出國報告（出國類別：研究 ）

赴新加坡參加 APEC 贊助之亞洲區域結核病研究及臨床試驗整合網絡(A-TRACTION)

服務機關：衛生福利部疾病管制署
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派赴國家：新加坡
出國期間：2018.3.18 ~3.21
報告日期：2018.4.30

目次

一、摘要

亞洲區域結核病研究及臨床試驗整合網絡 (簡稱 A-TRACTION) 會議中經過深入的討論，除了主辦新加坡和我國之外，包括柬埔寨、中國、香港、印尼、馬來西亞、日本、印度、菲律賓、蘇聯、泰國、越南等國 （依各國與會代表 given name 字母排座位），都表達對於未來合作的高度興趣．會中決議先以 50 位核心研究者進行合作，未來以人數 200 人為限舉辦年度會議，以結核病臨床研究為主．新加坡、越南、泰國則針對特定的議題提出近期合作的可能性．台灣則由萬芳醫院李枝新醫師代表研究者，表達該院對於多元研究合作的意願．整體來說，結核整合網絡對於提升台灣本土結核病控制並無直接幫助，但合作可大幅增加亞太區域其他國家學者和官員，對於台灣藉由結核病進行國際合作，配合新南向等政策的可見度，提升未來合作的便利以及切入其他新南向國家的可行性．

二、背景

目前結核臨床研究最蓬勃的是以南非為首的非洲地區，各大藥廠和基金會都以南非等國為主要的臨床試驗點，主要是因為該地區的結核病盛行率高，可以高效能的收案並且臨床試驗相關產業相對成熟．有鑒於此，同樣有大量結核病人的亞太結核病高負擔國家，例如中國、印度、越南、泰國、印尼，也相當有熱誠想要進入這個領域．新加坡大學 Nick Paton 教授 （曾為英國倫敦熱帶醫學背景的團隊執行 TRUNCATE Trial）為代表，申請了 APEC 經費，以亞洲區域結核病研究及臨床試驗整合網絡 (Asian Tuberculosis Research And Clinical Trials Integrated Organisational Network, A-TRACTION) 工作坊的形式，目標是促進亞太經濟體區域結核病研究網的形成，經費除了開會辦一場邀請亞太經合會經濟體的研究者來新加坡開會之外，還將成立一個數據資料平台先將各國願意加入研究的學者所提供的特定研究目的項目，促進臨床試驗研究合作的開端．希望未來可以跨國合作進行臨床試驗，以促進亞太地區相關臨床試驗發展．

三、目的

1. 透過研究會議瞭解新南向國結核病防治面臨問題，進而評估我國轉植技術之可行方案·
2. 了解不同形式的 APEC 工作坊辦理情形
3. 了解各國研發結核病疫苗之策略及進展及亞太地區對新疫苗臨床試驗的競爭力·

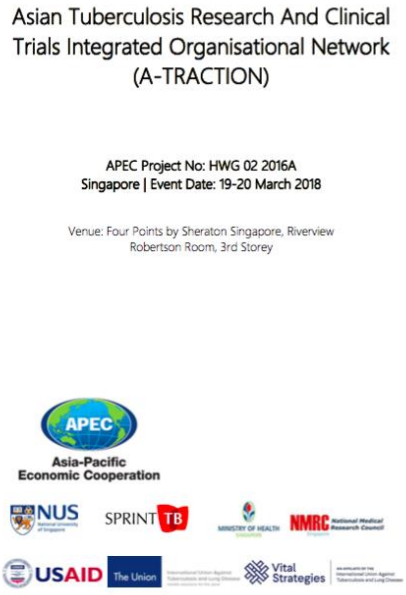
四、過程

1. 行程表：

日期	工作 日誌	地　　點	行　程　內　容
107/03/18	啟程	台北→新加坡	路程、抵達
107/03/19~ 107/03/20	APEC 會議	新加坡	參與討論
107/03/21	返程	新加坡→台北	路程

2. 內容：

亞洲區域結核病研究及臨床試驗整合網絡 (Asian Tuberculosis Research And Clinical Trials Integrated Organisational Network, A-TRACTION) 目標是促進亞太經濟體區域結核病研究網的形成，經費除了開會辦一場邀請亞太經合會經濟體的研究者來新加坡開會之外，還將成立一個數據資料平台先將各國願意加入研究的學者所提供的特定研究目的項目，促進臨床試驗研究合作的開端．希望未來可以跨國合作進行臨床試驗，以促進亞太地區相關臨床試驗發展．此會議還有國際抗癆聯盟在新加坡的亞太分部 (The Union, Singapore office)和美國國際發展署 (USAID) 支持，所以 Meera 有出席，並且 Vital Strategies 也派在菲律賓一起工作過的 Lenna 出席．



主持人 Nick Paton 教授，在結核病界研究相當有名，曾為英國倫敦熱帶醫學背景的團隊，並以執行一般非抗藥性結核病治療從六個月縮短成 2 個月含 Linazolid, Bedaquiline, Levofloxacin, 或 Delamanid 治療的 TRUNCATE Trial 為人知 (http://www.pasteur-kh.org/wp-content/uploads/2016/01/Session-5-1130-Paton_revised.pdf)

