participant characteristics (e.g. general population, TB contacts, healthcare workers, etc.) was also extracted. In studies that separately reported data from participants who developed TB very early (under 2 months of the start of the study), they were considered as prevalent TB cases and were excluded during extraction such that they did not contribute to the sample size for baseline QuantiFERON-TB results nor for the number of incident TB cases. When available, extracted data were stratified by TB preventive treatment use. For person-year information, we used the study mean or median as follow-up time if follow-up time was not disaggregated for every QuantiFERON-TB category.

評讀結果：■ 是　否　不清楚

Data extraction

Table S1. Characteristics of the studies included in the meta-analysis

Study	Study Type	Population	Country	Time period	Age	Sample size	Follow-up time	Time to incident TB case	TB Preventive Treatment	TB diagnosis	Incident TB cases	NOS Quality Score
Abdulkareem (2020)(1)	Prospective cohort	Tuberculosis case contacts	Iraq	2018 – 2018	Adults and children 1 to 90 years	401	6 months	3 to 6 Months	Unknown	Bacteriologically, radiologically	0–0.35 IU/ml: 0/323 0.35–20 IU/ml: 6/78	4
Altet (2015)(4)	Prospective cohort	Tuberculosis case contacts	Spain	2007 – 2013	Adults and children 0 to 100 years	937	4 Years	6 to 24 Months	No 0 %	Clinically confirmed through TB Control Program databases	0–0.35 IU/ml: 0/531 0.35–5 IU/ml: 4/135 5–10 IU/ml: 5/166 10–20 IU/ml: 6/105	5
Giri (2014)(10)	Retrospective cohort	Healthcare workers	United Kingdom	2009 – 2013	Adults and children 0 to 100 years	1258	1 Year	Not reported	Provided: Yes – 4 % Completed: 3 %	Bacteriologically, clinically	0–0.35 IU/ml: 0/1162 0.35–20 IU/ml: 0/96	
Kruczak (2014)(16)	Prospective cohort	High risk population: homeless, contacts, elderly	Poland	2007 – 2012	Adults and children 0 to 100 years	785	4 to 5 Years	6 to 20 Months	No 0 %	Clinically confirmed through local pulmonary clinic	0–0.35 IU/ 0.35–20 IU	
Noorbakhsh (2011)(21)	Prospective cohort	Tuberculosis case contacts	Iran	2006 – 2008	Children 0 to 19 years	49	1 Year	3+ Months	Unknown	Clinically	0–	
Tsou (2015)(27)	Prospective cohort	Elderly nursing home residents	Taiwan (Province of China)	2004 – 2009	Adults 65 to 100 years	139	5 years	4 to 5 Years	Unknown	Clinically		
Verhagen (2014)(28)	Prospective cohort	Tuberculosis case contacts	Venezuela (Bolivarian Republic of)	2010 – 2012	Children 0 to 15 years	140	1 Year	6 to 12 Months	No 0 %	Clinically confirmed throu national TB surveillance program		
Whitaker (2013)(29)	Prospective cohort	Healthcare workers	Georgia	2009 – 2011	Adults 18 to 100 years	319	2.2 Years	12 Months	Unknown	Clinically confirmed throu TB Control		
Zellweger (2015)(33)	Prospective cohort	Tuberculosis case contacts	Europe	2009 – 2013	Adults and children 0 to 100 years	3425	Median: 2.5	84 to 968 Days	Provided: Yes – 19 % Completed: Unknown %	Clinicall confirme national surveilla program		
Zenner (2017)(34)	Retrospective cohort	Migrants	United Kingdom	2009 – 2014	Adults and children 0 to 35 years	1320	Median: 2.2	Median: 1 year	No 0 %	Clinicall confirme national register		

Note: Assumed lower and upper age bound of 0 and 100 if study did not report the range of ages

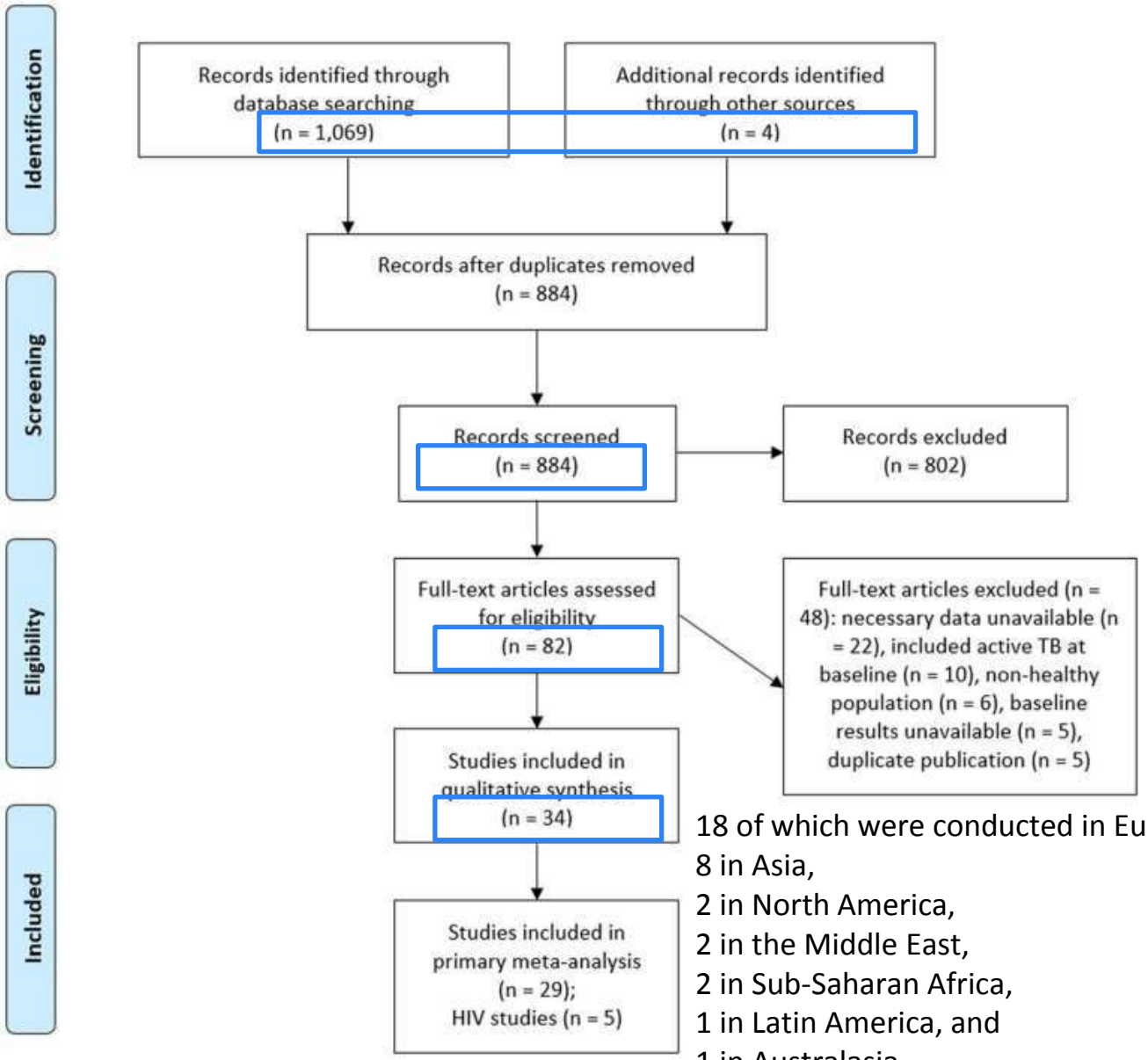


Fig. 1 Flow chart of study selection

18 of which were conducted in Europe,
8 in Asia,
2 in North America,
2 in the Middle East,
2 in Sub-Saharan Africa,
1 in Latin America, and
1 in Australasia

步驟 2：系統性文獻回顧的品質如何？(FAITH)
I - 是否只納入 (Included) 具良好效度的文章？

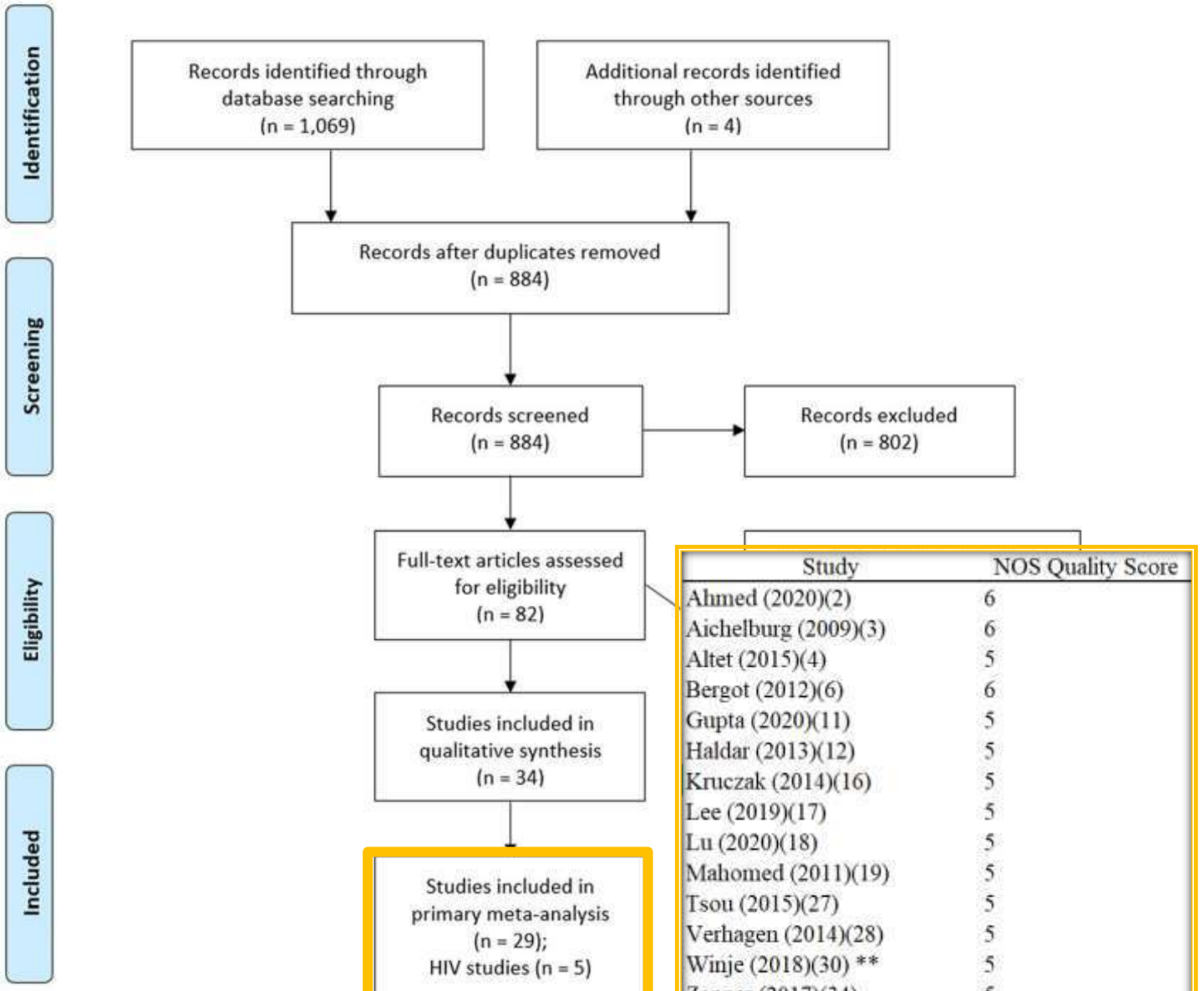
僅進行文獻判讀是不足夠，系統性文獻回顧只納入至少要有一項研究結果是極小偏誤的試驗。

Assessment of quality of included studies

We examined the quality of included studies using the Newcastle-Ottawa quality assessment scale (NOS) [16]. Potential scores range from 0 to 9 points, with higher scores representing higher quality studies. Study scores were based on the following criteria: selection of the study population, comparability between exposed and non-exposed groups, and assessment of the outcome.

