2012實證醫學月會報告

Interferon-γ Release Assays and Active Tuberculosis

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2012.01.16

縮寫表

- IGRA: Interferon-γ release assay (IGRA)
- TB: Tuberculosis
- LTBI: Latent tuberculosis infection
- TST: tuberculin skin test
- NAA: nucleic acid amplification
- PCR: polymerase chain reaction
- AFB: acid fast bacillus

臨床情境 (Clinical Scenario)

- 檢驗醫學部接到臨床醫師諮詢電話：
  - 目前肺結核病的診斷有賴於細菌培養。但細菌培養在急需確診和治療的病人身上常緩不濟急。
  - 所以驗檢驗科可否可引進**Interferon-γ release assay (IGRA)** 的檢驗，以幫助臨床醫師快速診斷active tuberculosis?

所形成的臨床問題

臨床單位的訴求

- 想新增檢驗項目IGRA
  - 可快速檢驗
  - 檢體為血液(或體液)
  - 幫助醫師及早診斷和治療

檢驗單位的疑問

- 我們目前用來診斷TB的指標有哪些?
- IGRA對於active TB的診斷是否有足夠的證據支持?
- 若真的要新增此檢驗項目，設備及試劑成本如何?是否有健保給付?

→ IGRA是否適用來診斷active TB?

Background Questions

- **Interferon-γ release assay (IGRA)是甚麼?**
- 診斷active TB的檢驗項目有哪些?
- 診斷active TB gold standard是甚麼?
- 目前本院用的指標有哪些?

Background Questions

- **Interferon-γ release assay (IGRA)是甚麼?**
- (source: http://www.cellestis.com/IRM/content/compinfo/pic_4_3pic1.gif)

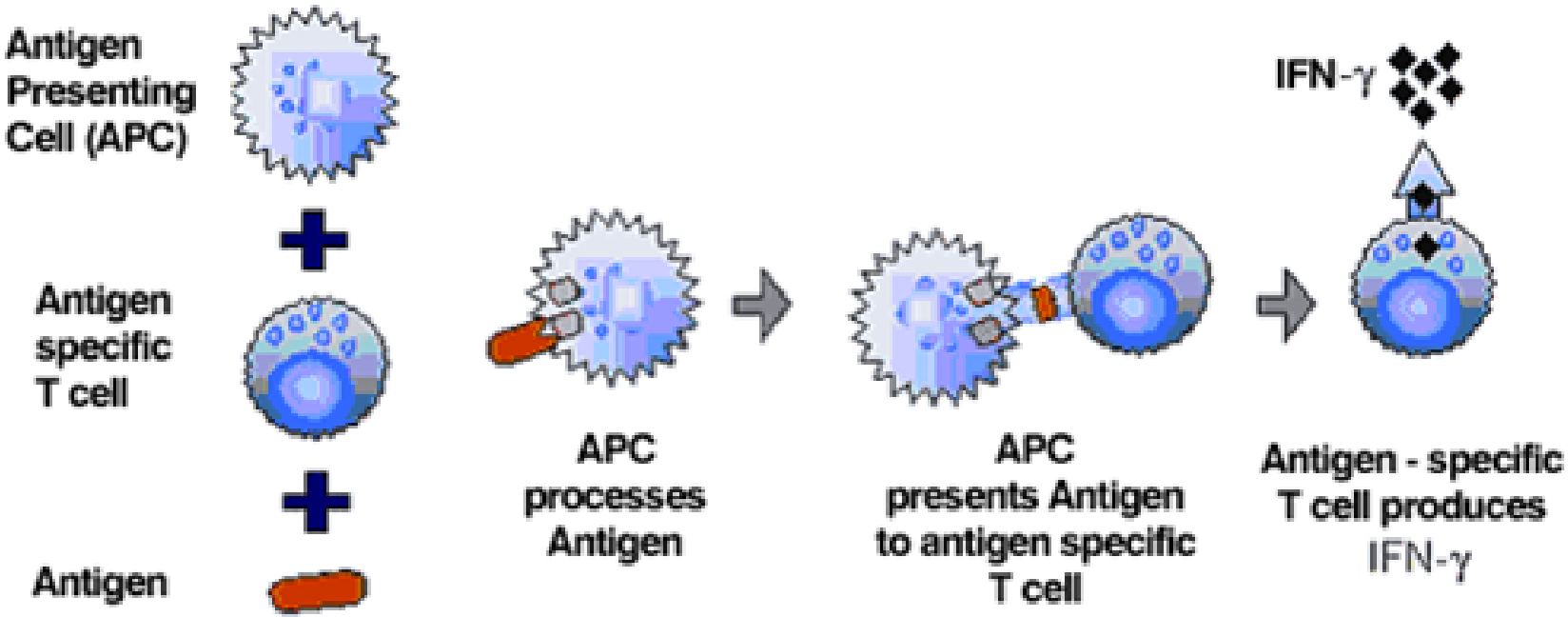
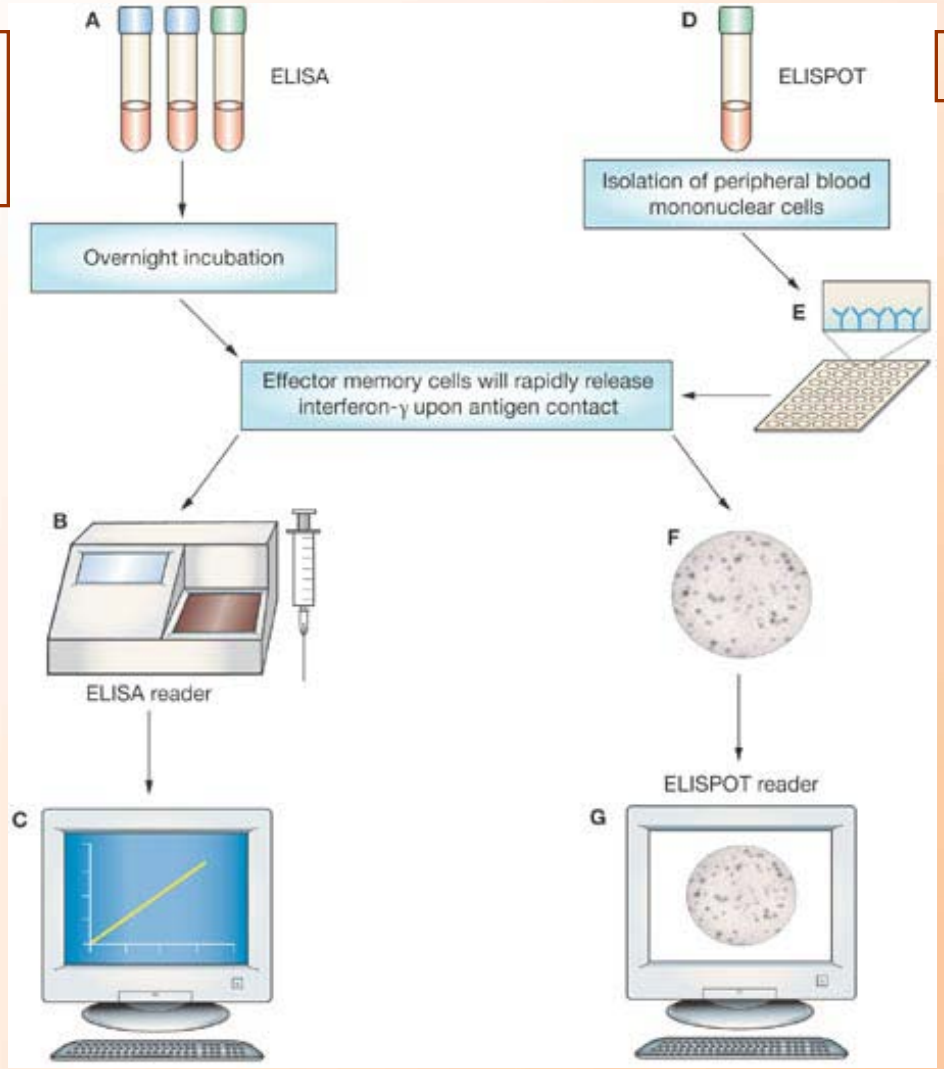


Figure 1 T-cell interferon-γ release assays for the diagnosis of *M. tuberculosis* infection

