計畫編號： MOHW110-CDC-C-31 5-112108

行政院衛生福利部疾病管制署(署內)110年度科技研究計畫

計畫名稱:

傳染病流行風險分析與時序建模及疫情預測研究

# 研 究 報 告

執行機構：疾病管制署主任祕書室

計畫主持人：關嬡嬡

研究人員：關嬡嬡

執行期間： 110 年 1 月 1 日至 110 年 12 月20日

# 目錄

# 中文摘要

本計畫之研究目的在應用統計分析與傳染病監測策略，以剖析與 瞭解我國流行病發生模式，從而利用數理統計方法，建立傳染病疫病 之模擬與預測模式，以提供疫病之預測及防疫措施之研判。研究方法將先以時間數列技術方法(Time-Series Analysis)進行疫病時間序列分析，瞭解歷年趨勢，由數據數列分解分析其整體趨勢、季節性、型態特徵及進行數據資料數理統計建模。第一年使用採用SARIMA、ETS、Hybrid時間數列技術方法之機器學習方法進行疫情總體分析監測、建立結核病之預測模式，資料來源為衍自疾管署傳染病監測系統資料，擷取2005年1月至2020年12月之月通報資料，以季節性整合自我相關移動平均模式 (Seasonal Auto-Regressive Integrated Moving Average)、指數平滑模式(Exponential Smoothing , ETS)、SARIMA-ETS融合模式來探討預測模式且比較每月觀察值與預測值 之誤差。製作台灣總體之結核病流行趨勢及發生率參考圖。結核病(TB)仍然是世界上最致命慢性傳染病之一。建立未來的結核病發生率預測模式工具有利於評量預防介入選擇和資源分配規劃。本研究第一年著重達成開發建立流行病預測的快速單變量預測模型。2005年1月至2017年6月台灣每月結核病發生率監測數據用於建模模擬(in sample simulation)，2017年7月至2020年12月用於模型偽樣本外預測驗證。構建並比較了包括季節性自回歸綜合移動平均 (SARIMA)、指數平滑 (ETS) 和 SARIMA-ETS 混合算法在內的建模方法。樣本內模擬訓練集和偽樣本外驗證集的建模性能通過均方根誤差 (RMSE)、平均絕對百分比誤差 (MAPE)、平均絕對誤差 (MAE) 和平均絕對比例誤差 (MASE)。 經過進行數據集分解分析，該結核病之時間數列資料分解模式分析疫情影響之研究，呈現

季節性及降低趨勢。從2005年1月到2020年12月，台灣共報告191,603 例結核病病例。結核病報告率在2005年最高（每10萬人年72.5例），2020年最低（每10萬人年33.5例），2005年1月至2020年12月台灣地區呈季節性、穩步下降趨勢。我們使用每月的發生率為單位之數據，築構預測模型。採用施行平穩轉化之疾病發生率數據、模型函數演算，進行以準確度指標逐步篩选和評估，分別選擇優化的SARIMA(3,0,0)(2,1,0)12、ETS和SARIMA-ETS-hybrid模型作為候選模型；在模型性能的結果評估方面，2005年1月至2015年6月SARIMA-ETS-hybrid 模型在 RMSE、MAE MAPE 和 MASE 的指標上優於ARIMA模型，在2017年7月-2020年12月模型測試中分別為 0.084、0.067、0.646%和 0.870-樣本預測測試數據集；在對未來進行預測並得出未來幾年的發生率值後，SARIMA-ETS-hybrid 模型預測2025、2030、2035結核病總發生率與2015年比較以推估預測下降程度。由於推估值有95%信賴範圍，實際未來疫情，仍需挹注落實防治作為之持續努力。結論：本研究計畫採用之時間序列模型可提供一種快速監測工具，裨助促進我國快速監測是否達成世衛組織消除結核病里程碑之工具。我們提出的 SARIMA-ETS混合模型在預測流行病發生率，對於未來之超前 12 個月或更短時間(<12個月內)之未來發生率之預測表現優於 SARIMA，並且所有模型都顯示出短期預測比長期預測有更好的表現。第一年已成功建立3種人工智慧預測模型(機器學習)及疫病預測演算，本計畫為二年期計畫，目前在第一年的成果將提供第二年更進一步做其他模式築構及預測演算，納入較細部人口條件及參數，包括導入性別、年齡風險因子等之監測資料進行比對，探討疫病趨勢之優化、精準的趨勢預測模式，並可望應用於跨其他疫病監測系統之建立。本研究計畫採用之時間序列模型可提供

一種快速監測工具，裨助促進我國達成世衛組織消除結核病的目標。我們提出的 SARIMA-ETS混合模型在預測流行病發生率，對於未來之超前 12 個月或更短時間(<12個月內)之未來發生率之預測表現優於 SARIMA，並且所有模型都顯示出短期預測比長期預測有更好的表現。第一年已成功建立3種人工智慧預測模型(機器學習)，本計畫為二年期計畫，目前在第一年的成果將提供第二年更進一步做其他模式築構及預測演算，納入較細部參數，第二年將持續導入性別、年齡風險因子等之監測資料進行比對，探討疫病趨勢之優化、精準的趨勢預測模式，並可望應用於跨其他疫病監測系統之建立。

英文摘要

# Applying SARIMA, ETS, and hybrid models for predication of tuberculosis incidence rate in Taiwan

Taiwan Centers for Disease Control, Ministry Health and Welfare, Taipei, Taiwan.

**Abstract**

**Background**

Tuberculosis (TB) remained one of the world's most deadly chronic communicable diseases. Future TB incidence prediction is a benefit for intervention options and resource-allocation planning. We aimed to develop rapid univariate prediction models for epidemics forecasting employment.

**Methods**

The surveillance data regarding Taiwan monthly TB incidence rates which from January 2005 to June 2017 were utilized for modelling simulation and from July 2017 to December 2020 for modelling validation. The modeling approaches including the Seasonal Autoregressive Integrated Moving Average (SARIMA), the Exponential Smoothing (ETS), and SARIMA-ETS hybrid algorithms were constructed and compared. The modeling performance of in-sample simulating training sets and pseudo-out-of-sample validating sets were evaluated by metrics of the root mean square error (RMSE), mean absolute percentage error (MAPE), mean absolute error (MAE), and mean absolute scaled error (MASE).

**Results**

A total of 191,603 TB cases were reported from January 2005 to December 2020 in Taiwan. The report rate of TB was highETS in 2005 (72.5 per 100,000 person- year) and lowETS in 2020 (33.5 per 100,000 person-year), from January-2005 to December-2020 showed a seasonality and steadily declining trend in Taiwan. The monthly incidence rates data were utilized to formulate these forecasting models. Through stepwise screening and assessing of the accuracy metrics, the optimized SARIMA $(3, 0, 0)\ (2, 1, 0)_{12}$, ETS and SARIMA-ETS-hybrid models were respectively selected as the candidate models. Regarding the outcome assessment of model performance, the SARIMA-ETS-hybrid model outperformed the ARIMA model in the metrics of RMSE, MAE MAPE, and MASE, which were 0.084, 0.067, 0.646%, and 0.870, in the pseudo-out-of-sample forecasting tETS dataset. After projecting ahead to the future and the resulting incidence values for the future years, the predicted TB incidences showed a 41.69% (range: 22.1%- 56.38%) reduction in 2025 and a 54.48% (range: 33.7%-68.7%) reduction in 2030 compared with the 2015 levels.

**Conclusion:**

This time series modeling might offer us a rapid surveillance tool for facilitating WHO's TB elimination goal. Our proposed SARRIMA-ETS or ETS model outperformed the SARIMA in predicting less or more than 12 months ahead of epidemics, and all models showed better short-term forecasting than long-term forecasting.

**Keywords:** TB incidence, SARIMA, SARIMA-ETS, time series modeling

# 第一章 前言

世界各先進國家為了瞭解及掌控重要傳染病的流行趨勢，均建有長期通報及預警監測系統，以觀察疫病的流行狀況。然而，多數監測系統僅止於描述個案發生個數、分布狀況及與過去同期流行個數之比較分析，並仰賴疾病監測人員多年經驗，進行判讀。然，隨著社會經濟、人類行為改變、醫療照護技術演進、環境變遷及土地開發、國際旅行及運輸的便捷…等快速變遷，傳染病流行模式或許有改變，甚或出現新興及再現之傳染病，使得疫情監控更趨複雜。

以結核病防疫分析、監測研究為例：依據世界衛生組織(World Health Organization, WHO)報告指出每年有 2 萬人死亡；超過800 萬，全球為迅速控制滅除結核病，需更有效擴增之控制程序(effective control programme)之施行層面，即世界衛生組織推薦的 DOTS 策略；世衛組織通過一個全球性政策， 其成功的關鍵組成部分結核病項目如下：1）政治承諾，2）病例發現-顯微鏡驗痰，3）監督下服藥療程(DOST)，4）供應確效的抗結核病藥物，5）標準化之記錄、報告和監測系統； 到 2005 年的目標設定治愈率 85%和檢測率 70%。結核病仍是全球傳染疾病防治重點國際 2012 年估計有 860 萬例活性 TB 新病例 1、2010 年有 880 萬結核病新病例被確診， 發生 120-145 萬例死亡，大部分發生在發展中國家；其中約 35 萬死亡發生在合併感染愛滋病毒患者。總計約三分之一世界人口感染結核桿菌(M. tuberculosis)，其中每年約 1 人口，發生新感染。然而，大多數感染結核桿菌不會引起結核病、90-95%感染維持無症狀。約90%感染結核桿菌為無症

狀 潛伏性 TB 感染（LTBI），10%潛伏性感染會在其一生中發展為顯性活性結核性疾病。但在合併感染愛滋病毒，在一年內發展為開放 活動性肺結核增加至約10%風險。若無有效治療，為活動性結核病 病例死亡率高達66%。自世界衛生組織於 1993 年宣布結核病為“全球衛生緊急情況(global health emergency)”，2006 年，遏制結核病夥伴關係制定全球計劃，以控制結核，旨在 2015 年前拯救1400 萬人生命； 此目標在 2015 年實現前的主要障礙，乃是由於HIV 結核病和多重抗藥結核病的出現。世界衛生組織呼籲政府致力於阻止結核病，須抓住一切可用機會；結核病發生率與死亡率雖持 續緩慢下降，逐步實現肺結核發生率目標和 2015 年目標，另在護 理質量、診斷、治療、加強實驗室，並在擴大結核病/愛滋病毒干預， 和 2015 年全球結核防治之夥伴關係-有重大進展。惟，主要挑戰依然存在：發生率與死亡率下降速度太慢，據目前下降速度，在有生之年結核病仍不會被根除；每年新增 440,000 多重抗藥性結核病(MDR-TB)，僅少數被妥適治療，此一應變需更加努力，以擴大和加強其作為 。