兩天的會議行程如下：

Agenda Day 1: Monday 19 March 2018, afternoon

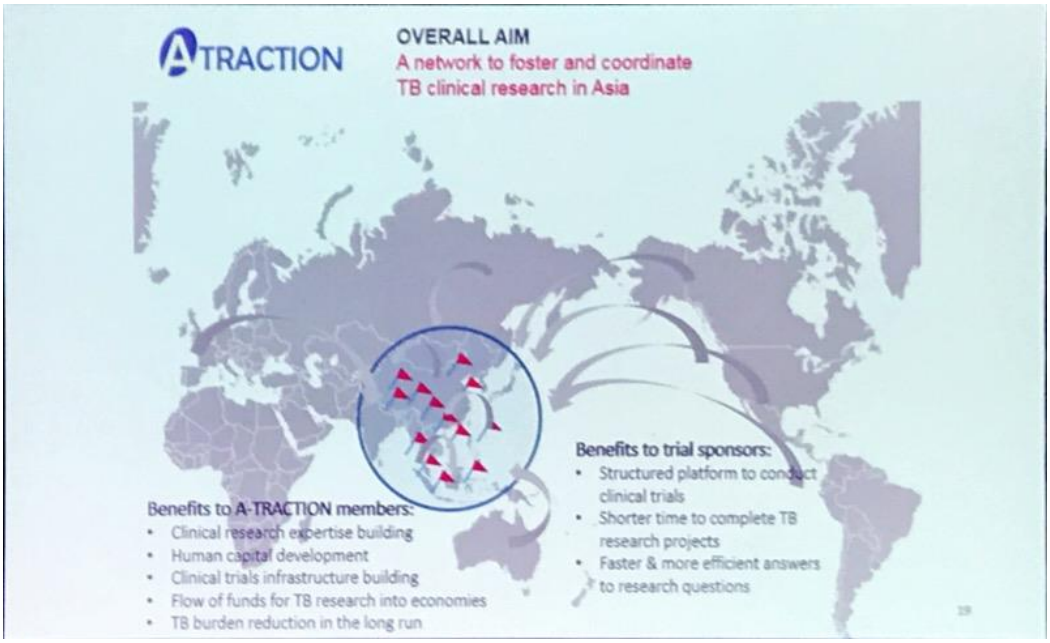
13.45	Reconvene	
13.50	Discussion of Asian TB Research Symposium: Value Organisation Funding	All
15.10	Tea break	
15.30	Discussion of Asian TB Clinical Research Network: Value Organisation & Governance Funding	All
17.00	Close	

Group dinner	Meet 6.45pm Lobby, Four Points (5 minutes' walk to restaurant – Shabestan)

Agenda Day 2: Tuesday 20 March 2018, morning

8.45	Arrival & Sign in	
9.00	Summary from Day 1	Nick Paton
9.15	A. Discussion of programme structure / content for annual research symposium AND / OR B. Discussion of initial projects for research network collaboration and funding	All
10.30	Coffee break	
11.00	Continue discussions	All
12.15	Summary and wrap-up	Nick Paton
12.30	Close	

第一天會議主要是要形成共識，上午的會議簡單中分成三個部分進行報告及討論，上午由 Pro. Peton 先釐清研究網絡組成的目的，他整理了最近幾年跟國際合作有關的文獻研究，發現居然都是跨洲的研究比較多，區域內的合作不成比例的低．



接下來讓各國代表自我介紹， 除了主辦新加坡和我國之外，依序為柬埔寨、中國、香港、印尼、馬來西亞、日本、印度、菲律賓、蘇聯、泰國、越南等國 （依各國與會代表 given name 字母排座位），一一自我介紹，其中能代表國家結核病計畫部門 (亦即有官方或官方代表)，除了我國之外，只有中國，泰國和越南，某種程度上也讓學者和官員認識交流．

台灣臨床研究報告則由萬芳醫院李枝新醫師代表研究者，除了報告台灣多重抗藥性結核病治療的成功現況，也介紹每個月非抗藥病人約有 20 位，以及強而有力的專家群以及品質優良的實驗室，可作為研究的後援。

Agenda Day 1: Monday 19 March 2018, morning

8.45	**Arrival & Registration**	
9.00	**Welcome, Introductions, Objectives**	Nick Paton
9.20	**TB clinical research sites in Asia** (5m each)	
	Cambodia: Institut Pasteur du Cambodge, Phnom Penh	Laurence Borand
	China: Beijing Chest Hospital	Yuhong Liu
	China: Shanghai Pulmonary Hospital	Wei Sha
	Hong Kong: Hong Kong TB & Chest Service	Chan Chi Kuen
	India: B J Medical College & Civil Hospital, Ahmedabad	Rajesh Solanki
	India: National Institute for Research in TB, Chennai	Padmapriyadarsini Chandrasekaran
	India: National Institute of TB and Resp. Diseases, Delhi	Rohit Sarin
	Indonesia: Universitas Padjadjaran, Bandung	Nina Ruslami
	Japan: Research Institute of Tuberculosis, Tokyo	Takashi Yoshiyama
	Malaysia: Inst. of Pulmonary Medicine, Kuala Lumpur	Zamzurina Abu Bakar
	Philippines: Quezon Institute, Quezon City	Jubert Benedicto
	Philippines: De La Salle Health Sciences Institute, Cavite	Victoria Dalay
	Russia: Natl. Med. Res. Ctr. Physiopulmon. & ID	Anastasiia Samoilova
	Taiwan: Tuberculosis Center, Wanfang Hospital	Chih-Hsin Lee
	Thailand: HIVNAT/Chulalongkorn University Hospital	Anchalee Avihingsanon
	Vietnam: Vietnam National Lung Hospital, Hanoi	Le Van Hoi
	Vietnam: OUCRU/HTD, Ho Chi Minh City	Guy Thwaites
10.45	**Coffee break**	
11.15	**TB Multicentre Networks in Asia** (10m each + 2m Qs)	
	National	
	China Tuberculosis Clinical Trial Consortium	Yuhong Liu
	India: National TB Consortium	Rohit Sarin
	Indonesia: INA-RESPOND	Muhammad Karyana
	Thailand Tuberculosis Research Network	Surakameth Mahasirimongkol
	Vietnam: VICTORY programme	Le Van Hoi
	Multinational	
	SPRINT-TB Asian TB Network	Nick Paton

第一天下午的會議，討論的主題為是否有需要辦一場研討會，而這個研討會需要哪些參與者；經過對合作形式和內容深入的討論，會中決議先以 50 位左右核心研究者進行合作，未來以人數 200 人以內為限，舉辦年度會議（提供年輕研究者與會機會），以結核病臨床研究為主，不依附於 Union 世界大會會議，可提升效率及減少經費支出．會中，中國和蘇聯分別提出有意願辦年會．但大家還是不曉得經費要來自哪個地方或哪個基金來源．