GFT-G-IT:
ESAT-6
CFP-10
TB7.7



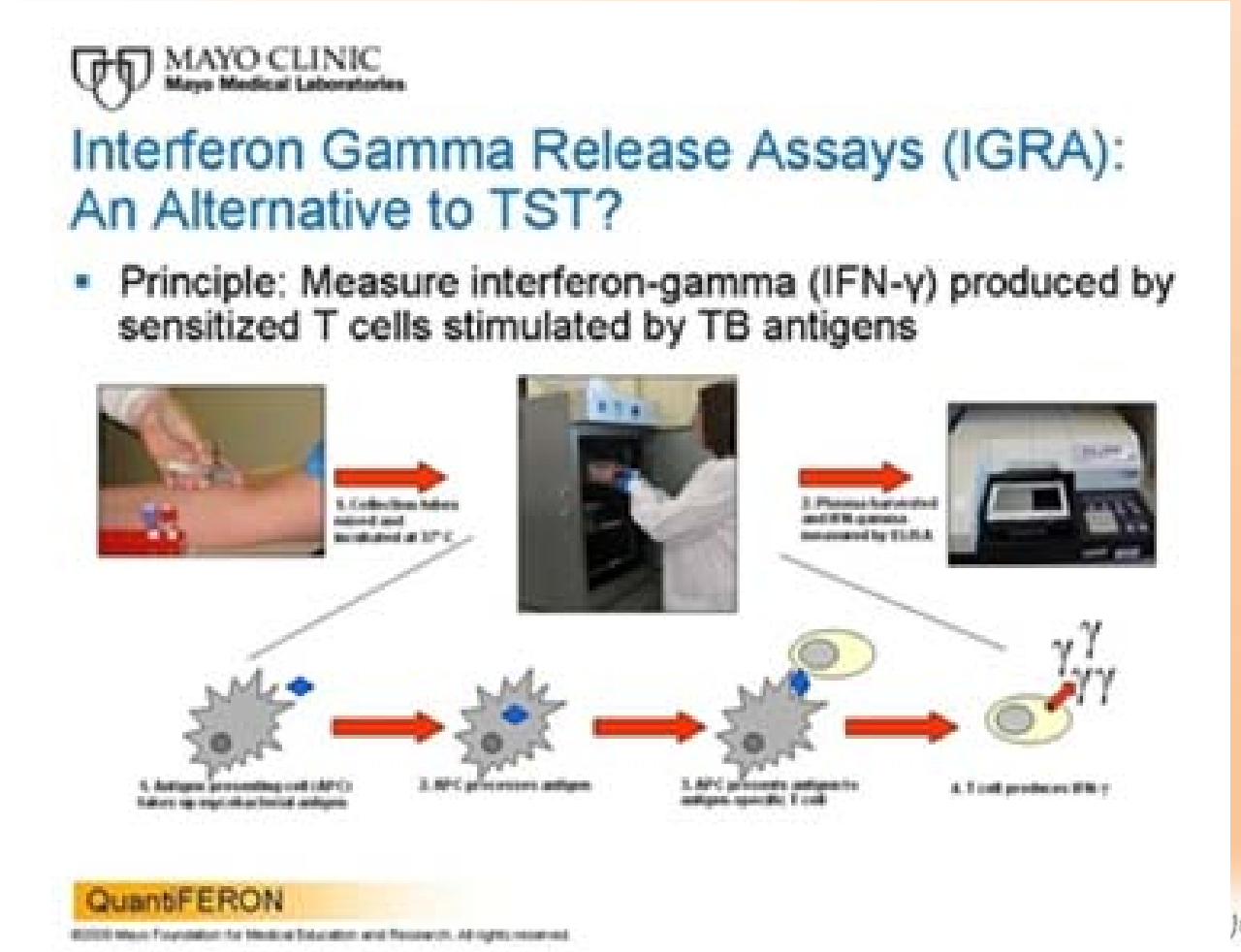
T-SPOT TB

Lange C *et al*. (2007) Rapid immunodiagnosis of tuberculosis in a woman receiving anti-TNF therapy *Nat Clin Pract Rheumatol* **3:** 528–534 doi:10.1038/ncprheum0571

nature CLINICAL PRACTICE RHEUMATOLOGY

Background Questions

- (source:)



Background Questions

- **Interferon-γ release assay (IGRA)是甚麼?**
- 診斷active TB的檢驗項目有哪些?

  AFB smear, culture (L-J, MGIT), BACTEC, NAA (E-MTD, PCR)
- 診斷active TB gold standard是甚麼?
- 目前本院用的指標有哪些?

- AFB: acid fast bacillus
- NAA: nucleic acid amplification
- PCR: polymerase chain reaction

搜尋UpToDate

- 關鍵字: **“Tuberculosis” “IGRA”**

Results from Searching: Summaries

UpToDate ONLINE

Database	UpToDate
Title of article	IGRAs for latent tuberculosis infection
Content	IGRAs are diagnostic tools for LTBI (Latent tuberculosis infection). The goal of testing for LTBI is to identify individuals who are at increased risk for the development of tuberculosis and therefore who would benefit from treatment of latent TB infection.

Results from Searching: Summaries

UpToDate ONLINE

Database	UpToDate
Title of article	Diagnosis of latent tuberculosis infection in adults
Content	In general, testing for latent TB infection is warranted to identify individuals who are at risk of new infection, and to identify individuals at increased risk of reactivation due to associated conditions.

Results from Searching: Summaries

UpToDate ONLINE

Database	UpToDate
Title of article	Diagnosis of latent tuberculosis infection in adults
Content	Patients with positive TST(tuberculin skin test) or IGRA results must undergo clinical evaluation to rule out active tuberculosis and to assess need for LTBI therapy. This includes evaluation for symptoms (eg, fever, cough, weight loss), physical exam, and radiographic examination of the chest.

Results from Searching: Summaries

UpToDate ONLINE

Database	UpToDate
Title of article	Rapid diagnostic tests for tuberculosis
Content	American Thoracic Society consensus conference recommendations for treatment, isolation, and contact investigations based upon clinical suspicion, AFB (acid fast bacillus) smear, and NAA (nucleic acid amplification) results.

Foreground Questions

- IGRA在診斷active TB的能力如何?

EBM的步驟

- Asking
  - 將臨床問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上

PICO

P Patient/Problem	A patient is suspected active TB
I Intervention	**Interferon-γ release assay (IGRA)**
C Comparison	Bacterial culture (gold standard)
O Outcome	Diagnosis accuracy for active TB

EBM的步驟

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上

Searching Strategy 1：
Finding out The Correct Keywords

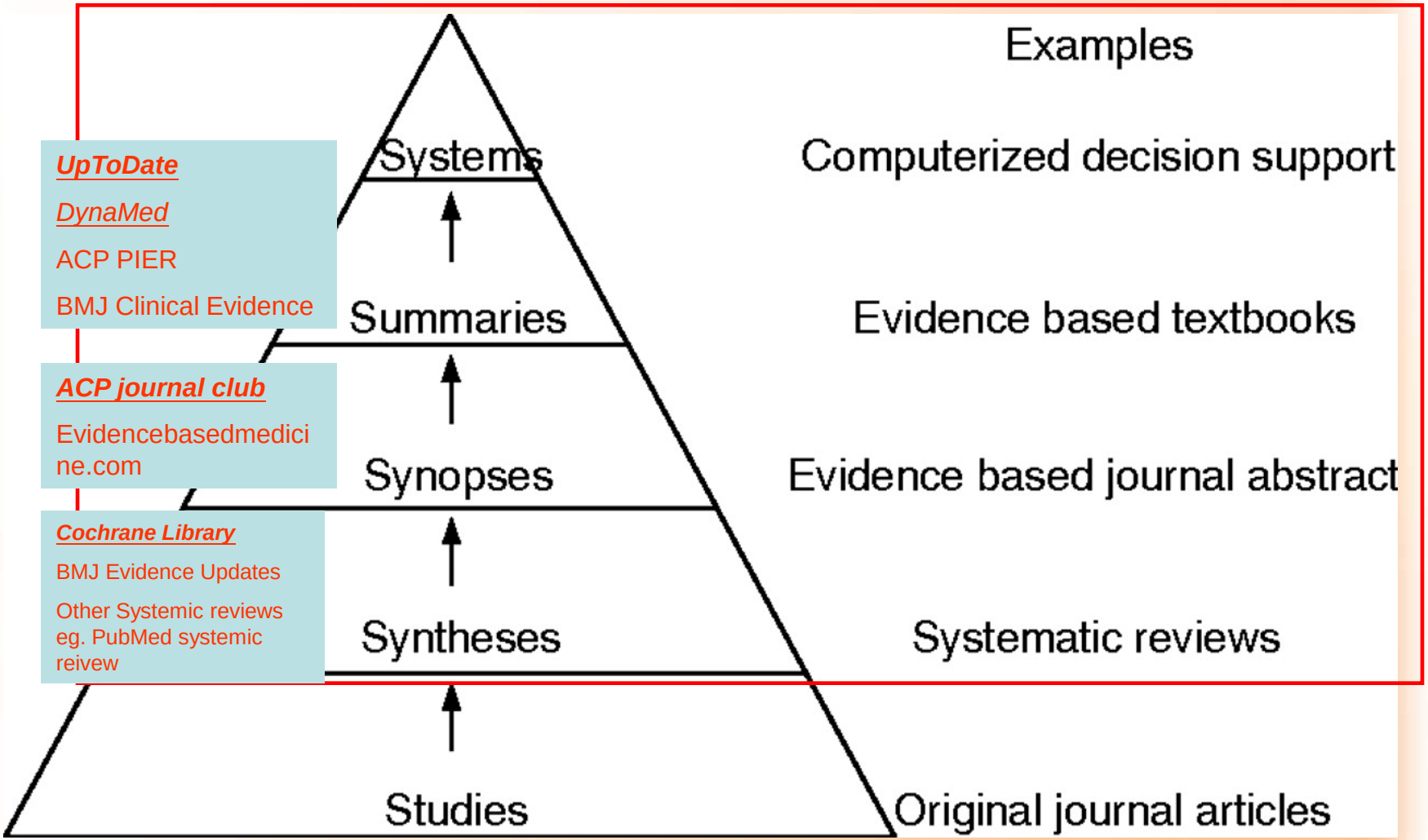
Keywords from PICO item
MeSH database to identify every term