臺灣目前整體屬於結核病中度流行地區，自 2005 至 2015 年 各年新發生結核病例個案數分別為 16,472 例(發生率值 72.5 /10 萬人口）、15,378 例(發生率值 67.4 /10 萬人口）、14,480 例(發生率粗估值 63.2 /10 萬人口）、14,265 例(發生率粗估值 62 /10 萬人口)、13336 例(發生率粗估值 57.8 /10 萬人口)、13231 例(發生率 粗估值 57.2 /10 萬人口)、126,345 例(發生率粗估值 54.5 /10 萬 人口）、12,338 例(發生率粗估值 53.0 /10 萬人口)、12,127 例(發生率粗估值 49.0 /10 萬人口)、例(發生率粗估值 48/10 萬人口)、例(發生率粗估值47 /10 萬人口)。目前共

有 6 個直轄市山地原住民區，以高雄市最多，共 3 個。新北市烏來區（原臺北縣烏來鄉）、桃園市復興區（原桃園縣復興鄉）、臺中市和平區（原臺中縣和平 鄉）及高雄市那瑪夏區、茂林區、桃源區（原高雄縣那瑪夏鄉、茂 林鄉、桃源鄉）。目前來自高風險疫區之外配之主要母國包括越南、印尼、菲律賓、泰國、馬來西亞；外籍移工之主要母國包括大陸、 越南、印尼、菲律賓、泰國、馬來西亞等。肺結核目前也是台灣地區最嚴重的慢性傳染病，每年約有約 14,000 例新發生個案，是所有法定傳染病新案人數之首位，高居所有法定傳染病的第一名。

本研究為兩年期研究，第二年度將以不同人口分群條件下，分 別進行時間序列數理模式推估。至於，未來台灣是否得以從中度發 生率國家進入低度發生率國家，是否可在2035年將結核病發生率降 到每10萬人口10例以下。全球約四分之一人口有LTBI，WHO分別於2015、2018 及 2020 年公布最新指引。過去因中低收入國家仍有許多結核病人未接受治療，世衛組織僅建議未滿5歲接觸者及愛滋感染者，進行LTBI治療，於2015年始建議結核病發生率每10萬人口100例以下的高及中高收入國家(臺灣為其一)，針對優先族群(易感染進展到發病)提供 LTBI的診斷與治療；2018年進而建議結核病高發生國家，指標個案為細菌學確認的肺結核病人之非愛滋感染的全年齡家 戶接觸者，在排除活動性肺結核之後，應該加強進行接觸者LTBI診 斷與治療；台灣自2016年全面對於結核病患之密切接觸者進行LTBI 篩檢及LTBI陽性之預防性投藥。2020年的世界衛生組織TB防治指引 改變不大，強調應打破所有執行障礙，讓倡議過的目標族群都得到 並完成結核病預防性治療(tuberculosis preventive treatmentTPT)，以利早日達到2035年每10萬人口10例以下目

標。並建議加強 三事：副作用監測，促進藥物治療的順從性與完成率，及在國家計 畫的管理、監測、評估下推展新處方。另包括考慮國內疫情以65歲以上病人占所有結核病人近60%比例，將檢視該年齡層發生率已逐年下降至2018年低於每10萬人200例，但仍為全國發生率4倍之多，於2018年配合國家長照機構優化政策，推動長照機構老人族群結核病主動發現暨LTBI治療整合計畫；此計畫與提升室內空氣品質，人口密集機構感染管制等策略互搭，強化主動發現，降低機構內群聚及再傳播發生，並降低結核病死亡率。另，臺灣LTBI診斷與治療將逐步推展至非接觸者的結核病優先族群，在2021-2025年期第二期國家結核病計畫，將逐步增加來自結核病高負擔國家的新住民，矯正機關收容人等優先族群，全面進行LTBI診斷與提升治療覆蓋率。本計畫將檢視、評估及預測相關措施是否可逐步達成2023年發生率降到每10萬人口10例以下國家結核防治計畫目標，讓臺灣正式進入低結核發生率國家之列。傳染病對人類的威脅，在人類歷史上未曾歇止；1998年台灣曾因腸病毒大流行，造成民眾大震撼，全球過去曾因於1889、1918、1957 及 1968 年發生世界性流感大流行，而地區性流行更是年年發生，而2003 年新興傳染病 SARS 的出現，更讓社會付出了相當大經濟成本。2019年COVID19出現，亦帶給全球新的防疫衝擊及運應而生之防疫科技發展之成功對抗。因此，建立監控各種重要傳染病的有效機制， 實為當務之急。本研究計畫工作重點將建立疾病預測模式，期能於提供監測工具，作為監測警訊，俾助提醒政府相關監測人員，及早因應準備、適時採取行動，以達防範或減災之功能。

本研究目的以建立結核病種疾病之預測模式為主，使用疾病管制署通報系統之資料做為建立預測模式之基礎，並加上性別、年齡、地理…等可能之影

響因子建立預測模式。

# 第二章 材料與方法

## 第一節疾管署通報資料分析

### 一、數據源

結核病病例和人口數據分別來自台灣疾病管制署（CDC）與台灣內政部網站。然後，隨後計算TB發生率。所有結核病例均通過臨床症狀初步診斷，並經細菌學和病理學檢查確診。在台灣，結核病是國家法定傳染病，醫院醫生必須及時報告病例，即結核病病例必須在 7 天內通過台灣疾病管制署授權的台灣結核病登記系統進行國家級監測。

研究期間包括從 2005 年 1 月到 2020 年 12 月診斷的病例，並根據確診病例的公開數據每月匯總和分析結核病發生率數據集（附錄 A：原始數據的可用性）。數據分為訓練數據和驗證數據。然後，分別基於2005年1月至2017年6月的數據（樣本內，訓練數據集）生成模擬模型。並且，預測測試模型基於2017年7月至2020年12月的數據（偽樣本外，預測測試數據集）。此後，我們 利用優化模型預測到 2030 年 12 月的未來預測。

### 二、STL分析

基於局部加權回歸（Loess）的季節性趨勢分解稱為 STL，最初由克利夫蘭於1990[14]年提出，被選為一種過濾程序，旨在將時間序列分解為趨勢、季節性

和剩餘部分。

## 第二節時間數列分析方法

### 一、SARIMA模型的構建

季節性自回歸綜合移動平均 (SARIMA) 模型是季節性 ARIMA6-10。 SARIMA 模型的一般形式如下： (p,d,q)(P,D,Q)S，其中 p 和 q 分別是自回歸 (AR) 和移動平均 (MA)分量的階數， d是差異的階數，P、D和Q是對應的季節階數，S 代表季節差異的步長。 SARIMA 模型是根據前面描述的基本原理建立的。我們通過 R 套件R套件功能函數式 函數構建它。作為一種自動預測模型，Ljung-Box Q 檢驗用於診斷殘差序列是否為白噪聲序列。根據最低 AIC [15]、AICc 或 BIC[15]自動選擇性能最佳的模型。

### 二、ETS模型

ETS 模型考慮給定時間序列的誤差、趨勢和季節性成分，並在選擇性能最佳的模型來模擬數據之前評估可能的替代模型 [12]. 主要三個參數是誤差、趨勢和季節性成分，其中可以是加法 (A)、乘法 (M) 或無 (N)。它是由 R 套件 ETS 函數構建的。作為結合指數平滑基礎的預測模型，ETS技術為Hyndman概述的R軟體提供了預測套件，Ljung-Box Q檢驗也用於診斷殘差序列是否為白噪聲序列。根據最低 AIC 15、AICc 或 BIC15 自動選擇性能最佳的模型。由於在

Hyndman [16] 概述的 R 軟件中提供了包含 ETS 技術基礎的函數套件。Ljung-Box Q 檢驗也用於診斷殘差序列是否為白噪聲序列。

三、混合模型

混合預測模型由以下等權重的模型組成，即0.5權重的ARIMA模型和0.5權重的ETS模型。由於在 Hyndman[16] 概述的 R 軟件包中提供了包含 SARIMA-ETS 混合技術基礎的自動預測模型。

## 第三節 模型評估指標

一、為了評估 SARIMA、ETS 或 SARIMA-ETS 模型的性能，測試了擬合值。在確定自動 ARIMA 模型的預測效率時採用了幾種性能指標，即 Akaike 信息準則 (AIC)[11]、均方根誤差 (RMSE) [17]、平均絕對誤差 (MAE) [17]、平均絕對百分比誤差 (MAPE) ) 和平均絕對縮放誤差 (MASE) [ 17,18]。許多研究人員已使用這些指標來評估準確性。對於這些指標，最小值對應於最佳方法。

二、 正確評估算法

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \hat{x}_i)^2}{n}}$$

$$MAE = \frac{1}{n}\sum_{i=1}^{n}|X_i - \hat{X}_i|$$

$$\mathrm{MAPE} = \frac{1}{N}\sum_{i=1}^{N}\left|\frac{\hat{x}_i - x_i}{x_i}\right| \times 100\%$$

$$\mathrm{MASE} = \frac{1}{N}\sum_{i=1}^{N}\left(\frac{|e_i|}{\frac{1}{N-1}\sum_{i=2}^{N}|\hat{x}_i - x_i|}\right)$$

where $X_i$ = real incidence rate , $\hat{X}_i$ = estimated incidence and $n$ = predictions number

where $X_i$ = real observed value , $\hat{X}_i$ = forecasting value, and $n$ = predictions number