第二天上午的會議，討論兩大主題，經費來源以及大家有興趣的研究主題．首先花了很多時間要大家分享如何爭取跨國研究的預算，先討論是否有國家的經費是可以作為跨國研究之用，討論的結果，跨國臨床研究的經費若欲使用國家的預算在各國都有實質上的困難，最好能夠申請國際合作的經費來支應早期的合作，建立模式和走向．泰國代表表示 E-Asia 可能可以申請部分的經費，中國、蘇聯等國都直接明說是否可以爭取藥廠的經費贊助．

接下來由已經有題目想徵求大家加入的合作案報告，分別是新加坡團隊提出在抗藥性病人治療期間若超過三個月未陰轉，要進行 MIC 相關研究；另外是越南團隊的代表 Guy 跟大家遊說加入已經由 Welcome Trust 資助的兒童結核腦膜炎的研究，他需要 400 個病人但是全越南目前只有 120-150 位，在場印尼的學者也有參加這個六個月高劑量臨床試驗．越南（病人的主動發現以及潛伏結核感染短程處方）泰國 (愛滋病人的短程潛伏結核治療)，針對特定的議題均提出近期合作的可能性．台灣則由萬芳醫院李枝新醫師代表研究者，表達該院乃至台灣的多重抗藥性團隊對於多元研究合作的意願．會中決議，願意起頭的國家請提 proposal 給 Pro. Paton，後續將提供給所有的代表參考．

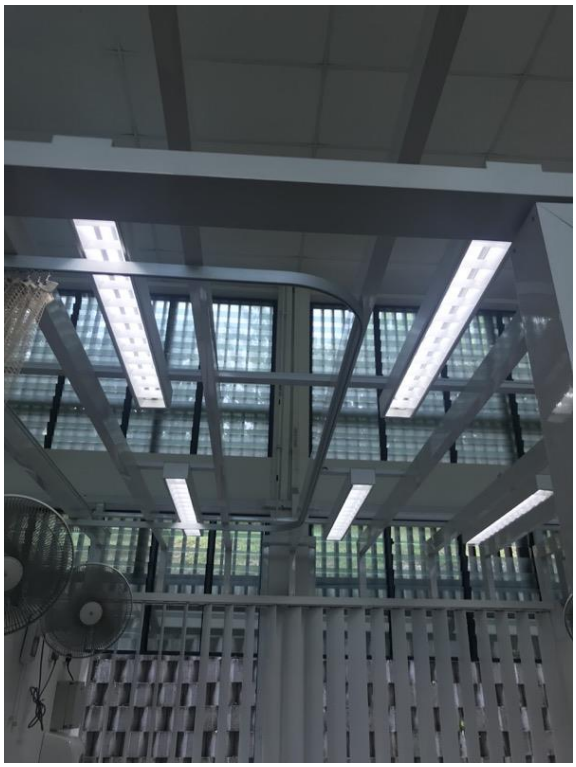
泰國的現任國家結核病計畫主任是 Dr. Phalin，我們在會議中討論如何經由溝通，能早一點瞭解自己國內進行中的結核病臨床試驗，將有助於 NTP 的發展，泰國從 2018 年開始，推動兒童接觸者檢查，Dr. Phalin 表達有機會希望台灣多跟泰國交流，增強他們政策的推廣正當性．

由於台灣今年新南向政策以越南北部為重點經營項目，此次代表出席的越南河內胸腔病院的副院長 Le Van Hoi，也是國家結核病計畫的代表衛生部執行的機構, 特別與我們交換將來在廣寧省合作要注意的事項以及實質如何完成，以及推動 2035 目標·

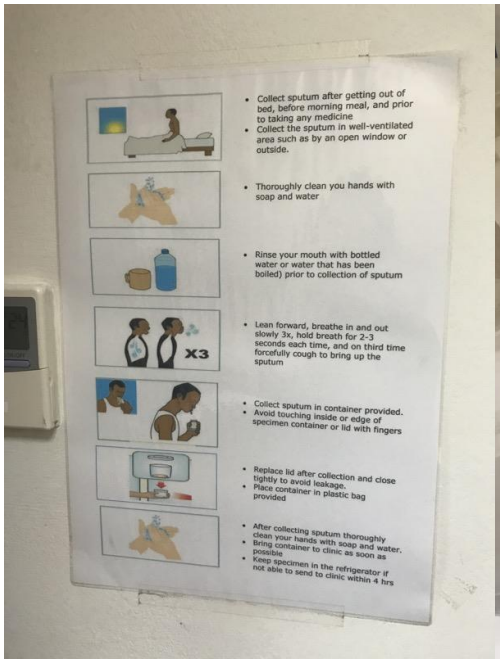
日本來的 JATA 代表，由結核病院 Fukujuji Hospital 的 Takashi Yoshiyama 出席該會議。

下午會議結束後，我和李醫師前往新加坡結核病防治中心，位在北邊的 TBCU 環境清幽外，看診中心已經三年前改建之後，不但美輪美奐，重點是完全符合感控和實務的要求，設計上盡善盡美．原則上把結核病人初診斷，複診追蹤和接觸者，在兩棟獨立的診所三個分開的空間看診，除了藥局共用外，一律不共用．挑高超過 3 公尺的天花板，以及負壓取痰室的設計，負壓 MDR-TB 病人看診室，到點都治和社工的配備以及完全自然通風的病人候診看診區．

掛號批價區超高的天花板，讓熱空氣上升，帶動自然循環，電燈管則架在一半高度，有效率又省電，完全不影響通風．



負壓取痰室


Collect sputum after getting out of bed, before morning meal, and prior to taking any medicine
Collect the sputum in well-ventilated area such as by an open window or outside.
Thoroughly clean you hands with soap and water
Rinse your mouth with bottled water or water that has been boiled) prior to collection of sputum
X3
Lean forward, breathe in and out slowly 3x, hold breath for 2-3 seconds each time, and on third time forcefully cough to bring up the sputum
Collect sputum in container provided.
Avoid touching inside or edge of specimen container or lid with fingers
Replace lid after collection and close tightly to avoid leakage.
Place container in plastic bag provided
After collecting sputum thoroughly clean your hands with soap and water.
Bring container to clinic as soon as possible
Keep specimen in the refrigerator if not able to send to clinic within 4 hrs


Check all Sputum Specimen Bottle
Before Putting for Despatch :
- Cap Properly Screw Tight
- Correct Patient Sticker