" interferon-γ release assay (IGRA) "

"active tuberculosis"

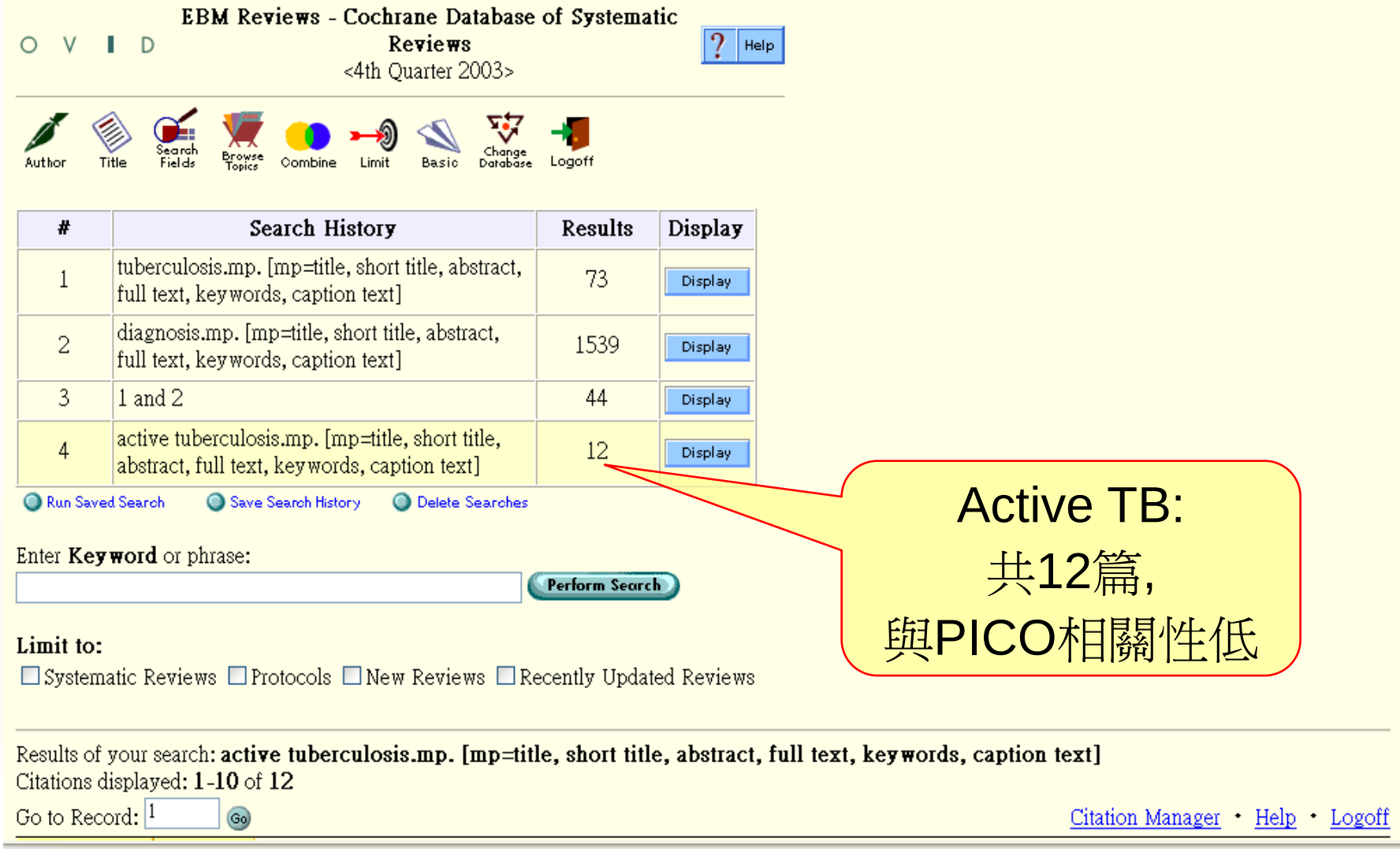
Search for Answers

Secondary database



搜尋Cochrane Database of Systemic Review

- **關鍵字: “active tuberculosis” →12篇**



EBM Reviews - Cochrane Database of Systematic Reviews
<4th Quarter 2003>

Help

Author | Title | Search Fields | Browse Topics | Combine | Limit | Basic | Change Database | Logoff

#	Search History	Results	Display
1	tuberculosis.mp. [mp=title, short title, abstract, full text, keywords, caption text]	73	Display
2	diagnosis.mp. [mp=title, short title, abstract, full text, keywords, caption text]	1539	Display
3	1 and 2	44	Display
4	active tuberculosis.mp. [mp=title, short title, abstract, full text, keywords, caption text]	12	Display

Run Saved Search | Save Search History | Delete Searches

Enter **Keyword** or phrase:

Perform Search

Limit to:

Systematic Reviews | Protocols | New Reviews | Recently Updated Reviews

Results of your search: **active tuberculosis.mp. [mp=title, short title, abstract, full text, keywords, caption text]**
Citations displayed: **1-10** of **12**

Go to Record: 1 Go

Citation Manager • Help • Logoff

Active TB:
共12篇,
與PICO相關性低

EBM Reviews - Cochrane Central Register of Controlled Trials

- Title: Characteristics of a diagnostic method for tuberculosis infection based on whole blood interferon-γ assay
- Journal:Kekkaku. 2006 Nov;81(11):681-6.
- Summary: IGRA可診斷latent tuberculosis infection (LTBI)且優於TST(無全文)

搜尋PubMed

- 關鍵字: **“Active TB + IGRA” (Limits: meta-analysis or RTC, Human, English)**

History

Search	Add to builder	Query	Items found
#10	Add	Search #1 AND #2 Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	7
#9	Add	Search #1 AND #2 AND #7 Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	1
#8	Add	Search sensitivity and specificity Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	8018
#7	Add	Search culture Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	6069
#6	Add	Search cultue Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	0
#2	Add	Search Interferon-γ release assays Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	26
#5	Add	Search active tuberculsis Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	0
#1	Add	Search active tuberculosis Limits: only items with abstracts, Humans, Meta-Analysis, Randomized Controlled Trial, English	172

PubMed文獻搜尋過程與結果

關　鍵　字	篇 數
#1 active tuberculosis	172
#2 Interferon-γ release assays	26
#3 culture	6069
#4 sensitivity and specificity	8081
#1 AND #2 AND #3 AND #4	1 (不適用)
#1 AND #2 AND #4	7 (2篇符合PICO)

搜尋到的文章標題

- Title: Interferon- γ release assays for the diagnosis of active tuberculosis: a systematic review and meta-analysis
- Journal: Eur Respir J 2011; 37: 100–111

搜尋到的文章標題

- Title: **IGRAs for active pulmonary TB diagnosis in adults in low- and middle-income countries: systematic review and meta-analysis.**
- Journal: J Infect Dis. 2011 Nov 15;204 Suppl 4:S1120-9. (無全文)

J Infect Dis. 2011 Nov 15;204 Suppl 4:S1120-9

- Results:
- 27 observational studies (17 QFT-GIT and 10 T-SPOT) evaluating 590 HIV-uninfected and 844 HIV-infected individuals.
- HIV-infected patients, pooled sensitivity 76% (45%-92%) for T-SPOT and 60% (34%-82%) for QFT-GIT.

J Infect Dis. 2011 Nov 15;204 Suppl 4:S1120-9

- Results:
- pooled specificity estimates were low for both IGRA platforms among all participants (T-SPOT, 61% [40%-79%]; QFT-GIT, 52% [41%-62%]) and among HIV-infected persons (T-SPOT, 52% [40%-63%]; QFT-GIT, 50%).