# 第三章 研究結果

## 第一節 疾管署通報資料分析

### 一、疾管署通報資料資料之蒐集與處理

確定病名/建檔年份/建檔月份/縣市/ 鄉鎮/性別/國籍/年齡層/確定病例數

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 結核病 | 2005 | 1 | 台中市 | 大甲區 | M | 本國籍 35-39 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大甲區 | M | 本國籍 65-69 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大甲區 | M | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 大安區 | F | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大安區 | M | 本國籍 30-34 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大安區 | M | 本國籍 70+ | 2 |
| 結核病 | 2005 | 1 | 台中市 | 大肚區 | F | 本國籍 4 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大肚區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大肚區 | M | 本國籍 45-49 | 2 |
| 結核病 | 2005 | 1 | 台中市 | 大肚區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大里區 | F | 本國籍 25-29 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大里區 | F | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 大里區 | M | 本國籍 70+ | 2 |
| 結核病 | 2005 | 1 | 台中市 | 大雅區 | M | 本國籍 40-44 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 大雅區 | M | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 中 區 | M | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 中 區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 太平區 | F | 本國籍 50-54 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 太平區 | M | 本國籍 30-34 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 太平區 | M | 本國籍 45-49 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 太平區 | M | 本國籍 70+ | 4 |
| 結核病 | 2005 | 1 | 台中市 | 北 區 | F | 本國籍 35-39 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北 區 | M | 本國籍 10-14 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北 區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | F | 本國籍 20-24 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | F | 本國籍 40-44 | 2 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | F | 本國籍 55-59 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | F | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | M | 本國籍 20-24 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | M | 本國籍 40-44 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 北屯區 | M | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 外埔區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 后里區 | F | 本國籍 55-59 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西 區 | F | 本國籍 65-69 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西 區 | M | 本國籍 20-24 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西 區 | M | 本國籍 40-44 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西 區 | M | 本國籍 65-69 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西 區 | M | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 西屯區 | F | 本國籍 50-54 | 1 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 結核病 | 2005 | 1 | 台中市 | 西屯區 | F | 本國籍 55-59 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西屯區 | M | 本國籍 50-54 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 西屯區 | M | 本國籍 70+ | 5 |
| 結核病 | 2005 | 1 | 台中市 | 沙鹿區 | F | 本國籍 55-59 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 沙鹿區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 沙鹿區 | M | 本國籍 45-49 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 沙鹿區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 東 區 | F | 本國籍 35-39 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 東 區 | M | 本國籍 50-54 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 東 區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 東勢區 | F | 本國籍 15-19 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南 區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南 區 | M | 本國籍 30-34 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南 區 | M | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | F | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | M | 本國籍 30-34 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | M | 本國籍 45-49 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | M | 本國籍 60-64 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | M | 本國籍 65-69 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 南屯區 | M | 本國籍 70+ | 3 |
| 結核病 | 2005 | 1 | 台中市 | 烏日區 | M | 本國籍 45-49 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 烏日區 | M | 本國籍 50-54 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 烏日區 | M | 本國籍 65-69 | 2 |
| 結核病 | 2005 | 1 | 台中市 | 烏日區 | M | 本國籍 70+ | 2 |
| 結核病 | 2005 | 1 | 台中市 | 神岡區 | F | 本國籍 70+ | 2 |
| 結核病 | 2005 | 1 | 台中市 | 神岡區 | M | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 梧棲區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 清水區 | F | 本國籍 70+ | 1 |
| 結核病 | 2005 | 1 | 台中市 | 清水區 | M | 本國籍 50-54 | 2 |
| 結核病 | 2005 | 1 | 台中市 | 清水區 | M | 本國籍 55-59 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 新社區 | M | 本國籍 50-54 | 1 |
| 結核病 | 2005 | 1 | 台中市 | 新社區 | M | 本國籍 60-64 | 1 |

.....(共取3000多頁/確定病例原始數據143958例)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 143936 | 結核病 | 2020 | 9 | 彰化縣 | 永靖鄉 | M | 本國籍 | 70+ | 1 |
| 143937 | 結核病 | 2020 | 9 | 彰化縣 | 田中鎮 | M | 本國籍 | 70+ | 2 |
| 143938 | 結核病 | 2020 | 9 | 彰化縣 | 伸港鄉 | F | 本國籍 | 70+ | 1 |
| 143939 | 結核病 | 2020 | 9 | 彰化縣 | 伸港鄉 | M | 本國籍 | 55-59 | 1 |
| 143940 | 結核病 | 2020 | 9 | 彰化縣 | 伸港鄉 | M | 本國籍 | 60-64 | 1 |
| 143941 | 結核病 | 2020 | 9 | 彰化縣 | 秀水鄉 | M | 本國籍 | 70+ | 1 |
| 143942 | 結核病 | 2020 | 9 | 彰化縣 | 社頭鄉 | F | 本國籍 | 70+ | 1 |
| 143943 | 結核病 | 2020 | 9 | 彰化縣 | 芳苑鄉 | M | 本國籍 | 70+ | 1 |
| 143944 | 結核病 | 2020 | 9 | 彰化縣 | 芬園鄉 | M | 本國籍 | 70+ | 1 |
| 143945 | 結核病 | 2020 | 9 | 彰化縣 | 員林市 | M | 本國籍 | 40-44 | 1 |
| 143946 | 結核病 | 2020 | 9 | 彰化縣 | 員林市 | M | 本國籍 | 55-59 | 1 |
| 143947 | 結核病 | 2020 | 9 | 彰化縣 | 員林市 | M | 本國籍 | 70+ | 1 |
| 143948 | 結核病 | 2020 | 9 | 彰化縣 | 埔鹽鄉 | F | 本國籍 | 25-29 | 1 |
| 143949 | 結核病 | 2020 | 9 | 彰化縣 | 埤頭鄉 | M | 本國籍 | 45-49 | 1 |
| 143950 | 結核病 | 2020 | 9 | 彰化縣 | 埤頭鄉 | M | 本國籍 | 70+ | 1 |
| 143951 | 結核病 | 2020 | 9 | 彰化縣 | 鹿港鎮 | M | 本國籍 | 70+ | 1 |
| 143952 | 結核病 | 2020 | 9 | 彰化縣 | 溪湖鎮 | F | 本國籍 | 25-29 | 1 |
| 143953 | 結核病 | 2020 | 9 | 彰化縣 | 溪湖鎮 | F | 本國籍 | 65-69 | 1 |
| 143954 | 結核病 | 2020 | 9 | 彰化縣 | 溪湖鎮 | M | 本國籍 | 70+ | 1 |
| 143955 | 結核病 | 2020 | 9 | 彰化縣 | 彰化市 | F | 本國籍 | 70+ | 3 |
| 143956 | 結核病 | 2020 | 9 | 彰化縣 | 彰化市 | M | 本國籍 | 65-69 | 1 |
| 143957 | 結核病 | 2020 | 9 | 彰化縣 | 彰化市 | M | 本國籍 | 70+ | 1 |
| 143958 | 結核病 | 2020 | 9 | 彰化縣 | 福興鄉 | M | 本國籍 | 70+ | 2 |
| 143959 | 結核病 | 2021 | 1 | 台中市 | 太里區 | F | 本國籍 | 65-69 | 1 |

本研究共取得約 143958 個結核病確定病例（計約3921頁）

二、資料整備與統計（請參附錄A）

三、內政部人口資料：本研究將自內政部之資料， 並依據該資料檔，彙整成台灣人口之分析總檔，以供進一步分析。

## 第二節 統計模型建立

### 一、 時間序列數據的一般初步分析

在192個月的研究期間，即從2005年1月至2020年12月，台灣共報告結核病例191,603例，平均每月發生率為每10萬人每月4.392例（範圍：2.287-6.937）。STL 分析，我們可以從每月的 TB 數據系列中分離出季節性和整體趨勢成分，並消除部分隨機噪聲或提醒成分。如圖 1 所示，季節性趨勢分解方法的結果產生了包括 12 個月隨機季節性在內的多個成分的總體趨勢；總體呈下降趨勢，2005 年最高（每 10 萬人年 72.5 人），2020 年最低（每 10 萬人年 33.5 人），發生率呈週期性變化（圖 1A、B、C）。可以明顯看出，台灣地區結核病的變化呈現出週期性，每年的變化過程中以一年（12個月）為周期，具有明顯的季節性，3月和5月出現兩個高峰，12月出現一個低谷。到 2 月的每個週期（圖 1 B、C）。

發生率數據集用於分析和製定模擬模型。我們應用的時間序列包括 192 個月度對數發生率數據集，這些數據集在季節性水平上以 12 的順序進行了平衡。Augmented Dickey-Fuller 檢驗的結果（Dickey-Fuller = -7.6315，滯後階數 = 1，PDickey-Full = 0.01 的替代假設：平穩）和 Ljung-Box 檢驗（X 平方 = 125.87，df = 1，PLjung -box = < 2.2e-16 替代假設：不獨立）這顯示 2005 年 1 月至 2020 年 12 月的時間序列具有平穩和自相關格式（圖 1A）。

二、 構建和比較建構模之性能的準確性：運用樣本內模擬訓練數據集，及偽樣本外數據集評估或驗證預測測試

為構建和評估模型的準確性，分別評估和驗證了模擬處理和預測性能。首先將數據系列樣本分群為(1)訓練數據集（in samples）即前150個數據集從2005年1月到2017年6月，(2)預測測試數聚集（pseudo-out-of-samples）即後續42個數據系列從 2017 年 7 月到 2020 年 12 月。接下來，利用 150 個數據集構建了三個訓練模型。第一，樣本中的最佳模擬 ARIMA 確定季節性 ARIMA (1,0,0) (2,1,0) 12 模式被選為性能最佳的 ARIMA 模型，其中 AIC= -335.62 的最小值，AICc= -335.17，BIC=-320.99。根據其 Ljung-Box Q 檢驗顯示 ARIMA (1,0,0) (2,1,0)12 模型與殘差的擬合度，該序列實現了 Q* = 62.283 的白噪聲，p-值 = 3.139e-06。第二，選擇 ETS (A, A, A) 模型 (AIC= -68.44, AICc= -63.81, BIC= -17.26) 作為表現最佳的 ETS 模型，Ljung-Box Q 測試顯示 Q* = 46.357， p 值 = 2.033e-07。第三，構建了一個混合模型，由以下模型組成：權重為 0.5 的 ARIMA 和權重為 0.5 的ETS（表 1，表 2）。

## 第三節 預測模型正確性評估

即計算提前 6 到30 個月的預測步驟。因此，建模的準確度指標分別基於來自 150 個樣本內訓練數據集構建的模擬模型的這些產量預測值進行估計。總體而

言，採用了幾個指標來評估這些首選模型的性能，包括用於比較的樣本內模擬和样本外預測。關於模擬擬合的性能，在 SARIMA-ETS-混合模型中，RMSE、MAE、MAPE 和 MASE 分別為 0.0585、0.0462、0.4613 和 0.5982，而在 0.0652、0.0514、0.5128%、4% 和 9% SARIMA (1, 0, 0) (2, 1, 0)12 模型。關於樣本外預測性能的表現，SARIMA-ETS模型中RMSE、MAE、MAPE和MASE分別為0.084、0.067、0.646%和0.870，而SARIMA-ETS模型為0.0924、0.0742、0.7196%和0.7196%。分別在 SARIMA (1, 0, 0) (2, 1, 0)12 模型中（表 2）。在這些建模結果評估中，SARIMA-ETS-hybrid 模型在近期預測中優於 SARIMA 模型，即基於顯示的準確性指標提前 3-12 個月。此外，兩個模型都顯示短期預測優於長期預測，例如，兩個模型的預測測試中前 3-12 個月的 MAPE 優於後 18-28 個月的 MAPE，如圖所示在表 2 中。

