出國報告（出國類別：開會）

赴巴黎參加 2023 年國際抗癆聯盟世界年會「54th Union World Conference on Lung Health」

服務機關：衛生福利部疾病管制署
姓名職稱：詹珮君 副組長
李品慧 防疫醫師
陳人睿 科員

派赴國家：法國
出國期間：**2023.11.13 ~11.20**
報告日期：**2024.01.24**

目次

壹、摘要

第 54 屆國際抗癆暨肺部健康聯盟世界年會大會的主題為「Transforming evidence into practice」將實證數據轉化為實務執行成果。本次 TB Science 不再像 2019 年以會前會方式進行，整合至大會議程同步進行。我國研究者於本次大會共發表 15 篇論文，包括臺灣利用全基因定序對抗藥性結核病不論是在國家的層級或者縣市地區的分析、雲端都治如何 COVID-19 期間升級、長照機構的長者潛伏結核感染治療的推動，以及在非愛滋結核病接觸者的 1HP 成果等也受到關注及討論。疫苗 GSK 疫苗 M72/AS01$_E$ 於 COVID-19 疫情後由比爾蓋茲基金會投資，去年進入臨床 3 期收案，尚待結果分享。而世界衛生組織今年持續與大會合作，有多個會場針對最新技術提供指引，包括新款不受 BCG 干擾的皮膚結核菌素測試(Cy TST，印度血清中心製造)實際應用與挑戰，全年齡層接觸者及高風險族群預防性投藥，多款短程處方的推廣，TB science 也針對 non-sputum based (例如：舌頭拭子採檢，糞便 Xpert 檢驗)，AI 在胸部 X 光影像辨識等診斷工具進化，進行分享與討論。同時也為 2023 年 UNHLM (聯合國 high level meeting) 共識會議後，為達到 2027 年 UNHLM 績效目標，繼續努力。

貳、背景

國際抗癆聯盟成立於 1920 年，1995 年更名為國際抗癆及肺部健康聯盟，近 3 年 COVID-19 的疫情衝擊，辦公室已緊縮編制。高峰時期約有近 3,000 名會員組成，來自 118 個國家臨床醫師、公衛管理政策制訂者、科學家、相關領域學者與第一線臨床醫療公衛工作人員等，是一個分有四個科學部門，全球共 14 間辦公室的非營利組織，主要任務在解決中、低收入國家所面臨之主要健康問題及挑戰，包括：結核病、愛滋感染、成人及兒童肺病、菸害控制及空氣汙染等。2035 年消除結核病：達到每 10 萬人口 10 人之發生率為全球目標，我國目前亦跟隨全球腳步，致力推行各項結核病防治工作，近年來國內不論在結核病發生率或死亡率上，雖有逐年下降的趨勢，但仍面臨諸多防治的挑戰。根據 WHO 2015 年後全球結核病防治策略指出新疫苗之研發及引進，係達成 2035 年消除結核病之重要關鍵，故藉由參加 2023 年國際抗癆及肺部健康聯盟世界年會，從中了解各國研發結核病疫苗之策略及進展，科技導入策略及實務運用經驗，作為我國將新疫苗、新藥物與技術工具納入國家預防結核病策略之依據。

參、目的

1. 了解研發結核病疫苗以及新診斷工具和藥物之新進展。
2. 本署同仁完成海報及口頭論文共 3 篇分享，並瞭解第一手的結核病相關之公共衛生政策及政策研究發展情況。
3. 後疫情時代，加強全球合作夥伴關係，且完成 2024 年 external review panel 的邀請。

肆、過程

一、行程表：本次會議之過程摘要如下表：

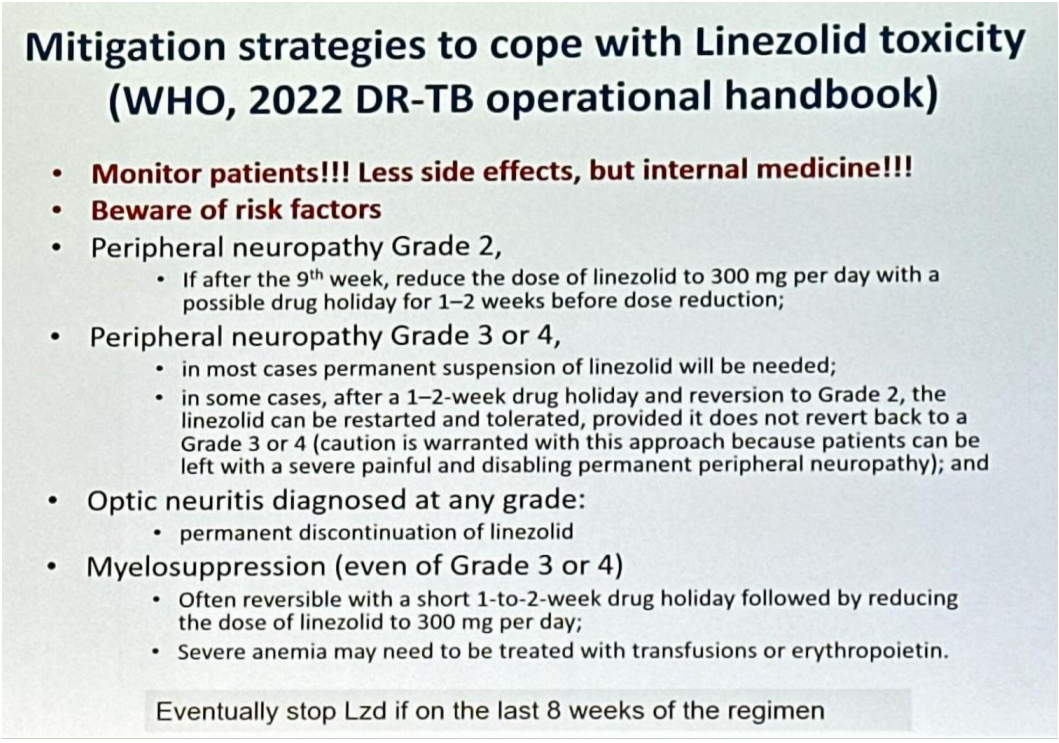
日期	行程及會議內容	重點報告	Special Events
2023/11/13	出發於杜拜轉機	-	-
2023/11/14	抵達巴黎	Workshops & Post-graduate Course	-
2023/11/15	Opening & Inaugural session	署內 2 篇(OA, SOA 報告)	Working groups (WG)
2023/11/16	Plenary/Symposia/poster discussion/E-poster/oral abstract presentation/short oral presentation/ Meet the Expert	本日有不同主題的 symposia; 署內 1 篇(e-poster)	
2023/11/17	Plenary/Symposia/poster discussion/E-poster/oral abstract presentation/short oral presentation/ Meet the Expert	本日有不同主題的 symposia	Side meetings: section & sub-section meetings / WG/ Satellite session (SS)
2023/11/18	Plenary/Symposia/poster discussion/E-poster/oral abstract presentation/short oral presentation/ Meet the Expert	本日有不同主題的 symposia	Rapporteur Closing Session
2023/11/19-20	出發->抵達台灣	-	-

二、重要會議內容摘要：

2023/11/14

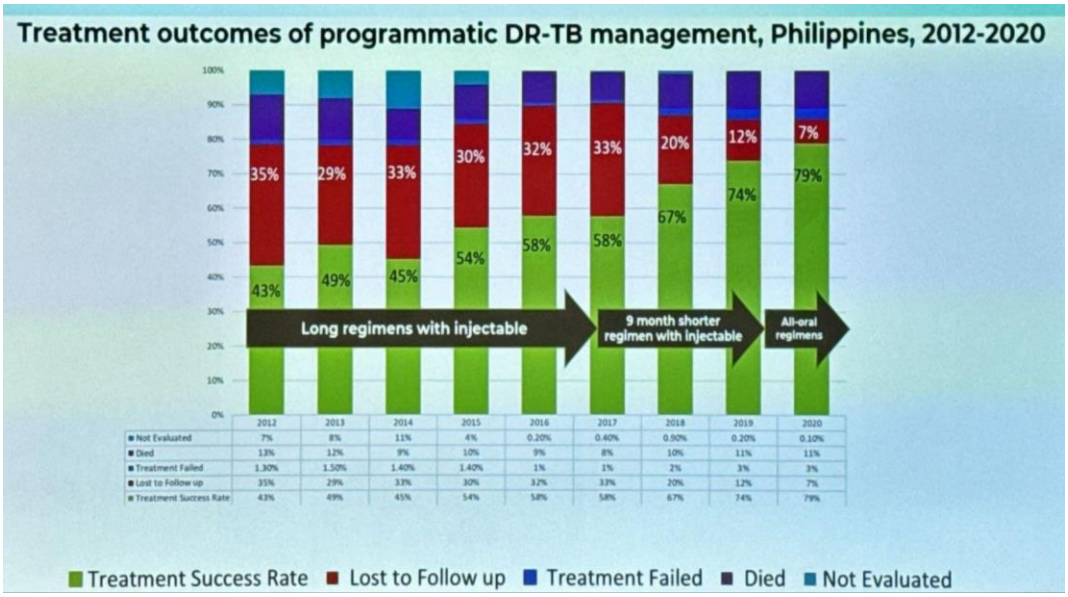
WS-07 Joint GLI-GDI workshop: using BPaL/M, diagnostic and treatment aspects

抵達巴黎後，直奔 Palais des Congrès 參加的第一個講堂。由於 WHO 在 2022 DR-TB 治療指引已建議可針對 RR/MDR-TB 病人使用 BPaLM 6-9 個月短程處方，若為 Pre-XDR 病人或無法耐受 MDR-TB 處方則建議使用 BPaL 處方，因此大會特別安排 Pre-conference workshop 介紹使用 BPaL 處方的臨床注意事項和和公衛推動經驗分享。由於處方中有 Linezolid，因此要特別注意該藥物的副作用監測，當出現周邊神經病變(grade 2)或貧血等骨髓抑制(grade 3-4)時，需先停藥 1-2 週再考慮給予較低劑量的 Linezolid (300mg/day)，但若出現視神經炎則不分嚴重程度須永久停藥。



菲律賓一直是抗藥結核病的高負擔國家，過去在長程 RR/MDR-TB 處方使用時其治療成功率低於 6 成，並伴隨著 3 成左右的病人失落，從引入短程含針劑 6-9 個月處方則治療成功逐步進步到 74%，改為全口服處方則進一步治療成

功率提升到 79%，失落率大幅下降到 7%。講者分享了 99 位病人使用 BPaL 處方的治療經驗，其中 41%是 Pre-XDR，75%的病人有開洞病灶，8%合併 HIV 感染，治療成功率達 98%，在治療結束後 6 個月追蹤發現持續治療成功的比例也達 90%。在治療的過程中，76%的病人在療程初期 1 個月就有 76%達到培養陰轉；89%的病人在 2 個月達培養陰轉，因此這個處方確實能大幅降低病人在社區傳播抗藥結核的機會。安全性監測方面比較需要注意的是菲律賓發現有 61%的病人出現任一程度等級的肝毒性，但出現肝毒性 AESIs (Adverse Events of Specific Interest) 事件有將近 3%是 grade 3 以上；任一程度等級之周邊神經病變則達 60%，其中 37%的周邊神經病變 AESIs 嚴重程度達 grade 3 以上，因此，約有 6 成的個案需調整 Linezolid 的使用劑量或治療時間。2023 年 Q4 菲律賓則著力於使用此處方的人員訓練和各項配套來進一步做全國推廣。



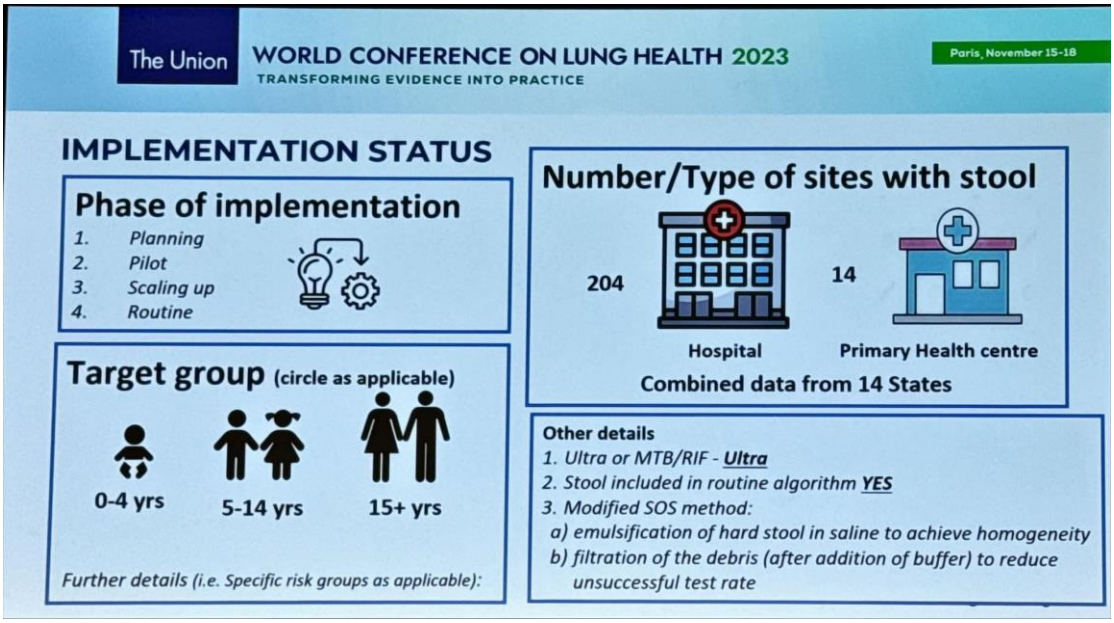
WS-03 Introduction and scale up of stool-based testing-sharing country results and practical lesson learned

SOS(Simple One-Step)方法：糞便前處理後進行 GeneXpert，以利增加兒童細菌學確診結核病的比例，將兒童糞便經過 SOS 步驟的處理並且 pilot 檢視沒問題後，用一般醫院就有的 GeneXpert 上機，增加 10%-20%不等的兒童結核病診斷。儘管 KNCV 在 COVID-19 疫情前就已經在發展 SOS 方法，但實際推廣跟真