J Infect Dis. 2011 Nov 15;204 Suppl 4:S1120-9

- **Conclusion:**

  In low- and middle-income countries, neither the tuberculin skin test nor IGRAs have value for active TB diagnosis in adults, especially in the context of HIV coinfection.

EBM的步驟

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上

Critical Appraisal

Valid: systematic review or diagnostic worksheet

Importance: what were the result?

Applicability: population and feasibility

搜尋到的文章標題

- Title: Interferon- γ release assays for the diagnosis of active tuberculosis: a systematic review and meta-analysis
- Journal: Eur Respir J 2011; 37: 100–111

What question did the systematic review addressed (PICO) 想要回答什麼問題？

■ 是	□ 否	□ 不清楚

評論：

The authors systematically reviewed and performed a meta-analysis of studies that simultaneously investigated the diagnostic performance **[O]** of IGRA **[I]** and culture **[C]** as markers for active tuberculosis **[P]**.

Is it unlikely that important, relevant studies were missed 沒有遺漏重要的文獻？

■是	□ 否	□不清楚

評論：

Retrieving the literature:

- All studies published in the PubMed, EMBASE, Cochrance-controlled central register of controlled trials from 2001/02 through 2009/11 that evaluated IGRA for the diagnosis of active TB in human were identified.
- According to the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement and the quality assessment of diagnostic accuracy studies (QUADAS) checklist.

Is it unlikely that important, relevant studies were missed 沒有遺漏重要的文獻？

■是	□ 否	□ 不清楚

評論：(***Retrieving the literature)***

(1) Type of study: any studies that evaluated the evidence of using IGRAs in order to dx active TB in human except for studies meet exclusion criteria

(2) Site: N.D.

(3) Subjects: human

(4) Test: IGRA (“T-spot” OR “Quantiferon” OR “interferon-gamma release assay” OR “ESAT-6” OR “CFP-10”)

(5) Disease: active tuberculosis

Were the criteria used to select articles for inclusion appropriate 選擇文獻的準則適當?

■是	□ 否	□ 不清楚

評論：

Selection of studies and data extraction: (by 2 reviewers)

◆Only included studies that reported the assessment of commercially available IGRAs in individuals with a clinical suspicion of active TB, performed on blood or biological fluids other than blood.

◆ The following types of studies were excluded 1) case reports, editorials and reviews on immunological studies; 2) laboratory studies; 3) animal studies; 4) studies performed with assays other than QFT-G-IT or T-SPOT.TB1; 5) studies not performed according to manufacturers' instructions

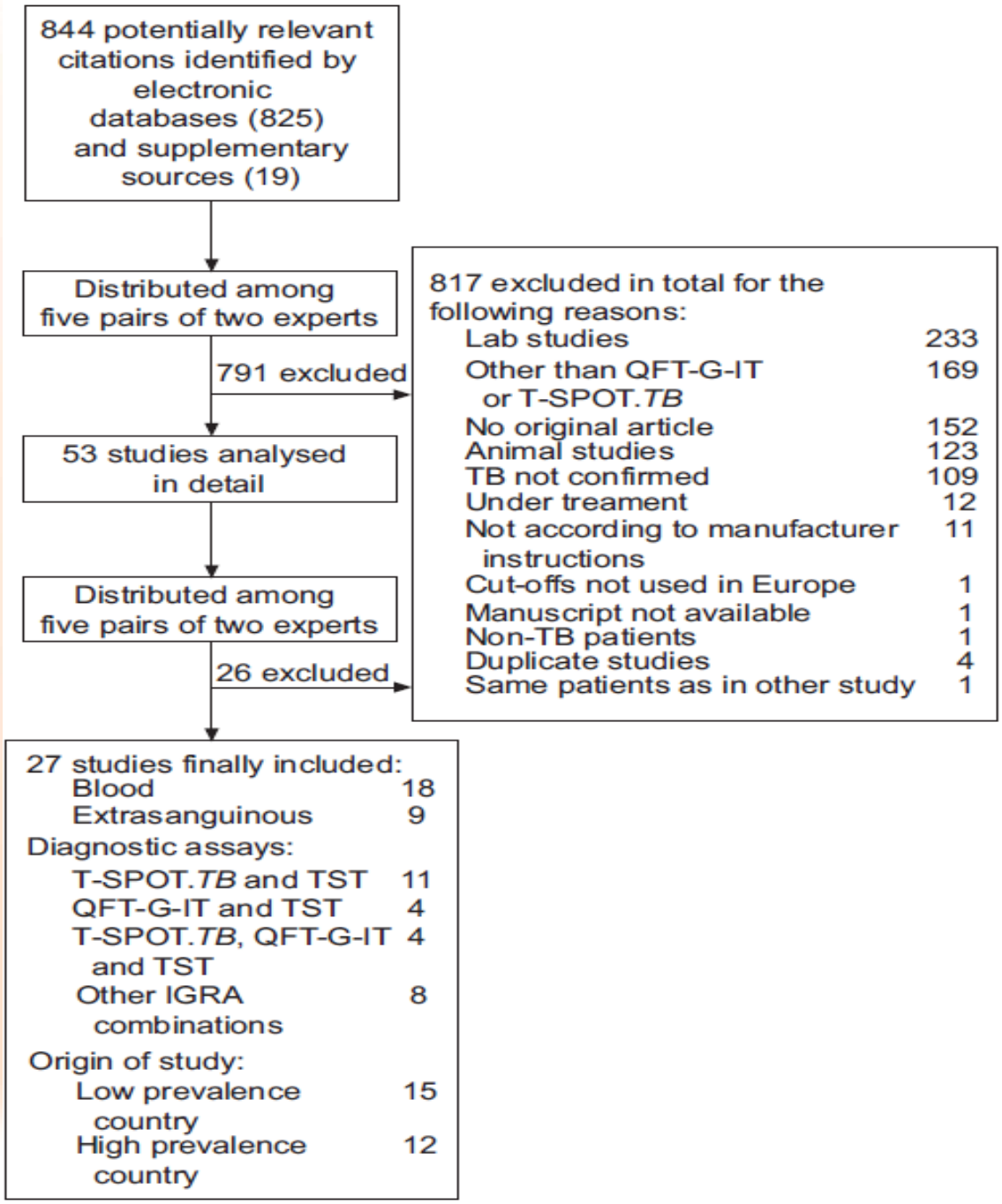
Were the criteria used to select articles for inclusion appropriate 選擇文獻的準則適當?

■是	□ 否	□ 不清楚

◆6) studies in adults where pulmonary TB was not confirmed by M. tuberculosis culture, characteristic histopathological findings and/or nucleic acid amplification tests in .50% of cases (in mixed studies, i.e. those without these strict criteria, data were analysed for the confirmed cases separately); 7) studies performed with cut-offs for positive test results that are not used in Europe; 8) studies where selected patients were treated for TB for 2 weeks prior to IGRA testing

◆Restricted to publications in English.

Flow Diagram for Study Selection



所引用研究統計表: (共27篇, 3821人)

TABLE 1 Characteristics of the included studies (also stratified for adults and children)

Variable	All individuals	Adults	Children
Country#			
South Africa	6/35 (17.1)	5/31 (16.1)	1/4 (25.0)
Italy	5/35 (14.3)	4/31 (12.9)	1/4 (25.0)
Germany	5/35 (14.3)	5/31 (16.1)	
Korea	4/35 (11.4)	4/31 (12.9)	
UK	2/35 (5.7)		2/4 (50.0)
Other	13/35 (37.1)	13/31 (41.9)	
Studies	27/27 (100.0)	23/27 (85.2)	4/27 (14.8)
Length of study months	16.8±8.7	16.2±7.9	23±10.4
Prospective design	26/27 (96.3)	23/23 (100)	3/4 (75)
Individuals enrolled	91 (148)	89 (131)	204.5 (75.5)
Studies enrolling immunocompromised patients	17/21 (81)	15/18 (83.3)	1/4 (25.0)
Studies enrolling HIV+ patients	14/21 (66.7)	13/15 (86.6)	1/4 (25.0)
Proportion of immunocompromised patients enrolled per study	28.3 (42.1)	30.8 (37.8)	NA
Immunocompromised patients enrolled per study	20 (38)	24 (39.5)	NA
Male:female ratio	2262:1559 (1.45:1)	1818:1167 (1.56:1)	444:392 (1.13:1)
Proportion of BCG immunised per study	53.8±25.3	42.1±19.9	74.2±21.4
Number of BCG immunised per study	62 (141)	27 (58)	201 (39.75)
Proportion of AFB smear positive patients	20 (41.6)	25 (45)	
Diagnostic assays			
T-SPOT.*TB*® and TST	11/27 (40.8)	10/23 (43.5)	1/4 (25.0)
QFT-G-IT and TST	4/27 (14.8)	3/23 (13.0)	1/4 (25.0)
T-SPOT.*TB*®, QFT-G-IT and TST	4/27 (14.8)	2/23 (8.7)	2/4 (50.0)
Others (IGRAs only)	8/27 (29.6)	8/23 (34.8)	