# 第四章 討論與建議

台灣結核病發生率的時間序列分析顯示出明顯的下降趨勢，從 2005-2020 年每 105 例/年 72.8 例下降到 33.5 例，屬於中等負擔，被認為低於全球平均水平，這可能是由於不斷改進的努力和近 年來的國家衛生政策制定。使用加法方法分解時間序列以檢查季節 性趨勢和特定模式。結果顯示，台灣結核病發生率呈穩步下降趨勢， 有季節性變化，兩個高峰主要出現在3、4、5月，低谷一般出現在11-2月。這些波動顯示早春高峰可能是由於過度擁擠和通風不良導 致結核病傳播，而在亞洲冬季農曆新年期間，城市之間的人口流動 以及人們在室內進行了大部分社交活動。此外，觀察到的結核病低 谷期季節性可能與結核病潛伏期的長短或監測操縱差距有關，需要 進一步調查證實。

我們將時間序列數據集轉換為對數格式，以平滑本研究中的波動性。通過自相關函數 (ACF)、偏自相關函數 (PACF) 和 Dickey-Fuller 檢驗或 Ljung-Box 檢驗（Dickey-Fuller 檢驗的增強版本），我們確定數據為依存分佈方式，表現出連續性相關性，即拒絕 H0：數據是獨立分佈的，本研究中批准的 TB 時間序列是“整體”自相關組。在應用SARIMA和SARIMA-ETS-hybrid模型預測台灣未來幾年結核病發生率方面，在建立模型的過程中採取了多項措施，以盡量減

少過度擬合或欠擬合的可能性。為了盡可能避免過擬合問題，我們使用了相對較大的樣本量，每月共 192 個數據點，包括控制情境不夠充分的時代，例如 2016 年之前沒有針對陽性個案接觸者進行 LTBI 篩選與治療。 在建模過程中，Ljung-Box測試用於估計模型是否充分利用了原始數據。當構建的模型不能充分捕捉數據集的底層結構時，就會發生欠擬合。如果殘差被確認為白噪聲，則可以得出結論，模型中欠擬合的可能性很小。自動重複識別、估計和診斷的過程，直到通過 R 編程獲得優化模型。

而在開發模型的評估中，我們將TB時間序列樣本分為樣本內模擬建模的訓練集，即前80%的數據，以及偽樣本外預測測試的測試集，即，其餘 20% 的數據。因此，我們分別成功地應用和構建了最優的 ARIMA、ETS 和 Hybrid 配置建模。基於指標，用於評估建模的準確性，包括均方根誤差 (RMSE)、平均絕對百分比誤差 (MAPE)、平均絕對誤差 (MAE) 和平均絕對縮放誤差 (MASE)。它顯示我們的模型中 <1 的指標顯示預測模型的性能優於樸素隨機遊走，並且均不大於 1；即，在樣本內模擬或偽樣本外預測期間都不比樸素的基準預 測方法差。樣本外預測的指標顯示，所有未來 3-12 個月的預測表現都小於和優於未來 18-24 個月的長期預測表現（表 2）。因此，我們得出結論，我們在驗證期內建立的算法展示了模型在驗證期內

的性能，有望預測未來，並且在預測 TB 發生率的短期潛在趨勢方面比長期結果更準確。此外，SARIMA-ETS-hybrid 預測模型在短期預測方面具有優越的性能，可以在未來 3-12 個月的短期內在製定迫在眉睫的流行病預警方面發揮作用。總體而言，3-12 之間的 MAPE 值領先 0.5% 左右，小於未來 15-30 個月的 0.6% 左右，並且兩者都具有類似趨勢，即隨著時間跨度的持續，預測的可信範圍逐漸擴大。並且 ARIMA-ETS 混合在近期預測中優於 ARIMA 和 ETS，即 18 個月以下，以及 ETS 在 18 個月以上的表現最好，ARIMA-ETS 優於 ARIMA。通過比較在未來 18 個月內的短期預測中具有最佳指標和最低 MAPE 的三個模型混合模型的性能，否則； ETS 模型在超過 18-30 個月的長期預測中具有更好的性能。我們的結果顯示，根據th的結果，SARIMA-ETS-混合模型優於 SARIMA 模型。

本研究在時間數列分析使用季節性模式來作為結核病之最佳模式，我們同時發現季節性與結核病發生率有明顯的關係。針對以後的研究議題可以更深入的探討資料的品質，並探討因衛生單位倡導LTBI之政策、對時間數列模式之影響；另外，我們探討氣溫與結核病之間的關係，未來有關其他氣象因素如溼度、空氣污染等相關影響， 皆值得我們探討與結核病之關係。

在以時間序列方法進行監測時要注意疾病每年之流行趨勢，包括衛生介入措施之變動，結核病每年之流行期時段，是否在預定範圍內；但如果有超過預測之範圍，在解讀警示點時就要多加留意。利用時間數列配合95信賴區間之發生率對於監測參考，不失為一可行之方法，確實可提供疾管署實際上線應用後之修正評估。我們的結果顯示，根據模　擬和預測模型中建模性能的準確性指標評估結果，SARIMA-ETS-混合 模型優於 SARIMA 模型。而且，短期預測總是優於長期預測（表 2）。亦即 SARIMA-ETS 混合模型優於 SARIMA 模型，但總體而言，短期未來預測優於長期未來預測。

全球結核病流行正朝著無結核病的未來世界邁進，即因結核病的終結而導致零死亡和零痛苦。為實現“終結結核病”目標，結核病發生率模型和算法的準確預測可以作為有效預防和控制結核病應用的有益工具之一。根據這項研究的預測數據，迄今為止的防控措施已有效實現台灣未來的里程碑；因此，與2015年的水平相比，我們的保守模式，以對數化平穩數據之建模及還原exponentail預測到2015至2025 年結核病發生率將減少近 50%。本研究採用SARIMA-ETS算法，除台灣已達到2015至2020年下降20%；預測2015至2030年台灣為下降54.77%(36.24-67.97%)。若採以原型數據輸入，　總體新發生率將於2025年可望達降低71.7%，

2030年降低 89.8%， 2035年降低100%里程碑 ，亦即2025年達成TB發生率降為： 20.51(95% CI: -6.3 - 47.4) TB case $10^5$per-year、減害71.71% (reduction range:108.74%- 34.68 %)，2030年達成TB發生率降至7.52(95% CI:-30.45 -45.49) TB case$10^5$ per-year、減害89.63%(range: 37.26-100%)。以性別分群，預測女性新發生結核病個數可望比男性，更早達成100%降低目標，女性約於2025年、男性約於2034年達至新生病例為0；則台灣將符合且可望提前達成世界衛生組織終結TB之目標。倘若採用，前者保守模擬與預測模式，為了加速實現世衛組織終結結核病的2025年目標減少70%目標，則需要注意加強綜合介入策略，例如積極探索新的有效的結核病預防方法；不斷加強對疫苗接種、先進診斷、治療、結核病合併症管理以及實現全民健康覆蓋和社會保護的量能。

在我們的研究中，根據預測範圍可信度值隨著時間遞延而逐漸擴大，短期預測比長期預測更加，因為升級的結核病干預措施的潛力可能會隨著人口結構的變化而動態變化未來在台灣。因此， 應不斷將新的觀測序列添加到序列中，以確保預測模型在實踐中提供可能的最佳預測。儘管如此，我們得出結論，我們的建模預測準確性是促進預測未來願景的有用工具。

未來疫情趨勢之監控與預警

有關 SARIMA 模型於預測疫情之實務操作方式，於應用於我國傳染病疫情之監控與偵測，可以基於係尋找一段傳染病疫情相對穩 定的時期作為基準，即基於假設未來情況與過去樣本間的各種社會 環境情況均相同的條件下，以精準預測未來；然而，此前題下，若 未來情況有所變化下，時間序列方法的預測能力則會下降，但是若 以預測值作為疫情的動態基準值，並採95%信賴區間的上界值作為疫情正常值之標準，若未來世界的疫情數量超過「預測值95%信賴區間的上界值」時，表示疫情相對過去情況嚴重，則為疫情失控爆發的 狀態，此即為一種非常變通的監控方式。因此，本研究所考量採用 此種變通之監測方式，將與 P Quénel, W Dab 的作法概念類似 (P Quénel, W Dab, Eur J Epidemiol . 1998 Apr;14(3):275-85. Influenza A and B epidemic criteria based on time-series analysis of health services surveillance data.)，使用 SARIMA 作為監控我國傳染病疫情爆發點之方法：將傳染病相對平穩的時間 作為 SARIMA 估計的時間區間，建立估計模型，並且建構基準值(預測值 95%信賴區間上界值)，作為衡量預測未來傳染病流行爆發之標準。根據世界衛生組織2020年報告，邁向里程碑進展報告書顯示，

實現2020年結束結核病戰略的里程碑進展2019年底，全球整體評估，

WHO大多數地區和許多結核病高負擔國家都無法實現「終止結核病策略」設定的2020年相關里程碑[19]。全球結核病發生率正在下降，但速度不足以達2020年的里程碑，即2015-2020年間結核發生率下降20% 的標。2015-2019年的累積降幅為9%（從142/100000降至130/100000新發病例），2018-2019年期間降幅為2.3%。慶幸的是，

WHO歐洲區幾乎達2020年里程碑，2015-2019年間結核 病發生率降低了19%，非洲地區也取得進展(降低16%)。總共有 78個國家即將達到2020年的里程碑。較積極的是世衛組織歐洲區域，幾乎達到2020年的里程碑，即2015年至 2019 年結核病發生率減少19%，和非洲

區域進展良好，減少了16%。共有78個國家有望達到 2020年的里程碑，其中包括七個結核病高負擔國家（柬埔寨、埃塞俄比亞、肯尼亞、納米比亞、俄羅斯聯邦、南非和美國 坦桑尼亞共和國）已經達到，其他三個高結核病負擔正在這樣做的國家（萊索托、緬甸）和津巴布韋）[19]。台灣則2015至2020年確已達結核病新發生率減少20%。推估未來台灣女性相較於男性之結核病新發生病例數，可望更早達成100%降低目標；推估各年齡人口結核病新發生病例數，65歲以上男性將可能是最遲達到0例個案之年齡人群。由於推估值有95%範圍，因此，實際未來疫情，仍需實際防治作為

之持續努力。

我們的預測模型存在一些侷限性。首先，我們模型的預測性隨著時間跨度的延長而降低，可信區間變得更寬，這顯示我們的模型在預測近期流行病方面比長期趨勢預測更好。通過結合機器學習推估預測疫情和人類判斷，有助未來流行病的決策過程可能會改善工作條件。其次，次年可導入分群比較於模型，或增加運用其他新的深度學習算法，包括例如神經元網絡技術、循環神經網絡和長短期記憶網絡或挑戰多元向量回歸時間序列數理統計技術，將有望增加預測精度。本研究著重嘗試使用R統計運算及構建模型，有低碳節能之優勢。