用百葉窗做成的牆壁完全沒有通風的限制

齊醫師和王醫師一共 12 位醫師，替新加坡所有的結核病人開處方，接觸者由這邊詢問，然後轉介來這邊檢查 （包括收容人）· 每年約完成 12000 名接觸者檢查業務，估計約有 7 成完成，但重點是是否都有匡列，他們自己覺得很難精進 · 他們很羨慕台灣在接觸者潛伏結核感染診斷與治療，能夠系統性的由政府管理接觸者以及新的短程處方的引進，確保使用正確又能有效提高民眾的接受度和完治率 ·

五、心得與建議

亞洲區域結核病研究及臨床試驗整合網絡 (Asian Tuberculosis Research And Clinical Trials Integrated Organisational Network, A-TRACTION) 順利成立，會議中經過對合作形式和內容深入的討論，會中決議先以 50 位左右核心研究者進行合作，未來以人數 200 人以內為限舉辦年度會議，以結核病臨床研究為主，不依附於 Union 世界大會會議，可提升效率及減少經費支出．主辦會議的可能人選，會中中國和蘇聯提出有意願開會，新加坡越南泰國則針對特定的議題提出近期合作的可能性．未來要討論的是，跨國臨床研究的經費若欲使用國家的預算在各國都有實質上的困難，最好能夠申請國際合作的經費來支應早期的合作，建立模式和走向．台灣則由萬芳醫院李枝新醫師代表研究者，介紹台灣結核病控制的狀況，以及表達該院對於多元研究合作的意願．整體來說，結核整合網絡對於提升台灣本土結核病控制並無直接幫助，但合作可大幅增加亞太區域其他國家學者和官員，對於台灣藉由結核病進行國際合作，配合新南向等政策的可見度，提升未來合作的便利以及切入其他新南向國家的可行性．

建議有三項：

1. 支持台灣有能力執行結核病臨床研究的團隊加入 A-TRACTION，未來有機會執行老人結核病疫苗等相關的試驗
2. 配合台灣團隊加入該會的活躍程度及國際合作部門的需求，可考慮於台灣舉辦 A-TRACTION 年會．
3. 新南向本期計畫可與河內胸腔病院透過國家結核病計畫既有的藍圖策略，讓我國結核病模組在廣寧推動，能符合越南政策方向．

六、附件

Minutes of the meeting to discuss formation of a TB clinical research network in Asia: Asian Tuberculosis Research and Clinical Trials Integrated Organisational Network (A-TRACTION)

Held at Four Points by Sheraton,
Singapore 19-20 March 2018

Attendees:

Zamzurina Abu Bakar	ZA	Institute of Pulmonary Medicine, Malaysia
Anchalee Avihingsanon	AA	HIVNAT/Chulalongkorn University, Thailand
Tara Bam	TB	International Union Against Tuberculosis and Lung Disease
Jubert Benedicto	JB	Quezon Institute, Manila, Philippines
Rahizan Binte Issa	RI	Institute for Medical Research, Malaysia
Laurence Borand	LB	Institut Pasteur, Phnom Penh, Cambodia
Alan Chi-Kuen Chan	ACKC	Hong Kong TB & Chest Service, Hong Kong
Anita Pei-Chun Chan	APCC	Ministry of Health and Welfare, CDC, Chinese Taipei
Padma Chandrasekaran	PC	National Institute for Research in TB, Chennai, India
Victoria Dalay	VD	De La Salle Health Sciences Institute, Cavite, Philippines
Martin Hibberd	MH	National University of Singapore
Le Van Hoi	LVH	Vietnam National Lung Hospital, Hanoi
Phalin Kramolwat	PK	Bureau of TB, Dept. of Disease Control, MoPH, Thailand
Muhammad Karyana	MK	Center for Resource Devt & Health Services, Indonesia
Chih-Hsin Lee	CHL	Tuberculosis Center, Wanfang Hospital, Taiwan
Eryong Liu	EL	Chinese Center for Disease Control and Prevention
Yuhong Liu	YL	Beijing Chest Hospital, China
Surakameth Mahasirimongkol	SM	Dept. of Medical Sciences, MoPH, Thailand
Igor Medvinsky	IM	Ministry of Health of the Russian Federation
Nicholas Paton	NP	National University of Singapore
Rovina (Nina) Ruslami	RR	Universitas Padjadjaran, Bandung

Anastasiia Samoilova	AS	Ministry of Health of the Russian Federation
Rohit Sarin	RSa	Natl. Institute of TB and Resp. Dis. (NITRD), New Delhi, India
Rajesh Solanki	RSo	B J Medical College & Civil Hospital, Ahmedabad, India
Guy Thwaites	GT	Oxford Uni. Clin. Res. Unit (OUCRU), Ho Chi Minh, Vietnam
Sha Wei	SW	Shanghai Pulmonary Hospital, China
Takashi Yoshiyama	TY	Research Institute of TB, JATA, Japan
Lin Zhou	LZ	Chinese Center for Disease Control and Prevention

Organisational support

Meera Gurumurthy	Vital Strategies / IUATLD
Leena Patel	Vital Strategies / IUATLD
Pauline Yoong	NUS

DAY 1 19th March, 9am – 5pm

INTRODUCTIONS AND OBJECTIVES

NP outlined the background to the meeting (limited international collaboration between TB clinical research centres within Asia, versus the substantial international collaboration between Asian institutions and centres outside Asia). The objectives of the meeting are to discuss the value of forming an Asian TB Clinical Research Network and how that might function; and the value of holding an annual Asian TB Clinical Research Symposium (presentation slides in Appendix).