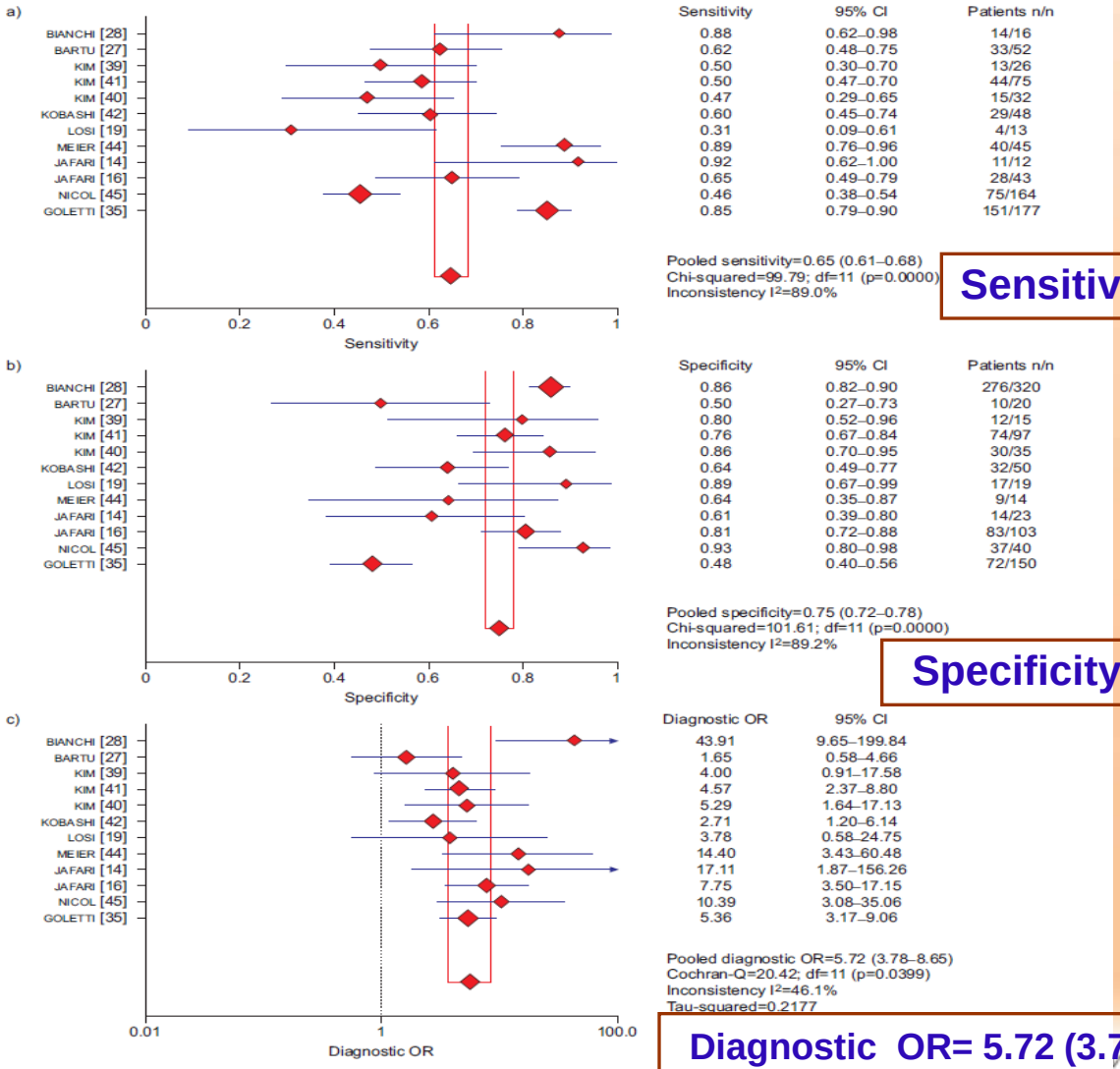
Data are presented as n/n total (%), mean±SD or median (interquartile range), unless otherwise stated. BCG: bacille Calmette–Guérin; AFB: acid fast bacilli; TST: tuberculin skin test; QFT-G-IT: QuantiFERON-TB® Gold in-tube; IGRA: interferon-γ release assay. #: 35 countries contributed to 27 studies.

Test characteristics 診斷工具的特性

- Sensitivity（敏感度）:
  - 有病者檢驗呈陽性的機率
- Specificity（特異性）:
  - 無病者檢驗呈陰性的機率
- Positive likelihood ratio（陽性相似比）:
  - 有病者/無病者 檢驗呈陽性的比率 LR+ = sens/(1-spec)
- Negative likelihood ratio（陰性相似比）:
  - 有病者/無病者 檢驗呈陰性的比率 LR- = (1-sens)/spec
- Positive predictive value (PPV)（陽性預測值）:
  - 測驗陽性者有病的機率 PPV. = P * Sen. / {P * Sen. + (1 - p)(1 - Spe.)}
- Negative predictive value (NPV)（陰性預測值）:
  - 測驗陰性者無病的機率 NPV. = (1 - P)Spe. / {P(1-Sen.) + (1 - P)Spe.}

Pre-test odds x Likelihood ratios = Post-test odds

Sensitivity, Specificity and OR of TST



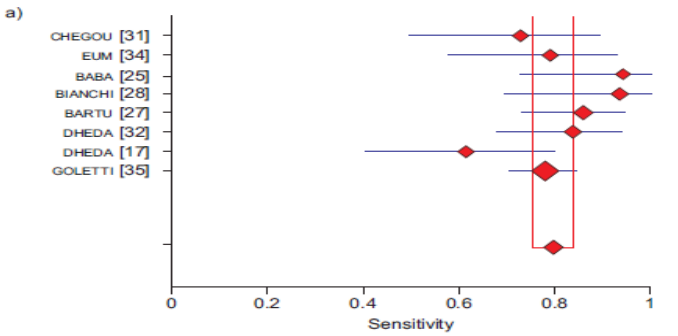
Sensitivity=0.65 (0.61-68)

Specificity=0.75(0.72-0.78)

Diagnostic OR= 5.72 (3.78-8.65)
PLR=2.6, NLR=0.47

FIGURE 2. Figure legend presented on following page.

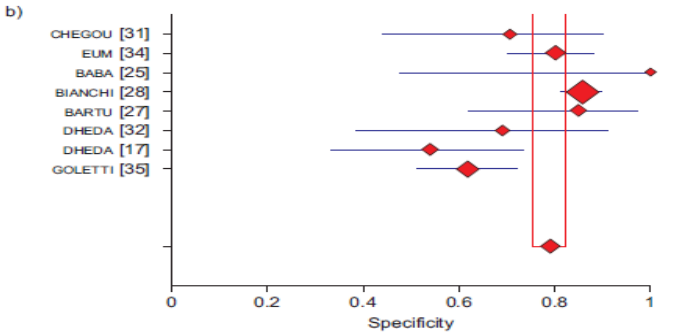
Sensitivity, Specificity and OR of QFT-G-IT



Sensitivity	95% CI	Patients n/n
0.73	0.50–0.89	16/22
0.79	0.58–0.93	19/24
0.94	0.73–1.00	17/18
0.94	0.70–1.00	15/16
0.86	0.73–0.94	43/50
0.84	0.68–0.94	31/37
0.62	0.41–0.80	16/26
0.78	0.71–0.84	121/155

Pooled sensitivity=0.80 (0.75–0.84)
Chi-squared=12.80; df=7 (p=0.0770)
Inconsistency I^2=45.3%

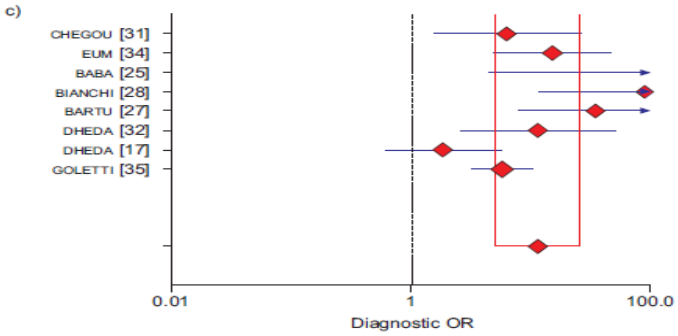
Sensitivity=0.80 (0.75-0.84)



Specificity	95% CI	Patients n/n
0.71	0.44–0.90	12/17
0.80	0.71–0.88	55/73
1.00	0.48–1.00	5/5
0.86	0.82–0.89	273/318
0.85	0.62–0.97	17/20
0.69	0.39–0.91	9/13
0.54	0.33–0.73	14/26
0.62	0.51–0.72	60/97