綜上所述，本研究第一年已成功達成築構時間序列數理統計模型，裨助於我們解讀結核病發生率和季節性的歷史趨勢，並達成精準推估預測趨勢對未來的影響，除對短期的疫情預警、資源配置和規劃有幫助；並裨助本署依照世界衛生組織指引，以數理統計推估朝著達成長期結核病疫情防治里程碑之趨勢，促進世衛組織控制結核病的長期目標並加強流行病防範。本研究計畫採用之時間序列模型可能為提供一種快速監測工具，以促進世衛組織消除結核病的目標。我們提出的SARRIMA-ETS 模型在預測流行病發生前 12 個月或更短時間方面的表現優於 SARIMA，並且所有模型都顯示出短期預測比長期預測有更好的表現。第一年已成功建立3種人工智慧預測模型(機器學習)，本計畫為二年期計畫，目前在第一年的成果將提供第

二年更進一步做其他模式築構及預測演算，納入較細部參數，第二年將持續導入性別、年齡風險因子等之監測資料進行比對，探討疫病趨勢之優化、精準的趨勢預測模式，並可望應用至跨其他疫病監測系統之建立。

# 參考文獻

**Reference**


1 Global tuberculosis report 2018. Available from: https://www.who.int/tb/publications/global_report/en/

2. Richard D. Turner, Graham H. Bothamley. Cough and the Transmission of Tuberculosis. The Journal of Infectious Diseases, Volume 211, Issue 9, 1 May 2015, Pages 1367–1372, https://doi.org/10.1093/infdis/jiu625

3. Graham R. Stewart, Brian D. Robertson & Douglas B. Young. Tuberculosis: a problem with persistence. Nature Reviews Microbiology volume 1, pages97–105(2003)

4. Floyd K1, Glaziou P, Zumla A, Raviglione M. The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. Lancet Respir Med. 2018 Apr; 6 (4): 299-314. doi: 10.1016/S2213 -2600 (18)30057-2.

5. K. Floyd, P. Glaziou, R. M. G. J. Houben, T. Sumner, R. G. White, and M. Raviglione. Global tuberculosis targets and milETSones set for 2016–2035: definition and rationale. Int J Tuberc Lung Dis. 2018 Jul; 22(7): 723–730. Published online 2018 Jul 1. doi: 10.5588/ijtld.17.0835

6. Coulombier D, Quenel P, Coignard B. Epiet. Time Series Module Arima Modelling Case study: Forecasting a time series using Box-Jenkins modeling Available: http://www.episouth.org/outputs/wp5/f_t_module/curso/day_4/Case% 20studies/jenkins.pdf

7. Kui Liu, Tao Li, Avina Vongpradith, Fei Wang, Ying Peng, Wei Wang, Chengliang Chai, Songhua Chen, Yu Zhang, Lin Zhou, Xinyi Chen, Qiao Bian, Bin Chen, Xiaomeng Wang, Jianmin Jiang. Identifcation and Prediction of Tuberculosis in Eastern China: Analyses from 10-year Populationbased Notifcation Data in Zhejiang Province, China. Sci Rep. 2020 May 4;10(1):7425. doi: 10.1038/s41598-020-64387-5.

8. Wang Y, Xu C, Zhang S, Wang Z, Zhu Y, Yuan J. Temporal trends analysis of human brucellosis incidence in mainland China from 2004 to 2018. Sci Rep. 2018 Oct 26;8(1):15901. doi: 10.1038/s41598-018-33165-9.

9. Domenico Benvenuto, Marta Giovanetti, Lazzaro Vassallo, Silvia Angeletti, Massimo Ciccozzi. Application of the ARIMA model on the COVID-2019 epidemic dataset Data Brief. 2020 Feb 26;29:105340. doi: 10.1016/j.dib.2020.105340. eCollection 2020 Apr.

10. SH Mohammed, MM Ahmed, AM Al-Mousawi, A Azeez. Seasonal behavior and forecasting trends of tuberculosis incidence in Holy Kerbala, Iraq. Int J Mycobacteriol 7 (4), 361-367.

11. Taiwan National Infectious Disease Statistics System. https://nidss.cdc.gov.tw/ch/SingleDisease.aspx?dc=1&dt=3&disease=010

12. Ministry of Interior Taiwan. Statistics: annual report of the Ministry of the Interior. Available from:

https://www.moi.gov.tw/files/site_stuff/321/1/month/month _en.html.

13. Taiwan Centers for Disease Control, Department of Health. Taiwan Tuberculosis Control Report. Available from: https://www.cdc.gov.tw/En/InfectionReport/List/SOIzsdQ5fRn3xPZOleIb0w

14. Cleveland, R. B., Cleveland, W. S. & McRae, J. E. STL: A seasonal-trend decomposition procedure based on loess. J Official Stat 6, 3–73. (1990).

15. Aho, K.; Derryberry, D.; Peterson, T. (2014), "Model selection for ecologists: the worldviews of AIC and BIC", Ecology, 95 (3): 631–636, doi:10.1890/13-1452.1.

16. Hyndman, R. J., Koehler, A. B. & Snyder, R. D. A State Space Framework for Automatic Forecasting Using Exponential Smoothing Methods. Int J Forecasting 18, 439–454 (2002).

17. Elisabeth Woschnagg. Evaluating forecast accuracy. University of Vienna Department of Economics 2004. Available by: https://homepage.univie.ac.at/ robert.kunst/procip.pdf

18. Rob J. Hyndman. Another look at forecast-accuracy metrics (MASE) for intermittent demand. Available from: https://robjhyndman.com/papers/foresight.pdf

19. Global tuberculosis report 2020.

表一 模型參數比較

Table 1. Hyperparameters used in the machine learning models

| N 0 | Series | Model | ETSimated parameter | AICc / Accuracy | Residuals check (Ljung-Box tETS dat) |
|---|---|---|---|---|---|
| 1 | Training set of TB incidence (150 observations) | ARIMA(1, 0, 0)(2, 1, 0)[12] by R, package: forecast, function: R套件功能函数式 | Coefficients: ar1=-0.2399, sar1= -0.6395, sar2=-0.2443, drift =-0.0038 s.e. 0.0866 0.0882 0.0907 0.0002 sigma^2 ETSimated as 0.00475: log likelihood= 172.81 | AIC=-335.62, AICc=-335.17, BIC=-320.99; RMSE= 0.0652 MAPE= 0.5127 | Residuals from ARIMA(1, 0, 0)(2, 1, 0)[12] with drift, Q* = 62.283, df = 20, p-value = 3.139e-06, Model df: 4. Total lags used: 24 |
| 2 | Simulation set of TB incidence (192 observations) | ARIMA(3, 0, 0)(2, 1, 0)[12] by R, package: forecast, function: R套件功能函数式 | Coefficients: ar1=0.1283, ar2= 0.1111, ar3=0.2527, sar1= -0.6137' sar2=-0.3464, drift= -0.0041 sigma^2 ETSimated as 0.005094: log likelihood=219.89 | AIC=-425.79 AICc=-425.14 BIC=-403.44 RMSE= 0.0652, MAPE=0.5213 | Residuals from ARIMA(3, 0, 0)(2, 1, 0)[12] with drift Q* = 34.641, df = 18, p-value = 0.01048, Model df: 6. Total lags used: 24 |
| 3 | Training set of TB incidence (150 observations) | ETS(A,A,A) | Smoothing parameters: alpha= 0.0102, beta = 0.0101, gamma= 1e-04; | AIC= -68.44, AICc=- 63.81, BIC=-17.26 RMSE= 0.0581, MAPE =0.4591 | Residuals from ETS(A, A, A); Q* = 61.132, df = 8, p-value = 2.793e-10 ; Model df: 16. Total lags used: 24 |
| 4 | Simulation set of TB incidence (192 observations) | ETS(A, A, A) , Call: ets(y = M) | ETS(A, A, A) Call: ets (y = M) Smoothing parameters: alpha = 0.0738, beta = 1e-04, gamma = 1e-04 , | AIC=-25.56 AICc= -22.04 BIC =29.82 RMSE= 0.0618, MAPE= 0.4870 | Residuals from ETS(A, A, A); Q* = 51.531, df = 8, p-value = 2.073e-08 ; Model df: 16. Total lags used: 24 |
| 5 | Training set of TB incidence (150 observations) | ARIMA-ETS | Hybrid forecast model comprised of the following models: arima with weight 0.5 , ETS with weight 0.5 | RMSE=0.0585 MAPE= 0.4613 | Could not find appropriate degrees of freedom for this model |
| 6 | Simulation set of TB incidence (192 observations) | ARIMA-ETS | Hybrid forecast model comprised of the following models: arima with weight 0.5, ETS with weight 0.5 | RMSE=0.0512 MAPE=0.5058 | Could not find appropriate degrees of freedom for this model |

表二 模型樣本內預測表現之測試

Table 2 Evaluation of the models' accuracy of the SARIMA. ETS and SARIMA-ETS hybrid in forecasting underlying trend (pseudo out-of-sample) performance

Prediction: TB incidence (cases per 100000-month); Hybrid: SARIMA-ETS-hybrid

*95%CI of PV: 95% confidence interval of predictive value for TB incidence

| Ahead time | Actual-value (cases per $10^5$-month | models | Prediction ( cases per $10^5$-month) | 95%CI of PV | RMSE | MAE | MAPE | MASE |
|---|---|---|---|---|---|---|---|---|
| 3 months 2017-09 | 3.55 | SARIMA$(1,0,0)(2,1,0)_{12}$ | 3.43 | 2.77-4.14 | 0.086 | 0.058 | 0.575 | 0.753 |
| | | ETS | 3.49 | 2.93-4.14 | 0.077 | 0.058 | 0.569 | 0.746 |
| | | Hybrid | 3.39 | 2.77- 4.13 | 0.081 | 0.056 | 0.554 | 0.726 |
| 6 months 2017-12 | 3.3 | SARIMA | 3.34 | 2.76-4.15 | 0.069 | 0.047 | 0.459 | 0.606 |
| | | ETS | 3.29 | 2.76-3.97 | 0.060 | 0.046 | 0.449 | 0.593 |
| | | Hybrid | 3.4 | 2.79-4.15 | 0.064 | 0.045 | 0.445 | 0.587 |
| 12 months 2018-6 | 3.15 | SARIMA | 3.58 | 2.9-4.51 | 0.088 | 0.062 | 0.598 | 0.606 |
| | | ETS | 3.47 | 2.9-4.14 | 0.079 | 0.061 | 0.586 | 0.785 |
| | | Hybrid | 3.69 | 3.03-4.51 | 0.082 | 0.060 | 0.578 | 0.776 |
| 18 months 2018-12 | 3.15 | SARIMA | 3.16 | 2.55- 4.0 | 0.090 | 0.069 | 0.668 | 0.898 |
| | | ETS | 3.09 | 2.55- 3.73 | 0.080 | 0.065 | 0.627 | 0.849 |
| | | Hybrid | 3.23 | 2.62- 4.0 | 0.084 | 0.066 | 0.639 | 0.859 |
| 24 months 2019-6 | 3 | SARIMA | 3.4 | 2.64- 4.4 | 0.092 | 0.074 | 0.714 | 0.960 |
| | | ETS | 3.26 | 2.64- 4.02 | 0.079 | 0.065 | 0.627 | 0.812 |
| | | Hybrid | 3.41 | 2.64- 4.4 | 0.084 | 0.068 | 0.655 | 0.881 |
| 30 months 2019-12 | 3 | SARIMA | 2.89 | 2.38-3.51 | 0.091 | 0.073 | 0.699 | 0.942 |
| | | ETS | 2.90 | 2.28- 3.69 | 0.079 | 0.064 | 0.619 | 0.833 |
| | | Hybrid | 2.98 | 2.28- 3.9 | 0.084 | 0.067 | 0.646 | 0.870 |