TB CLINICAL RESEARCH SITES IN ASIA

The following presentations were given that described activities at individual TB clinical research sites in Asia (presentation slides in Appendix)

LB, Cambodia: Institute Pasteur du Cambodge, Phnom Penh, Cambodia

YL, China: Beijing Chest Hospital, China

SW, China: Shanghai Pulmonary Hospital

ACKC, Hong Kong: Hong Kong TB and Chest Service

RSo, India: BJ Medical College and Civil Hospital

PC, India: National Institute for Research in Tuberculosis (NIRT)

RSa, India: National Institute of Tuberculosis and Respiratory Diseases (NITRD)

RR, Indonesia: Universitas Padjadjaran, Bandung

TY, Japan: Research Institute of Tuberculosis, Tokyo

ZA, Malaysia: Institute of Pulmonary Medicine, Malaysia

JB, Philippines: Quezon Institute

VD, Philippines: De La Salle Health Sciences Institute

AS, Russia: Ministry of Health of the Russian Federation

CHL, Taiwan: TB Center, Wanfang Hospital

AA, Thailand: HIVNAT/Chulalongkorn University Hospital

LVH, Vietnam: Vietnam National Lung Hospital

GT, Vietnam: Hospital for Tropical Diseases, Ho Chi Minh City

TB MULTICENTRE NETWORKS IN ASIA

The following presentations were given that described the activities of Asian national TB clinical research networks, then Asian multi-national TB clinical research networks (presentation slides in Appendix).

National TB clinical research networks

YL, China: China TB Clinical Trial Consortium (CTCTC)

PC, India: India National TB Consortium (ITRC)

MK, Indonesia: The Indonesia Research Partnership on Infectious Disease (INA-RESPOND)

SM, Thailand: Thailand Tuberculosis Research Network (ThaiTURN)

LVH, Vietnam: Vietnam Integrated Center for TB and Respirology Research (VICTORY)

International networks

NP, Singapore: Singapore Programme of Research Investigating New approaches to Treatment of Tuberculosis (SPRINT-TB) Asian TB Network

GT, Vietnam: Oxford University Clinical Research Unit (OUCRU) Asian TB Network

DISCUSSION OF ASIAN TB RESEARCH SYMPOSIUM (1)

Chaired by GT, Vietnam

RSa, India: Need to consider how this fits with the existing conferences, mainly The Union conference and American Thoracic Society conference. There are some unique issues in Asia. Important to have an opportunity to learn from each other. For funding and research priorities it is important to understand what has already been done, what does not work and what does, and make informed decisions about research priorities. A TB research symposium would be an important opportunity to share Information regarding new diagnostics, treatment options, research ideas/focus, and funding

avenues.

PC, India: Need to consider the audience for this meeting, its purpose, and what is the advantage over other meetings.

JB, Philippines: Important to know what is going on in the region; will make it easier to foster collaborations. Could join on to the Union Asia-Pacific (UAP) meeting which offers separate locations for satellite meetings; can have an A-TRACTION research meeting/symposium within the UAP meeting. For the content, could have countries present their own-country/centre initiated research studies. Even though funders/donors may be from outside Asia, it's acceptable if the idea originates from the country. Would be useful to provide training/insight into how to access funds to help countries pursue their research interests – most of us have problems gaining access to funds.

IM, Russia: It is the relationship between private companies and hospitals that drives activities/collaborations in clinical trials in Russia. There is no central network for conducting trials. Think there would be value in emulating networks that have been described in other Asian countries. Would like to explore different models of funding

GT, Vietnam: There is also a mix of funding models in Asia – some are commercial funded, some are government funded.

LVH, Vietnam: A symposium would be of value not only to share ideas in research, but also to do small collaborative studies. It could provide support to young researchers. The research community could provide inputs for TB control policies and foster the relationship between researchers and policy makers. Agee can align with Union Asia Pacific regional conference, but may need to hold additional meetings/conferences

TB, IUTLD: Important to engage policymakers in research outputs/dissemination. We do research at different levels – how do we translate that to the policymakers in the countries? A Union project called The Asia Pacific Member of Parliament Alliance, could fit well with a regional clinical research symposium – to share results and may generate Government political and financial support for the endeavours. In Indonesia, the Universal Health Coverage (research funding from Tobacco tax for Tobacco/TB related research) shows how can generate country-level funding. Similarly other countries can engage policymakers and media to generate research funding.

GT, Vietnam: Should the meeting be purely research-based or combined policy/advocacy/community?

PK, Thailand: Both, but important to determine who should be the correct invitee/focal point for the country – who can combine policymakers and researchers?

JB, Philippines: Focus should be research but research can be packaged such that it is palatable for policymakers, administrators (and media), then it will make the symposium more relevant and impactful.

RSa, India: No denying that research must eventually feed into policy change etc., the focus of this could be mainly driven by research – focus, priorities, agenda and results of clinical research ongoing in the country.

PC, India: Do we need to have a separate meeting? Consider the example of separate HIV meetings: CROI (basic science) and IAS (policy) are separate. The Union meeting is mainly implementation/ operational research. We need to define what kind of meeting we want it to be. Do we want to be a pre-meeting before the Union meeting? Or do we want to be an independent meeting? I think should try to focus on clinical research; especially representations/visibility of activities happening

in Asian countries.

LB, Cambodia: I am in favour of the symposium to share what we are all doing, develop exchanges and possibly build research programmes together. We should be more represented in clinical trials, globally. We need to get together to get more funding. We don't have that here, compared to Africa. A symposium should include training on clinical research. Agree about advocacy: we should work with NTPs etc. but there are many other platforms for that.

VD, Philippines: Yes, we should have a regional symposium. Will increase visibility and will allow us to share results/data and challenges/issues faced while conducting trials

GT, Vietnam: At which stage should you engage policy makers?

LB, Cambodia: Before, useful to engage so results can be translated.

RSa, India: Policy makers/programme managers have research priorities; but this symposium could be to know about what is happening in research (design, implementation challenges, results, data, etc.).

APCC, Taiwan: National TB Programs are usually not aware of what is happening with TB clinical trials. These deviate from standard treatment so it's useful to engage NTP to get support for DOTS, follow-up etc. Should increase discussion on how NTPs can support research; should not become a barrier. It's important to communicate both positive and negative outcomes of trials back to NTP; to have a dialogue between government and partners (researchers and funders)

ACKC, Hong Kong: Before we conduct a clinical trial, we have to seek approval from the relevant authority. It may not be necessary to engage the policymaker every

time but if we are doing a clinical trial that will produce results it will be better to engage the policymakers before the start.