Pooled specificity=0.79 (0.75–0.82)
Chi-squared=37.10; df=7 (p=0.0000)
Inconsistency I^2=81.1%

Specificity=0.79(0.75-0.82)



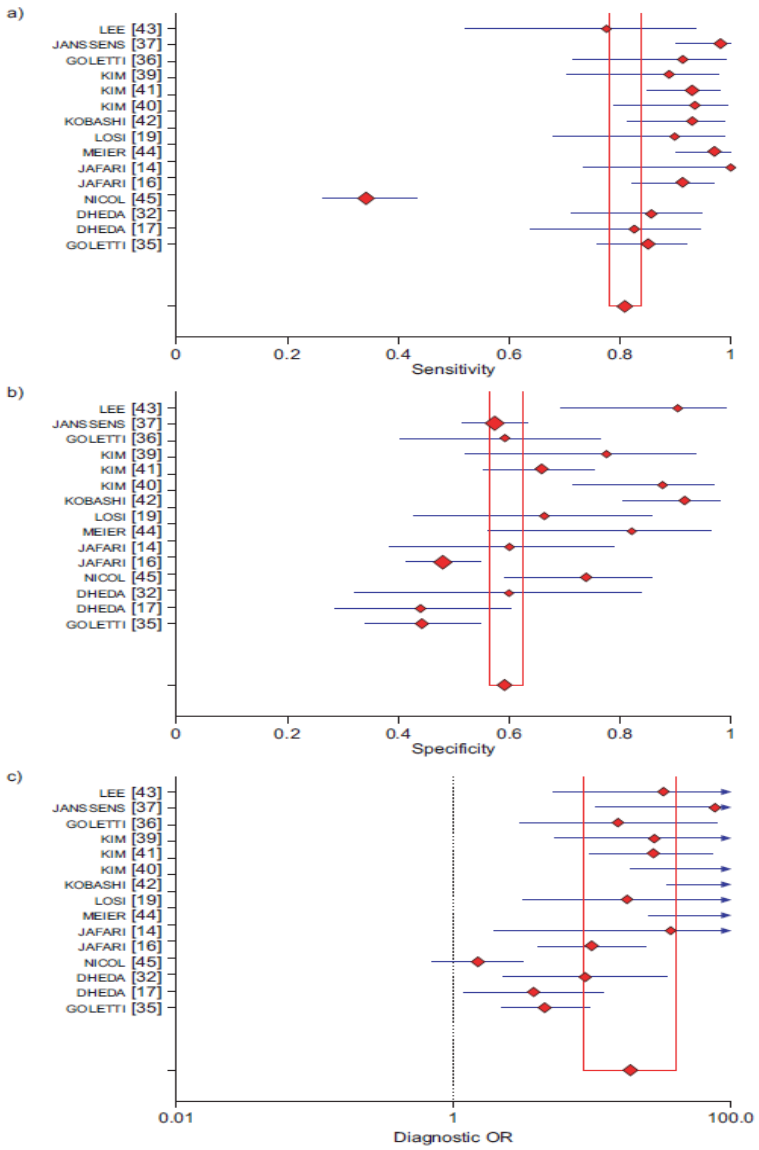
Diagnostic OR	95% CI
6.40	1.57–26.03
15.41	5.07–46.86
128.33	4.54–3624.88
91.00	11.73–705.93
34.81	8.05–150.56
11.63	2.68–50.40
1.87	0.62–5.63
5.77	3.30–10.09

Pooled diagnostic OR=11.47(5.12-25.69)
Cochran-Q=21.71; df=7 (p=0.0028)
Inconsistency I^2=67.8%
Tau-squared=0.8101

Diagnostic OR= 11.47(5.12-25.69)
PLR=3.81, NLR=0.25

FIGURE 3. Forest plots of sensitivity, specificity and diagnostic odds ratio of QuantiFERON-TB® Gold in-tube performed on blood samples. Data represent pooled values that were computed on all tuberculosis cases (culture-confirmed and non-confirmed cases) where data on both sensitivity and specificity were available (8 studies). If values were computed including all studies that have reported sensitivity (13 studies), pooled sensitivity was 77% (95% CI 75–80%; I^2=64.5%). df: degrees of freedom.

Sensitivity, Specificity and OR of T-SPOT TB



Sensitivity	95% CI	Patients n/n
0.78	0.52–0.94	14/18
0.98	0.91–1.00	57/58
0.91	0.72–0.99	24/27
0.89	0.71–0.98	24/27
0.93	0.85–0.98	70/75
0.94	0.79–0.99	30/32
0.93	0.82–0.99	42/45
0.90	0.68–0.99	18/20
0.97	0.90–1.00	70/72
1.00	0.74–1.00	12/12
0.92	0.83–0.97	65/71
0.35	0.27–0.43	46/133
0.86	0.71–0.95	36/42
0.83	0.64–0.94	24/29
0.85	0.76–0.92	75/88

Pooled sensitivity=0.81 (0.78–0.84)
Chi-squared=208.78; df=14 (p=0.0000)
Inconsistency I^2=93.3%

Sensitivity=0.81 (0.78-0.84)

Specificity	95% CI	Patients n/n
0.90	0.70–0.99	19/21
0.58	0.52–0.63	176/306
0.59	0.41–0.76	19/32
0.78	0.52–0.94	14/18
0.66	0.56–0.75	64/97
0.88	0.72–0.97	29/33
0.92	0.81–0.98	46/50
0.67	0.43–0.85	14/21
0.82	0.57–0.96	14/17
0.60	0.39–0.79	15/25
0.48	0.42–0.55	118/245
0.74	0.60–0.85	37/50
0.60	0.32–0.84	9/15
0.44	0.29–0.60	19/43
0.44	0.34–0.55	43/97

Pooled specificity=0.59 (0.56–0.62)
Chi-squared=90.27; df=14 (p=0.0000)
Inconsistency I^2=84.5%

Specificity=0.59(0.56-0.62)

Diagnostic OR	95% CI
33.25	5.32–207.77
77.17	10.55–564.56
15.35	3.06–76.99
28.00	5.45–143.72
27.15	9.996–73.79
108.75	18.48–640.03
161.00	34.03–761.81
18.00	3.22–100.49
163.33	24.95–1069.30
36.90	1.96–693.39
10.07	4.20–24.10
1.50	0.73–3.11
9.00	2.34–34.61
3.80	1.22–11.83
4.59	2.25–9.36

Pooled diagnostic OR=18.86 (8.72–40.77)
Cochran-Q=74.44; df=14 (p=0.0000)
Inconsistency I^2=81.2%
Tau-squared=1.7259

Diagnostic OR= 18.86 (8.72-40.77)
PLR=1.96, NLR=0.32

FIGURE 4. Figure legend presented on following page.

Were the included studies sufficiently valid for the type of question asked

選擇的文獻有效回答所問的問題?

■是	□ 否	□ 不清楚

評論：

◆IGRAs had a higher sensitivity and lower negative likelihood ratio than TST markers.

(LR+ ≧4 valuable, ≧10 good; LR- ≦0.6 useful, ≦0.1 good.)

	sensitivity	specificity	PLR	NLR
TST	0.65	0.75	2.6	0.47
QFT	0.80	0.79	3.81	0.25
T-SPOT	0.81	0.59	1.96	0.32

Were the included studies sufficiently valid for the type of question asked
選擇的文獻有效回答所問的問題?

■是	□ 否	□ 不清楚

評論：

- Diagnostic sensitivities of IGRAs were higher than TST but NOT high enough to use as a rule out test for TB.
- Low specificity may indicate limited value of IGRAs to distinguish latent M. TB infection form active TB.

Were the results similar from study to study
各研究的結果相似?

☐是	■ 否	☐不清楚

評論：

The heterogeneity and inconsistency between some studies in this analysis is significant.

Conclusions

- Diagnostic sensitivities of IGRAs were not high enough to use as a rule out test for TB.
- Low specificity may indicate limited value of IGRAs to distinguish latent M. TB infection form active TB.

Evidence-based Medicine 2011 Levels of Evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

EBM的步驟

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上

應用到臨床上

- 和TST相比, IGRAs不易受BCG 或NTM干擾, 且有較高的靈敏度.
- 但IGRAs無法區別LTBI 和active TB, 因此目前多用於LTBI的偵測.
- IGRAs特異性較低, 所以仍無法當作active TB的確診工具.
- 醫療成本的考量: 經本院評估, 進行一次IGRA約需新台幣5000~6000元(含儀器耗材成本和人員操作費用), 明顯高於NAA (PCR)的方法.