評讀結果：■是　否　不清楚

- Assessment of quality of included studies
  - Newcastle-Ottawa quality assessment scale (NOS)
    - Selection of cohorts 研究對象的選擇(0-4*)
    - Comparability of cohorts 暴露組和非暴露組之間的是否具有比較的意義(0-2*)
    - Assessment of outcome研究結果(0-3*)
    - 滿分為9*分，分數越高代表研究品質越好



Study	NOS Quality Score
Ahmed (2020)(2)	6
Aichelburg (2009)(3)	6
Altet (2015)(4)	5
Bergot (2012)(6)	6
Gupta (2020)(11)	5
Haldar (2013)(12)	5
Kruczak (2014)(16)	5
Lee (2019)(17)	5
Lu (2020)(18)	5
Mahomed (2011)(19)	5
Tsou (2015)(27)	5
Verhagen (2014)(28)	5
Winje (2018)(30) **	5
Zenner (2017)(34)	5

Fig. 1 Flow chart of study selection

步驟 2：系統性文獻回顧的品質如何？(FAITH)

T - 作者是否以表格和圖表「總結」 (Total up) 試驗結果？

應該用至少 1 個摘要表格呈現所納入的試驗結果。若結果相近，可針對結果進行統合分析 (meta-analysis)，並以「森林圖」(forest plot) 呈現研究結果，最好再加上異質性分析。

Data analysis

Incidence rate ratios (referred to as relative risks in this paper) for each study were computed by using the total number of cases that progressed to active TB and accumulated person-time information for each IGRA category. We then used a novel Bayesian meta-regression method [17] to analyze data from included studies and generate a continuous risk curve for the association between IGRA values and risk of progression to active TB. This method allowed us to incorporate random-effects across studies and include heterogeneous data with various IGRA categories. The primary advantage of this method is that it is able to take any IGRA range (e.g. 0–0.35, 0.35–1, 4–10, 0.35–20, etc.) as input and use integration techniques to derive continuous risks over the entire distribution of IGRA values. Detailed methods and equations can be found in the supplementary material. We separately analyzed studies where the study population were people living with HIV (PLHIV).

評讀結果：■是　否　不清楚

- Bayesian meta-regression method貝式回歸
  - 依據現有的實驗數據來推論未來發生的機率
  - 例如:北極的冰山在2050年完全融化的概率
    - 這個事情完全沒有發生過，所以無法用頻率來代替概率表示，只能研究過去幾十年，北極冰山融化的速率(IGRA數值)，來預測北極的冰山在2050年完全融化(active TB)的概率

張紹勳， 張任坊 (2019)。
《人工智慧AI與貝葉斯Bayesian迴歸的整合：應用STaTa分析》。臺北：五南。

Bayesian meta-regression method貝式回歸分析

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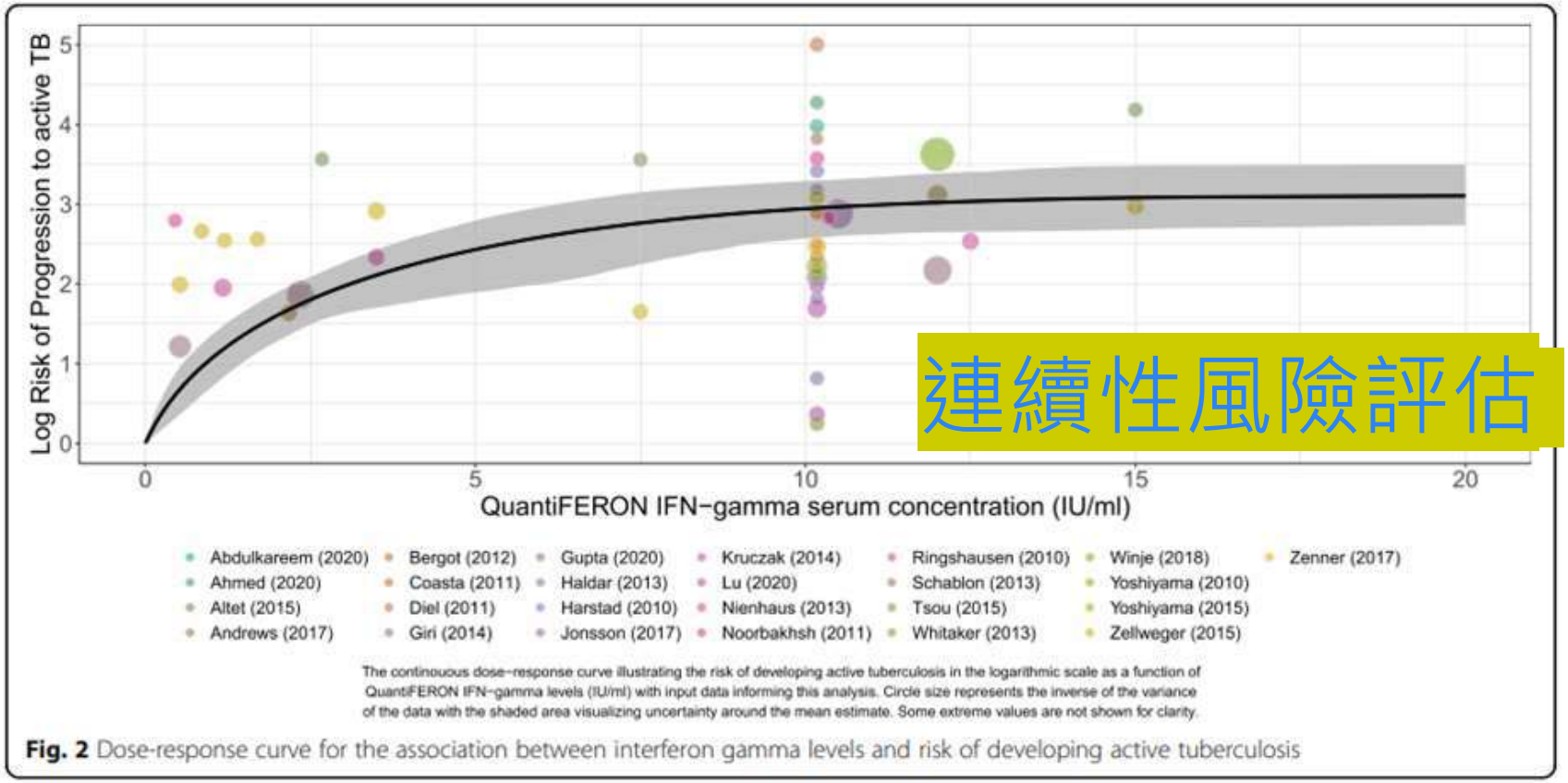


Fig. 2 Dose-response curve for the association between interferon gamma levels and risk of developing active tuberculosis

Dose-response relationship

Table 1 Risk of progression to active TB across IFN-gamma levels (IU/ml) by model

IFN-gamma levels (IU/ml)	Relative Risk (95% Uncertainty interval)					
	Primary Analysis	High Quality Studies[a]	Received TPT	No TPT	Adults	Children
0.00	REF	REF	REF	REF	REF	REF
0.10	1.18 (1.07 to 1.32)					
0.20	1.37 (1.15 to 1.63)					
0.30	1.55 (1.23 to 1.93)					
0.35	1.64 (1.28 to 2.08)					
0.40	1.74 (1.32 to 2.24)					
0.50	1.93 (1.42 to 2.54)					
0.70	2.31 (1.63 to 3.09)					
1.00	2.90 (2.02 to 3.88)					
2.00	4.99 (3.61 to 6.65)					
3.00	7.16 (5.07 to 9.65)					
4.00	9.32 (5.85 to 13.06)					
5.00	11.38 (6.64 to 16.38)					
6.00	13.31 (7.37 to 19.43)					
7.00	15.07 (8.63 to 22.07)					
8.00	16.61 (10.31 to 24.16)					
10.00	19.00 (13.08 to 26.90)	15.16 (7.38 to 31.92)	19.10 (12.87 to 29.37)	18.74 (11.01 to 30.36)	9.85 (6.20 to 15.17)	10.24 (2.96 to 33.94)
12.00	20.53 (14.13 to 29.62)	16.74 (7.90 to 35.79)	21.35 (14.11 to 32.55)	20.75 (12.04 to 34.15)	10.78 (6.79 to 16.66)	11.90 (3.47 to 39.68)
15.00	21.82 (14.65 to 32.57)	18.18 (8.39 to 40.54)	23.26 (14.95 to 37.08)	22.39 (12.88 to 38.79)	11.75 (7.14 to 18.99)	13.44 (4.03 to 45.99)
20.00	22.31 (15.43 to 33.00)	18.74 (8.69 to 41.61)	23.82 (15.26 to 37.92)	22.94 (13.27 to 39.56)	12.22 (7.43 to 19.48)	14.04 (4.33 to 46.61)

[a]Sensitivity analysis excluding studies with NOS score < 5

NOTE: TPT (TB preventive treatment). In the TPT subgroup analyses, data inputs into the models were stratified by whether studies provided any TPT. The children subgroup analysis included data for individuals below 18 years, while the adult subgroup analysis included data for those 18 years and older

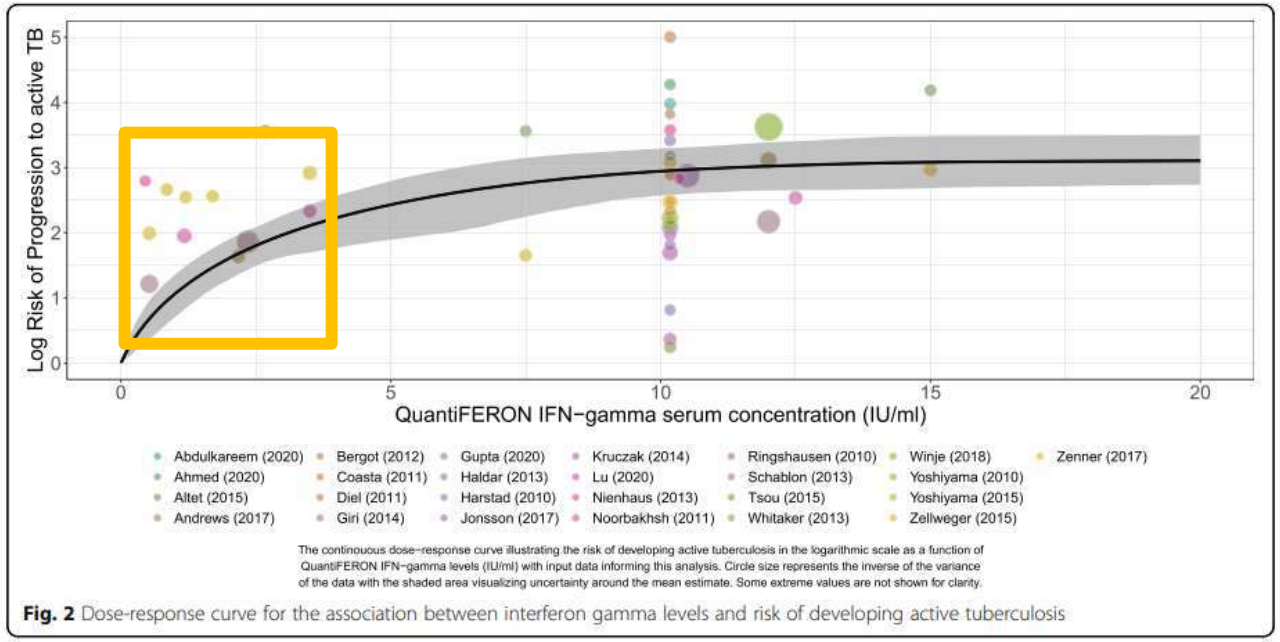


Fig. 2 Dose-response curve for the association between interferon gamma levels and risk of developing active tuberculosis