## 表三 應用模型於推算、預測未來結核病發生率

Table 3 Tuberculosis incidence forecasting until 2030 using the SARIMA and SARIMA-ETS-hybrid models by output exponation data following pre-logarithm input

| | ARIMA | | | ETS | | | ARIMA-ETS-hybrid | | |
|---|---|---|---|---|---|---|---|---|---|
| Year (reduction*) | TB incidence: TB cases per 100000-year (*) | | | TB incidence: TB cases per 100000-year (*) | | | TB incidence: TB cases per 100000-year (*) | | |
| | Forecast value | Lo. 99.5% | Hi. 99.5% | Forecast value | Lo. 99.5% | Hi. 99.5% | Forecast value | Lo. 99.5% | Hi. 99.5% |
| 2021 | 32.380 | 26.317 | 39.839 | 32.471 | 27.016 | 39.028 | 32.495 | 27.589 | 38.150 |
| 2022 | 31.052 | 24.818 | 38.853 | 30.888 | 25.547 | 37.345 | 30.762 | 25.618 | 36.769 |
| 2023 | 29.261 | 23.008 | 37.214 | 29.382 | 24.158 | 35.735 | 29.331 | 23.790 | 36.121 |
| 2024 | 27.955 | 21.298 | 36.695 | 27.949 | 22.844 | 34.195 | 27.875 | 22.102 | 35.054 |
| 2025 | 26.646 (41.69%) | 19.933 (56.38%) | 35.620 (22.06%) | 26.586 (41.82%) | 21.601 (52.73%) | 32.721 (28.40%) | 26.531 (41.95%) | 20.561 (55.01%) | 34.138 (25.30%) |
| 2030 | 20.803 (54.48%) | 14.286 (68.74%) | 30.294 (33.71%) | 20.706 (54.69%) | 16.328 (64.27%) | 26.258 (42.54%) | 20.671 (54.77%) | 14.636 (67.97%) | 29.138 (36.24%) |

*reduction= (Final incidence rate - incidence rate in 2015)/ incidence rate in 2015. WHO milestone and targets for TB incidence rate reduction in 2020, 2020, 2025 and 2030 by 20%, 50%, 80% compared with the 2015 (Int J Tuberc Lung Dis. 2018 Jul; 22(7): 723 - 730).

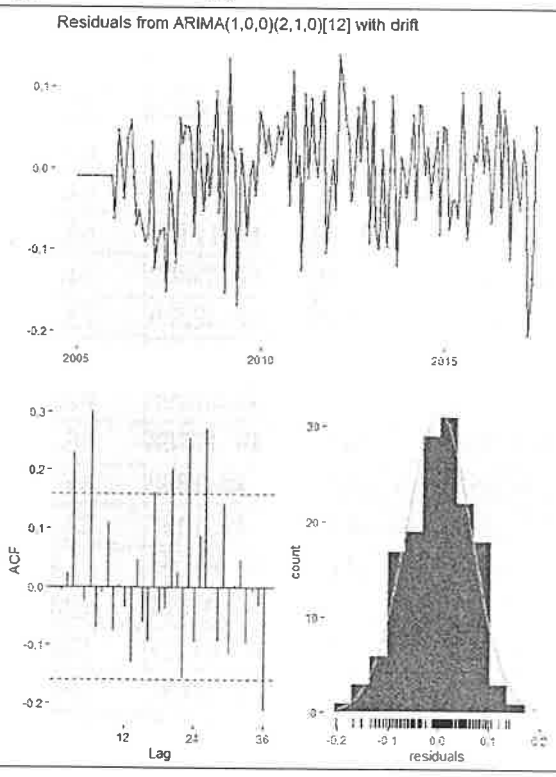
Table 4 Tuberculosis incidence rate forecasting until 2030 using the SARIMA models by original data

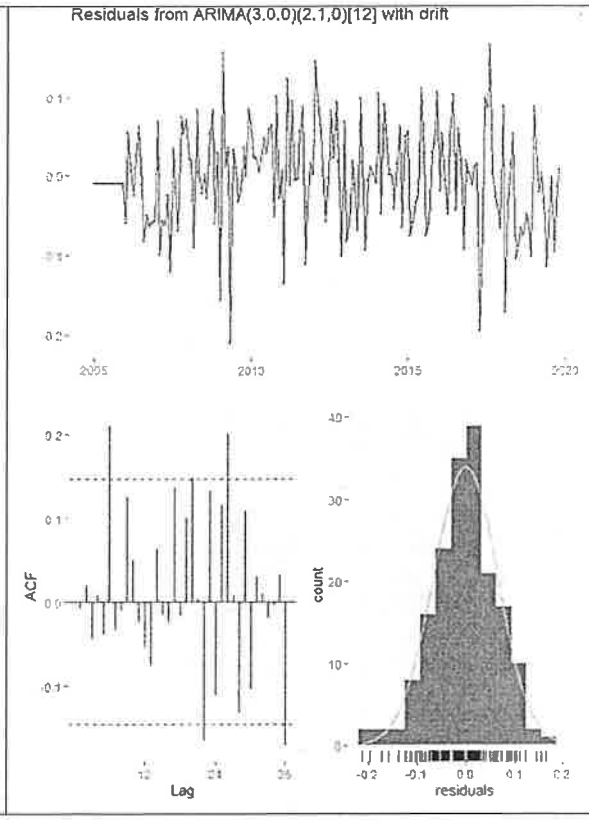
| date | Incidence | Lo. 99.5% | Hi. 99.5% | *reduction | Hi | Lo |
|---|---|---|---|---|---|---|
| | TB incidence: TB cases per 100000-year (*) | | | % | | |
| 2021 | 30.90322 | 18.8969 | 42.90954 | 57.37487 | 73.93531 | 40.81443 |
| 2022 | 28.30518 | 11.32568 | 45.28468 | 60.95837 | 84.37837 | 37.53837 |
| 2023 | 25.70715 | 4.911589 | 46.5027 | 64.54187 | 93.2254 | 35.85834 |
| 2024 | 23.10911 | -0.90353 | 47.12175 | 68.12537 | 101.2463 | 35.00449 |
| 2025 | 20.51107 | -6.33588 | 47.35802 | 71.70887 | 108.7391 | 34.6786 |
| 2026 | 17.91303 | -11.4963 | 47.32239 | 75.29237 | 115.857 | 34.72774 |
| 2027 | 15.31499 | -16.4507 | 47.08073 | 78.87587 | 122.6907 | 35.06106 |
| 2028 | 12.71696 | -21.242 | 46.67596 | 82.45937 | 129.2994 | 35.61937 |
| 2029 | 10.11892 | -25.9 | 46.13788 | 86.04287 | 135.7242 | 36.36155 |
| 2030 | 7.520881 | -30.4464 | 45.4882 | 89.62637 | 141.9951 | 37.25766 |
| 2031 | 4.922843 | -34.8976 | 44.7433 | 93.20987 | 148.1346 | 38.2851 |
| 2032 | 2.108303 | -39.6243 | 43.84094 | 97.092 | 154.6543 | 39.52974 |
| 2033 | -0.27323 | -43.5626 | 43.01617 | 100.3769 | 160.0864 | 40.66735 |
| 2034 | -2.87127 | -47.7948 | 42.05227 | 103.9604 | 165.9239 | 41.99687 |
| 2035 | -5.46931 | -51.9696 | 41.03097 | 107.5439 | 171.6822 | 43.40556 |

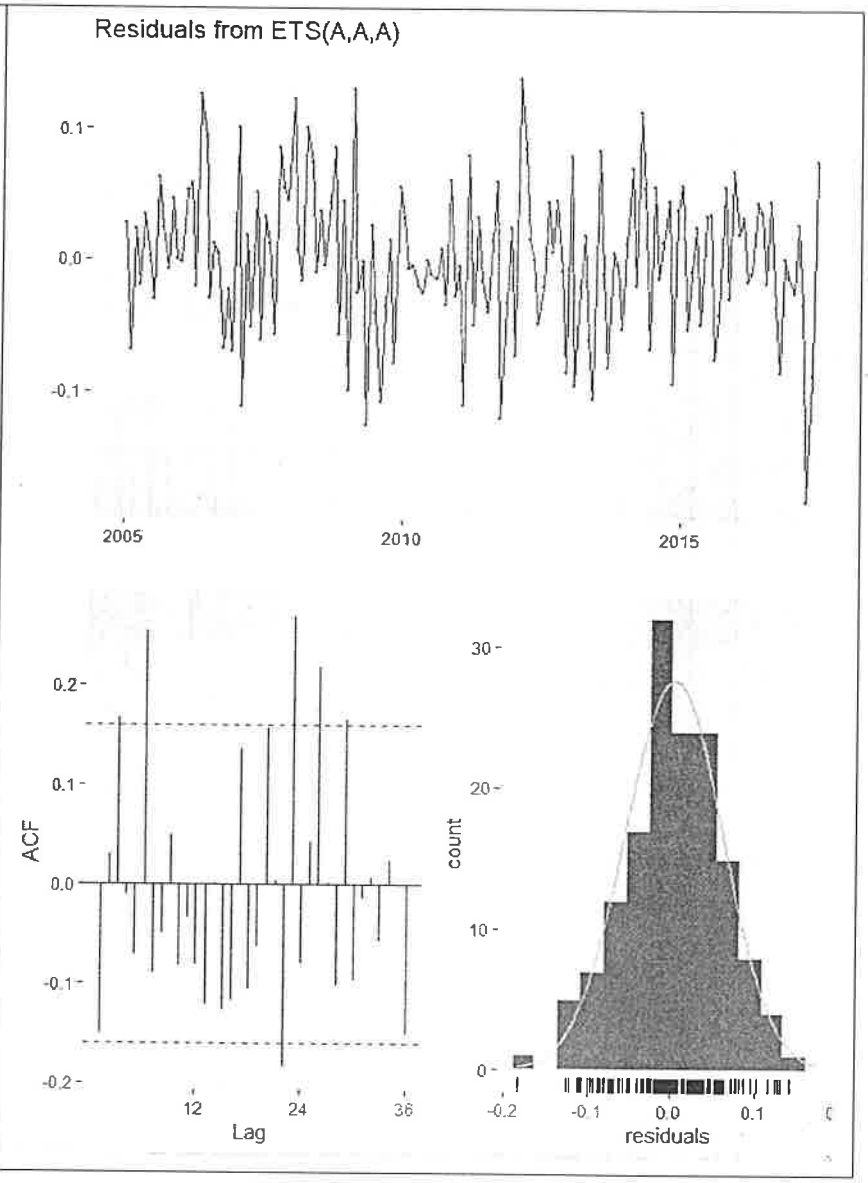
*reduction= (Final incidence rate - incidence rate in 2015)/ incidence rate in 2015. WHO milestone and targets for TB incidence rate reduction in 2020, 2020, 2025 and 2030 by 20%, 50%, 80% compared with the 2015 (Int J Tuberc Lung Dis. 2018 Jul; 22(7): 723 - 730).