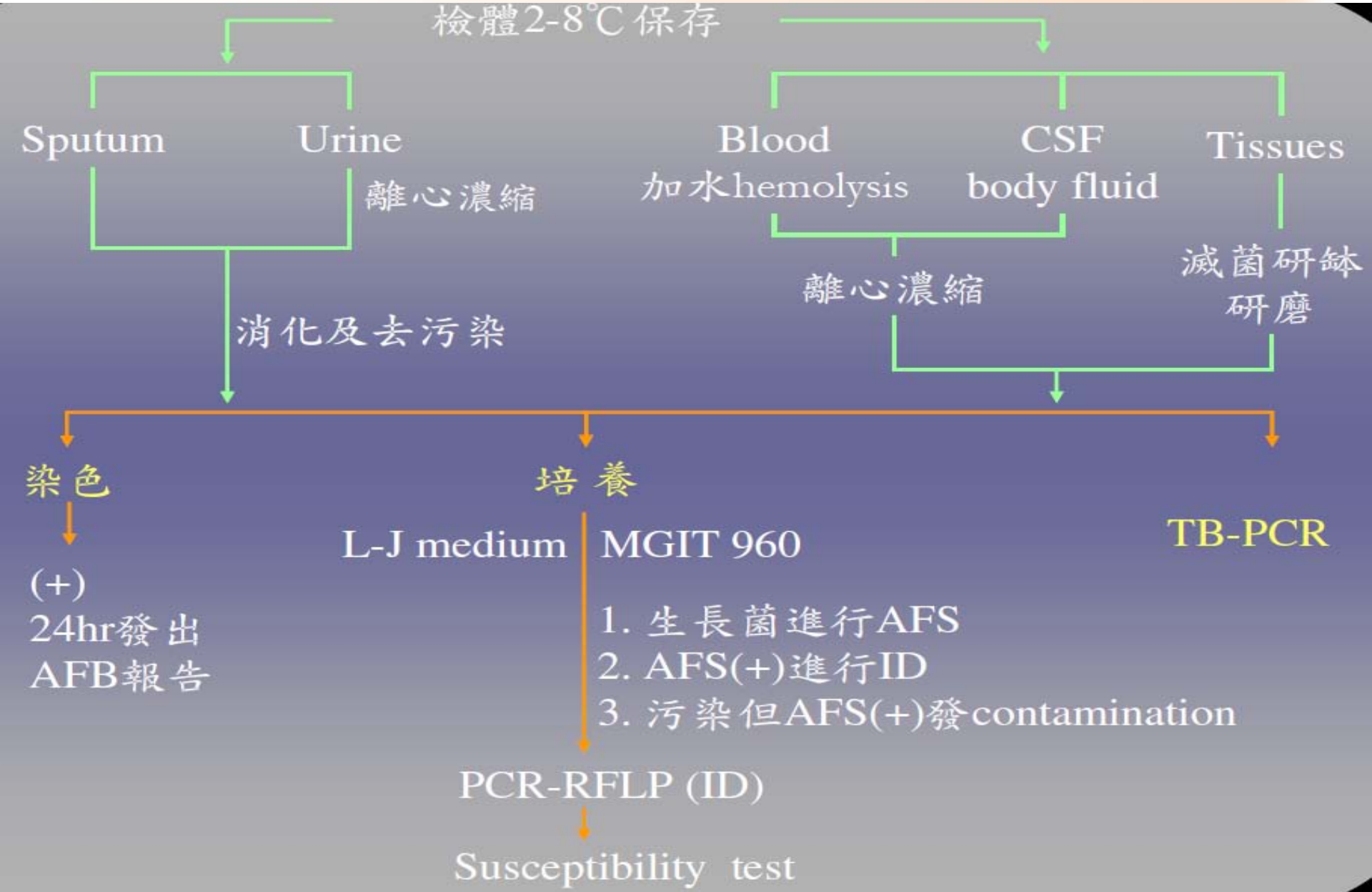
Grades of Recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	level 4 studies ***or*** extrapolations from level 2 or 3 studies
D	level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

謝謝聆聽

高雄醫學大學附設中和紀念醫院
Chung Ho Memorial Hospital Kaohsiung Medical University

檢驗部TB檢驗流程



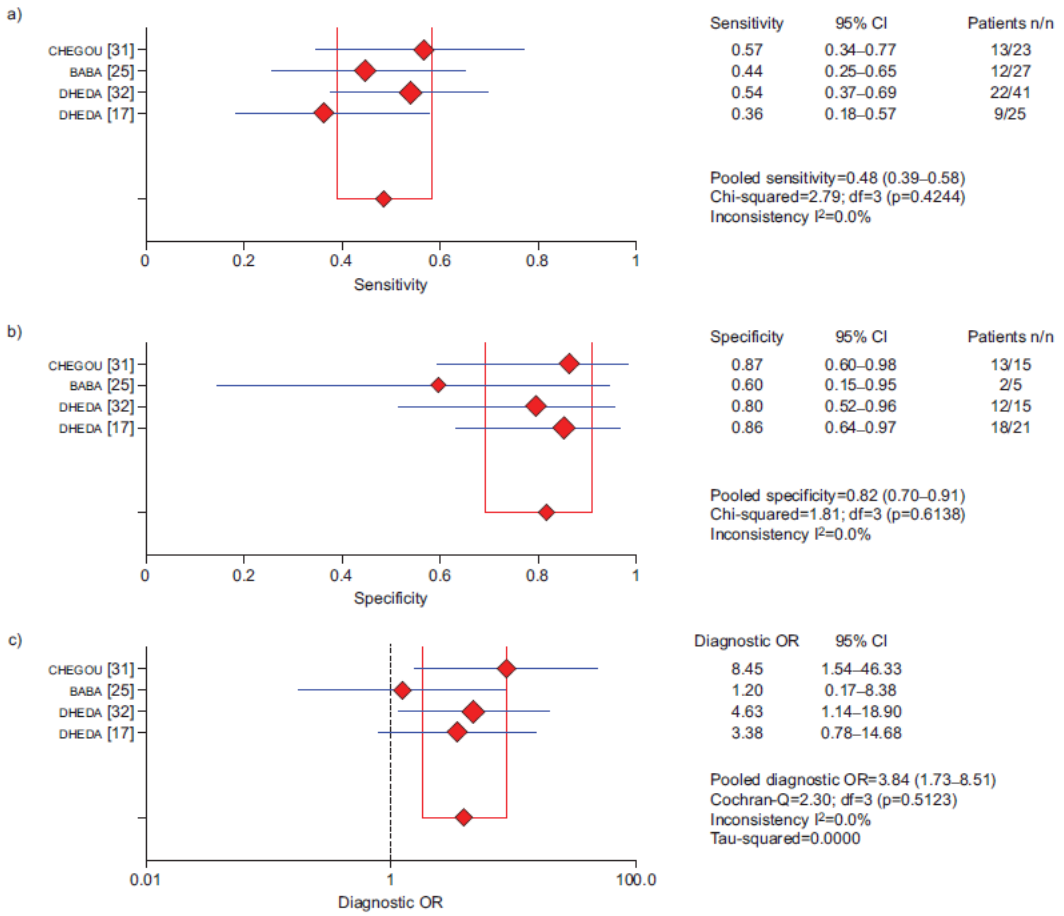


FIGURE 5. Forest plots of sensitivity, specificity and diagnostic odds ratio of QuantiFERON-TB® Gold in-tube performed on extrasanguinous samples. Sensitivity data represent pooled values that were computed on all tuberculosis cases (culture-confirmed and non-confirmed cases). All studies reported data on both sensitivity and specificity. df: degrees of freedom.