NOTE: TPT (TB preventive treatment). In the TPT subgroup analyses, data inputs into the models were stratified by whether studies provided any TPT. The children subgroup analysis included data for individuals below 18 years, while the adult subgroup analysis included data for those 18 years and older

步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

在理想情況下，各個試驗的結果應相近或具同質性，若具有異質性，作者應評估差異是否顯著(卡方檢定)。根據每篇個別研究中不同的 PICO 及研究方法，探討造成異質性的原因。

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

- 卡方檢定 ✕
- 敏感性(sensitivity analysis)：Newcastle-Ottawa quality assessment scale (NOS)
- 次群組分析(Subgroup analysis)：結核病病例接觸者、醫療相關人員、移民、HIV患者
- 另外針對年齡:成人（ > 18 歲）兒童（ < 18 歲）以及是否投藥治療進行比較。

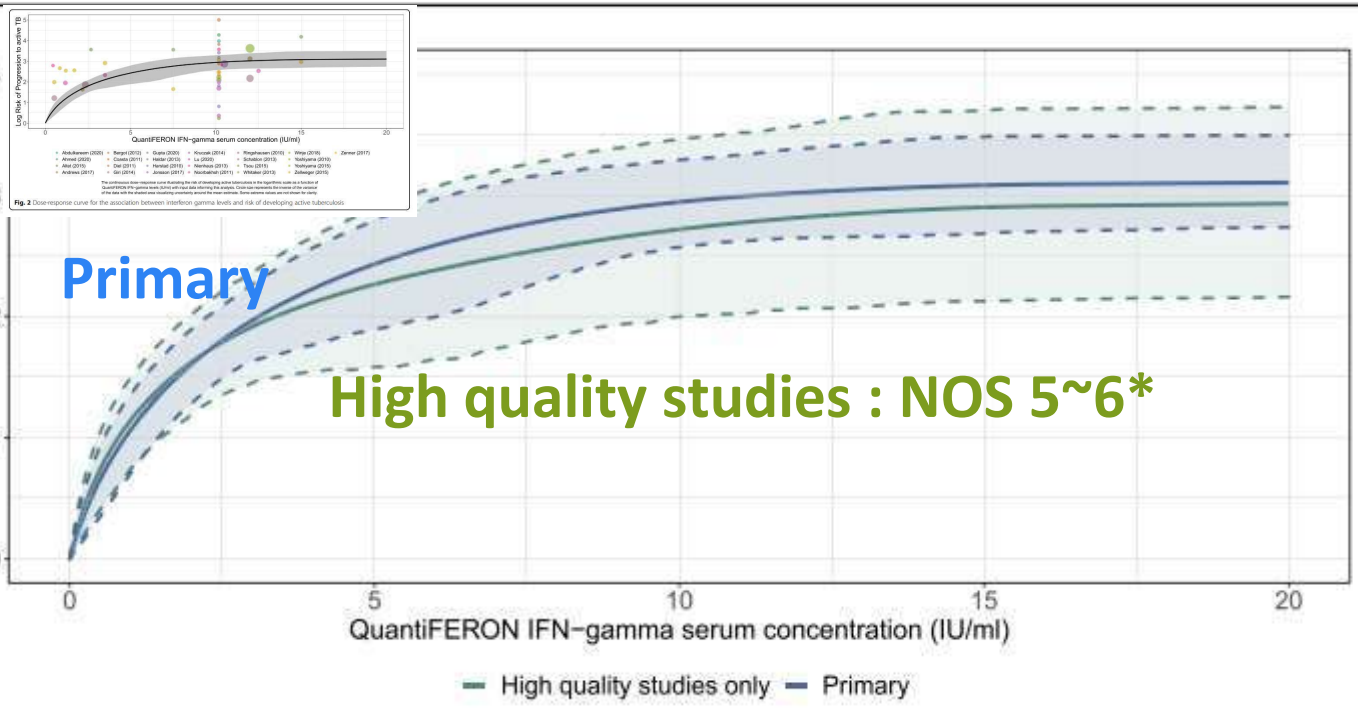
評讀結果：■是　否　不清楚

步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)

敏感性(sensitivity analysis)

- 敏感性分析（ sensitivity analysis ）：將某些不合適的論文（ NOS 低）刪除後，看看剩餘論文合併效果是否會因此更改，藉以測試綜合性效果的穩定度。



IFN-gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.04 (0.89 to 1.22)
0.20	1.07 (0.82 to 1.38)
0.30	1.09 (0.77 to 1.50)
0.35	1.10 (0.75 to 1.56)
0.40	1.11 (0.74 to 1.60)
0.50	1.12 (0.72 to 1.67)
0.70	1.12 (0.69 to 1.72)
1.00	1.12 (0.66 to 1.76)
2.00	1.05 (0.61 to 1.67)
3.00	0.99 (0.55 to 1.66)
4.00	0.95 (0.46 to 1.76)
5.00	0.92 (0.40 to 1.95)
6.00	0.90 (0.36 to 2.00)
7.00	0.88 (0.36 to 1.97)
8.00	0.88 (0.36 to 1.91)
10.00	0.88 (0.36 to 1.82)
12.00	0.91 (0.34 to 1.94)
15.00	0.94 (0.35 to 2.09)
20.00	0.94 (0.36 to 2.08)

Note: The ratio of relative risks were computed by dividing the relative risks from the model including only high quality studies (N=11) by those from the Primary model

Fig. 3 Sensitivity analysis results (excluding studies with NOS quality score < 5)

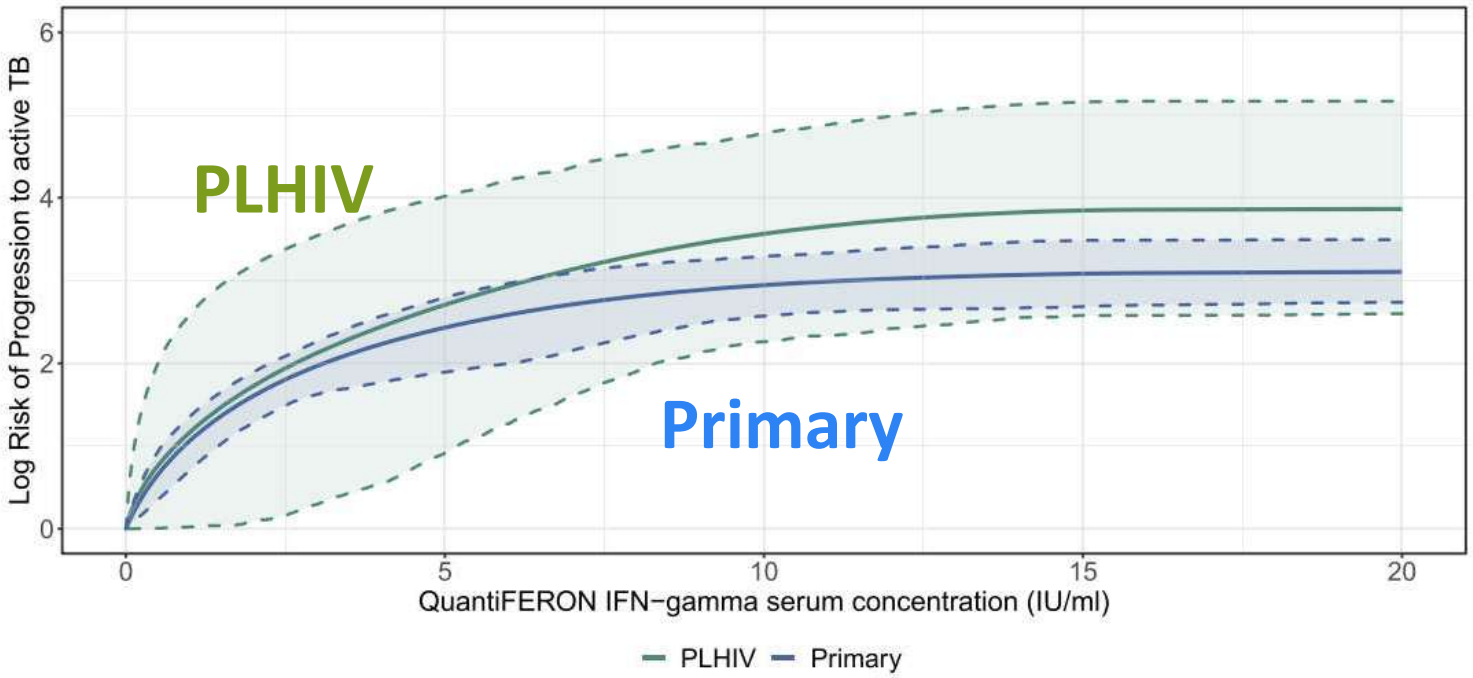
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

a: comparing PLHIV with HIV−negative individuals



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.12 (0.78 to 2.00)
0.20	1.20 (0.65 to 2.78)
0.30	1.28 (0.56 to 3.36)
0.35	1.31 (0.53 to 3.59)
0.40	1.33 (0.50 to 3.81)
0.50	1.38 (0.45 to 4.17)
0.70	1.45 (0.39 to 4.68)
1.00	1.51 (0.33 to 5.05)
2.00	1.58 (0.22 to 5.40)
3.00	1.62 (0.19 to 5.32)
4.00	1.68 (0.19 to 5.30)
5.00	1.76 (0.21 to 5.27)
6.00	1.84 (0.26 to 5.46)
7.00	1.94 (0.32 to 5.85)
8.00	2.05 (0.39 to 5.64)
10.00	2.30 (0.50 to 6.79)
12.00	2.54 (0.54 to 8.14)
15.00	2.73 (0.57 to 8.98)
20.00	2.70 (0.58 to 8.77)

Note: The ratio of relative risks were computed by dividing the relative risks from the PLHIV (N=5) model by those from the Primary model