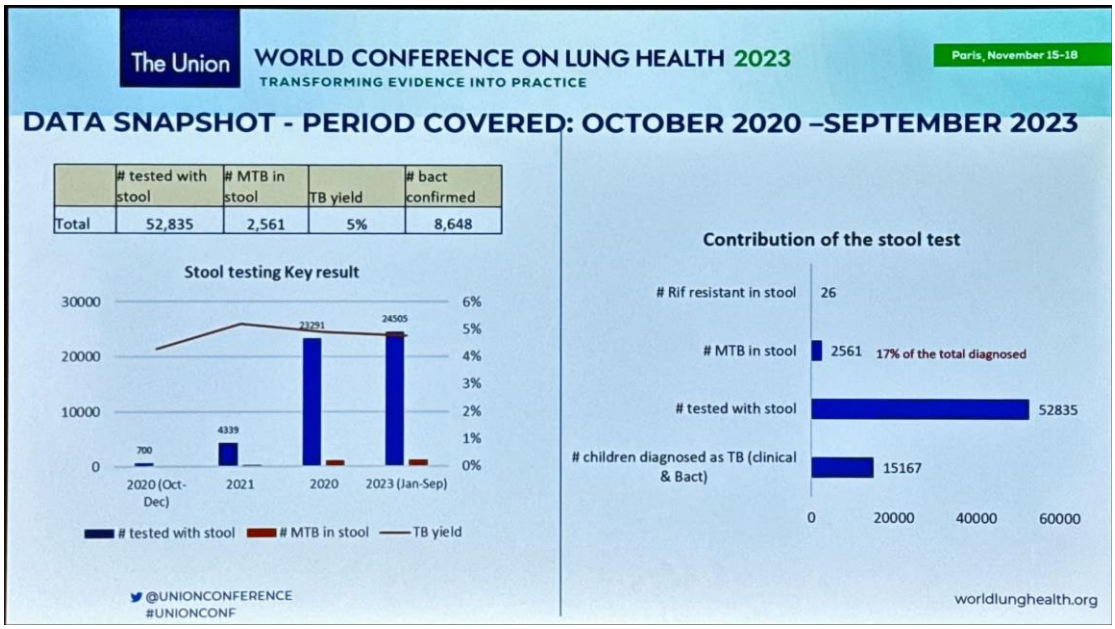
正能協助兒童結核病的診斷，還有頗長的一段路要走。在臺灣，5 歲以下的兒童疑似結核病人數一年不超過 10 位，雖然 2023 年已提供科技計畫資源協助臨床實驗室引進 SOS 前處理方法，但從過去 1 年之執行成果來看，並未成功地利用此技術來協助兒童個案完成結核病診斷。

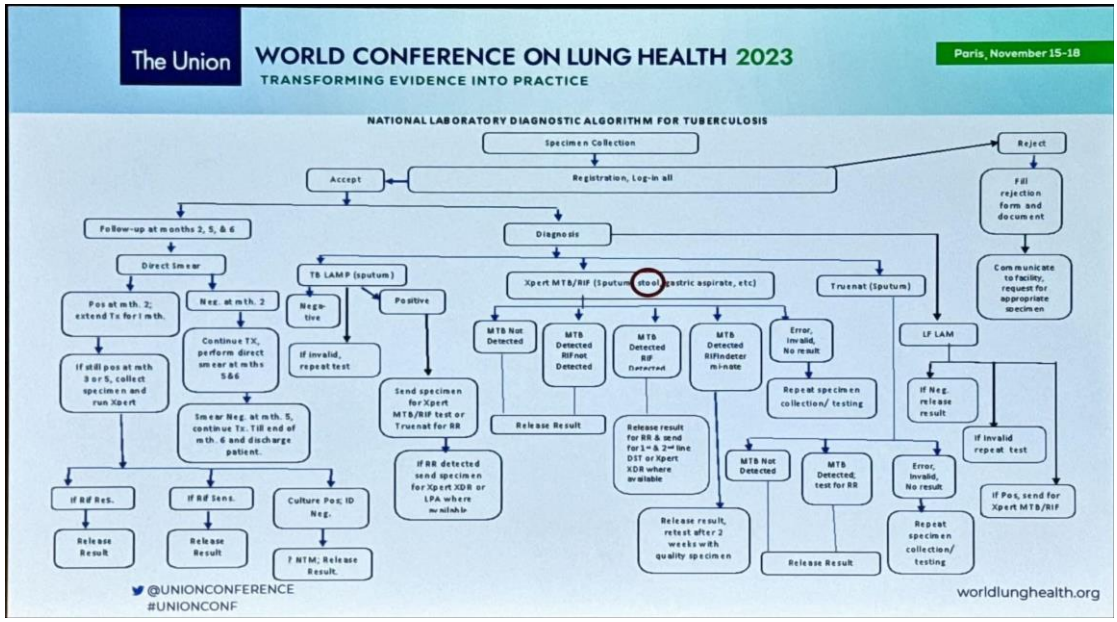
而這次 workshop，KNCV 及 USAID 等單位顯然也在過去幾年發現這個問題，故邀集各國分享推廣的經驗與挑戰，非洲諸國透過支持已陸續展開。在沒有實質證據的情況下，很難說服家屬，所以，最常見的應用，反而是拿來說服已經發病的孩子接受治療。與會分享的國家如 Ethiopia、Tanzania、Kyrgyzstan、Zimbabwe 及 Nigeria 等，運用共同的簡報模版，就推展此診斷技術至醫療機構及公衛健康中心之歷程、運用方式、使用時機及協助額外確診的量有多少，一一分享。

以下以 Nigeria 為例 (Nigeria 也是整場會議最會 campaign 自己國家，並且非常擅長獲取國外資源)：Nigeria 已推廣至 204 家醫院和 14 個衛生所(照片為各國簡介 Implementation Status 之簡報模版)，目前，這個檢驗已經納入 Nigeria 的國家指引。

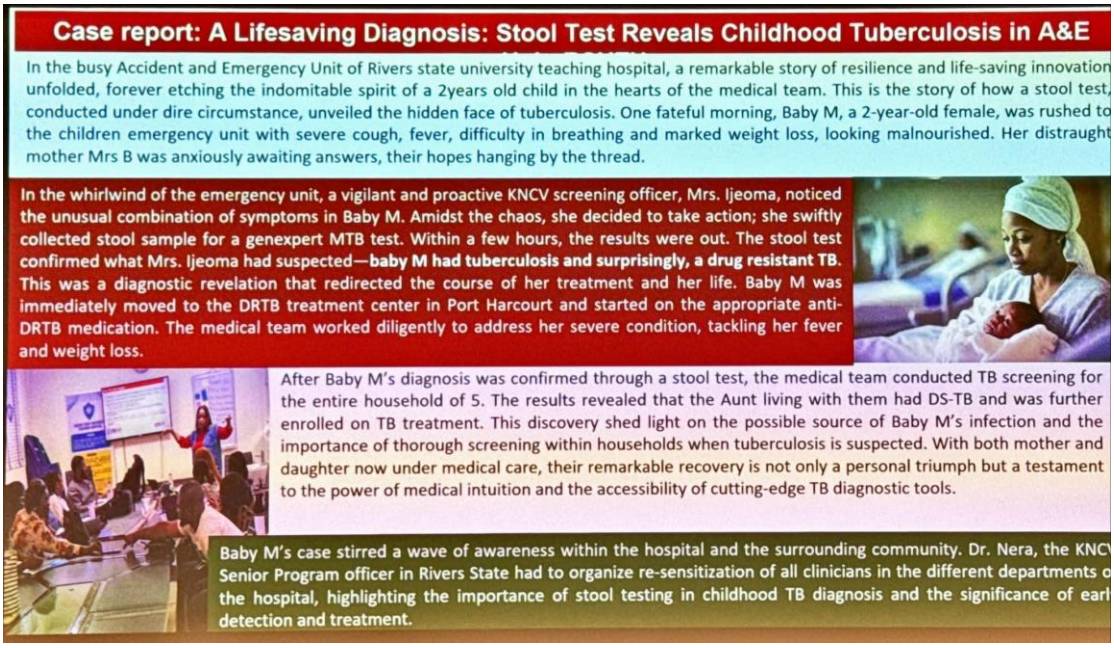


這段時間蒐集到的檢體，光 2023 年(統計截至 9 月)就篩檢了 2 萬多個檢體，最後有 2,561 位的糞便檢體被檢驗出 MTBC 菌，占了診斷確診 TB 的兒童(15,167 位)之 17%，比例相當高。

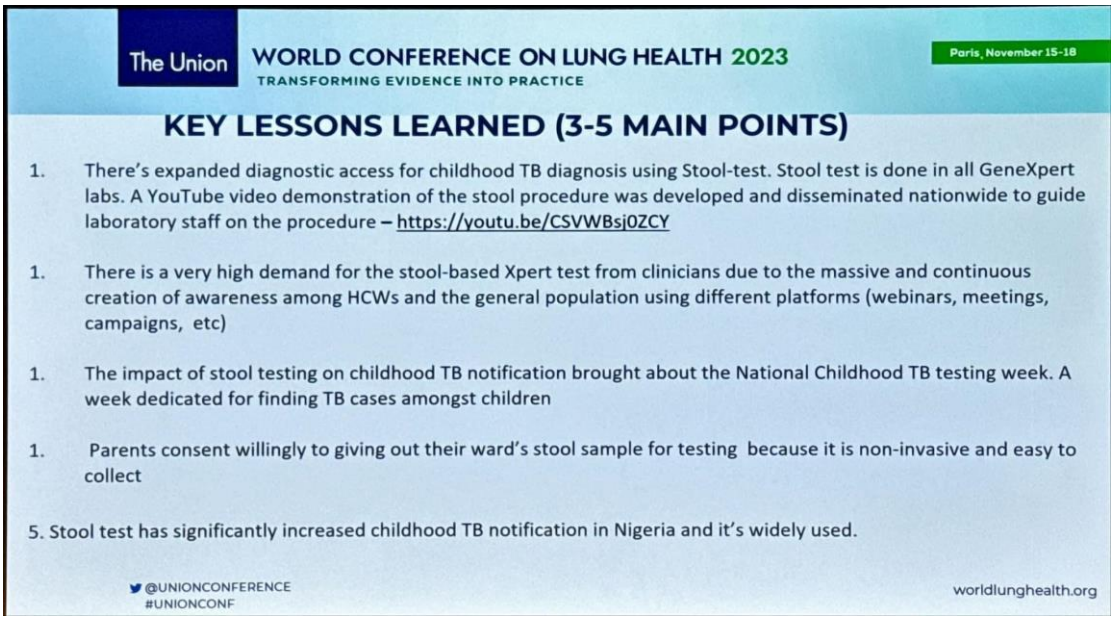




報告並提到有個 2 歲孩子案例，透過糞便的 SOS 前處理及 GeneXpert 診斷，進而發現家中的阿姨是病人，得以同時治療傳染源及 2 歲的兒童結核病人。



Nigeria 透過 YouTube 平台，將教育訓練廣為宣導，所以該國各大實驗室只要有 Xpert 儀器，皆可執行糞便前處理，也是本次報告中，執行得最為徹底的國家。技術推廣更關鍵的是，醫師必須了解這個檢驗項目，並且開出 order，故持續進行醫師的教育訓練是很重要的。



後續不一一貼出其他國家 slide 內容，統整常見的挑戰包括如下：

1. 如果可執行的實驗室不夠多，可考慮轉介檢體，也是一種可以減少診斷障礙的策略。

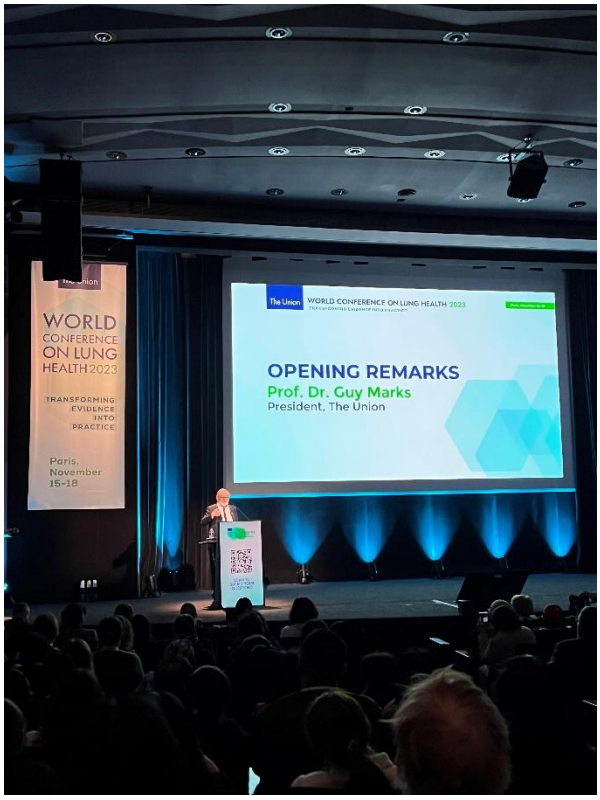
2. 因為 Xpert XDR 儀器設計為 10-color module，所以未來需要更多的 operational research 提供臨床應用的參考數據。

3. 要系統性地要求送驗和通報綁在一起，才會有利於後續的監測和接觸者檢查。

4. 檢驗的結果應能常規在 medical information system 正式發報告，以利追蹤。

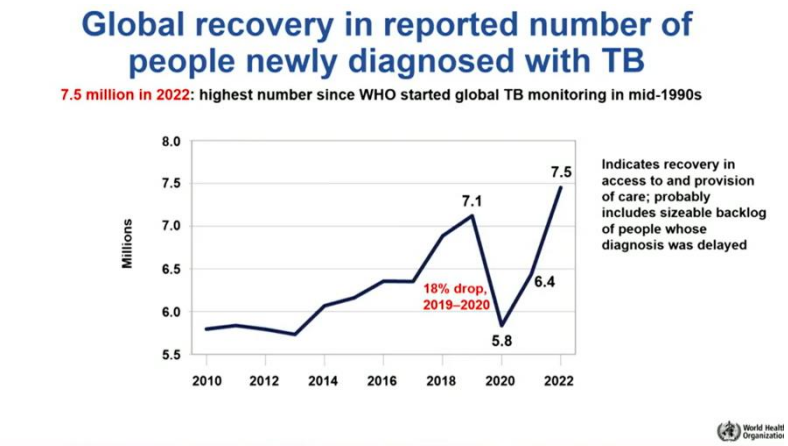
2023/11/15

Opening session & global end TB symposium 2023

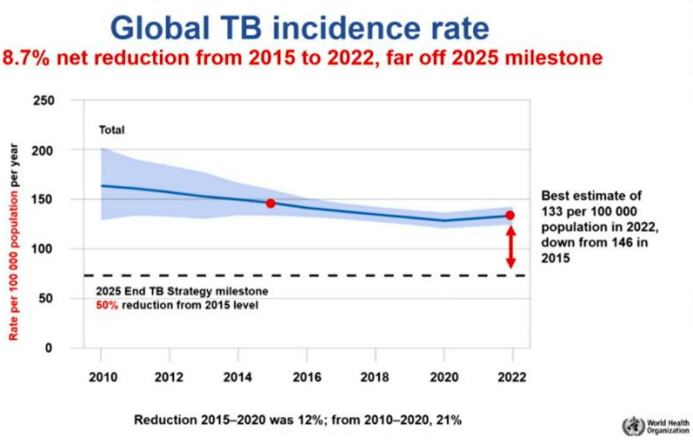


11/15 一早，TB Survivor-Rhea Lobo 上台詢問現場與會者：Can you believe after 4 long years, please thank you all are here.後大會正式起跑，Opening Session 的大禮堂場地不大，不少人站著聆聽各個重量級人物的歡迎致詞，包括 The Union 主席 Professor Guy Marks：It is wonderful to bring Union family together here in person. 歷經 COVID-19 超過三年的奮戰，大家終於回到巴黎，舉辦實體年會，也驚訝於今年是歷屆投稿件數最多的一年，大會為了審查篩選與議程安排花了不少心力，勉勵大家持續掌握各種新藥、技術及疫苗的進展，將研究數據納入政策執行，繼續堅定地往消除結核的目標前進。