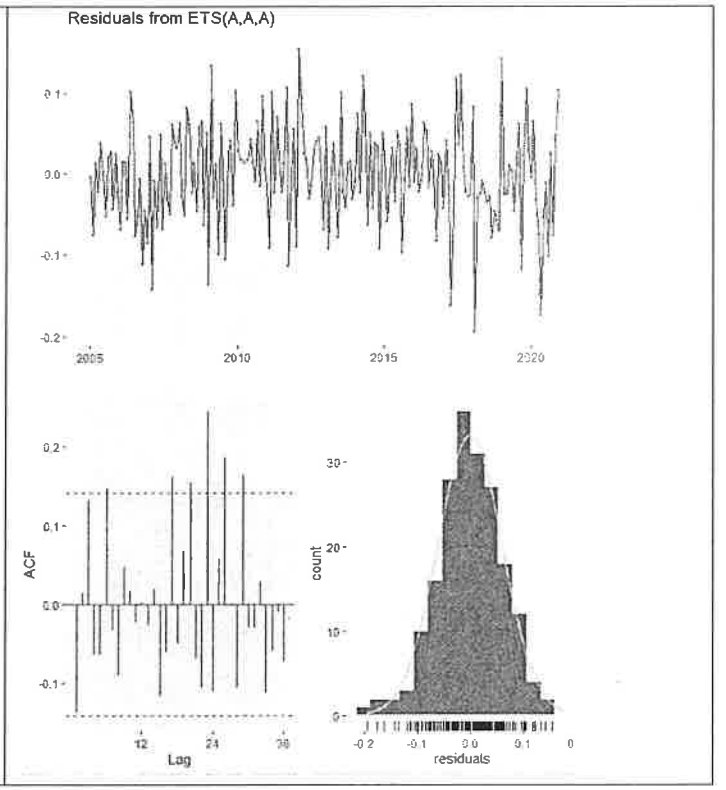
**negative number would be considered as zero

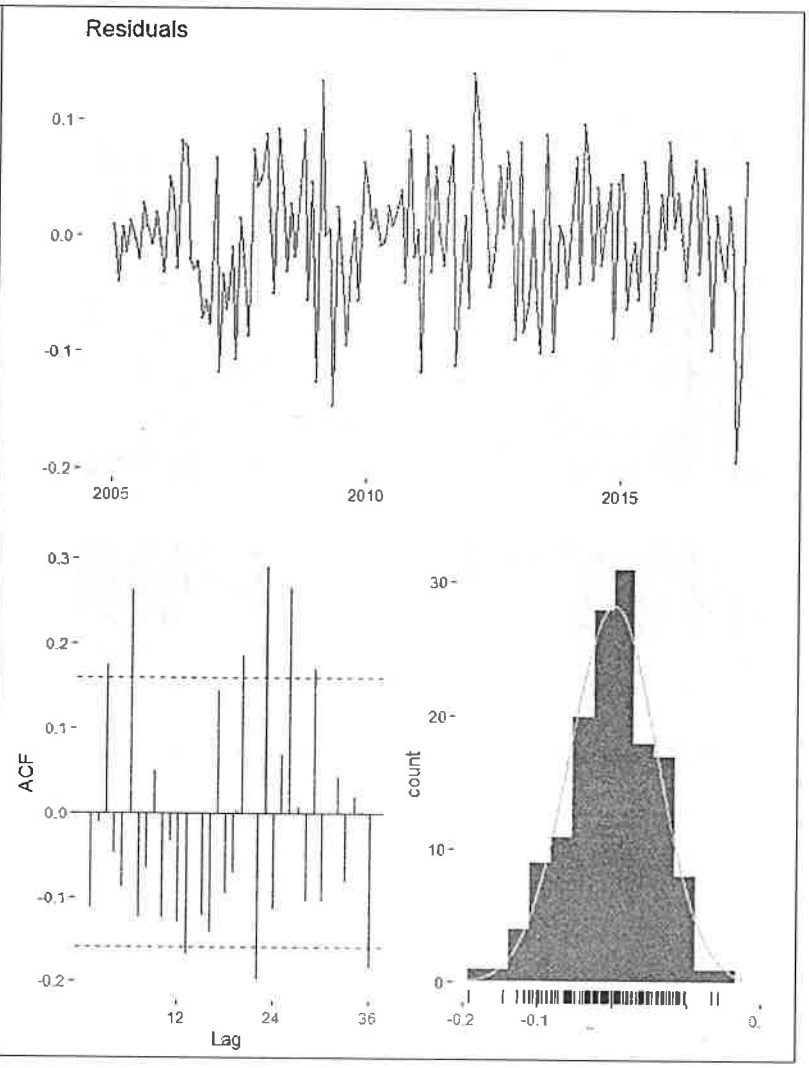
Table 5 模型算法之參數診斷分析

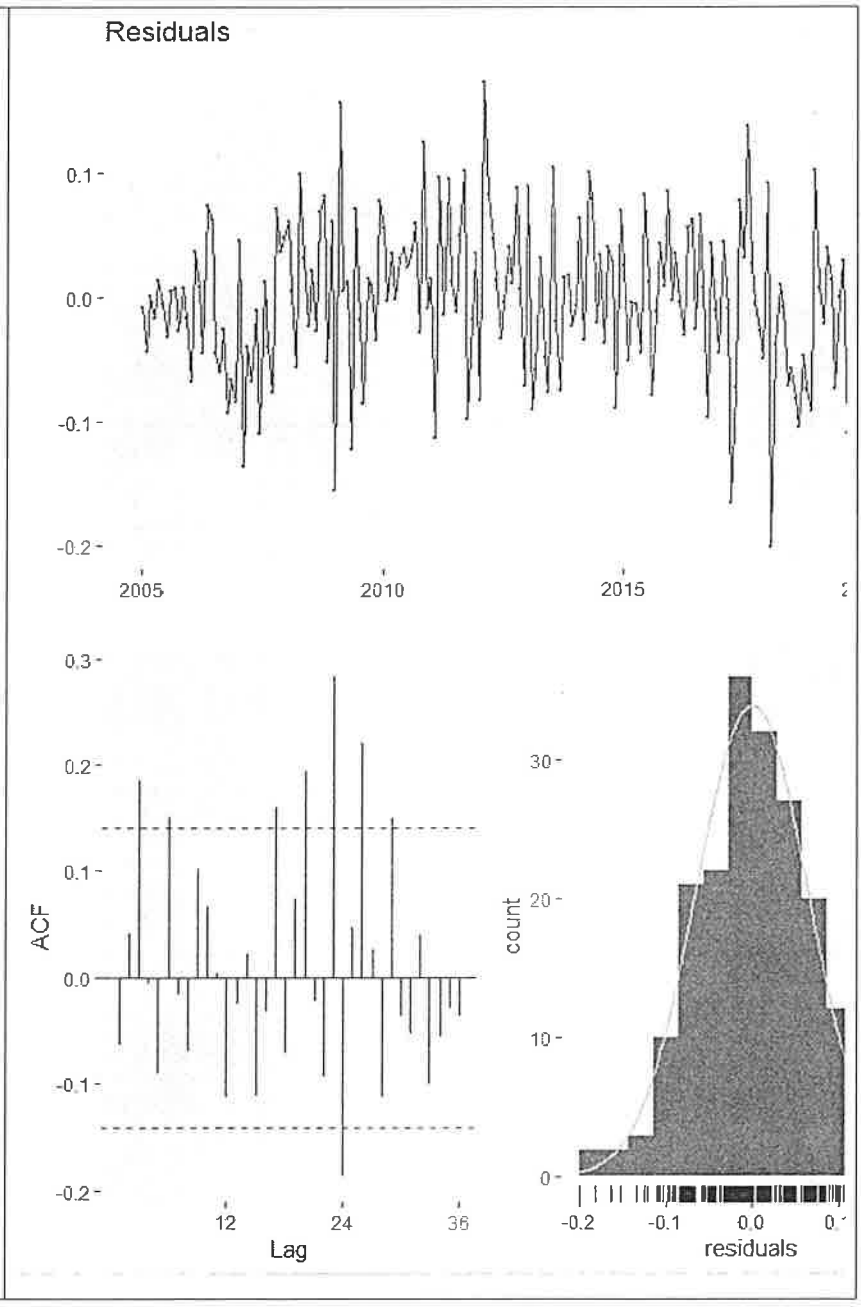
| N0 | Series | Model | 模型參數診斷：係數診斷 |
|---|---|---|---|
| 1 | Training set of TB incidence (150 observations) | ARIMA(1,0,0)(2,1,0)[12] |  |

| | | | |
|---|---|---|---|
| 2 | Simulation set of TB incidence (192 observations) | ARIMA(3,0,0)(2,1,0)[12] by R, package: forecast, function: auto.arima |  |

| | | | |
|---|---|---|---|
| 3 | Training set of TB incidence (150 observations) | ETS(A,A,A) |  |

| | | | |
|---|---|---|---|
| 4 | Simulation set of TB incidence (192 observations) | ETS(A, A, A), Call: ets(y = M)<br><br>a heuristic |  |

| | | | |
|---|---|---|---|
| 5 | Training set of TB incidence (150 observations) | ARIMA-ETS |  |

| | | | |
|---|---|---|---|
| 6 | Simulation set of TB incidence (192 observations) | ARIMA-ETS Hybrid |  |