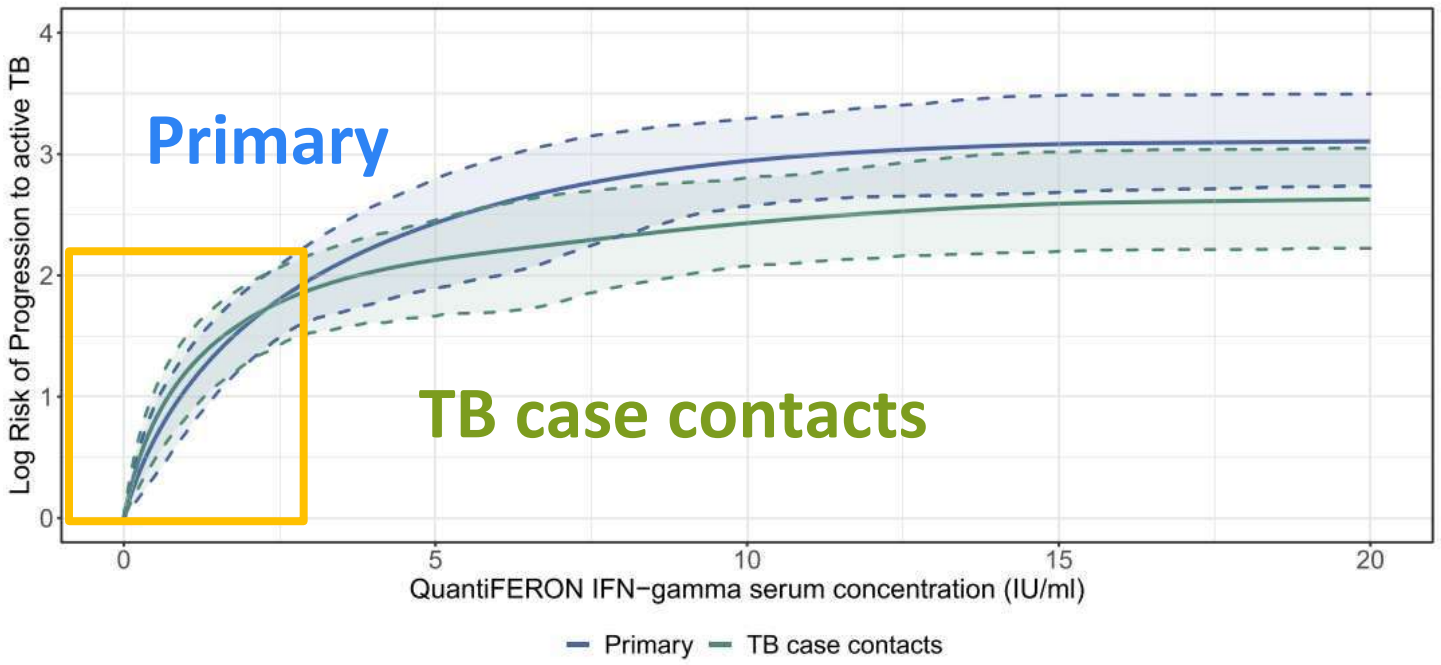
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

b: comparing TB case contacts with primary analysis



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.07 (0.91 to 1.22)
0.20	1.12 (0.85 to 1.39)
0.30	1.15 (0.81 to 1.53)
0.35	1.16 (0.79 to 1.59)
0.40	1.17 (0.78 to 1.63)
0.50	1.19 (0.76 to 1.70)
0.70	1.20 (0.74 to 1.78)
1.00	1.18 (0.71 to 1.79)
2.00	1.06 (0.65 to 1.57)
3.00	0.94 (0.57 to 1.42)
4.00	0.85 (0.48 to 1.37)
5.00	0.77 (0.41 to 1.38)
6.00	0.72 (0.36 to 1.38)
7.00	0.67 (0.33 to 1.26)
8.00	0.64 (0.35 to 1.15)
10.00	0.62 (0.37 to 1.01)
12.00	0.62 (0.36 to 1.04)
15.00	0.64 (0.35 to 1.10)
20.00	0.65 (0.36 to 1.11)

Note: The ratio of relative risks were computed by dividing the relative risks from the TB case contacts (N=14) model by those from the Primary model

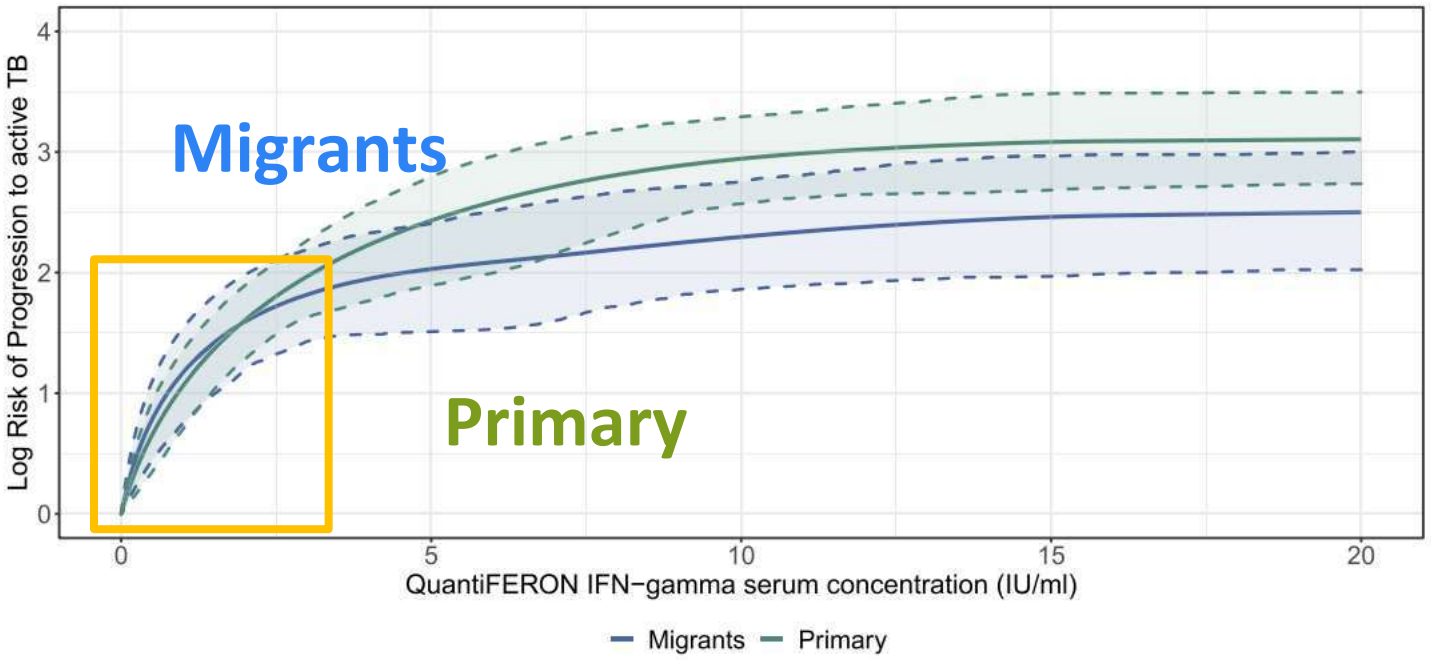
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

c: comparing migrants with primary analysis



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.06 (0.90 to 1.24)
0.20	1.10 (0.84 to 1.42)
0.30	1.13 (0.80 to 1.56)
0.35	1.14 (0.78 to 1.61)
0.40	1.15 (0.77 to 1.65)
0.50	1.16 (0.74 to 1.71)
0.70	1.17 (0.70 to 1.81)
1.00	1.15 (0.66 to 1.83)
2.00	1.02 (0.60 to 1.61)
3.00	0.89 (0.51 to 1.45)
4.00	0.79 (0.42 to 1.35)
5.00	0.71 (0.35 to 1.31)
6.00	0.64 (0.31 to 1.25)
7.00	0.60 (0.30 to 1.13)
8.00	0.57 (0.30 to 1.04)
10.00	0.54 (0.30 to 0.94)
12.00	0.55 (0.29 to 0.96)
15.00	0.57 (0.29 to 1.01)
20.00	0.57 (0.29 to 1.02)

Note: The ratio of relative risks were computed by dividing the relative risks from the migrants (N=4) model by those from the Primary model

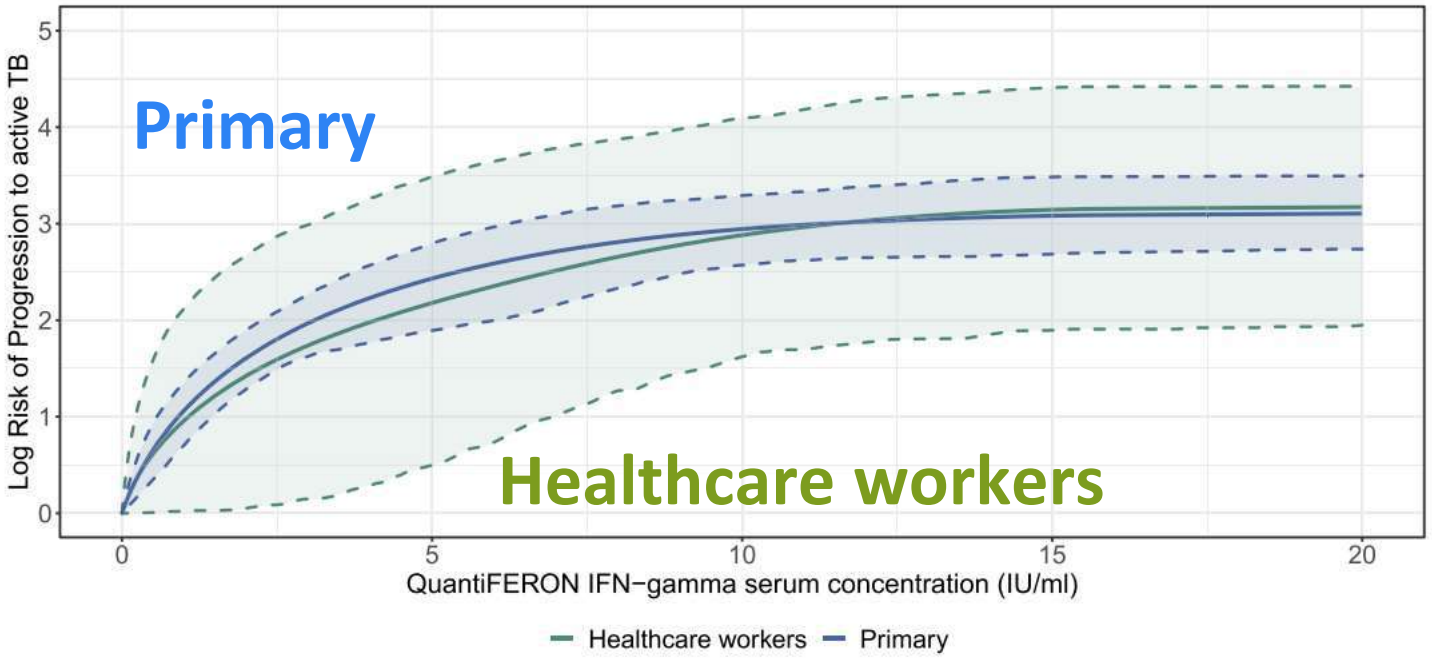
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

d: comparing healthcare workers with primary analysis



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.03 (0.79 to 1.54)
0.20	1.05 (0.66 to 1.95)
0.30	1.07 (0.57 to 2.29)
0.35	1.07 (0.54 to 2.42)
0.40	1.08 (0.51 to 2.51)
0.50	1.09 (0.46 to 2.68)
0.70	1.10 (0.39 to 2.93)
1.00	1.10 (0.31 to 3.14)
2.00	1.07 (0.20 to 3.09)
3.00	1.05 (0.15 to 3.08)
4.00	1.04 (0.13 to 3.15)
5.00	1.05 (0.14 to 3.20)
6.00	1.06 (0.14 to 3.32)
7.00	1.08 (0.17 to 3.34)
8.00	1.11 (0.19 to 3.29)
10.00	1.18 (0.26 to 3.31)
12.00	1.26 (0.26 to 3.79)
15.00	1.33 (0.28 to 4.18)
20.00	1.33 (0.30 to 4.27)

Note: The ratio of relative risks were computed by dividing the relative risks from the healthcare workers (N=7) model by those from the Primary model