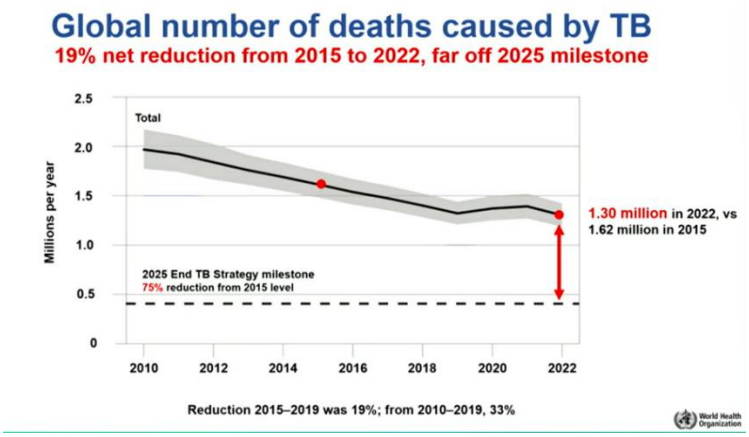
按照慣例，大會 Opening 後，隨即是最新發表之全球結核病報告 Global Tuberculosis Report。本年依然由非常有魅力之 WHO Global Tuberculosis Programme(GTB)「Tuberculosis monitoring, evaluation and strategic information」部門其 Unit Head，Katherine Floyd，用神似菸嗓又略為慵懶的聲音向大家報告 2022 年最新現況、192 國或各分區流行病學發展趨勢。

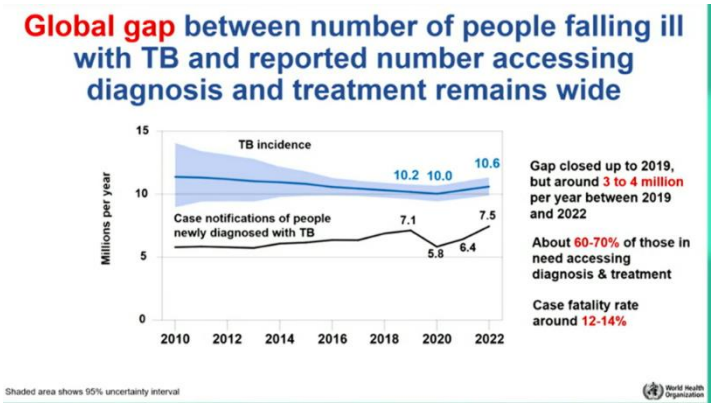


整體來說，全球歷經 2 年 COVID-19 後，2022 年 TB 新案數終於從 2020 年 580 萬人上升至 750 萬人，可視為 TB 醫療照護服務量能復甦回穩，部分 TB 延遲診斷案例慢慢回流，故發生率略為上升，但推測可能在 2023 或 2024 下降。2022 全球 TB 新案人數最多前三名之國家為：印度(27%)、印尼(10%)及中國大陸(7%)。死亡人數也不再劇烈增加。儘管如此，TB 仍為全球致命死因第二位，僅次於 COVID-19，也無法達成 UN high-level meeting 2018-2022 與 End TB Strategy 設定的目標。



End TB Strategy 2025 milestone 為 TB 發生率應達 2015 年 50%之降幅，全球目前僅 8.7%，仍有好長一段距離；但以國家層次來看，目前 87 個國家已達超過 20%降幅；同樣的，死亡數 2025 milestone 應達 2015 年 75%之降幅，目前僅 15%，就國家層次來看，47 個國家已達超過 35%降幅。





如想達到 2025 milestones，則2025年以前必須每年下降 10%，致死率降低 6.5%，而這需要確保每個人都得到最妥適照護與標準處方治療。值得關注的是，TB 經通報診斷人數與實際感染發病的人數的落差受COVID-19大流行影響而驟增，雖然逐年縮小，但仍持續存在 300-400 萬人之落差。

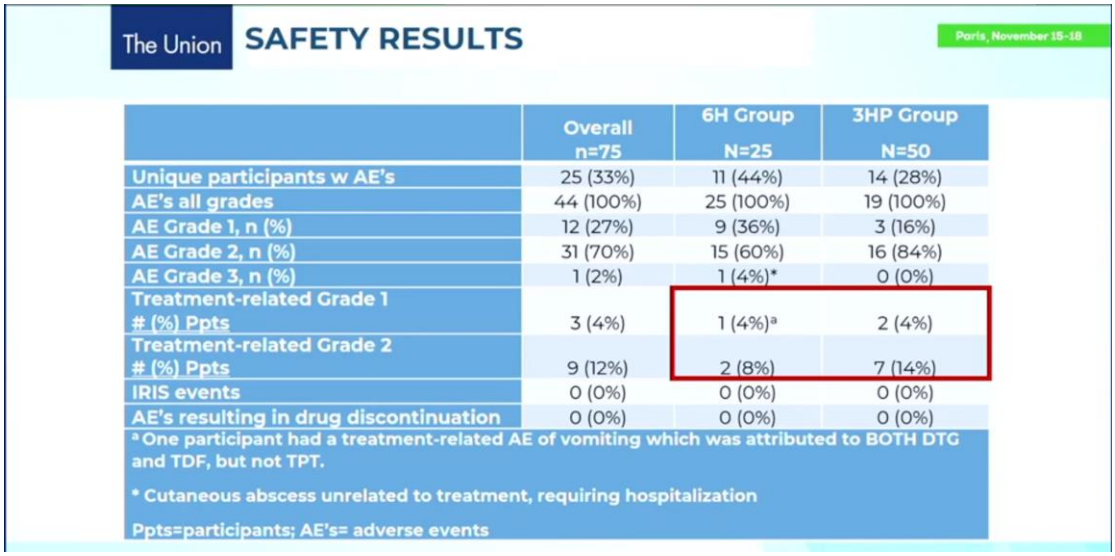
檢視 UN high-level meeting 的目標，2018-2022 應有 4,000 萬人接受治療，現有 3,400 萬人，達成率 84%，但 49%TB 個案及家庭支出在治療過程中面臨災難性負擔，幾乎所有高負擔國家皆無法達到 Universal Health Coverage。但慶幸的是治療成功率以及快速分子檢測服務覆蓋率已逐年提升。

目標之二，2018-2022 目標應有 3,000 萬人接受 TB 感染預防性治療，現完成 1,550 萬人，達成率 52%，但 people living with HIV 族群已完成 1,130 萬人，遠超過目標數 600 萬人。2022 年接受預防性治療的人數已大於 2019 年，尤其發病風險高的家戶內接觸者顯著增加。

如要持續推進 End TB Strategy 目標，TB 診斷、治療及預防等相關必要的服務就必須穩定提供，但整體預算仍少於 2019 年將近 10%，且全球估計五大 TB 決定因子中，以營養不良最為嚴重，在在顯示資源缺乏問題嚴重。儘管研究經費不足，但最新檢驗技術、藥物及疫苗依然持續推進，接續幾天的議程也將逐一討論。

LB01-100-15 DOLPHIN TOO: 3HP for TPT in ART-naive PLHIV with HIV initiating DTG-based ART: a phase I/II study

在 DOLPHIN 臨床試驗，使用 DTG-based ART (anti-retroviral therapy) 兩週後，再開始使用 3HP 得到不錯的結果，但是如果在從來沒有使用 ART 的 HIV 病人，3HP 仍然可以不影響病人的病毒量嗎？在南非進行了 DOLPHIN TOO，使用 6H 當對照組來看看 3HP 這個介入組，合併 ART 使用在從來沒有使用 ART 的 HIV 病人身上，就安全性和病毒抑制而言，有沒有什麼不同。就安全性而言，兩組都沒有 Grade III AE，也沒有觀察到 IRIS (immune reconstitution inflammatory syndrome, IRIS) ；



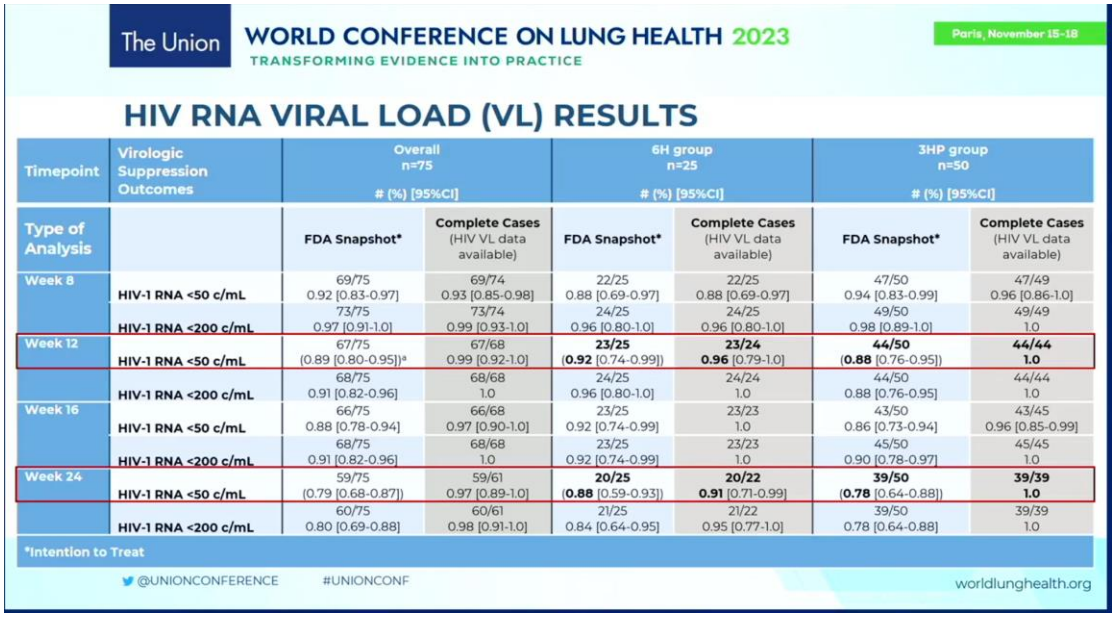
	Overall n=75	6H Group N=25	3HP Group N=50
Unique participants w AE's	25 (33%)	11 (44%)	14 (28%)
AE's all grades	44 (100%)	25 (100%)	19 (100%)
AE Grade 1, n (%)	12 (27%)	9 (36%)	3 (16%)
AE Grade 2, n (%)	31 (70%)	15 (60%)	16 (84%)
AE Grade 3, n (%)	1 (2%)	1 (4%)*	0 (0%)
Treatment-related Grade 1 # (%) Ppts	3 (4%)	1 (4%)[a]	2 (4%)
Treatment-related Grade 2 # (%) Ppts	9 (12%)	2 (8%)	7 (14%)
IRIS events	0 (0%)	0 (0%)	0 (0%)
AE's resulting in drug discontinuation	0 (0%)	0 (0%)	0 (0%)

[a] One participant had a treatment-related AE of vomiting which was attributed to BOTH DTG and TDF, but not TPT.

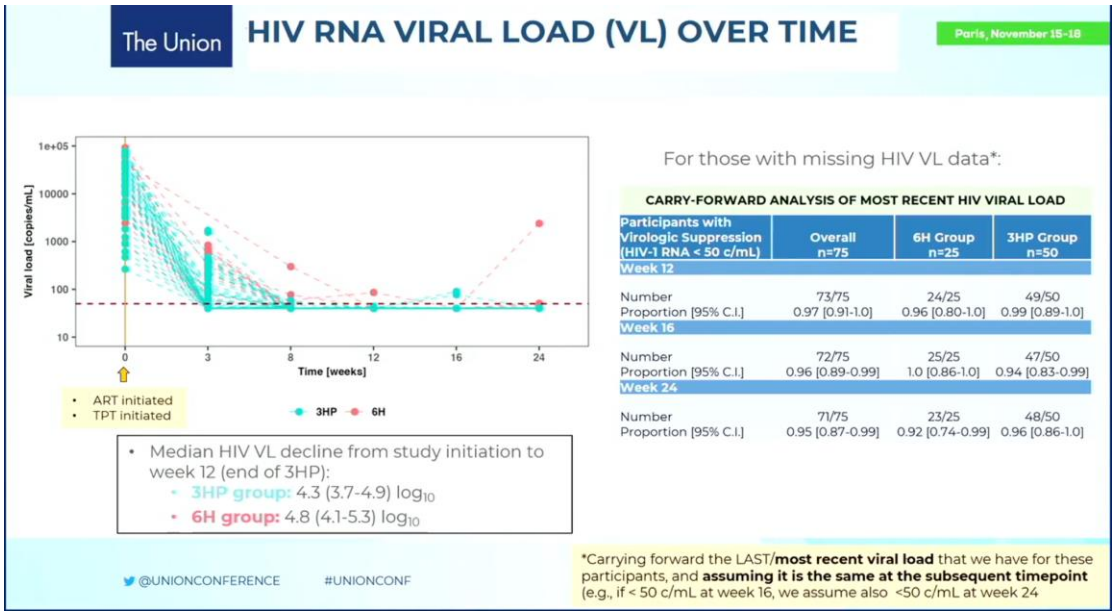
* Cutaneous abscess unrelated to treatment, requiring hospitalization

Ppts=participants; AE's= adverse events

就病毒量而言，由於 3HP 組有較多的人沒有回來抽血，所以在 12 週，能夠達到 HIV-1 RNA <50copies/ml 的比例，顯示 FDA Snapshot (intention to treat, ITT) 0.92 vs. 0.88 (6H vs.3HP)，如果是用 complete cases 的概念 (即只計算有抽到血的當分母)，則為 0.96 vs. 1.0；同樣的在 24 週的追蹤， 在使用 3HP 與 6H 兩組，viral suppression FDA Snapshot 定義為 0.88 vs. 0.78， 若以 complete cases 來算則為 0.91 vs. 1.0。



從另外一個觀點來看，只要達到病毒量測不到，那之後就當作已經測不到，即使之後沒有按照規定來抽血 (so-called amputation carry-forward analysis of most recent HIV VL)；在第 12 週兩組的 VL suppression proportion 其實是 0.96 vs. 0.99 (6H vs.3HP)，第 16 週 1.00 vs. 0.94，第 24 週則是 0.92 vs. 0.96。



由此可知，病人可以從一診斷 HIV 就同時開始接受 LTBI 治療，若選用 DTG based 的 ART，同時使用 3HP，對病毒量的壓制程度沒有差異；一方面可以減少病人一開始 ART 還沒有效，病人就發展成 TB 的機會，另一方面，也可以減少等待 viral suppression，造成 loss to follow-up 的問題。南非有 500 萬