PC, India: There is a difference between inform vs. involve/engage. Clinical trials are not really top agenda/priority for programmes versus implementation or operational research. Therefore inform but not necessarily engage. Could replicate the BRICS network model: lead project from one country replicated in other countries/collaborate.

AA, Thailand: For the symposium we can have some sections for researchers, and another section for policymakers. We can combine multiple aspects to one symposium. HIV has so many symposia, there are but not so many in TB. Can start off with knowledge-sharing session, then ongoing research (design, progress, etc.), lastly engagement with programme/policy.

NP, Singapore: Few of the TB meetings have a clinical research focus. Despite the existing numerous HIV meetings, there was still room for an Asia Pacific HIV conference that started 2 years ago and attracts 300-400 people; oriented towards junior researchers. Held in Asia so accessible to most countries to travel. Could be a model.

GT, Vietnam: Should it be a smaller clinical research meeting and leave the policymaking and advocacy to the Union meeting?

PC, India: Could be 1.5 days: 1 day for basic science and translational research + half day advocacy (to make the meeting/network more visible)

GT, Vietnam: what would we say/communicate to policy makers/advocates?

PC, India: Showcase already available results/data etc.

GT, Vietnam: There may be 2 meetings then – the clinical research meeting and the policy making meeting. Who is interested in scientific meeting vs policy meeting vs both? [show of hands: most interested in clinical research/science meeting, a few willing to attend both; none for policy meeting only]

RR, Indonesia: We work together with the government. Yes, we want to change what is happening, but hopefully the evidence for change comes from ourselves, from Asia, not from others. We want the symposium to solve the problems efficiently and not for every site to do the same thing.

NP, Singapore: Advantage of a smaller meeting – we can present research in progress, at the intermediate, development stages (difficult at large international meetings because competition for time favours completed research). A smaller group means a friendlier environment. A slightly larger meeting, 100 – 150 means we can include the juniors as well. Preferred size? [Show of hands: most support for < 50 or 50-100; few for 100-200; none for >200]

RSa, India: For brainstorming, <50 better. For sharing could be 100-200. Therefore need to define the objective of the meeting: is it brainstorming for new ideas/strategies, or sharing of info?

LB, Cambodia: One option will be to have the meeting with the approximate number of people to work on the projects based on the network that we are going to create. Can we brainstorm about ideas, collaborate, work together and gain visibility at larger meetings (Union)?

NP, Singapore: For brainstorming I see this as functional part of the research network rather than a scientific symposium which is more for education/ sharing research.

MH: Should have a meeting to develop an agenda for the network – to define research

idea, collaborate (and have a meeting to facilitate this). Can separate the network research agenda meeting and the symposium.

DISCUSSION OF ASIAN TB CLINICAL RESEARCH NETWORK (1)

Chaired by NP, Singapore

Purpose / value of network

NP, Singapore: Is there value for an Asian TB clinical research network? Already existing national networks. Is there a need for another one?

AA, Thailand: Every time that I go to a HIV conference, they focus more on African country, it seems like Asia is being left behind, in every aspect, not just HIV. Asians are unique, the food, the culture and this may affect the drug action, drug absorption. There are so many aspects that we can look at specifically for Asians. We can collect more data together, it will be stronger, more powerful for publication. So we should have an Asian network, apart from the benefits already mentioned – the sharing.

RSa, India: Strength to Asian voice both at global level and at in-country level

SM, Thailand: Need for Asian specific network backed up by scientific/clinical reasons: Asian host transcriptome different, Asian Mtb strains different, contributes to different treatment responses. We cannot explain why mortality is higher in our operational settings. These are the biological reasons why we need to focus on Asian TB.

ACKC, Hong Kong: TB patient profiles in Asia different with difference between countries also: DR-TB, paediatric TB, TB meningitis etc. Good to have a network that

can complement each other's research studies with inputs into research design, etc.

RR, Indonesia: Agree there is a need for an Asian research network. Data from Africa about evidence for dosing, drug-drug interactions, polymorphism etc. Good/important to have Asia specific research studies to generate our own data to answer safety and efficacy data

NP, Singapore: Agree need more Asian data, but do we need another network for that? What value?

GT, Vietnam: Would increase generalisability, reproducibility, efficiency (relying on central data management, laboratory management, use of specific procedures in trials, etc. capacity building). TB as an epidemic is very different in Asia (not largely driven by HIV but mostly smoking, diabetes, etc.)

ZA, Malaysia: Advantage for smaller countries like Malaysia where there are no existing networks, so may benefit being part of studies with other countries that can help generate evidence for local practice.

TY, Japan: In Japan, TB is mainly in ageing population and in diabetics, therefore it would be useful to understand what other countries face/experience and learn from how they manage.

SM, Thailand: A network would allow sharing of experiences with international collaborators; publications of national research may be in national journals which may not be accessible due to language barrier. This network can also interact with the larger networks. How is this network different from BRICS (it has RIC without B & S)?

<u>Network organisation</u>

NP, Singapore: How should the network work with the existing national networks? Pick the best sites to work directly with the network, or to work through the existing national networks' governance structure?

YL, China: It would be better for the country to join the Asian network through the existing network rather than individual sites joining the network separately. How to balance the sites' studies/activities in their participation in CTCTC, ACTG, Asian network?

SW, China: Maybe could select a subset of sites from CTCTC to work on the Asian network?

EL, China: Important to collaborate with NTP instead of working with the network or individual sites.

RSa, India: We already have an existing network with framework and research agenda (already includes research institutes, Govt., programmes etc.). Therefore best to collaborate directly with the ITRC

RSo, India: Any hospital, medical college will come through this route.

MK, Indonesia: Can work with existing network and network can reach out to appropriate sites/bodies.

LVH, Vietnam: For Victory network, NTP provides technical assistance and financial support + training courses. So it would help to work through the network.

SM, Thailand: Can keep existing collaborations, but easier if you go through the

network because everyone in the national network will already know each other. Gives the national network responsibility/ownership.

GT, Vietnam: For TB trials, every country needs to go through NTP (because all patients are treated through NTP and medicines are available only through NTP). Therefore need to go through programme but need a "champion" for the network who will really drive the network's agenda and activities forward with the existing country-level network and programme.