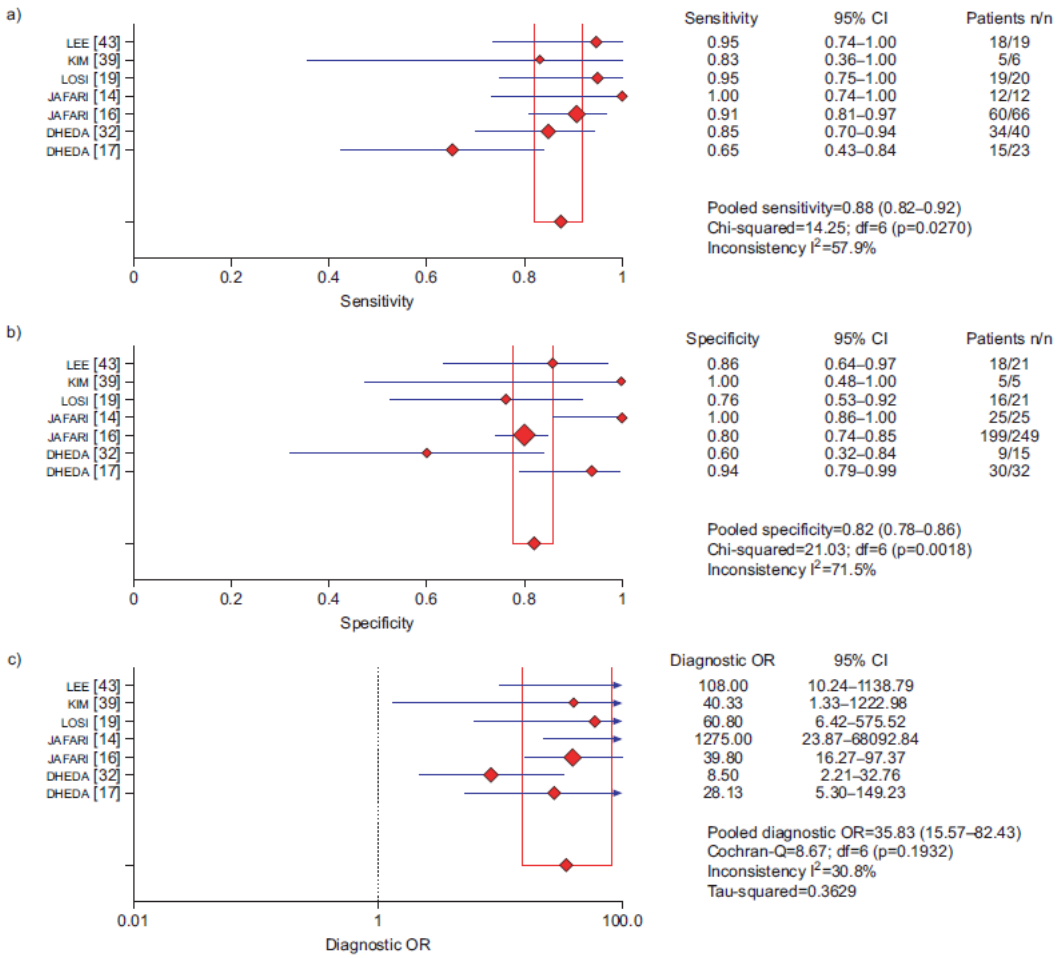
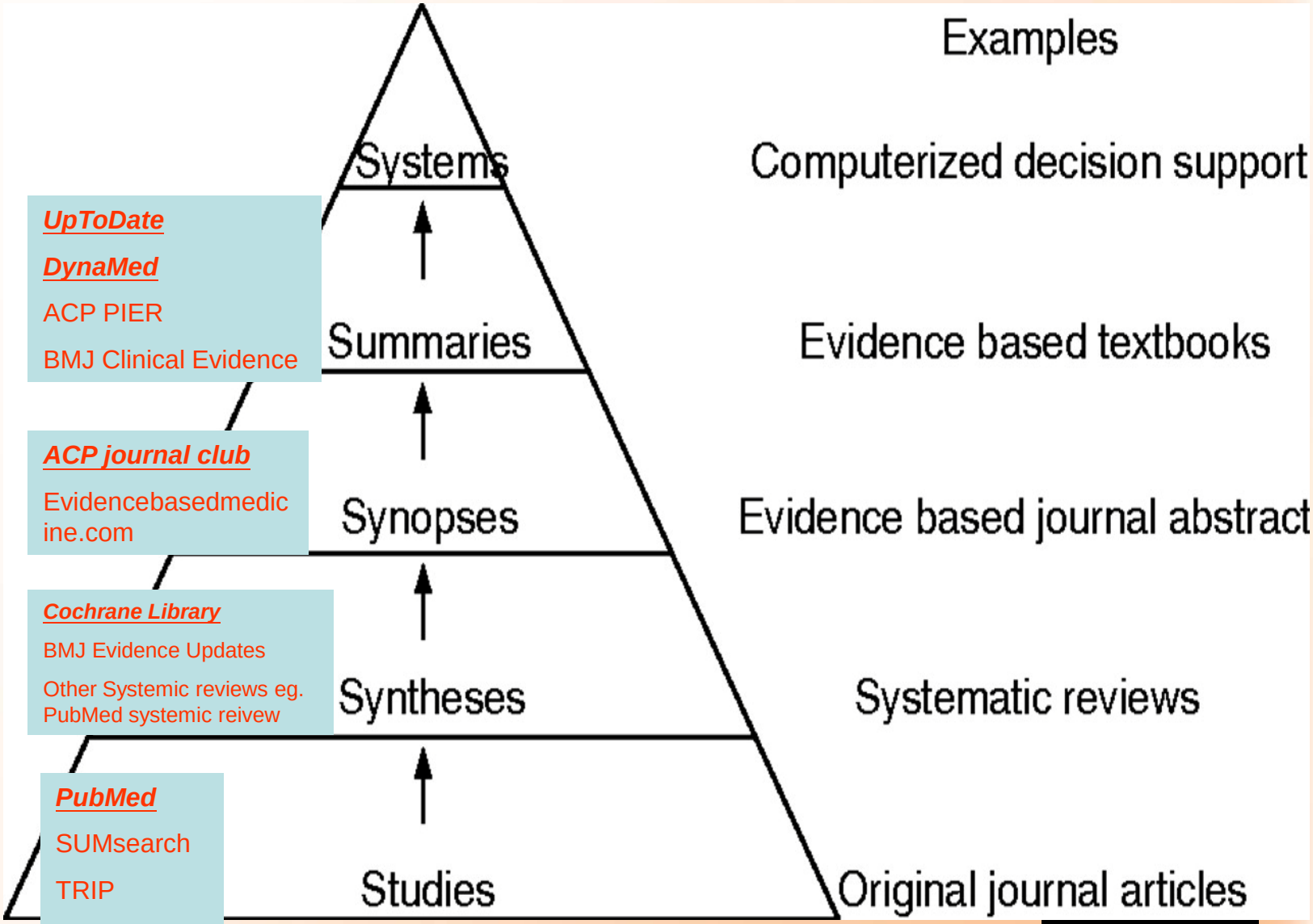


FIGURE 6. Forest plots of sensitivity, specificity and diagnostic odds ratio of T-SPOT.*TB*® performed on extrasanguinous samples. Sensitivity data represent pooled values that were computed on all tuberculosis cases (culture-confirmed and non-confirmed cases). All studies reported data on both sensitivity and specificity. df: degrees of freedom.

The "5S" levels of organisation of evidence from healthcare research

Brian Haynes, R Evid Based Med 2006;11:162-164



Potential actions while waiting for tuberculosis culture result

Potential actions while waiting for tuberculosis culture result

Potential action	NAA results	High clinical suspicion of tuberculosis				Low clinical suspicion of tuberculosis			
		AFB smear (+)		AFB smear (-)		AFB smear (+)		AFB smear (-)	
		Action without NAA results	Action with NAA results	Action without NAA results	Action with NAA results	Action without NAA results	Action with NAA results	Action without NAA results	Action with NAA results
Treat	(+)	Yes	Yes	Yes	Yes	Yes	Yes	No	?
Isolate	(+)	Yes	Yes	Yes	Yes	Yes	Yes	No	?
Begin contact investigation	(+)	Yes	Yes	No	Yes	Yes	Yes	No	No
Treat	(-)	Yes	?	Yes	?	Yes	No	No	No
Isolate	(-)	Yes	?	Yes	No	Yes	No	No	No
Begin contact investigation	(-)	Yes	No	No	No	Yes	No	No	No

Adapted from Catanzaro, A, Davidson, BL, Fujiwara, PI, et al, Am J Respir Crit Care Med 1997; 155:1804.

Tuberculosis direct amplified tests in AFB smear-positive versus smear-negative patients

Tuberculosis direct amplified tests in AFB smear-positive versus smear-negative patients

	Overall, percent	Smear-positive, percent	Smear-negative, percent
Sensitivity	77/80*	95/96*	48/53*
Specificity	96/99*	100•	96/99*
PPV	57/85*	100•	24/58*
NPV	99•	86/90*	99•

PPV: positive predictive value; NPV: negative predictive value.
* All numbers represent percentages. When two numbers are given for a particular entry, they represent the percentages obtained from the two types of direct amplification tests. For some results, the Gen-Probe assay had the higher value and for others, the Roche assay was higher. The table does not identify which values are associated with either assay. The wide differences shown in the table for positive predictive value in the overall and smear-negative columns cannot be used to infer that one of the tests was superior, both because the two tests were studied on different samples and because the confidence intervals for the results would overlap. If one manufacturer sought to claim superior performance for its test, that claim would have to be based on results from a controlled, head-to-head clinical trial.
• Single values indicate the two assays had the same value.

Results from Searching: Summaries

UpToDate ONLINE

Database	UpToDate
Title of article	Interferon-gamma release assays for latent tuberculosis infection
Content	IGRAs cannot distinguish between latent infection and active TB disease, and should not be used for diagnosis of active TB in adults.