PLHIV, 有 100 萬的 LTBI 需要治療，這個試驗可望提供一些證據，給需要 rifapentine 才能夠吃完，但又剛診斷的 PLHIV。

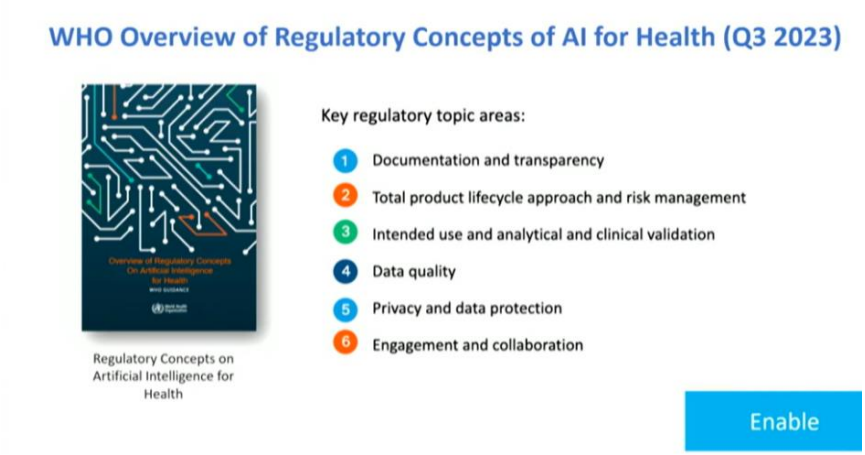
2023/11/16

PL-02 AI-generated TB care and prevention

自 2012 年開啟了 deep neural network 和 machine learning，近年來人工智慧在各個領域益發蓬勃發展，在醫療和健康照護方面，如果我們去搜尋相關的文獻就發現，近年來 AI 的使用特別是在放射影像和病理的相關研究所佔最多。目前來說因為數位健康和攜帶式裝置的進步，使得搭配此類的結核病篩檢工具，例如胸部 X 光等，配上 computer-aided detection(CAD)的 AI 技術，在缺乏影響診斷醫師的 TB 高負擔國家，便可使用這樣的工具來計算疑似有結核病病灶的 X 光片，依據其結核病的可能分數來做篩檢和分流，後續再使用 Xpert 等 point-of-care 的快速分子檢驗來診斷出結核病。目前已有 12 種商用的 CAD 平台可以使用。

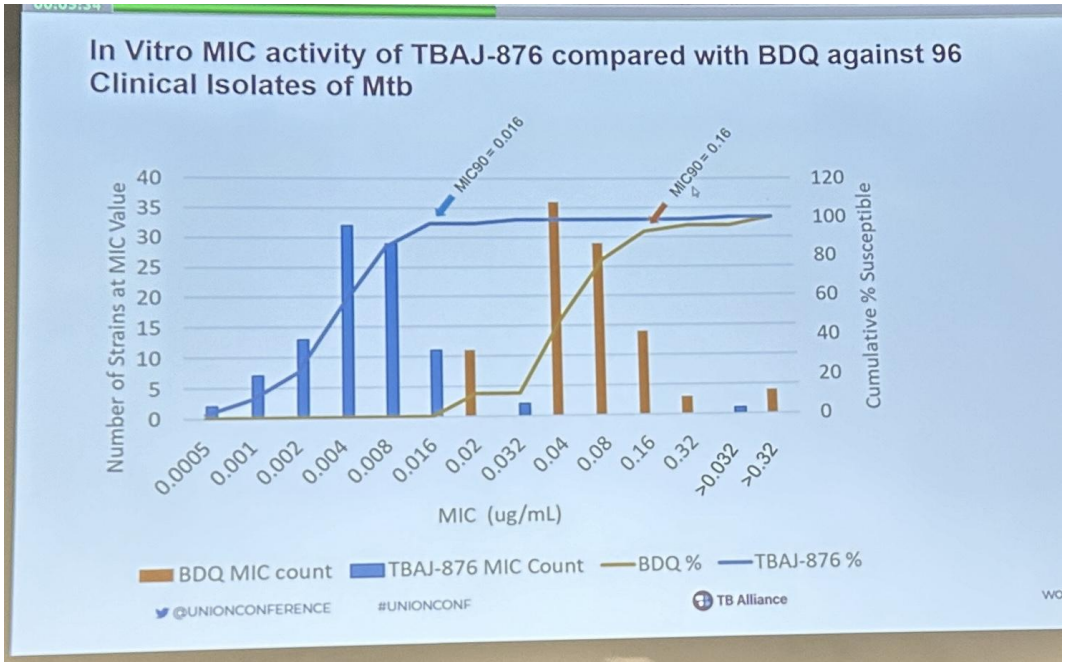
因此人工智慧這樣的工具在 TB care cascade：篩檢、診斷、治療、預防等領域如何應用已成最紅的課題之一。而由於 CAD 的判讀經評估後發現已接近人為判讀的正確率，世界衛生組織對於結核病系統性篩檢的建議也已從 2016 年對於 digital health 和 AI 所持保留的態度，轉變為 2021 年建議：當無法人工判讀 X 光時，CAD 等 AI 技術可作為 15 歲以上的年齡層進行肺結核篩檢和分流的取代方式。WHO 也著手進行 AI 進行篩檢等產品應具備哪些特質(target product profile)以及這些 CAD 軟體產品要如何進行 Prequalification。除了 X 光的判讀，現正進行的研究還包括聽診肺部的肺音或病人的咳嗽音來進行 AI 學習，以區分出可能疑似肺結核的病人。除了篩檢和分流結核病，分子檢驗抗藥結核病的 Hain test(Genotype MTBDRplus second line)需要人為判讀(抗藥位點是否出現 band)來取得藥物敏感性試驗結果，目前也正在發展 AI 判讀。就治療應用層面來說，特別是抗藥結核的治療，除了標準處方之外，臨床上會使得病人無法使用標準處方而得考慮個人化醫療(或精準醫療)的因素非常多，包含依據藥物敏感試驗結果還有哪些藥物可以使用，各種二線藥物本身的殺菌或滅菌能力，以及對於病灶組織穿透的局部藥物濃度，副作用(包含病人本身的體質和所使用的其他共病藥物造成藥物間的交互作用)和治療機構或該國家能取得哪一種二線藥物等因素有關，AI 可以學習各種情境並給予不同處方組合分數，進而建議病人在標準處方之外還有哪些用藥選擇，達到最有利的個別化治療方式。

但是 AI 的使用仍有很多亟待處理的問題，包含可能加重醫療不平權，隱私安全的問題，還有演算的過程可能被視為黑盒子無法得知其過程；因此 AI 的使用目前應遵循的原則包含: 1. Protect autonomy, 2. protect human well-being, safety, and public interest, 3. ensure transparency, 4. foster responsibility and accountability, 5. ensure inclusiveness and equity, 6. promote AI that is responsive and sustainable. 世界衛生組織也自 2018 年起對於 AI 使用於健康照護的領域來提出重點的 regulatory concepts 包含領域 1. documentation and transparency, 2. total product lifecycle approach and risk management, 3. intended use and analytical and clinical validation, 4. data quality, 5. privacy and data protection, 6. engagement and collaboration.

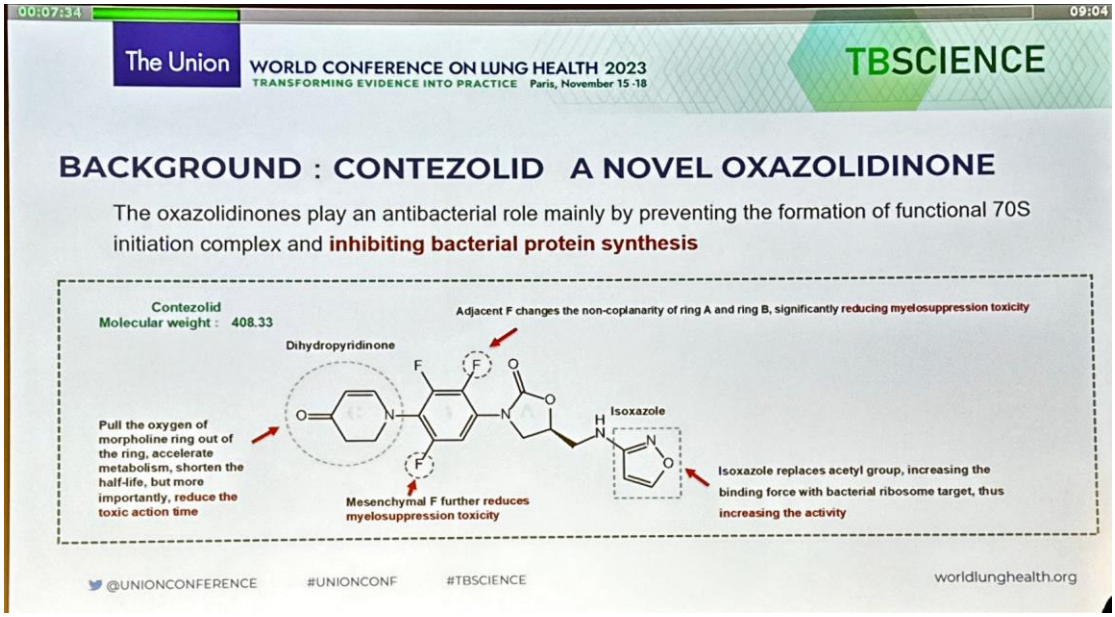


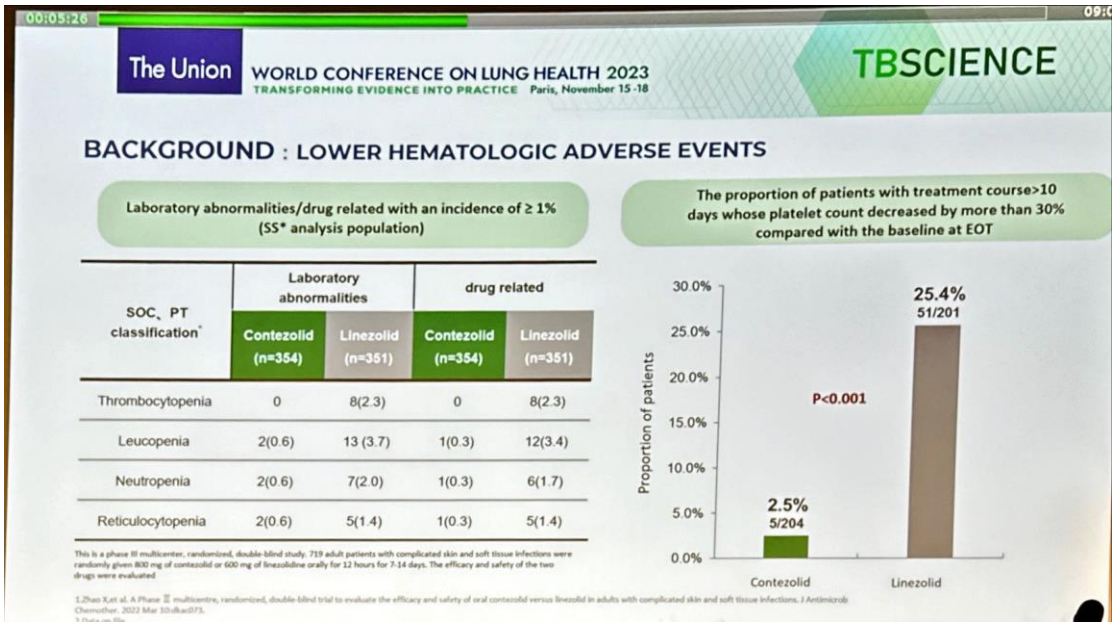
OA13 Advances in Drug and Vaccine Development

TBAJ-876 是由 TB alliance 發展中的第二代 diarylquinoline, 相較於目前正在使用的 Bedaquiline (BDQ)有更好的體外抗結核菌的功效，MIC 更低且其代謝物 TBAJ-876M3 的 MIC 也低於 BDQ，針對 BDQ 的抗藥位點 Rv0678 突變所造成的 efflux pump 活化也有更強的抵抗力，此外也比較少發生 QT prolong，可能比 BDQ 更為安全，目前狗的動物實驗(3.7 倍劑量)中並未觀察到 QT prolong。目前 TBAJ-876 正在進行 phase 2 收案中，使用 25, 50, 100 mg 合併 linezolid 和 pretomanid 使用於 DS-TB 病人。



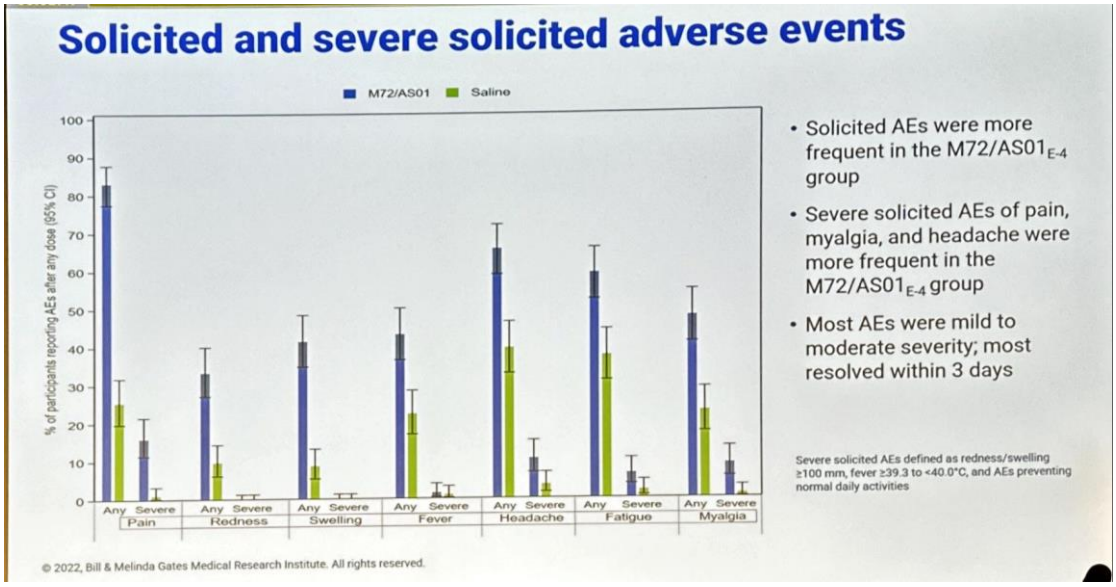
另一個受注目的藥物：contezolid 為新一代的 oxazolidinone，功能為形成抑制 70s 起始的複合體來抑制細菌蛋白質合成。目前觀察到對於骨髓抑制的比例相較於 linezolid 來得低；MIC50, MIC90 和 linezolid 接近。目前尚未看到和 linezolid 有 cross-resistance。