NP, Singapore: In summary, agreed best to go through country-level network (for those where it exists), and for directly through sites (where such networks don't exist – which may even be a catalyst for formation of a national level network)

Governance structure

NP, Singapore: Can learn something from NIH funded TB networks. INSIGHT is a network that did many large-scale HIV trials (4000-6000 patients each, with over 200 sites globally). They developed a system of working through existing national networks, or sometimes developed them, each one led from a country coordinating centre. Then there were 4 international coordinating centres to which each national coordinating centre reported, with a steering committee to oversee. This worked well, but maybe we don't need the international coordinating centres. Scientific steering committee, national coordinating centre and sites enough?

AA, Thailand: We worked with INSIGHT and ACTG. Structure is totally different. In INSIGHT, countries had good representation, with ideas coming from countries not just from the scientific committee. All members can access the database and sample storage by submitting a proposal for access. We take turns on who to be on the author list/manuscript. This gives the sites more opportunities to contribute. ACTG is more stringent in terms of limiting access and more paperwork, but if they approve an idea,

they usually try to find funding to support that idea. For TB, we also work with TBTC, but they are very traditional /inflexible in their approach.

NP, Singapore: how does governance structure work with ACTG vs INSIGHT?
AA, Thailand: ACTG works with separate clinical sites, not a national structure. For Thailand, we have Chiang Mai and HIVNAT, they count as different sites. For INSIGHT, they count Thailand as a country.

NP, Singapore: So the INSIGHT one sounds more like the arrangement suggested for A-TRACTION working with national networks.

PC, India: Maybe we should learn from the limitations of ACTG. The steering committee was made up of people who were not directly involved in the research. Would prefer model where steering committee members are involved directly. There should be a representative from each country and then leave the day-to-day follow up to each national coordination group. The steering committee should monitor and decide which direction the network should follow.

NP, Singapore: Should all countries have representation on the steering committee? What about individual sites in countries that don't have a national network – group under another centre?

PC, India: Steering committee should have representations from all countries; can have different working groups; would only review scientific robustness of research/proposal and then pass onto country level coordinating focal points for implementation; monitor timelines for projects

YL, China: Management of network: the managerial aspect and the scientific aspect should include people outside Asia.

NP, Singapore: Do we necessarily need to invite people from outside Asia or do we have the capacity to do it ourselves with our resources in Asia?

YL, Singapore: The research agenda, the research priority should be decided by the network itself in Asia. But for the technical part, it would be a value add if we had advice from other experts.

GT, Vietnam: Probably experts from outside Asia at a scientific advisory but not at an organisational level. Although we are a big region and have a lot of expertise, it may not be a bad thing to have advice from outside the region.

AA, Thailand: Could ask WHO to join the group perhaps; or outside institute such as Kirby institute in Australia.

Funding

NP, Singapore: How could we get funding? Will existing networks or government be able to support? For example, travel costs, time to participate in this kind of discussion? Do we have to find central funding to keep making this happen? Can we leave this to individual countries and/or existing networks?

PC, India: Need to consider why will someone (WHO, USAID, UNITAID, BMGF) fund this. Need to promote the value of the network – our conclusion is that Asians are biologically different from Africans for example.

GT, Vietnam: We need a solid idea to take to the funders, get funded, and demonstrate success and then that can be used as a basis for funding the network itself.

PC, India: The way we got funding from the Indian Consortium is that our goal is to end TB. So we need a value strong enough to convince sponsors.

GT, Vietnam: We need a study strong enough to convince. A clear scientific idea to show that we can do something.

NP, Singapore: Agree, I have experienced a number of networks. The ones that take off are those with a concrete project at the start. Need to find a small initial implementable project around which the network can form. The initial funding from APEC includes some funding for network activities for the next 1 year (1 meeting, 1 small project). We can discuss the possible research agenda tomorrow.

ZA, Malaysia: Malaysian governments are hard to approach for these type of studies. We have to source for our own funding. It is quite difficult to support for the network and the meetings.

LB, Cambodia: 5% initiative from Global Fund – if we can show that this network would strengthen GF's activities on the ground. NRF- funding for symposiums

TB, Singapore: There are country-level funding opportunities. Indonesia has money available at national and sub-national level (from tobacco tax). Most of the spending is only 10% of existing funding; if we approach 20 governors, we will at least receive funding from two. Vietnam – similar opportunities exist for tapping funds available with the Public Health program. Cambodia – we are meeting with Minister of Finance/Health Ministry to establish Health Funds (from tobacco/alcohol tax) for activities that are aligned with the national level priorities. The Union can leverage on the relations we have to fund some of the participants. But we have to come up with a strong and sound proposal to convince the sponsors.

DAY 2, 20th March, 9am – 12.30pm

SUMMARY FROM DAY 1

Summary given by NP

Site and network presentations

These showed substantial existing capacity at sites and some well-coordinated intra-country networks. Currently two networks doing clinical studies between Asian countries, but clearly considerable potential for enhancing intra-Asian international collaboration

Symposium

Two models seem to be supported: A. Small size group (<50) for discussing research plans, sharing updates; B. Medium group (50-150) to allow attendance by juniors to present research data, discussing ongoing research, sharing updates

Consensus for agenda based on clinical research, but aware of need to make relevant to policy-makers. Either tag onto Union conference or country network meetings, or stand alone. No final consensus.

Clinical research network

Everyone agreed it would be of value: increased research efficiency, increase overall research activity, promote Asian research agenda (different disease, e.g. less HIV than Africa), generalizability, capacity building, technical support especially for clinical trials

Discussions on structure favoured model of joining the national networks through points of leadership plus including individual sites.

Governance with steering committee with representation from every participating country. Also consider representatives of global bodies such as WHO and Union. External (ex-Asia) members to contribute in scientific advisory role in areas where specific expertise is lacking. Communication: face to face meetings preferred.

Funding for research network: Build-in cost into project costs, funding from existing networks to support participation in the Asian network, international donors – USAID, WHO, ANRS, NTPs?
Need a small achievable project to start/implement in next 6-12 month and a larger project longer term.

DISCUSSION OF ASIAN CLINICAL RESEARCH NETWORK (2)

What can individual countries partners contribute to the network?