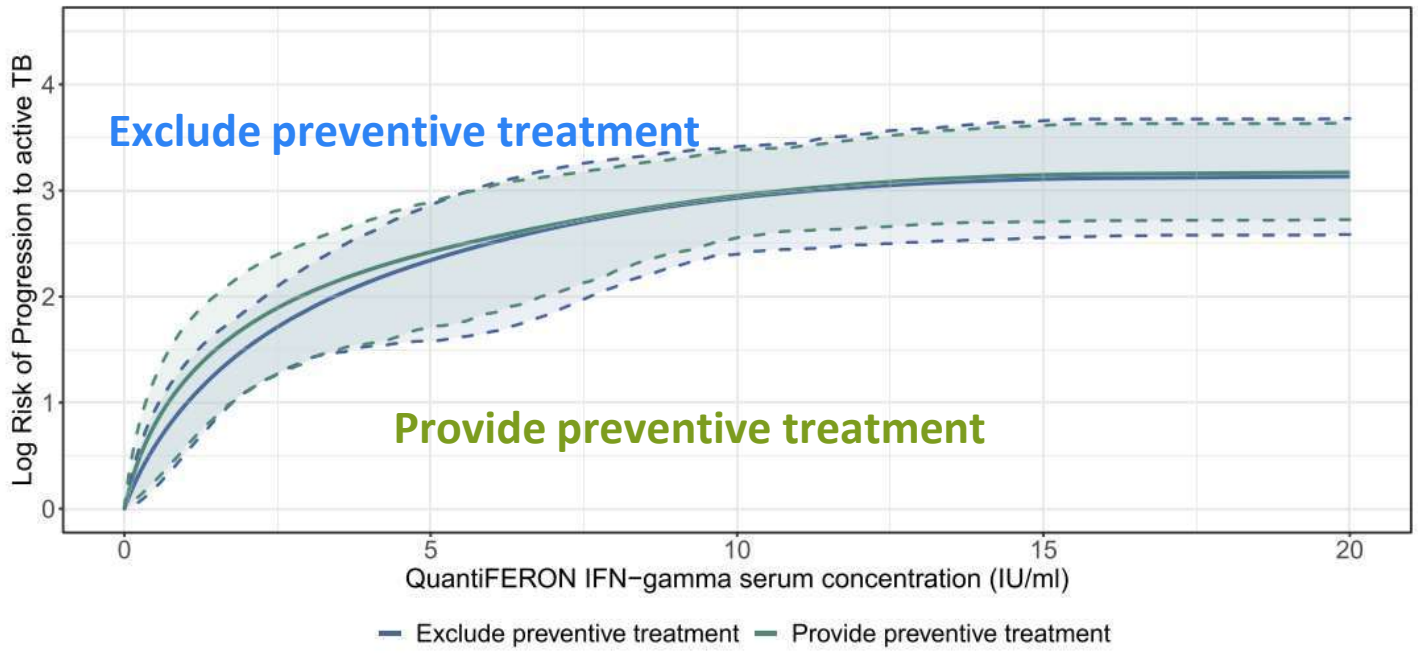
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

e: comparing studies providing preventive treatment with studies not providing preventive treatment



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	0.93 (0.73 to 1.15)
0.20	0.90 (0.60 to 1.27)
0.30	0.88 (0.53 to 1.37)
0.35	0.87 (0.51 to 1.41)
0.40	0.86 (0.49 to 1.44)
0.50	0.86 (0.47 to 1.49)
0.70	0.85 (0.42 to 1.60)
1.00	0.85 (0.40 to 1.67)
2.00	0.87 (0.43 to 1.67)
3.00	0.91 (0.44 to 1.75)
4.00	0.97 (0.42 to 1.91)
5.00	1.02 (0.39 to 2.23)
6.00	1.05 (0.37 to 2.41)
7.00	1.06 (0.39 to 2.29)
8.00	1.05 (0.45 to 2.13)
10.00	1.03 (0.52 to 1.92)
12.00	1.03 (0.49 to 1.92)
15.00	1.03 (0.46 to 2.04)
20.00	1.02 (0.47 to 1.95)

Note: The ratio of relative risks were computed by dividing the relative risks from the non−preventive treatment (N=14) model by those from the preventive treatment (N=6) model

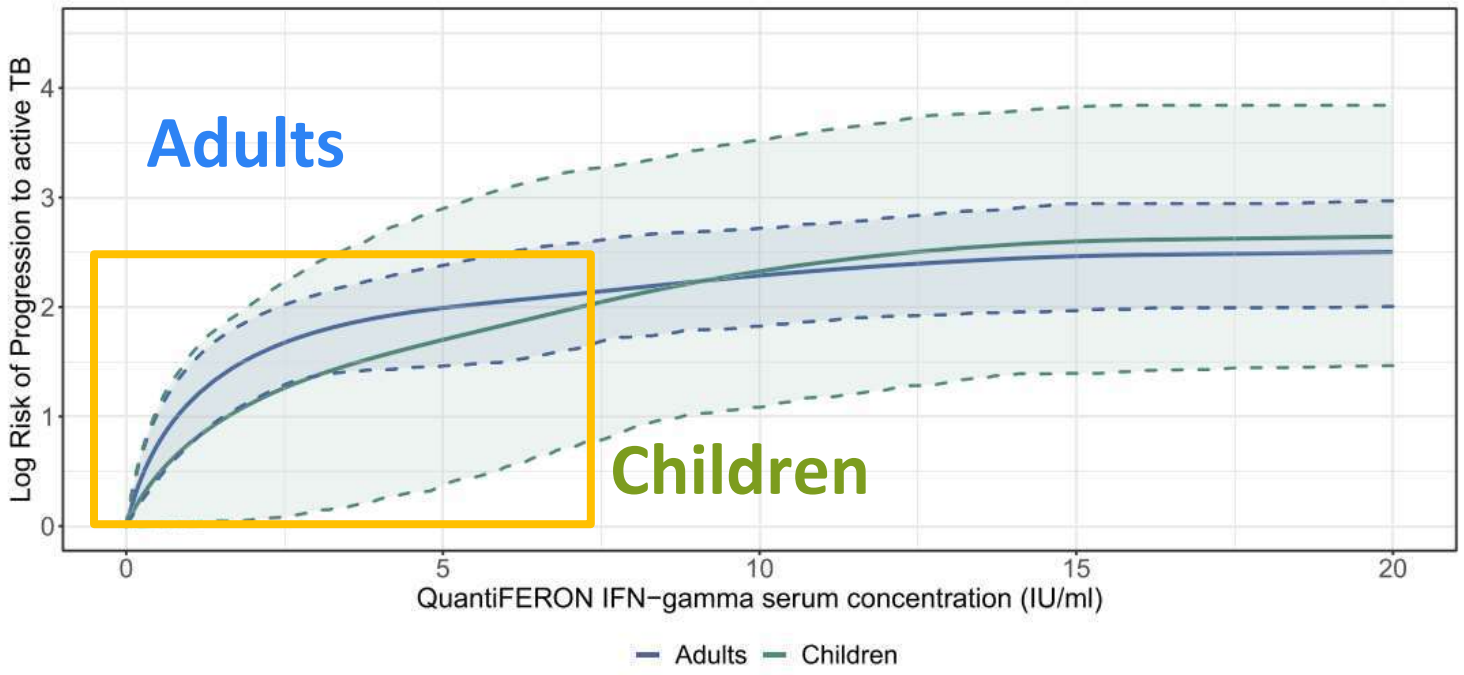
步驟 2：系統性文獻回顧的品質如何？(FAITH)

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

敏感性(sensitivity analysis)

次群組分析(subgroup analysis

f: comparing adults with children



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.10 (0.85 to 1.30)
0.20	1.19 (0.77 to 1.59)
0.30	1.27 (0.72 to 1.85)
0.35	1.30 (0.71 to 1.98)
0.40	1.33 (0.69 to 2.09)
0.50	1.39 (0.67 to 2.31)
0.70	1.49 (0.64 to 2.71)
1.00	1.60 (0.61 to 3.26)
2.00	1.77 (0.56 to 4.63)
3.00	1.82 (0.49 to 5.28)
4.00	1.80 (0.42 to 5.49)
5.00	1.71 (0.36 to 5.41)
6.00	1.59 (0.31 to 4.81)
7.00	1.45 (0.28 to 4.16)
8.00	1.33 (0.27 to 3.84)
10.00	1.20 (0.27 to 3.49)
12.00	1.15 (0.25 to 3.47)
15.00	1.11 (0.23 to 3.18)
20.00	1.09 (0.24 to 3.20)

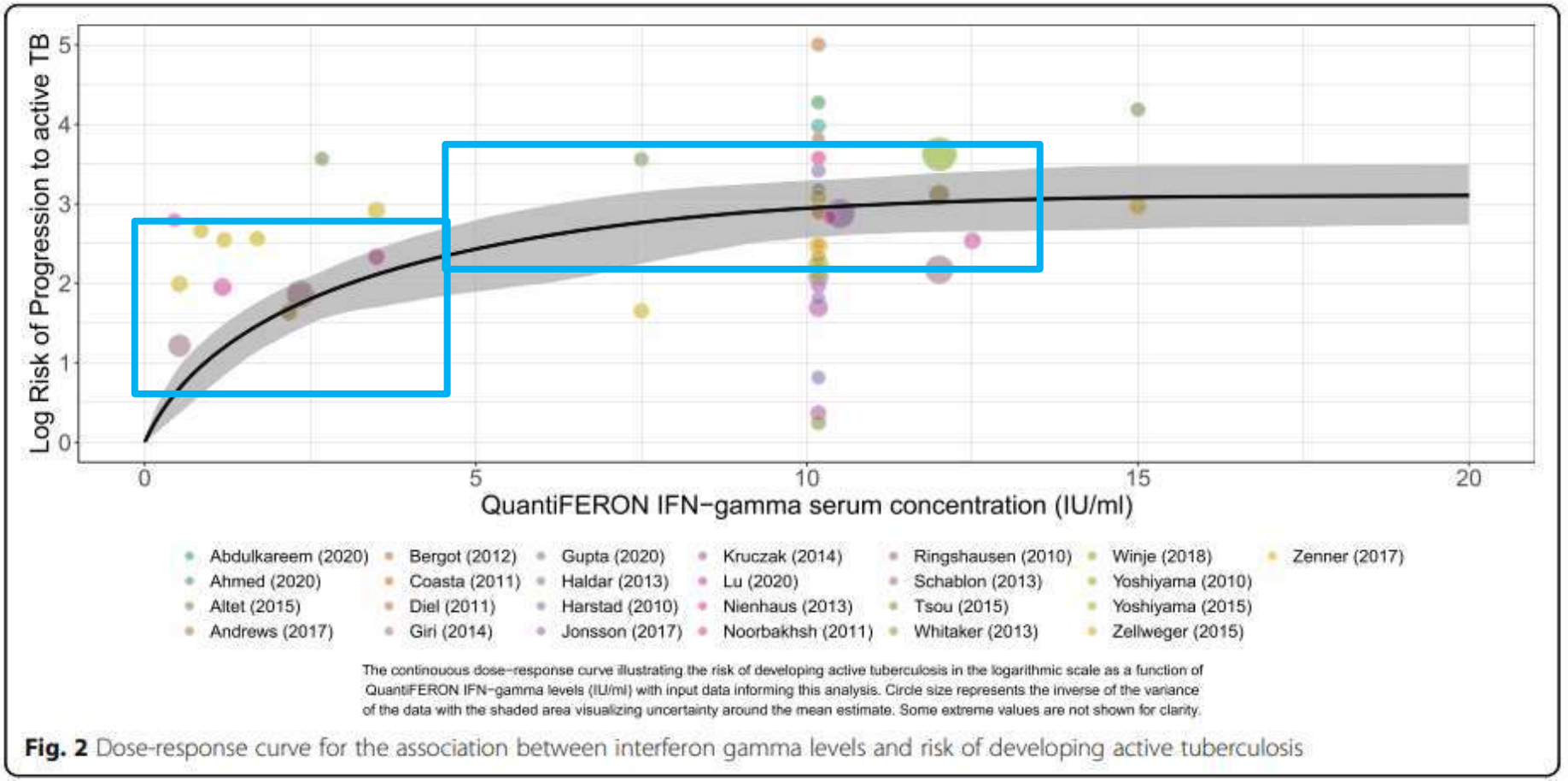
Note: The ratio of relative risks were computed by dividing the relative risks from the adult (N=7) model by those from the children (N=4) model

臺北市立萬芳醫院
·委託財團法人臺北醫學大學辦理·

Discussion

Discussion 1

Our continuous dose-response curve indicates that the risk of incident TB sharply increases between IFN-gamma levels of 0 and 5 IU/ml after which the risk continued to increase moderately but at a slower pace until reaching 15 IU/ml where the risk levels off.