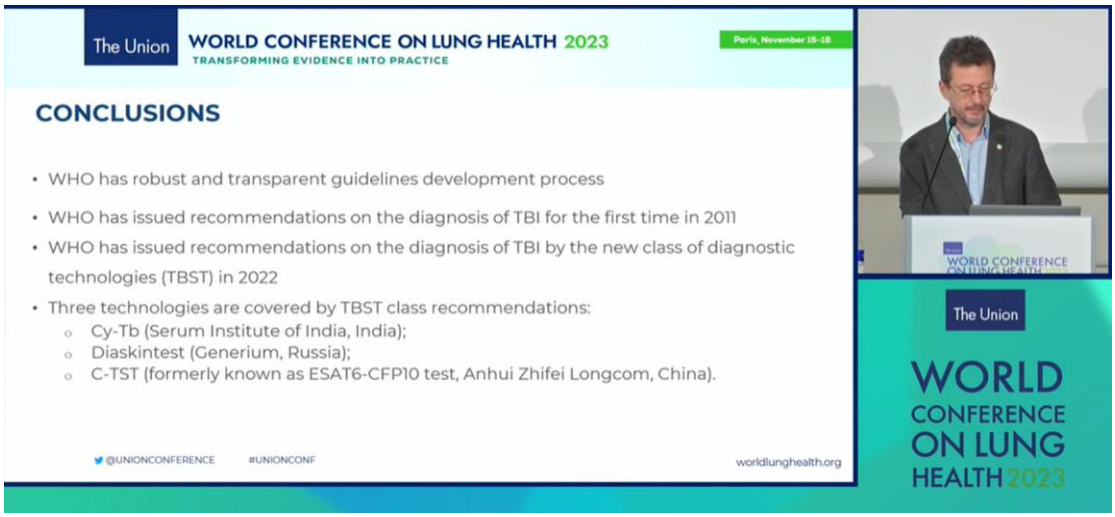
疫苗的部分，2020 年 Gates MRI (medical research institute)從 GSK 取得繼續 M72/AS01E 的疫苗研究 license，目前正在進行的是在南非做 phase 2 針對 PLHIV

進行安全性以及 immunogenicity 研究(MESA-TB), 收案為 16-35 歲 PLHIV 約收案 400 位，收案條件為 VL<200 copies/ml 且 CD4>=200 cells/uL，過去使用過 TPT 但並未發生 TB disease，觀察接種第二劑 12 個月後是否發病。收案已在 2022 年 8 月截止，目前看起來安全性的部分主要為疼痛肌肉酸痛和頭痛出現的比例較高，大部份接種 3 天內會恢復。



SP12 Mtb antigen-based skin tests (TBSTs) – new class of tests for the detection of TB infection

利用 IGRA 的抗原 (ESAT-6+ CFP-10)，做出了新的皮膚測試方法，與傳統的皮膚結核菌素 PPD 的 TST 做區隔，名稱為 Mtb antigen-based skin tests, TBSTs，WHO 的 Alex Korobitsyn 一再強調，這個診斷工具的概念，已經在 2022 年的 TBI (tuberculosis infection) 新的診斷技術指引中，有前提的建議使用，目前的證據還在 low certainty of the evidence。過去人們總是批評 WHO 推薦新的診斷工具的動作太緩慢，跟不上時代，這次 WHO 願意在早期就 endorse 是看到 TBI 診斷的重要性，所以演講時直接說，希望大家不要說三道四的，請一起向前努力的碎碎念，讓聽眾如我不覺莞爾。由於需要的設備少，應用 TBSTs 主要的門檻在於施打皮內注射與判讀訓練，專家們認為，學理上能夠避免 BCG 造成偽陽性的 TBSTs， 值得在開發中國家推廣，增加 TBI 治療前診斷的準確性(比不提供檢驗直接叫民眾吃藥來得有說服力)，先取得民眾的信任，減少 2/3-3/4 不必要的治療，進而增加 TPT 被接受的機會。



印度 Serum Institute of India (SII) 繼俄羅斯與中國的 TBSTs，推出名為 Cy-Tb 的產品。William J Foundation, India 的 Dr. Shamim M Mannan 分享了一些在印度做研究時遇到的困境，主要是對民眾來說，沒有疾病卻需要治療，是一個當地還不太能接受的觀念；治療的處方也還沒辦法大量使用短程處方，也是民眾顧慮的部分；許多工作人員反映，TBSTs 因為要人工判讀，差異是存在的，所以他也提出希望有自動判讀，用 AI 取代人為測量。除了在印度進行臨床試驗，美國 CDC 在印度也透過研究，支持更多證據的收集，尤其是希望能夠取得全年齡層的 TBSTs 與接觸史或者發病之間相關的證據，廠商 SII 目前正積極地以歐洲的 EMA 為目標，希望能夠取得藥證。

臺灣基本上還有蠻多護理師有 intradermal 的技術，但是隨著時間過去，台灣目前只剩下 2 歲以下的兒童，需要 TST，其他的持針練習來自 BCG 注射，所以判讀的機會越來越少。倘若 TBSTs 真的可以有等同 IGRA 一樣的表現，價格又更便宜合理，那麼臺灣可能考慮採購，既維持技術並且提供診斷。所以我們就很積極地請 WHO 的 Alex 幫忙，看看廠商有沒有興趣在臺灣申請許可證，但因為 SII 沒有來現場擺攤，Alex 協助我們與廠商用 E-mail 聯繫，回國後也順利取得 2023 年下半年相關的研究資訊和在臺灣銷售的報價。評估起來，Cy-TB 報價比臺灣 IGRA 還要昂貴，再加上還需要病人 48-72 小時來回診判讀，對已經習慣只需要來一趟的臺灣民眾，將是一項挑戰。另外，Cy-TB 目前還沒有 5 歲以下的資料，靜待廠商取得 EMA 的許可證之後，我們再評估是否需要完成本土使用之評估。

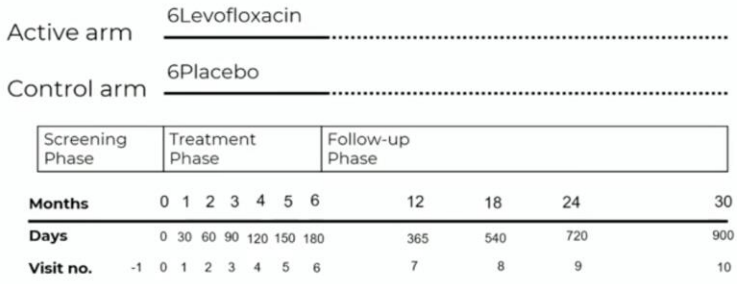
LB02 The Union/CDC late-breaker session on TB (treatment and clinical trials)

LB02-106-16 The effectiveness of levofloxacin for the treatment of latent TB infection among household contacts of patients with multidrug-resistant TB: The VQUIN MDR Trial

The VQUIN MDR Trial 隨機分派 2,041 人之前，找到 61 co-prevalent TB 所有年齡層，分成 placebo 和 levofloxacin 介入，重點是在開始治療前用 CXR 和痰液 Xpert 陰性嚴格篩檢家戶內接觸者。

TRIAL DESIGN

VQUIN MDR-TB prevention study



During protocol development, the VQUIN trial collaborated with a second trial evaluating levofloxacin in children and adolescents (TB CHAMP) to align outcomes, drug formulation & dosing

30 個月 ITT population，追蹤是否有細菌學確診，incidence rate ratio: 0.55，但因為發病的人很少，95%信賴區間很寬跨過 1。

INCIDENCE OF TB AMONG ALL PARTICIPANTS (ITT POPULATION)

Intention to treat population	Levofloxacin	Levofloxacin incidence per 100 person-years	Placebo	Placebo incidence per 100 person-years	Incidence rate ratio (95% CI)	P-value
Intention to treat population	**n=1023**		**n=1018**			
Completed 30 months follow up or reached a trial end-point, n (%)	996 (97.4%)	--	999 (98.1%)	--	--	--
Total follow-up, person-years	2,586.1	--	2,564.6	--	--	--
Bacteriologically-confirmed, n	6	0.232	11	0.429	0.55 (0.19, 1.62)	0.278
Clinically-diagnosed only, n	1	0.039	2	0.078	0.49 (0.045, 5.46)	0.566
Either bacteriologically-confirmed or clinical TB, n (%)	7	0.271	13	0.507	0.54 (0.20, 1.46)	0.226

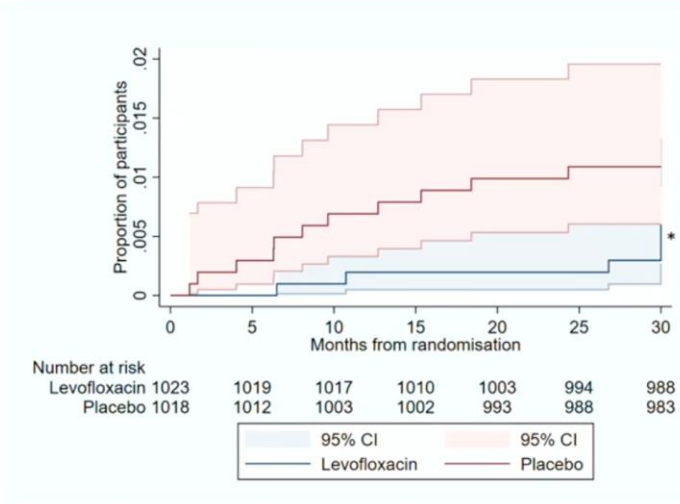
Primary effectiveness outcome is shown in the yellow row

INCIDENCE OF TB AMONG ALL PARTICIPANTS (ITT POPULATION)

Intention to treat population	Levofloxacin	Levofloxacin incidence per 100 person-years	Placebo	Placebo incidence per 100 person-years	Incidence rate ratio (95% CI)	P-value
Intention to treat population	**n=1023**		**n=1018**			
Completed 30 months follow up or reached a trial end-point, n (%)	996 (97.4%)	--	999 (98.1%)	--	--	--
Total follow-up, person-years	2,586.1	--	2,564.6	--	--	--
Bacteriologically-confirmed, n	6	0.232	11	0.429	0.55 (0.19, 1.62)	0.278
Clinically-diagnosed only, n	1	0.039	2	0.078	0.49 (0.045, 5.46)	0.566
Either bacteriologically-confirmed or clinical TB, n (%)	7	0.271	13	0.507	0.54 (0.20, 1.46)	0.226
Per protocol population	**n=700**		**N=844**			
Total follow-up, person-years	1,783.7	--	2,145.3	--	--	--
Bacteriologically-confirmed, n	3	0.168	6	0.280	0.60 (0.15, 2.39)	0.474
Clinically-diagnosed only, n	0	0.000	1	0.047	Not estimated	--
Bacteriologically-confirmed or clinical TB, n	3	0.168	7	0.326	0.52 (0.14, 1.99)	0.338

Primary effectiveness outcome is shown in the yellow row

KAPLAN MEIER CURVE OF TIME TO A DIAGNOSIS OF CONFIRMED TB TO 30 MONTHS



*3/6 intervention cases detected at 30 months.

在副作用的部分，levofloxacin 組與控制組有 18.9%的差異， 沒有 Gr 3-4 的肝毒性副作用，發生副作用的人多集中在 Gr 1-2，因為副作用而造成停藥的比例在兩組分別是 7.4% vs. 1.1%, 差異達到 6.3% 有統計顯著，但是相當低且安全。透過全基因定序，3/8 位指標與接觸者配對，已完成定序比較，2 個是 control 組, 1 位是 levofloxacin 組，但 3 位都跟指標無關 (講者是說 "had not been infected by their enrolled index cases)；至於全基因定序的抗藥位點偵測，目前 2/2 levofloxacin 組，4/6 控制組，是 MDRTB，但目前這 8 個菌株都沒偵測 levofloxacin 抗藥。

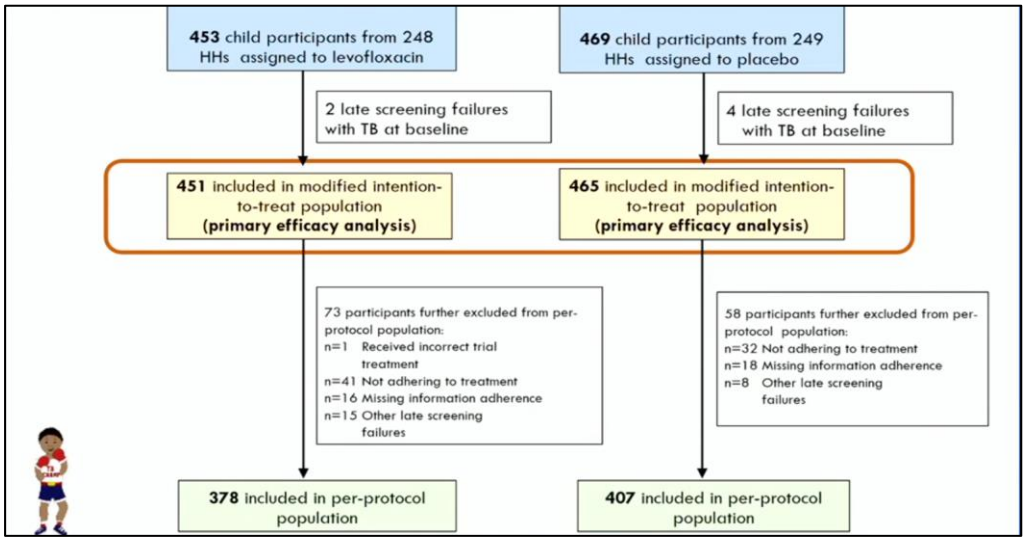
ADVERSE EVENTS (INTENTION TO TREAT POPULATION), PER SUBJECT

Variable	Levofloxacin (N=1023)	Placebo (N=1018)	Risk difference	P-value
Participants taking at least one dose of study drug	960 (93.8%)	962 (94.5%)	-0.7 (-3.5, 2.2)	0.65
Participants with one or more adverse events, n (%)				
Total – Any Grade 1-4	306 (31.9%)	125 (13.0%)	**18.9% (14.2, 23.6)**	<0.0001
Grade 1 or 2 adverse event	290 (30.2%)	111 (11.5%)	**18.7% (14.0, 23.3)**	<0.0001
Grade 3 or 4 adverse event	29 (3.0%)	19 (2.0%)	1.0% (-0.3, 2.4)	0.140
No adverse events	354 (68.1%)	837 (87.0%)	**-18.9% (-23.6, -14.2)**	<0.0001
Participants, with an adverse event AND stopped taking study drug permanently, n (%)				
Total – Any Grade 1-4	71 (7.4%)	11 (1.1%)	**6.3% (4.3, 8.2)**	**<0.0001**
Grade 1 or 2 adverse event	59 (6.2%)	7 (0.7%)	**5.4% (3.6, 7.3)**	**<0.0001**
Grade 3, pregnancy only	4 (0.4%)	3 (0.3%)	0.1% (-0.4, 0.6)	0.701
Grade 3, non-pregnancy related grade 3-5 adverse events*	8 (0.8%)	1 (0.1%)	**0.7% (0.1, 1.3)**	**0.019**
Grade 3 or 4 hepatotoxic event*	1 (0.1%)	0 (0%)	0.1	N/A
Grade 3 or 4 musculoskeletal event*	1 (0.1%)	0 (0%)	0.1	N/A

Secondary safety outcome shown in the yellow shaded row.
Grade 3-4 adverse events were graded by a blinded Expert Clinical Panel.
Bolded comparisons indicate confidence limits do not cross the null.