IM, Russia: We would like to contribute to research studies. There are two systems. Clinical research is financed by the Ministry of Healthcare, Russian Federation. There is also a system of internal grants, which finance clinical research. We can invite Asian countries to take part in mutual research in TB. In such way we can attract grants, and attracts the grants of the participating countries to develop research in TB. We represent the National Research Centre; the centre that organises TB research in the Russian Federation and would like to have more conversations with representatives in the Asian countries. We would also like to take part in the clinical trials which take place in Asia. It will be more interesting, not only for us, but also for our colleagues because we have a lot of TB patients and the type of patients we have may be different. Probably not possible for clinical trials to be funded with local money as these are normally funded by pharmaceutical companies.

LB, Cambodia: we would be interested to be part of network to work on trials. We could contribute by enrolling patients into trials but also contribute by designing and

running common projects. We have to work on a project to show that we are a viable network.

EL/SW/YL, China: We agree that China should be part of this network. We have a large number of patients and research sites. We can contribute by contributing patients into clinical trials. CTCTC can collaborate with regional network and other country networks to join trials in other countries or open our ongoing trials to other countries.

ACKC, Hong Kong: We have some experience based on previous collaboration with TBTC, and we have very good lab support, so HK is very keen to be a part of the network. We can contribute via capacity building activities (lab based)

MK/RR, Indonesia: We need to align with national priorities to be able to gain funding. Similar to Russia, it is difficult to get money for clinical trial (usually only pharma-funded). There is money from government, but limited by regulations, reporting requirements and the amount is small. And also, if we want to ask for governmental funding, we have to apply 2 years in advance.

PC/RSa, India: India can contribute technical expertise for protocol development, determining priority area for this region; NITRD/NIRT are part of SRL network as well as WHO coordinating/training centre so can help with capacity building. For funding, we have a mechanism to support research/activities (ITRC, National Task Force) – both have funding; if we are convinced about protocol, can get it funded.

TY, Japan: we have few patients; main contribution would be capacity building (lab).

ZA/RI, Malaysia: We want to participate in studies. There is funding for local studies with Ministry of Science, but stiff competition and very small amount. The money we get will likely be just sufficient to get drugs and we may still need international funders to fund the rest.

VD/JB, Philippines: Can contribute patients and technical expertise. May be funding available if the group's proposal is aligned with NTP priority; also from PCHRD (Philippines Council for Health Research and Development).

APCC/CHL, Taiwan: Few patients so limited contribution. If MDR-TB related research, can find some funding support for local existing manpower.

PK, Thailand: There is funding through MOH for Thailand contribution to research. Could contribute through genomics research – there is Thai funding for that.

AA, Thailand: Funding through E-Asia fund is available for projects that have >3 partners/collaborators. Also Newton Fund and Euraxel.

GT, Vietnam: Contribute to designing clinical trials; proposal needs to be competitive for funding; important to use clinical trials to answer several other questions other than just the intervention (biomarkers, PK-PD, treatment response). Wellcome trust is keen on multi-country, multi-centre CTs for TB; therefore have good opportunity.

LVH, Vietnam: Can access country's funding for Vietnam's contribution to a multi-country trial (Ministry of Science – but have not tried before).

NP, Singapore: In summary, based on these and other conversations, it appears to be possible to tap into country-funding for local contributions to trials/clinical research studies in Vietnam, Thailand, Russia, Philippines, India, China. In Malaysia, Indonesia and Cambodia, this may not be feasible. Ideally we need to target international funding agencies for a common proposal: USAID, WHO, Wellcome trust, etc.

Research agenda

Consensus from discussion: focus on Clinical Research/Trial with several sub-studies which address some basic science questions.

Ideas proposed for studies that could involve the network:

Ka–Lip Chew, Singapore
Using Sensititre plate to follow changes in drug susceptibility (MIC) on treatment and relate this to clinical outcomes. Capacity building for lab to introduce new technique. Capacity building for research infrastructure: sample transport. Useful to share pooled information generated from the relational database.
GT/PC already working on longitudinal MIC changes in Vietnam/India.
Decision to share protocols and explore further what is being done and how a common proposal can integrate/add-on further

GT, Vietnam
Wellcome Trust funded trial childhood TB Meningitis, to assess whether 6 months intensive Rx is as good as the standard 12 months and whether addition of aspirin reduces disability (trial in adults showed that high-dose aspirin reduced death in adults). Trial will start in 6-12 mo. Only Vietnam in Asia so far. Protocol draft is developed. Guy will circulate protocol/proposal to anyone interested.

PC, India
Put treatment cascade (information) data from all the countries into a consolidated paper/report? Similar to what was shown in PloS Subbaraman paper. General support for this idea.

LVH, Vietnam
Willing to consider other sites for several studies: ACF with mobile X-rays; New (shorter) TB regimen for LTBI control in high-risk contact groups; all funded studies

AA, Thailand

Latent TB Rx in early ART-treated pts. INH+RFP for 4 weeks or INH+RFP weekly for 12 weeks. To determine which regimen is more appropriate for Asian population. PK/safety of dolutegravir dosing regimen (BID) in Asian population. No funding yet.

NP, Singapore:

We need to find a way to coordinate/circulate proposals – NUS can coordinate initially until someone else in a position to take this on.

We have APEC seed money potentially available for next meeting and for database development activity

We should plan another meeting (within 6 months) with a small group to brainstorm and finalise proposals to take to funding bodies.

DISCUSSION OF ASIAN RB RESEARCH SYMPOSIUM (2)

NP, Singapore: This would be separate from the network meeting to develop research proposals. Small meeting to discuss ongoing research – perhaps a fixed time slot for each country (~1 hour) to share ongoing or completed research studies.

PC, India: will need secretariat to coordinate proposals/participation & organisation in symposium

NP, Singapore: Agreed that Singapore can start off and provide secretariat support for the first year with existing APEC and other Singapore grant support to see through next meeting on proposal development and first symposium. Once governance structure is established, then we can decide how to move forward with secretariat with the intention being that other countries would take this on in rotation.

Plan to circulate minutes and plans for next steps within 4 weeks.

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