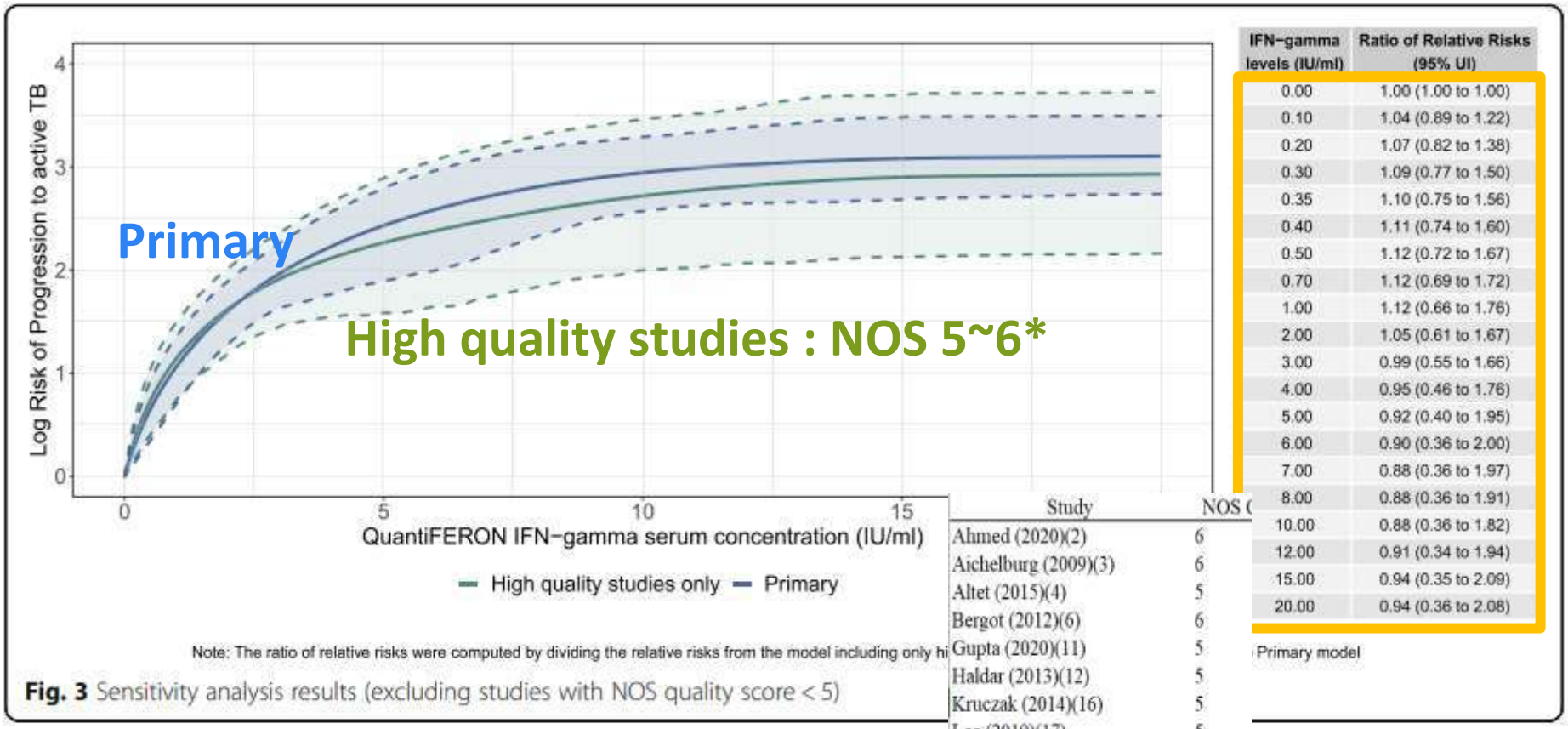


The continuous dose−response curve illustrating the risk of developing active tuberculosis in the logarithmic scale as a function of QuantiFERON IFN−gamma levels (IU/ml) with input data informing this analysis. Circle size represents the inverse of the variance of the data with the shaded area visualizing uncertainty around the mean estimate. Some extreme values are not shown for clarity.

Fig. 2 Dose-response curve for the association between interferon gamma levels and risk of developing active tuberculosis

Discussion 2

Sensitivity analyses revealed that our findings are robust to the quality of the studies as the results did not differ significantly by the quality of studies.



IFN-gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.04 (0.89 to 1.22)
0.20	1.07 (0.82 to 1.38)
0.30	1.09 (0.77 to 1.50)
0.35	1.10 (0.75 to 1.56)
0.40	1.11 (0.74 to 1.60)
0.50	1.12 (0.72 to 1.67)
0.70	1.12 (0.69 to 1.72)
1.00	1.12 (0.66 to 1.76)
2.00	1.05 (0.61 to 1.67)
3.00	0.99 (0.55 to 1.66)
4.00	0.95 (0.46 to 1.76)
5.00	0.92 (0.40 to 1.95)
6.00	0.90 (0.36 to 2.00)
7.00	0.88 (0.36 to 1.97)
8.00	0.88 (0.36 to 1.91)
10.00	0.88 (0.36 to 1.82)
12.00	0.91 (0.34 to 1.94)
15.00	0.94 (0.35 to 2.09)
20.00	0.94 (0.36 to 2.08)

Study	NOS (
Ahmed (2020)(2)	6
Aichelburg (2009)(3)	6
Altet (2015)(4)	5
Bergot (2012)(6)	6
Gupta (2020)(11)	5
Haldar (2013)(12)	5
Kruczak (2014)(16)	5
Lee (2019)(17)	5
Lu (2020)(18)	5
Mahomed (2011)(19)	5
Tsou (2015)(27)	5
Verhagen (2014)(28)	5
Winje (2018)(30) **	5
Zenner (2017)(34)	5

Fig. 3 Sensitivity analysis results (excluding studies with NOS quality score < 5)

Discussion 3

Our findings show that the risk for incident TB is 2.90-fold higher at 1 IU/ml, 10.38-fold higher at 5 IU/ml, 19.00-fold higher at 10 IU/ml, 21.82-fold higher at 15 IU/ml, and 22.31-fold higher at 20 IU/ml

Table 1 Risk of progression to active TB across IFN-gamma levels (IU/ml) by model

IFN-gamma levels (IU/ml)	Relative Risk (95% Uncertainty interval)					
	Primary Analysis	High Quality Studies[a]	Received TPT	No TPT	Adults	Children
0.00	REF	REF	REF	REF	REF	REF
0.10	1.18 (1.07 to 1.32)	1.23 (1.09 to 1.39)	1.26 (1.		.24 (1.1 to 1.39)	1.13 (1.00 to 1.41)
0.20	1.37 (1.15 to 1.63)	1.45 (1.19 to 1.77)	1.50 (1.		.46 (1.2 to 1.76)	1.26 (1.00 to 1.81)
0.30	1.55 (1.23 to 1.93)	1.67 (1.29 to 2.14)	1.74 (1.16 to 2.50)	1.48 (1.10 to 1.94)	1.69 (1.3 to 2.12)	1.37 (1.01 to 2.19)
0.35	1.64 (1.28 to 2.08)	1.78 (1.34 to 2.32)	1.86 (1.19 to 2.74)	1.56 (1.12 to 2.09)	1.80 (1.3 to 2.30)	1.43 (1.01 to 2.38)
0.40	1.74 (1.32 to 2.24)	1.88 (1.39 to 2.50)	1.98 (1.		.90 (1.4 to 2.47)	1.49 (1.01 to 2.57)
0.50	1.93 (1.42 to 2.54)	2.10 (1.50 to 2.84)	2.22 (1.		.11 (1.5 to 2.81)	1.60 (1.01 to 2.95)
0.70	2.31 (1.63 to 3.09)	2.52 (1.71 to 3.53)	2.68 (1.47 to 4.33)	2.15 (1.38 to 3.09)	2.52 (1.7 to 3.45)	1.81 (1.02 to 3.67)
1.00	2.90 (2.02 to 3.88)	3.14 (2.10 to 4.45)	3.37 (1.81 to 5.64)	2.67 (1.68 to 3.93)	3.09 (2.1 to 4.32)	2.13 (1.03 to 4.73)
2.00	4.99 (3.61 to 6.65)	5.08 (3.29 to 7.50)	5.59 (3.01 to 9.41)	4.56 (3.03 to 6.52)	4.70 (3.1 to 6.66)	3.10 (1.06 to 7.67)
3.00	7.16 (5.07 to 9.65)	6.80 (4.27 to 10.67)	7.65 (4.01 to 12.38)	6.54 (4.09 to 9.88)	5.89 (3.9 to 8.25)	3.95 (1.15 to 11.06)
4.00	9.32 (5.85 to 13.06)	8.31 (4.69 to 14.30)	9.53 (4.75 to 15.19)	8.50 (4.62 to 13.49)	6.73 (4.1 to 9.57)	4.72 (1.28 to 14.53)
5.00	11.38 (6.64 to 16.38)	9.63 (4.87 to 18.00)	11.26 (5.52 to 18.08)	10.42 (4.85 to 17.51)	7.33 (4.3 to 10.81)	5.48 (1.45 to 18.14)
6.00	13.31 (7.37 to 19.43)	10.83 (5.17 to 21.46)	12.90 (6.33 to 20.97)	12.28 (5.31 to 21.43)	7.80 (4.5 to 12.19)	6.30 (1.72 to 21.91)
7.00	15.07 (8.63 to 22.07)	11.99 (5.67 to 24.60)	14.54 (7.61 to 23.07)	14.11 (6.38 to 24.60)	8.27 (5.0 to 13.19)	7.23 (2.03 to 25.37)
8.00	16.61 (10.31 to 24.16)	13.13 (6.29 to 27.22)	16.17 (9.37 to 25.01)	15.84 (8.08 to 26.98)	8.79 (5.6 to 14.14)	8.25 (2.46 to 27.55)
10.00	19.00 (13.08 to 26.90)	15.16 (7.38 to 31.92)	19.10 (12.87 to 29.37)	18.74 (11.01 to 30.36)	9.85 (6.2 to 15.17)	10.24 (2.96 to 33.94)
12.00	20.53 (14.13 to 29.62)	16.74 (7.90 to 35.79)	21.35 (14.11 to 32.55)	20.75 (12.04 to 34.15)	10.78 (6.7 to 16.66)	11.90 (3.47 to 39.68)
15.00	21.82 (14.65 to 32.57)	18.18 (8.39 to 40.54)	23.26 (14.95 to 37.08)	22.39 (12.88 to 38.79)	11.75 (7.4 to 18.99)	13.44 (4.03 to 45.99)
20.00	22.31 (15.43 to 33.00)	18.74 (8.69 to 41.61)	23.82 (15.26 to 37.92)	22.94 (13.27 to 39.56)	12.22 (7.4 to 19.48)	14.04 (4.33 to 46.61)

IGRA NEGTIVE

IGRA POSITIVE

[a]Sensitivity analysis excluding studies with NOS score < 5

NOTE: TPT (TB preventive treatment). In the TPT subgroup analyses, data inputs into the models were stratified by whether studies provided any TPT. The children subgroup analysis included data for individuals below 18 years, while the adult subgroup analysis included data for those 18 years and older

Discussion 4

The dose-response relationship found in this meta-analysis can be used to help guide clinical decisions to perform additional tests and treat latent tuberculosis infection within the context of TB programs and local epidemiology.