LB02-107-16 Efficacy and safety of levofloxacin preventive therapy in child and adolescent household contacts of multidrug-resistant TB: the TB-CHAMP double-blind placebo-controlled, cluster randomised trial

在南非進行的兒童 TB-CHAMP 收案對象一開始只有 5 歲以下，後來才拓展到 5 歲以上，收案隨機分派約 450 人之前，找到 32 co-prevalent TB，5 歲以上必須要有 IGRA/TST 陽性，或者 HIV 感染，才能加入臨床試驗 (實際執行之後發現只有 20%陽性，原本估計的是 40%)，重點是在開始治療前用 CXR 和抽胃液 Xpert 陰性嚴格篩檢家戶內接觸者。



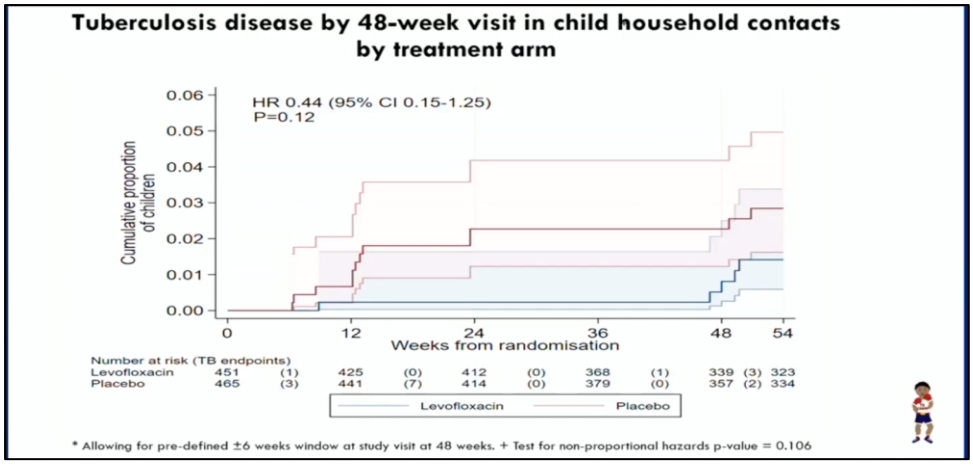
所有人分成 placebo 和 levofloxacin 介入兩組，對象也是篩檢 MDRTB 成人指標的家戶內接觸者，但沒有強調用甚麼方式排除活動性結核。因為是在南非，在兩組有 34%的 HIV 暴露過但沒有 HIV 感染的兒童，以 3 歲左右為主，48 週 modified ITT population，追蹤確診結核病，incidence hazard ratio: 0.44，但因為發病的人很少，95%信賴區間很寬跨過 1。

Primary efficacy analysis- mITT population

		LVX	Placebo	Total
All participants		451	465	916
Participants with ERC adjudicated TB endpoint during overall study follow-up		7 (1.6%)	14 (3.0%)	21
	Confirmed TB	3	7	10
	Unconfirmed TB	4	7	11
Primary efficacy analysis				
Participants with TB endpoint by 48 weeks*		**5 (1.1%)**	**12 (2.6%)**	**17**
	Confirmed TB	3	7	10
	Unconfirmed TB	2	5	7
Hazard ratio (95% CI), LVX vs placebo$		**0.44 (0.15-1.25)**		
P-value		**0.121**		

Number needed to treat: 56

* Allowing for pre-defined ±6 weeks window at study visit at 48 weeks.
$ Hazard ratio estimated adjusting for site, age group and allowing for household clustering.



Grade 3 的副作用也是非常低，levofloxacin 組與控制組分別 0.9% vs. 1.7%，沒有差異；在試驗前就特別要注意的 arthritis/arthralgia/tendinopathy (any grade)可以看到 levofloxacin 組與控制組分別 1.3% vs. 0.9%，沒有差異。所以講者不斷地強調 extremely safe，levofloxacin 組只有 6 位因為副作用停藥，而 placebo 組則只有 1 位停藥。

兩個研究都因為，估計的發病率要比實際收案的高太多，後來需要更大的 sample size，但不太可能更大規模，或者追蹤更久；所以利用貝氏模式將兩個研究資料一起分析，不過這種現實和理想的差距（加上時效）應該是流病學家，因為估計的方式，在 RCT 前後，必須（但無法）面對的挑戰。

TB-CHAMP: Primary safety analysis

	LVX	Placebo	Total
All participants receiving ≥1 study treatment dose	452	469	921
Grade ≥3 adverse events at least possibly associated with study drug			
Number of events	5	8	13
Participants with ≥1 event(s)	4 (0.9%)	8 (1.7%)	12
Hazard ratio (95% CI), LVX vs placebo*	0.52 (0.16-1.71), P= 0.285		

$ Analyses based on time to first event.
Hazard ratio estimated adjusting for site, age group and allowing for household clustering.

Secondary safety endpoints: pre-specified adverse events

	LVX	Placebo	Total
All participants receiving ≥1 study drug dose	452	469	921
Arthritis/arthralgia/tendinopathy (any grade)			
Number of events	7	4	11
Participants with ≥1 event(s)	6 (1.3%)	4 (0.9%)	10
Hazard ratio (95% CI), LVX vs placebo*	1.32 (0.35-4.98), P=0.686		

ANALYTIC METHODS

Main analyses

- Primary analysis: Compared the incidence rate ratio of TB to 30 months in the ITT population
- Secondary safety analysis: Compared grade 3-4 AEs up to 21 days post treatment, among those starting treatment.

Secondary Bayesian analysis

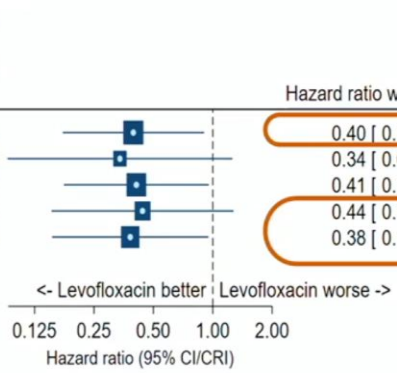
- Bayesian analysis comparing the TB incidence between groups was performed[1], applying priors from the TB CHAMP trial.
- This approach allowed 'borrowing' of information between trials[2,3]
- Potentially increases power, compared to stand-alone analyses
- Methods were pre-specified before unblinding the results of either trial.
- Outcome was confirmed or clinical TB at 54 weeks, reflecting duration of follow-up in TB CHAMP

[1]TB CHAMP is a phase 3 randomized trial of levofloxacin versus placebo to treat children and adolescent contacts of patients with RR/MDR-TB. Bayesian analyses were performed in collaboration with UCL.
[2]Weights given to age and TB infection status, based upon expert elicitation
[3]MTurner RM et al, BC Med Res Methodol 2022

Estimated treatment effect of levofloxacin on time to TB disease by 54 weeks: results from TB-CHAMP and V-QUIN

V-QUIN

Analyses	Levofloxacin n with endpoint / N	Placebo n with endpoint / N	Hazard ratio with 95% CI/CRI
Overall estimate: IPD meta-analysis	8 / 1474	21 / 1483	0.40 [0.17, 0.90]
V-QUIN: standard analysis	3 / 1023	9 / 1018	0.34 [0.09, 1.25]
V-QUIN: Bayesian analysis*	3 / 1021	9 / 1015	0.41 [0.18, 0.95]
TB-CHAMP: standard analysis	5 / 451	12 / 465	0.44 [0.15, 1.26]
TB-CHAMP: Bayesian analysis*	5 / 448	12 / 464	0.38 [0.15, 0.94]

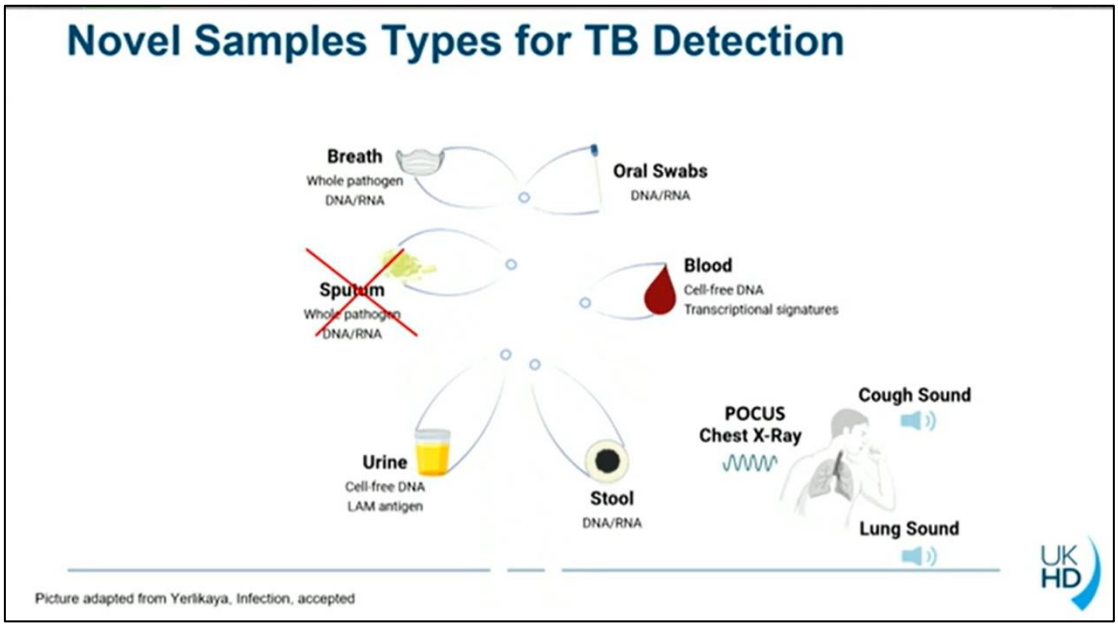


* Treatment effect in V-QUIN was estimated while "borrowing" information from TB-CHAMP, and vice versa; allows levofloxacin efficacy to differ between the study populations, and increases power compared to corresponding standalone analyses of each study. IPD = individual patient data; CI = confidence interval; CRI= credibility interval (for Bayesian results)

排除掉方法學上的瑕疵，VQUIN 和 TB-CHAMP 副作用很少，接受度很高；依照台灣我們的資料， 治療有效性也有類似的結果，甚至更好，但我們的副作用就是比較無法容忍，看到人家的 trials 十足羨慕，對方的民眾耐受性怎麼這麼好。

2023/11/17

TBS3B Diagnostic innovation-TB science: Non-sputum based testing



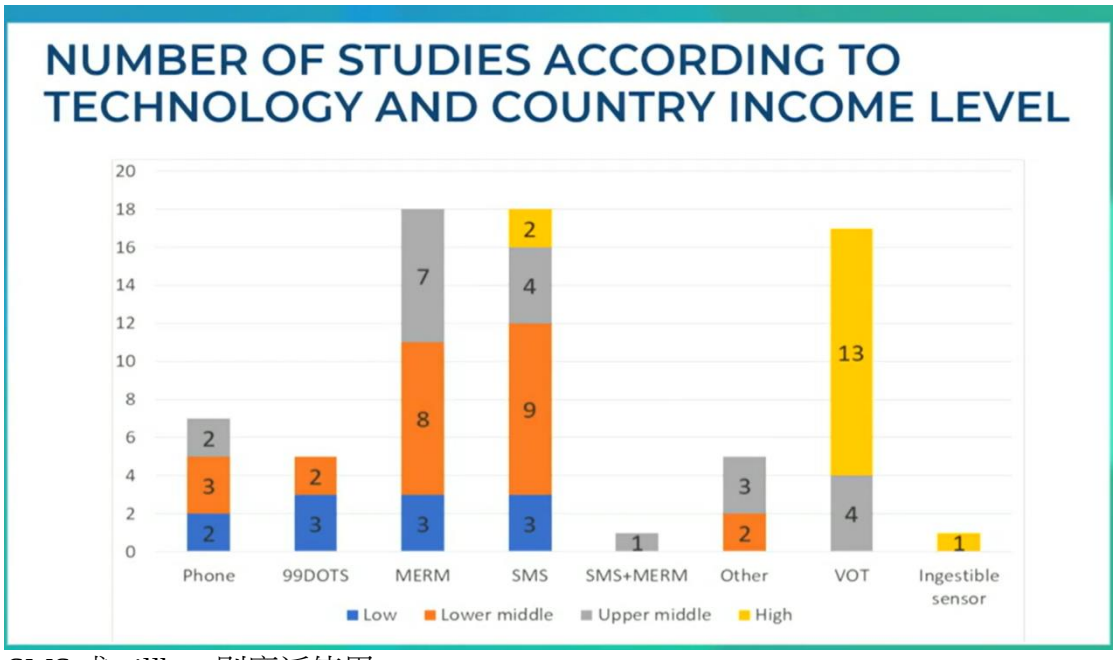
創新的非痰檢驗包含：檢測呼出氣體殘留的 TB DNA、尿液中 cell free DNA 或 LAM 抗原、口腔拭子檢測 DNA、血液中 cell free DNA 或轉譯標記、糞便中 DNA、RNA 或者使用咳嗽聲或聽診的呼吸聲等，參考其他的疾病控制例如 HIV、梅毒、瘧疾、SARS-CoV2 的 POC，或低價的自我篩檢工具，容易使用也容易取得，使得篩檢或診斷結核病變得更容易。Tongue swab：敏感度雖然較低(13-98%)，但專一度相對不錯(80-100%)，在動物身上 tongue swab 算是比較常用的檢測方式，特別對於不易取得痰檢體的兒童用 swab 進行分子檢測，目前在住院的病童身上進行的研究發現和臨床診斷的一致性相當高，也能找出更多原本使用傳統的檢測 smear 無法診斷的兒童 TB 個案，但若同時取得的 tongue swab 其 TB 培養為陰性就會有缺乏標準參考值的問題。在 HIV 個案使用，可以增加 40% TB 診斷陽性率，在應用上仍需考慮如何把這個工具優化，可能可以使用在大批民眾的篩檢活動，因為現場留痰相較於 tongue swab 仍是比較耗時，或是考慮 pooling 或多次送驗檢體，設計不同的篩檢流程，考慮進一步在實務上運用的評估。

利用呼出氣體來檢驗 TB DNA，陽性率會隨著個案本身痰檢體的價數而增加，不過要由呼出氣體檢測出來需要搭配不同的裝置，來攔截呼出的菌體，例如：具有 filter 的吹管，當然如果個案肺功能不佳時檢測的陽性率也會受到影響。

若是使用口罩來檢出需要 24 小時的收集時間，每三小時病人要戴一小時口罩來做，對於沒有明顯咳嗽症狀的病人也可使用，整體的敏感度和專一度約 65%和 100%。E-nose 的敏感度和專一度約 80%和 84%，目前在印尼進行大型的 validation study，但小規模的 validation study 目前看來 ROC 的 AUC 較低。Cepheid Host Response cartridge 目前也正在進行五歲以下的兒童評估。

SP33 The impact of digital adherence technologies on TB care: Results from ASCENT and other studies

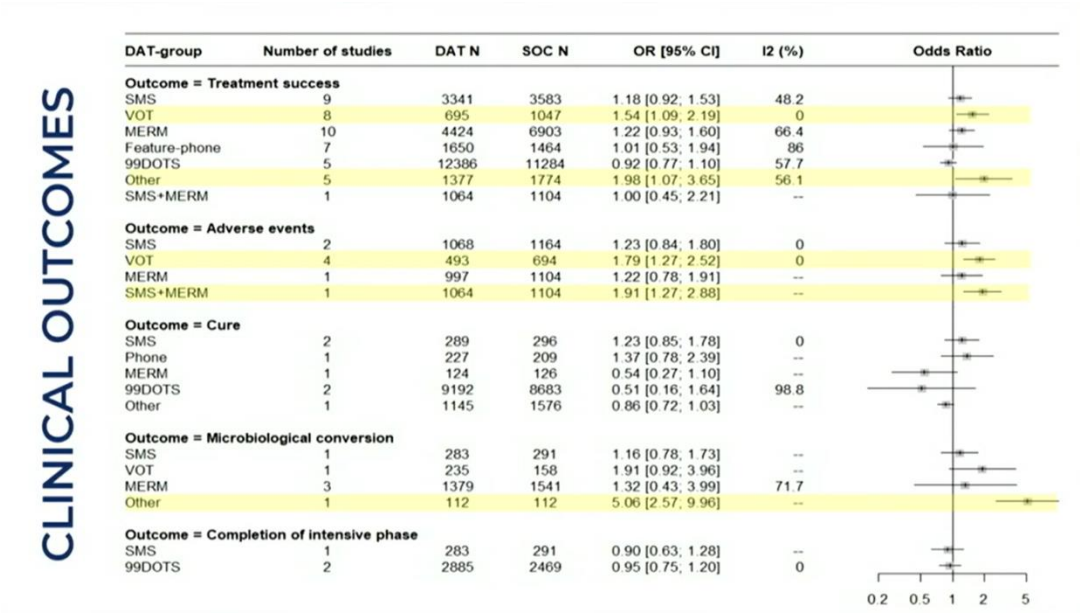
如同 11/15 場次，11/17 KNCV 再次帶來有關 digital adherence technologies (DATs)的研究，開場同樣由 Professor Katherine Fielding 簡報，針對 2022-2023 年發表 DATs 相關研究成果系統性文獻回顧與分析於共 70 篇，DAT 研究類型集中在 SMS、VOT 及 pill box，而智慧型手機應用程式(application)，譬如 Facebook、WeChat、WhatsApp 等免費社群軟體則獨立分出另一類(other)；講者觀察 DAT 類型在不同經濟規模國家的分布，發現 VOT 明顯集中在中高或高收入國家，



SMS 或 pillbox 則廣泛使用。

從臨床治療結果觀察，VOT 跟其他(other)類型對改善治療結果有較明顯的影響，且就副作用反映傳達，也有顯著差異，loss to follow up 也較低。但如探討服藥順從度(Adherence)，因涉及各國研究對服藥次數之計算方式、服藥區間採計、評估的時間點皆有不同，故順從度分析結果分歧較大，即使是同一類型

DAT 也呈現不同結果。後續講者認為也應著重個案使用經驗或相關質性研究報告。



11/17 場次還安排了東歐國家 Republic of Moldova (摩爾多瓦共和國，近鄰 Romania 與 Ukraine) 分享 VST (Video Supported Treatment) 經驗，受試者為 120 名(~49%)結核病個案與 60 名醫療及公衛人員(~70%)，主要探討 VST 使用受哪些因子影響、了解 TB 個案使用經驗、挑戰以及 VST 是否能減省個案金錢與時間。從個案回饋的經驗顯示，服藥過程錄影多半可在 2 分鐘之內完成、操作失敗可能是軟體臨時故障無法使用、個案操作錯誤、網路訊號微弱、個案忘記使用、手機無法充電或不見等原因，而個案沒有按時上傳服藥錄影，大部分會在隔天或同一天接到提醒，或經由個案主動聯繫；使用者經驗調查中，7 成個案認為使用 VST 能與 TB 公衛個管人員保持聯繫，5 成個案認為工作或旅行時亦可很輕鬆地使用，6 成認為即使身邊有其他人包圍，亦不妨礙；但反過來說，整體而言，約有一半的人無法在外輕鬆使用 VST 完成服藥；另就個案服藥時間與費用減省計算，服藥時間可省下 40 至 60 分鐘，支出則視服藥地點減省交通花費，多則可達 100(USD)。

如同本次有關 DATs 各場次之分享趨勢，我國都治方式近年亦逐漸納入數位科技輔助都治執行，搭配個人手機使用兼具 Live video call(視訊通話)或 self-portrait(自拍)功能之行動應用程式(App)。雖然我國使用之 DATs 與 ASCENT

Team 主要跨國研究類型之 DAT 不同，且我國都治需求族群較為年長，人口特徵與基礎建設亦不同，但依舊面臨類似問題。

Moldova 講者 Cristina Celan 在聽眾提問時補充了該國 VST 如何觀察副作用，該國 VST 軟體於個案啟動服藥影片上傳時，同步跳出副作用回報選項，詢問服藥的身體反應與感受，如無異狀可逕自上傳，如表達不舒服，則 VST 跳出 adverse effect 選項供病人選擇，直接傳送至 doctor 或 health worker。就副作用觀察，我國則設計獨立功能，不限服藥視訊當下反映，如有不適即可輸入文字描述症狀或以照片表達，個案專屬之關懷員收到訊息後將立即連繫，並反映至衛生所公衛個管人員後續處理。這表示大家共同追求數位工具的功能完整性，考慮個案基本服藥過程的各種需求。

議程中常提問 adherence 分析難題或 DAT 類型眾多應如何抉擇，就目前來看，VOT(VST)是最能直接掌握每日服藥劑量的工具，pill box 跟 medical label 僅為間接取得的服藥紀錄，但最終仍需各國盤點該國環境、資源條件與個案特質，才能選擇最適切的 DAT。

此次從 11/15 場次 SS04 Digital adherence technologies in TB care: key results and lessons from the Adherence Support Coalition to End TB (ASCENT) trial 簡報主題「Process Evaluation of ASCENT Trial」可知，相較於前兩年的簡報重點著重各國導入經驗分享，今年則已進展至導入後之數據蒐集、運用與調整，思考如何運用 DAT 執行過程收錄至後端資料庫後之數據並即時回饋至第一線人員，才能更有效地協助個案管理。

2023/11/18

SP49 Into the unknown: Drug-resistant TB in pregnancy

懷孕發生結核病會增加母親的死亡率，特別是又合併感染 HIV 的懷孕婦女，過去的觀察性研究發現懷孕期間結核病的發生率並未特別增加，但常在產後六個月上升。當然胎兒的預後可能出現早產/低體重/週產期死亡等情況。

一開始由印度的專家介紹懷孕婦女在不同孕期，被診斷為藥物敏感性結核/抗藥結核病的臨床表現和胎兒的預後的系列病例報告，懷孕婦女的臨床結核病表現可能並不典型或 subclinical(細菌學或影像學符合結核病但並沒有明顯的臨

床症狀)特別是合併 HIV 感染，統合過去的六篇文獻發現 58%(95% CI: 23-93%)的孕婦並沒有臨床症狀，此外如果使用 Xpert ultra 作為診斷工具也可能因為細菌量低而 detected very low，此時若無抗藥病人的接觸史但 Rif 抗藥檢測陽性有可能是偽陽性，此時要開始給予抗藥結核病的治療，以及二線抗結核藥物在對胎兒毒性的資料不清楚的情況下，臨床就可能會陷入是否在早期孕程(少於 24 週)建議終止懷孕要積極治療抗藥結核的難題。由於在懷孕期間會出現 modulated immunity 使得 Th1 cytokine(IL-12, interferon gamma)下降類似 TB tolerating environmental，而在產後這些免疫反應反轉在產後六個月逐漸恢復原本的免疫狀態，產生類似 immune reconstruction inflammatory syndrome (IRIS) 造成 TB 的症狀惡化而被診斷出來，除了 TB 以外包括 cryptococcosis, coccidioidomycosis, hepatitis B&C 都有在產後急速惡化的報告。目前在懷孕的 HIV 婦女的研究初步發現血清中 kinurenine/tryptophan 比值可以用來作為診斷活動性結核病的參考，AUC =0.95(Adu-Cyamfi et al. CID 2021)

南非擁有全球最大的懷孕 cohort，在 2019 年以前的治療結果發現整體，長程和短程處方的成功率為 63, 67, 55%，主要是因為短程處方的失落率較高(35%), 自 2023 年起懷孕的 RR-TB 病人治療的建議改為使用 BDLL 和 BDL, 事實上在南非懷孕 HIV 婦女能持續就醫回診只有 74%， 而且統計產後 HIV 婦女在產後六個月要花至少八次回診去尋求醫療照顧，主要因為有很大一部分的就醫障礙在於 HIV 和 TB 的醫療服務沒辦法能和兒童的醫療服務整合。此外也談到許多臨床試驗將懷孕個案排除於收案對象是極不公平的，常被歸類於”特殊族群”或”脆弱”族群，但對於大多數的婦女懷孕生產是很平常的經歷，並不特殊而且懷孕女性並非兒童等無法自主決定的脆弱族群，因此我們會更缺乏懷孕女性使用這些新藥或 repurposed drugs 的實證資料。

伍、心得與建議

2019 年之後，歷經 3 年 COVID-19 奮戰，2023 年回到了國際抗癆暨肺部健康聯盟的起源地，也是總部所在地之法國巴黎，舉行實體年會，與會者彼此相互問聲 How are you？原本是極為平常的招呼，此次聽來別具意義。

Global Tuberculosis Report 2023 告訴大家，由於 COVID-19 的影響，讓我們又回到了 2019 年流行趨勢，但在此次大會，可以發現各種創新檢驗工具、疫苗臨床試驗研究、藥物研發以及人工智慧在 TB 檢測診斷的進展，各種新知蓬勃發展；而大會主題為「Transforming evidence into practice」將實證數據轉化為實務執行成果，即迫切希望各國能重視 TB，爭取資源、提供技術與積極引進最新的防治策略，並轉化為本土經驗。

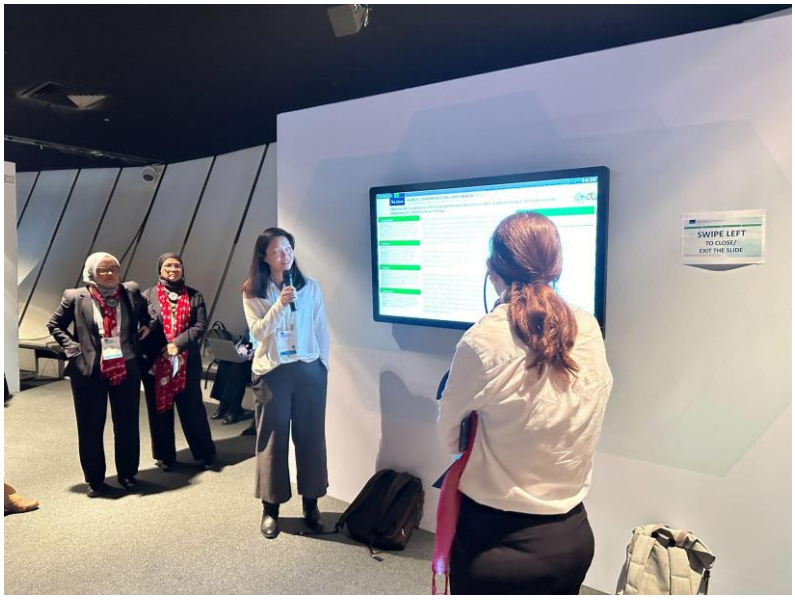
儘管創新結核病疫苗 M72/AS01E 終獲得 the Gates Foundation 與 Wellcome Trust 資助進入臨床 3 期，目前靜待追蹤 2 年結果出爐(預計 2024 年底)，然仍有 VPM1002 等 16 種 Candidate 的研究持續進行；而我國國內目前也積極推動各種新的短程處方，並投入科技計畫資源，執行小型先驅研究，亦於山地原鄉地區投入研發資源開發 AI 影像 X 光判讀技術，後續可望進一步整合運用於實務中；而都治整合數位工具之推動、流程標準化，亦仰賴各層面實務整合與人員訓練規劃。未來仍持續參考國際發展，從數位科技、公衛管理或健康照護體系及民眾三大方向，搭配本土執行效益分析研究調整執行方式，共同努力在 2027 年達到 UNHLM (聯合國 high level meeting) 的績效目標。

建議有二項：

1. 結核病新疫苗、新藥物、新檢驗工具與診斷技術應盡快評估，並規劃本土運用模式。
2. 強化全球夥伴關係建立，運用國際人脈，完成國家型計畫評核。

陸、附件（照片及摘要）

本次大會詹珮君副組長、李品慧醫師、陳人睿科員之發表



EP14-1133-16 Nationwide surveillance of emerging rifampicin resistance after implementation of short-course regimens for TB preventive therapy

SOA08-863-15 Effectiveness of latent TB infection treatment among residents in long-term care facilities, Taiwan

OA11-286-15 The evolution of electronic directly observed therapy in TB treatment: before, during and after the COVID-19 pandemic in Taiwan

臺灣參加 54th Union 年會之成員大合照

臺灣疾管署慢性傳染病組成員

The Union
The Official Journal of The International Union Against Tuberculosis and Lung Disease

The International Journal of Tuberculosis and Lung Disease (IJTLD)

PAGES S1 - S725
ISSN 997–1098

VOLUME 27 SUPPLEMENT 1 NOVEMBER 2023

ABSTRACT BOOK

WORLD CONFERENCE ON LUNG HEALTH 2023 OF THE INTERNATIONAL UNION AGAINST TUBERCULOSIS AND LUNG DISEASE (THE UNION)

PARIS, FRANCE
15 – 18 NOVEMBER 2023

SOA08-863-15 Effectiveness of latent TB infection treatment among residents in long-term care facilities, Taiwan

P.H. Lee,[1] C.H. Liu,[1] P.C. Chan,[1] P.W. Chu,[1] Y.Y. Liao,[1] C.F. Feng,[1] H.Y. Lo,[1] C.C. Lee,[1] [1]Taiwan Centers for Disease Control, Chronic Infectious Disease Division, Taipei, Taiwan.
e-mail: leepinhui@cdc.gov.tw

Background: More than 60% of Tuberculosis(TB) patients in Taiwan were age≥ 65 years with highest age-specific incidence of 111.3 per 100,000 population in 2021. In long-term care facilities(LTCFs), the risk of TB transmission would be higher than the elderly in communities. Testing and treatment of LTBI had been conducted in voluntary participating LTCFs since 2018. The aim of our study is to evaluate the effectiveness of Tuberculosis preventive therapy(TPT) in LTCFs.
Design/Methods: We conducted a retrospective cohort study to enroll health care workers(HCWs) and residents in LTCFs from 2018 to 2021. We used IGRA testing and the TPT regimen including 9H, 4R, 3HR and 3HP were provided for free among those with positive/indeterminate IGRA results. We collected the demographic characteristics and BMI, dialysis, having/ever smoking history of participants. Logistic regression model was applied for factors associated with non-completion of TPT. Furthermore, we used Cox proportional hazard model to evaluate the effectiveness of TPT.
Results: A total of 4742 participants with positive/indeterminate IGRA results was enrolled. After excluding HCWs and those found to be active TB within 100 days after the date of IGRA testing, 3772 residents with median age of 79.5 years(IQR 69.6-86.3) were eligible for analysis. The TPT coverage was 74.3%. The majority of initial chosen regimen was 9H(60.5%), following by 3HP(27.3%), 3HR(8.2%) and 4R(4%). Factors associated with non-completion of TPT included age(aOR=1.02, 1.01-1.03), IGRA of mitogen-nil<0.5(aOR=1.85, 1.30-2.62), and regimen of 3HR(aOR=2.39, 1.63-3.51) and 9H(aOR=2.38, 1.85-3.07). We followed the eligible participants till Oct. 10, 2022 and identified 25 incident active TB cases with incidence rate of 321.4/100,000. Those without TPT were more likely to develop active TB(aHR=4.96, 2.21-11.12) than those receiving TPT after adjusting age and gender (Table 1).