PLoS One. 2017 Nov 2;12(11):e0187313. doi: 10.1371/journal.pone.0187313. eCollection 2017.

A borderline range for Quantiferon Gold In-Tube results

Jerker Jonsson [1 2], Anna Westman [3 4], Judith Bruchfeld [2 5], Erik Sturegård [6], Hans Gaines [1 2 5], Thomas Schön [7 8]

Table 1. Categorical distribution of follow-up QFT results when retesting those with initial result in the borderline range (0.20–0.99 IU/ml).

				Result of follow-up QFT test (IU/ml)					
Initial result (IU/ml)	Total (n)	Percent-age retested (n)	Median days to retest (IQR)	Indeter-minate	Negative (<0.20)	Border-line negative (0.2–0.34)	Border-line positive (0.35–0.99)	Positive (>0.99)	Total retested
Borderline negative (0.20–0.34)	1664	20.9% (348)	52 (25–112)	1.2% (4)	66.1% (230)	13.2% (46)	12.9% (45)	6.6% (23)	100.0% (348)
Borderline positive (0.35–0.99)	1992	33.7% (671)	38 (20–84)	1.3% (9)	42.5% (285)	12.2% (82)	26.7% (179)	17.3% (116)	100.0% (671)
All borderline (0.20–0.99)	3656	27.9% (1019)	42 (21–92)	1.3% (13)	50.5% (515)	12.6% (128)	22.0% (224)	13.6% (139)	100.0% (1019)

19.5%

54.7%

Conclusions

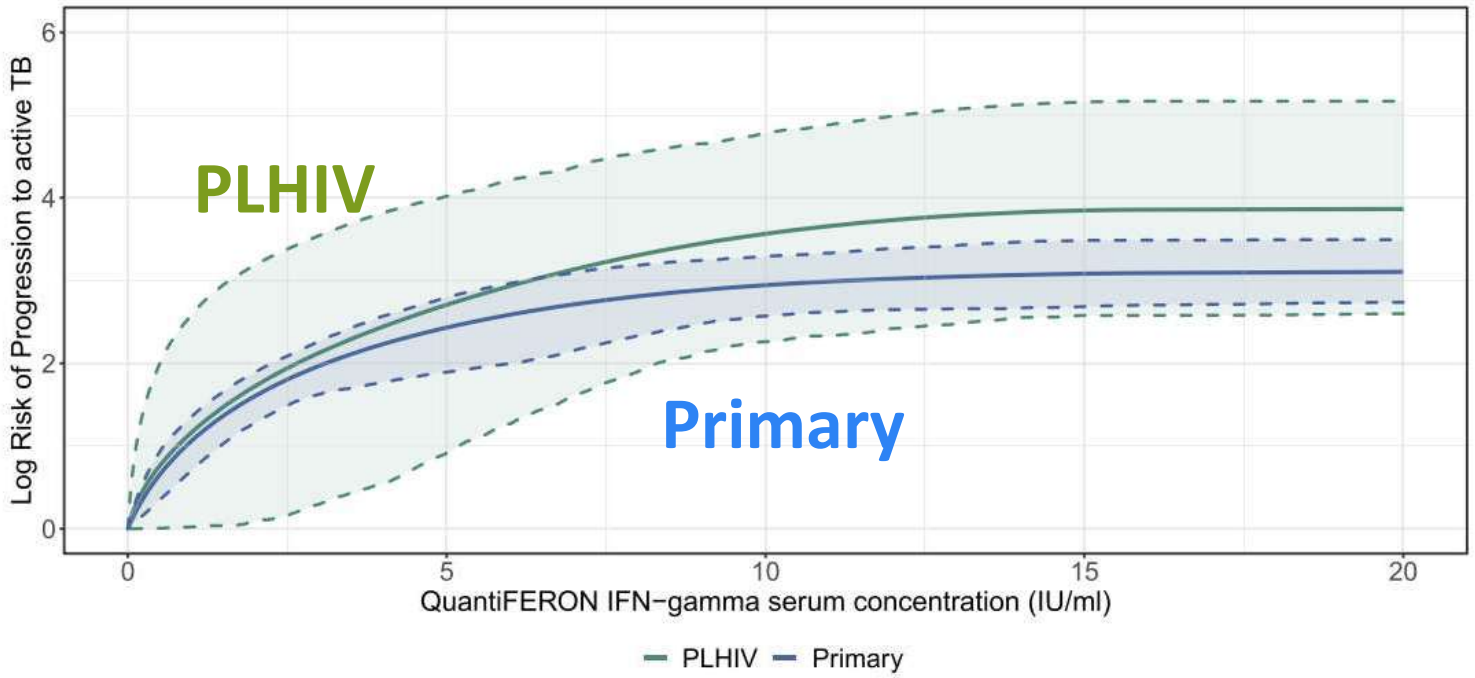
We recommend retesting of subjects with QFT results in the range 0.20–0.99 IU/ml to enhance reliability and validity of the test. Half of the subjects in the borderline range will be negative at a level <0.20 IU/ml when retested and have a very low risk of developing incident active TB.

https://doi.org/10.1371/journal.pone.0187313

Discussion 5

Compared to our primary curve that excluded studies where the entire study population is HIV positive, the dose-response relationship was substantially higher in studies among HIV positive individuals.

a: comparing PLHIV with HIV−negative individuals



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.12 (0.78 to 2.00)
0.20	1.20 (0.65 to 2.78)
0.30	1.28 (0.56 to 3.36)
0.35	1.31 (0.53 to 3.59)
0.40	1.33 (0.50 to 3.81)
0.50	1.38 (0.45 to 4.17)
0.70	1.45 (0.39 to 4.68)
1.00	1.51 (0.33 to 5.05)
2.00	1.58 (0.22 to 5.40)
3.00	1.62 (0.19 to 5.32)
4.00	1.68 (0.19 to 5.30)
5.00	1.76 (0.21 to 5.27)
6.00	1.84 (0.26 to 5.46)
7.00	1.94 (0.32 to 5.85)
8.00	2.05 (0.39 to 5.64)
10.00	2.30 (0.50 to 6.79)
12.00	2.54 (0.54 to 8.14)
15.00	2.73 (0.57 to 8.98)
20.00	2.70 (0.58 to 8.77)

Note: The ratio of relative risks were computed by dividing the relative risks from the PLHIV (N=5) model by those from the Primary model

Discussion 5

Compared to our primary curve that excluded studies where the entire study population is HIV positive, the dose-response relationship was substantially higher in studies among HIV positive individuals.

JOURNAL ARTICLE

Detection and Prediction of Active Tuberculosis Disease by a Whole-Blood Interferon-γ Release Assay in HIV-1–Infected Individuals FREE

Maximilian C. Aichelburg, Armin Rieger, Florian Breitenecker, Katharina Pfistershammer, Julia Tittes, Stephanie Eltz, Alexander C. Aichelburg, Georg Stingl, Athanasios Makristathis, Norbert Kohrgruber ✉

Clinical Infectious Diseases, Volume 48, Issue 7, 1 April 2009, Pages 954–962,

IGRAs are sensitive tools for predicting TB progression among PLHIV

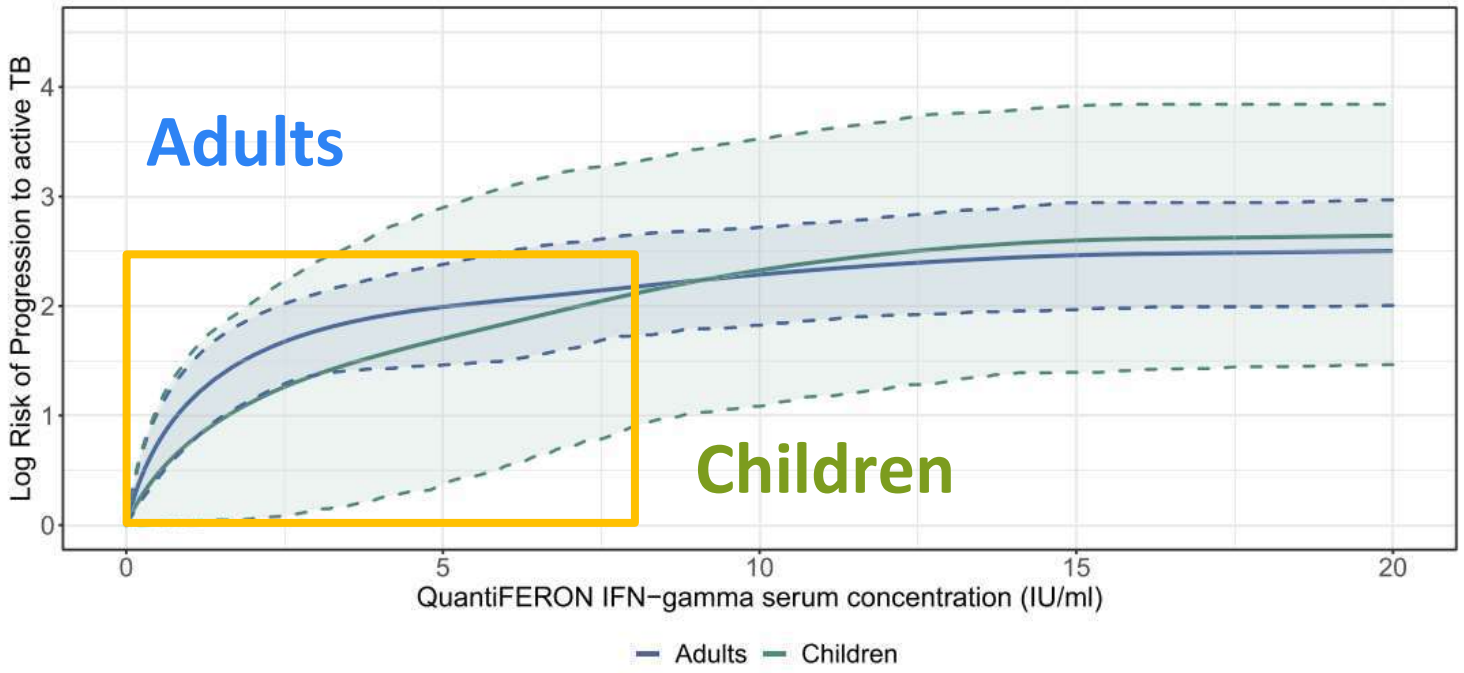
Characteristics of active tuberculosis. In this study, 11 individuals received a diagnosis of active tuberculosis. Six patients had pulmonary tuberculosis, 1 had extrapulmonary tuberculosis, and 4 had miliary tuberculosis. The QFT-GIT assay results were positive in 10 and negative in 1 individual. Thus, for the diagnosis of active tuberculosis, the sensitivity of the QFT-GIT assay was 90.9% (95% CI, 62.3%–98.4%).