	Number of active TB patients	person-year	incidence rate per 100,000	Univariate analysis HR (95% CI)	Multivariate analysis aHR (95% CI)
Men	18	4102.9	438.7	2.33 (0.97-5.57)	2.95 (1.23-7.11)
Women	7	3674.6	190.5	1	1
Age (years)				1.06 (1.02-1.11)	1.06 (1.02-1.10)
TPT, Yes	10	6143.5	162.8	1	1
TPT, No	15	1634	918	5.65 (2.54-12.58)	4.96 (2.21-11.12)

Abbreviations: HR, hazard ratio; aHR, adjusted hazard ratio; TPT, tuberculosis preventive therapy

Table 1. Risk of active TB among residents eligible for TPT in long-term Care Facilities (n=3772).

Conclusions: The regimen of 9H and 3HR were associated with non-completion of TPT which significantly reduced risk of TB and the subsequent transmission in LTCFs.

SOA08-864-15 Situational analysis of TB preventive treatment coverage among under-fives in Uttar Pradesh, India

S. Bhatnagar,[1] R. Saxena,[1] R. Dofe,[2] S. Joshi,[2] S. Dixit,[2] D. Baliga,[2] P. P.S.,[2] A. Yadav,[2] D. Gupta,[2] A. Rajeev,[2] S. Chandra,[2] R. Ramachandran,[2] [1]Government of Uttar Pradesh, State Health Department, Lucknow, India, [2]TB Support Network, Office of the World Health Organisation (WHO) Representative to India, WHO Country Office, New Delhi, India.
e-mail: stoup@rntcp.org

Background and challenges to implementation: India has the highest estimated burden of tuberculosis infection globally. Prevention of tuberculosis (TB) disease by treating TB infection in susceptible population is one of the core pillars of India's end-TB strategy. TB preventive treatment (TPT) guidelines recommend TB screening of household contacts (HHC) and initiation of preventive treatment to eligible contacts.
This observational study aims to assess the TPT cascade interventions targeting the household contacts below 5 years age from 2019-2022 in Uttar Pradesh, India.
Intervention or response: TPT cascade information of under five years children who were contacts of bacteriologically confirmed drug sensitive pulmonary TB cases from year 2019 to 2022 was extracted from the country's digital TB surveillance platform (Ni-kshay).
Key informant interviews (KII) were conducted to understand the strategies to increase the TPT coverage. Quantitative data was analysed using SPSS software. Transcripts of the KII were analysed with software R version 4.2.3 with package "RQDA" using thematic content analysis.
Results/Impact: In Uttar Pradesh, 621,588 bacteriological confirmed cases were diagnosed from 2019-2022. The number of household contacts eligible for TB screening were 1,963,903 of which 90.9% were screened. Observed contact to case ratio was 3.15:1. Among the screened individuals, 0.44% children below 5-years of age had TB. The proportion of eligible children given TPT showed a progressive increase in coverage from 17.6% in 2019 to 65% in 2022. Qualitative assessment showed that partnership strategies, uninterrupted procurement and supply of regimens for TPT, understanding the patient's perception of threat towards getting TB, along with continuous supportive supervision from the program were the key context specific strategies which enabled this scale-up.
Conclusions: The study recommends effective implementation of contextualized strategies - supply of TPT regimens, testing facilities and strategic interventions to

OA11-286-15 The evolution of electronic directly observed therapy in TB treatment: before, during and after the COVID-19 pandemic in Taiwan

J.-J. Chen,[1] C.-F. Feng,[1] P.-C. Chan,[1] H.-Y. Lo,[1] P.-W. Chu,[1] C.-C. Lee,[1] [1]Taiwan Centers for Disease Control, Division of Chronic Infectious Diseases, Taipei, Taiwan.
e-mail: tender1119@cdc.gov.tw

Background and challenges to implementation: Since 2006, Taiwan's Directly Observed Treatment, Short-course (DOTS) program has relied mainly on in-person DOT that trained workers provide care and medication to TB cases through home visits. The coverage of the DOTS program is as high as 98%. In 2015, an electronic Directly Observed Therapy (eDOT) app was developed as a complement to in-person DOT for TB patients who faced mobility, lifestyle and privacy issues. Until 2020, the eDOT usage rate remained at less than 5%. However, during the COVID-19 outbreak in 2021, due to the control regulations, a significant increase (30%) in the eDOT use was observed.

Intervention or response: We conducted a retrospective analysis of the use of eDOT and in-person DOT for TB patients and their contacts with latent TB infection (LTBI) who received community-based DOTS in 2021-2022. Inpatients and residents in long-term care facilities were excluded from the population. Demographic data and treatment outcomes were collected and analyzed using a multi-variate logistic regression.

Results/Impact: The eDOT usage rate for 5,363 DS-TB patients and 7,768 contacts collected were 33.5% and 28.4% respectively. Demographic data revealed that women had a higher eDOT usage rate than men, as well as younger population compared to their older counterparts (Table). After adjusting sex and age, the population using eDOT had significantly better treatment outcomes than their counterparts who received in-person DOT for both TB patients (OR = 1.474, $p < 0.001$) and LTBI contacts (OR = 2.031, $p < 0.001$), indicating that eDOT was effective during the pandemic.

		N	%	eDOT	%	Treatment completion: Treatment success	%	p value*	Adjusted Odds Ratio (95% CI)
DS-TB		5,363	100	1,796	33.5	4,561	84.8		
sex	female	1,665	31.0	619	37.2	1,450	87.1	0.012	1.24 (1.05-1.07)
	male	3,698	69.0	1,177	31.8	3,101	83.9		Ref.
age	<65 years	2,495	46.5	1,159	46.5	2,262	90.7	<0.001	3.26 (1.90-2.68)
	≥65 years	2,868	53.5	637	22.2	2,289	79.8		Ref.
DOT type	eDOT	1,796	33.5	-	-	1,609	89.6	<0.001	1.47 (1.23-1.77)
	In-person DOT	3,567	66.5	-	-	2,942	82.5		Ref
LTBI contacts		7,766	100	2,207	28.4	6,845	88.1		
sex	female	3,802	48.9	1,116	29.4	3,167	83.0	0.999	1.0 (0.87-1.15)
	male	3,966	51.1	1,091	27.5	3,498	88.2		Ref.
age	<65 years	5,622	72.4	1,886	33.5	5,076	90.3	<0.001	1.78 (1.54-2.05)
	≥65 years	2,146	27.6	321	15.0	1,769	82.4		Ref
DOT type	eDOT	2,207	28.4	-	-	2,060	93.3	<0.001	2.03 (1.69-2.45)
	In-person DOT	5,561	71.6	-	-	4,785	86.0		Ref.

Abbreviations: DOT = Directly Observed Therapy; eDOT= electronic Directly Observed Therapy
* chi-square test

Table. Multi-variate logistic regression for treatment outcome among patients with drug-susceptible TB (DS-TB) and contacts with latent TB infection (LTBI).

Conclusions: eDOT was a practical solution to the challenges posed by social distancing regulations during the COVID-19 pandemic. The equal or even better treatment outcome makes it possible for this digital tool to be utilized in TB care in community in post-pandemic period. More studies to tackle-down the low uptake rate of the eDOT app are warranted.

OA11-287-15 Adolescent, caregiver and health provider perceptions of TB treatment supervision during the COVID-19 pandemic in Lima, Peru

B. Roman Sinche,[1] F. Dorodea,[2] K. Tintaya,[1] S.S. Chiang,[3,4] [1]Socios En Salud Sucursal Perú, Tuberculosis (TB) Program, Lima, Peru, [2]Texas A&M International University, Business Programs, Houston, United States of America, [3]Alpert Medical School of Brown University, Department of Pediatrics, Providence, United States of America, [4]Hasbro Children's Hospital, Division of Pediatric Infectious Diseases, Providence, United States of America.
e-mail: broman_ses@pih.org

Background: In Peru, tuberculosis treatment is administered at a health facility under direct supervision of health providers. However, during the COVID-19 pandemic, selected patients were allowed to take treatment at home under the supervision of family members or health providers via synchronous or asynchronous videos.

This study explored the perspectives of adolescents (10-19 years old) who completed tuberculosis treatment, their caregivers, and health providers regarding facility-based vs. home-based treatment.

Design/Methods: Between August-October 2022, we conducted 16 focus groups (7 of adolescents, 6 of caregivers, and 3 of health staff) using semi-structured guides. Two investigators independently developed codes, applied codes to the transcripts, and identified emerging themes. After each step, they compared results and resolved disagreements through discussion.

Results: Health providers explained that they allowed home-based treatment only if they perceived the patient and family to be responsible and committed to treatment completion, and if adverse treatment events were mild and infrequent. They reported that home-based treatment was reliable and effective for these selected adolescents. This was confirmed by adolescents and caregivers, all but one of whom reported good adherence with home-based treatment.

Participants explained that, unlike facility-based treatment, home-based treatment did not interfere with daily activities (e.g., studying, working, etc.) and reduced the risk of other infections, TB-related stigma (from being seen receiving TB treatment), and transportation costs. However, some adolescents lacked access to a cell phone, meaning that supervision had to be by family

EP14-1132-16 Improved TB preventive treatment outcome using short regimens in a person-centred approach among TB household contacts in Yogyakarta, Indonesia

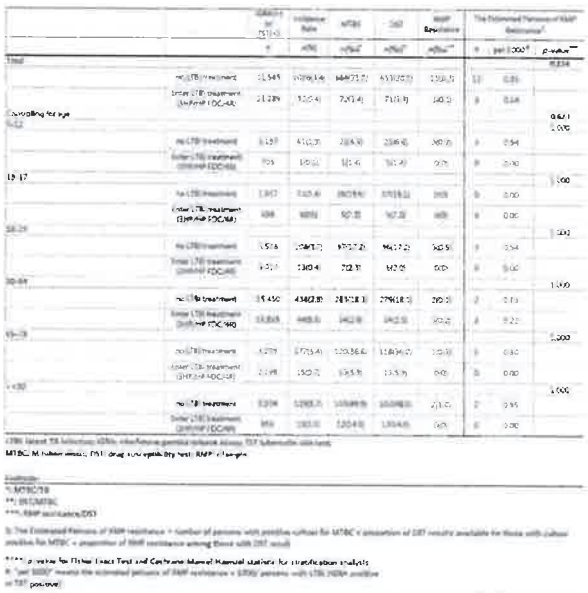
F. Felisia,[1] R. Triasih,[2] B. Weri Yolanda Nababan,[1] G. Yoki Sanjaya,[3] S. Candra Dewi,[4] E. Sri Rahayu,[5] L. Unwanah,[6] G. Chan,[7] P. du Cros,[7] [1]Gadjah Mada University, Centre for Tropical Medicine, Faculty of Medicine, Public Health and Nursing, Sleman, Indonesia, [2]Universitas Gadjah Mada/Sardjito Hospital, Department of Pediatric, Faculty of Medicine, Public Health and Nursing, Sleman, Indonesia, [3]Universitas Gadjah Mada, Department of Health Policy and Management, Faculty of Medicine, Public Health and Nursing, Sleman, Indonesia, [4]Yogyakarta City Health Office, Infectious Disease Control, Yogyakarta, Indonesia, [5]Yogyakarta City Health Office, Prevention and Control of Communicable Diseases and Immunization, Yogyakarta, Indonesia, [6]Yogyakarta City Health Office, Disease Prevention and Control Services-Data Management & Health Information System, Yogyakarta, Indonesia, [7]Burnet Institute, TB Elimination and Implementation Science Working Group, Melbourne, Australia.
e-mail: rina_triasih@yahoo.com

Background and challenges to implementation: The end TB strategy highlights the importance of tuberculosis preventive treatment (TPT) in high-risk groups. Coverage of TPT in Indonesia is inadequate, and persons who start TPT often don't complete treatment. World Health Organization-recommended shorter TPT regimens are effective in reducing risk of active TB with higher completion rates than longer regimens.
In 2020, Zero TB Yogyakarta (ZTBY) implemented person-centered contact investigation and shorter TPT regimen provision in collaboration with primary health care centers.
Intervention or response: Household contacts of persons with bacteriologically confirmed TB (index case) from January 2020 to August 2022 were assessed for eligibility for TPT and given a 3-month TPT regimen (3RH or 3HP). A dedicated nurse monitored contacts on TPT for treatment adherence and side effects every week in the first month and every two weeks in the next months. Contacts were also able to contact the ZTBY nurse by phone or ask for home visits at any point if they had any concerns.
Side effects were managed by referring people to the nearest health facility. Completion of TPT was defined as 80% intake of their regimen within 120 days since treatment was started.
Results/Impact: A total of 1016 contacts were eligible for TPT: 772 (78.8%) started short regimen TPT with 706 (91.5%) completing their TPT. Reporting any side effect was associated with non-completion of TPT in univariate analysis (OR 1.89 CI 1.17-3.16) and in multivariate analysis (aOR 3.59 C 1.80-7.29).
Conclusions: High rates of TPT uptake and completion can be achieved among household contacts through person-centered care and use of shorter regimens. Development of any side effect is a risk for not completing TPT. Side effect monitoring and management while on TPT is vital for improving TPT completion.

EP14-1133-16 Nationwide surveillance of emerging rifampicin resistance after implementation of short-course regimens for TB preventive therapy

P.-C. Chan,[1,2,3] Y.-X. Lin,[1] P.-H. Lee,[1] P.-W. Chu,[1] J.-J. Chen,[1] C.C. Lee,[1] [1]Centers for Disease Control, Division of Chronic Infectious Disease, Taipei, Taiwan, [2]College of Public Health, National Taiwan University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan, [3]National Taiwan University Hospital, National Taiwan University College of Medicine, Department of Pediatrics, Taipei, Taiwan.
e-mail: pcanita.tw@cdc.gov.tw

Background and challenges to implementation: The monitoring of rifampin resistance at both population and individual levels is crucial for implementation of short-course regimens for TB preventive therapy (SR-TPT) program.
Intervention or response: The results of drug susceptibility test (DST) testing on isolates were presented for both SR-TPT and control groups and the estimated rifampin resistance at population levels was calculated in reverse by confirming levels of rifampin resistance proportional to bacteriological confirmation. For contacts who developed TB after SR-TPT, M. tuberculosis isolates of paired index patients and contacts were compared with 10-loci MIRU-VNTR typing.



Results/Impact: From April 2008 to December 2021, a total of 52,834 latent tuberculosis infected (LTBI) contacts whose index patients identified as no rifampin resistance were enrolled in our study and were followed until July 2022. Among them, 21,289 received SR-TPT