Detection and Prediction of Active Tuberculosis Disease by a Whole-Blood Interferon-γ Release Assay in HIV-1–Infected Individuals | Clinical Infectious Diseases | Oxford Academic (oup.com)

Discussion 6

The relative risk of incident TB was lower for children compared to adults at the lower end of the curve before converging at 7.5 IU/ml.

f: comparing adults with children



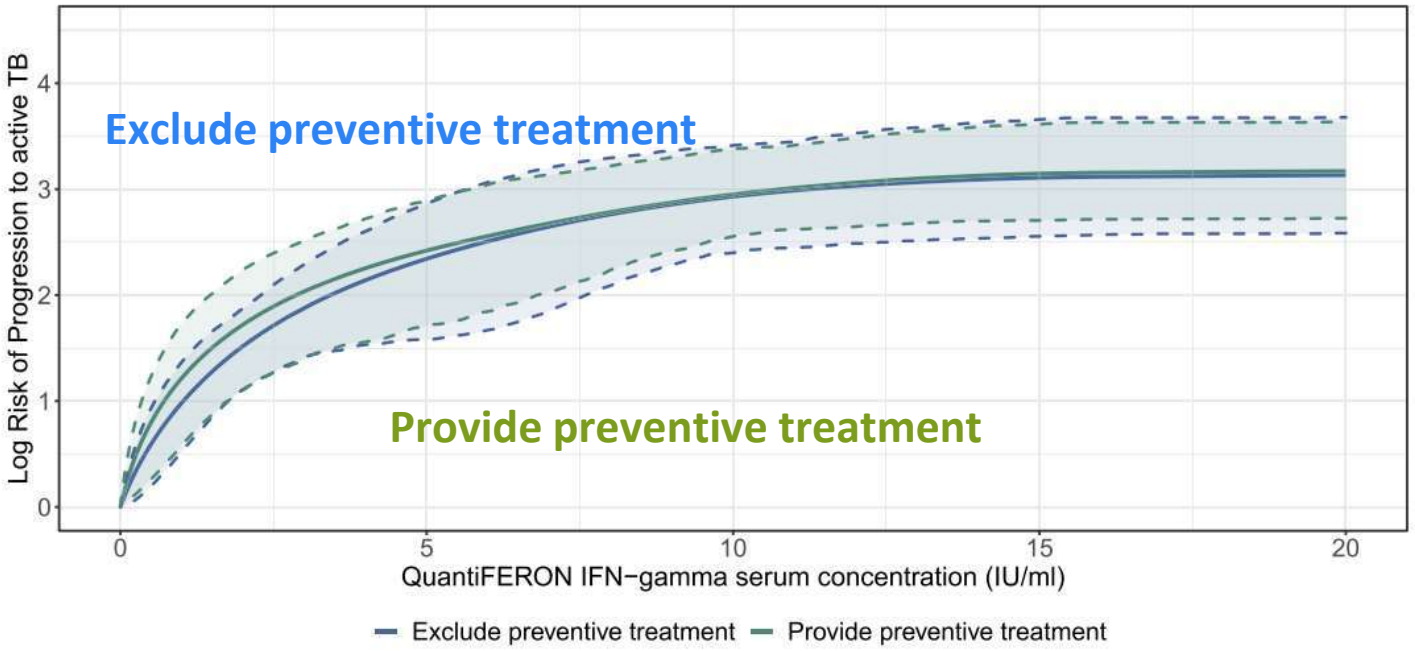
IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	1.10 (0.85 to 1.30)
0.20	1.19 (0.77 to 1.59)
0.30	1.27 (0.72 to 1.85)
0.35	1.30 (0.71 to 1.98)
0.40	1.33 (0.69 to 2.09)
0.50	1.39 (0.67 to 2.31)
0.70	1.49 (0.64 to 2.71)
1.00	1.60 (0.61 to 3.26)
2.00	1.77 (0.56 to 4.63)
3.00	1.82 (0.49 to 5.28)
4.00	1.80 (0.42 to 5.49)
5.00	1.71 (0.36 to 5.41)
6.00	1.59 (0.31 to 4.81)
7.00	1.45 (0.28 to 4.16)
8.00	1.33 (0.27 to 3.84)
10.00	1.20 (0.27 to 3.49)
12.00	1.15 (0.25 to 3.47)
15.00	1.11 (0.23 to 3.18)
20.00	1.09 (0.24 to 3.20)

Note: The ratio of relative risks were computed by dividing the relative risks from the adult (N=7) model by those from the children (N=4) model

Discussion 7

The lack of difference in the curves can be due to the fact that only a small proportion of participants accepted treatment in studies where it was provided

e: comparing studies providing preventive treatment with studies not providing preventive treatment



IFN−gamma levels (IU/ml)	Ratio of Relative Risks (95% UI)
0.00	1.00 (1.00 to 1.00)
0.10	0.93 (0.73 to 1.15)
0.20	0.90 (0.60 to 1.27)
0.30	0.88 (0.53 to 1.37)
0.35	0.87 (0.51 to 1.41)
0.40	0.86 (0.49 to 1.44)
0.50	0.86 (0.47 to 1.49)
0.70	0.85 (0.42 to 1.60)
1.00	0.85 (0.40 to 1.67)
2.00	0.87 (0.43 to 1.67)
3.00	0.91 (0.44 to 1.75)
4.00	0.97 (0.42 to 1.91)
5.00	1.02 (0.39 to 2.23)
6.00	1.05 (0.37 to 2.41)
7.00	1.06 (0.39 to 2.29)
8.00	1.05 (0.45 to 2.13)
10.00	1.03 (0.52 to 1.92)
12.00	1.03 (0.49 to 1.92)
15.00	1.03 (0.46 to 2.04)
20.00	1.02 (0.47 to 1.95)

Note: The ratio of relative risks were computed by dividing the relative risks from the non−preventive treatment (N=14) model by those from the preventive treatment (N=6) model

Discussion 8

Finally, the findings from this study bring into question the predictive value for progression to active TB of IGRAs.

Predictive value of interferon-γ release assays for incident active tuberculosis: a systematic review and meta-analysis

Molebogeng X Rangaka, Katalin A Wilkinson, Judith R Glynn, Daphne Ling, Dick Menzies, Judith Mwansa-Kambafwile, Katherine Fielding, Robert J Wilkinson, Madhukar Pai

The strength of
development of
moderate, with
even in IGRA-p
positive individ
follow-up. This
and in historica
review is that n
high prognostic

As discussed elsewhere,[64] another possible explanation for the poor predictive ability of existing tests for latent *M tuberculosis* infection is that a single or cross-sectional TST or IGRA result cannot resolve the underlying phenotypes because they do not capture information about when infection occurred and how the infection was fully, partly, or not eliminated by the host. All but two studies[27, 28] included in this review reported results of only one IGRA or TST test at baseline. Serial IGRA testing might show interesting underlying phenotypes that have different histories and trajectories.[65] Without serial testing, the underlying phenotypes are not distinguishable, undermining the predictive value of a single test result.

Discussion

1. IFN-γ落在 0 和 5 IU/ml 之間時，active TB 的風險急劇增加

2. 對於每個陽性結果來說，未來的罹病風險並不相同
   單純只顯示陽性或陰性， 容易忽略高風險族群的罹病風險

3. 過高的 IFN-γ數值，是潛伏感染進展為活動性 TB 的重要指標。

4. 本篇的貝氏分析結果可用於幫助臨床進行醫療決策(borderline)

5. IGRAs對於預測HIV患者由LTBI進展為active TB具有高度的敏感性

6. 幼兒免疫系統發育不完全，影響QuantiFERON抗原管的免疫反應，
   對於結果容易產生干擾

7. IGRA判讀不應只侷限在定性分析

Strengths and Limitations

1. In our meta-regression we were able to include data with different IFN-gamma categories into a singular analysis while incorporating between study heterogeneity in our uncertainty estimation.

2. This is an advantage over traditional methods that would have to take the midpoint of IFN-gamma categories rather than use information of the entire category as done in this study.

3. Our study is the first meta-analysis to examine TB risk over the entire distribution of IFN-gamma levels, allowing for improved identification of individuals who may be at highest risk for progressing to active TB.

4. Finally, we were able to stratify results by important at risk populations to evaluate for potential confounding and effect modification.

Strengths and Limitations

1. First, we could not assess for effect modification by known risk factors for progression to active TB
   including tobacco smoke, alcohol consumption, diabetes, malnutrition, and indoor air pollution, as these data were not routinely included in studies.

2. Second, several studies included in our systematic review used passive-follow-up for detection of active TB through national TB registries.

3. Third, our quality assessment indicated that almost all studies have some source of bias as all studies were considered to be of low to moderate quality.

4. Fourth, most studies were conducted in low to intermediate TB burden countries, potentially limiting the generalizability of our findings.

5. Fifth, time since infection may impact results as recent infection is associated with higher risk for active TB.

6. Finally, we may have missed articles as we restricted our search to two databases.

Recommendations for Future Work

1. We found that the risk of incident TB is not the same for everyone with a positive IGRA reaction.

2. Future cohort studies should therefore collect granular data on IGRA levels and the associated risk of progression to active tuberculosis.

3. Future studies may also incorporate additional risk factors for progression to active tuberculosis such as alcohol, smoking, malnutrition, and diabetes to identify individuals at greatest risk of subsequent TB.

臺北市立萬芳醫院
·委託財團法人臺北醫學大學辦理·

Discussion

Discussion

1. We developed a dose-response risk curve for the progression to active TB as a function of a continuous measure of IGRA values.
2. Our findings show that the current practice of dichotomizing IGRA test results simplifies the TB infection disease continuum.
3. The findings of this study showed that the risk of active TB development is not the same for everyone with a positive IGRA, with higher IGRA values being strongly associated with disease progression.
4. With IGRAs starting to scale up in high TB burden areas, the findings from this study can help clinicians make informed decisions by providing different relative risks of progression to active TB for a range of IGRA values within the borderline zone and very high IGRA reactions.
5. More investigations using detailed quantification of IGRA values will help to find more accurate estimates of the dose-response relationship and allow for a reexamination of the predictive power of IGRA tests.

討論：發出IGRAs報告時是否需新增備註說明

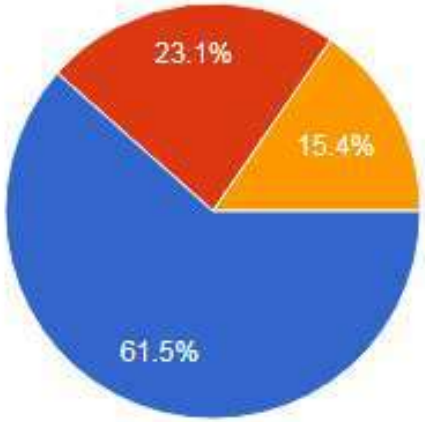
- 維持目前報告格式
  (定性報告與檢驗數值同時呈現不另行備註)
- 針對高風險族群(HIV患者)備註警語
- 需要參考更多文獻
- 簽退、投票連結與QR code：

https://forms.gle/iNk571qbAH5eGSnK6

發出IGRAs報告時是否需新增備註說明

複製

26 則回應



- 維持目前報告格式 (定性報告與檢驗數值同時呈現不另行備註)
- 針對高風險族群(HIV患者) 增加備註警語
- 需要參考更多文獻以進行評估