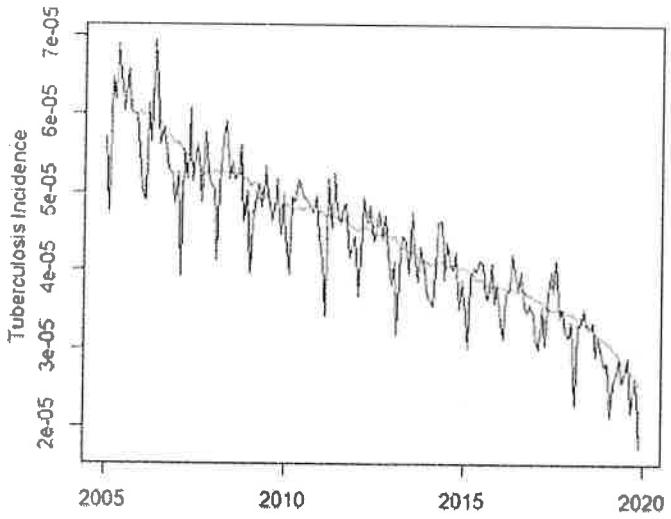
Visits

# 統計圖

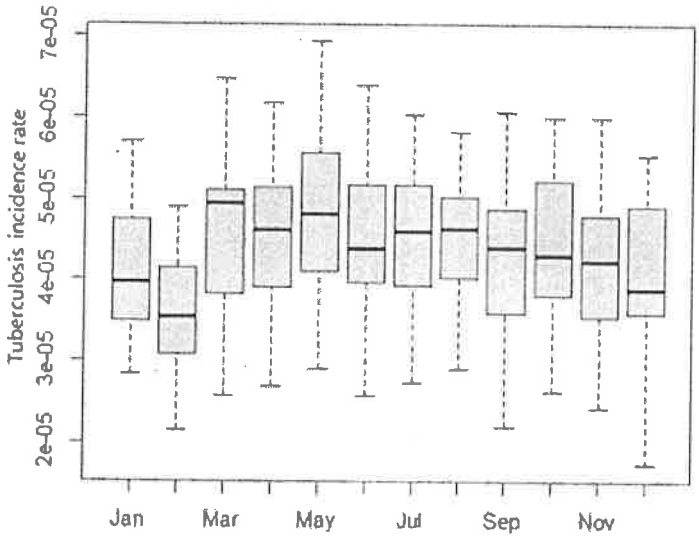
## 結核病流行趨勢

Fig 1

A)




B)



c)

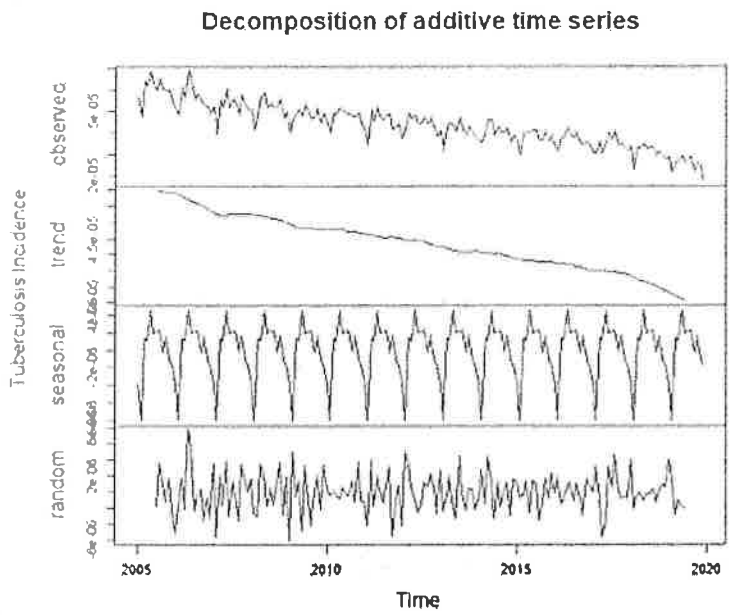


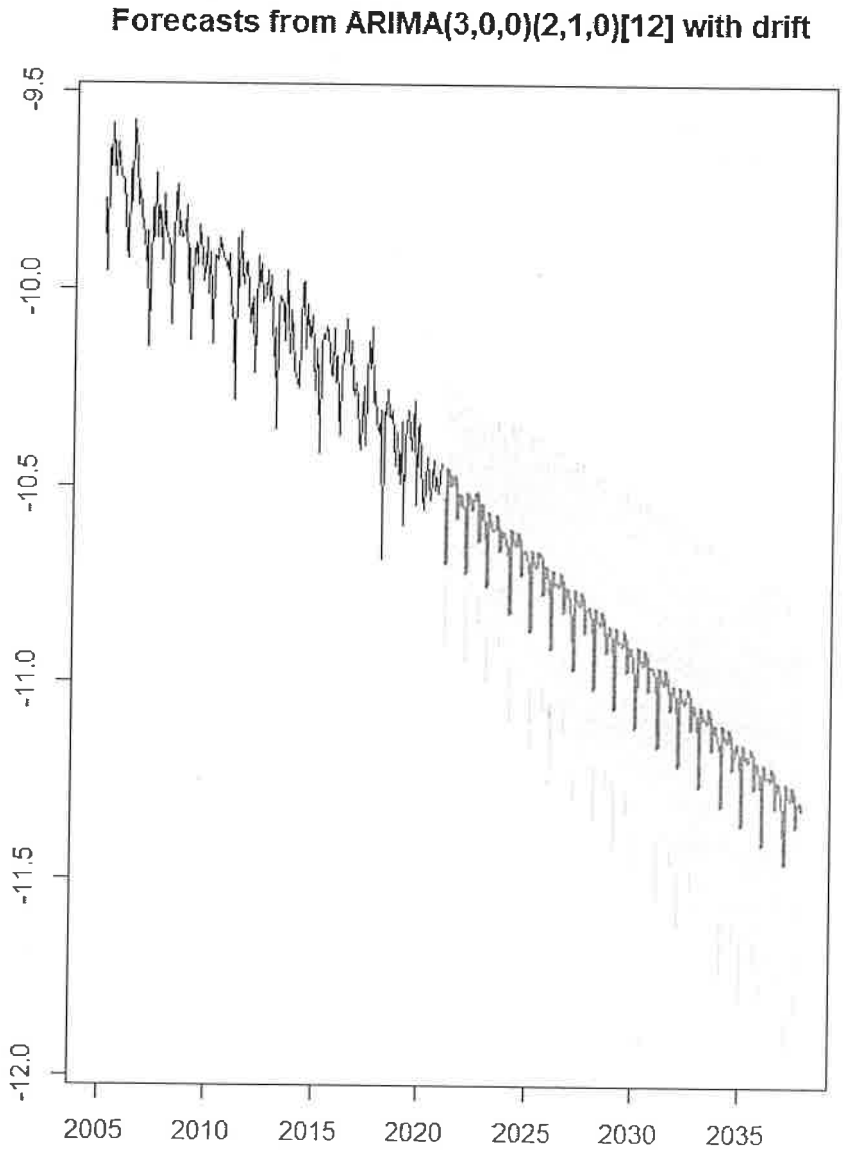

**Fig**. 1 Tuberculosis incidence time series analysis: A) Tuberculosis incidence with a steady declining trend from 2005-2019. B) Seasonality with two peaks occurring in March and May and a trough in November to the next February. C) Decomposition of the time series.

未來推估預測圖

Fig 2

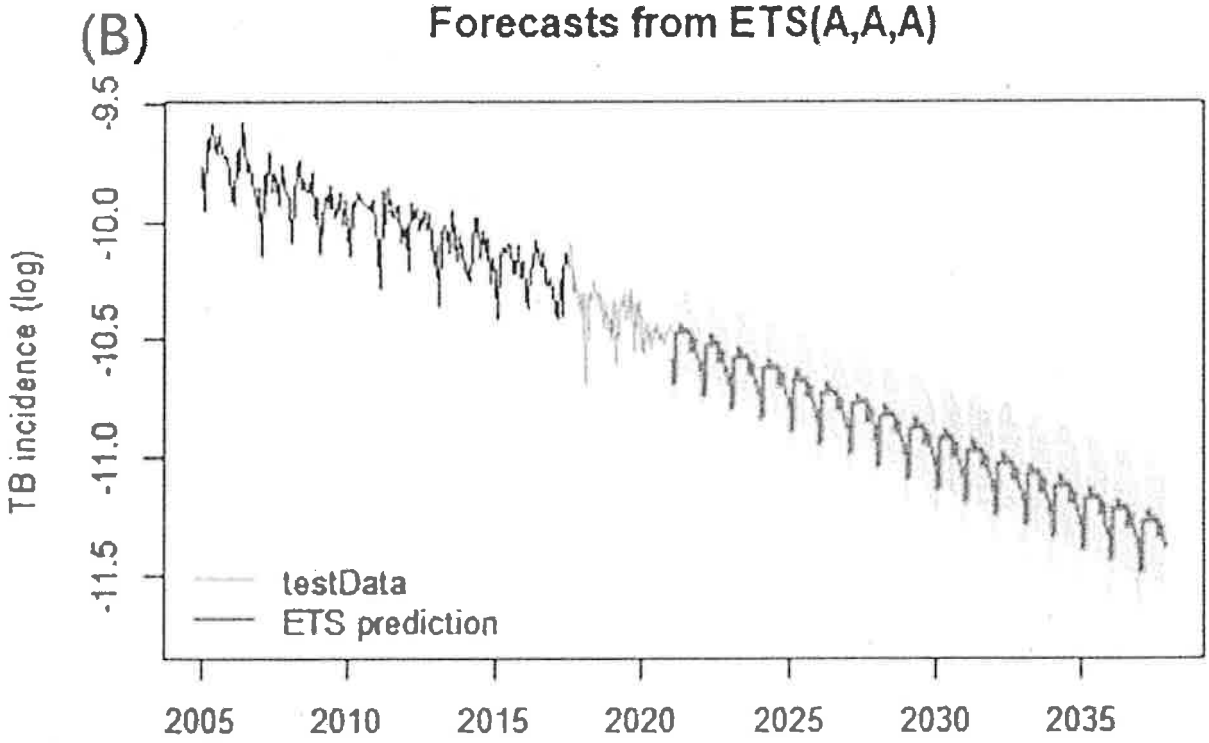
Tuberculosis incidence forecasting until 2030 using the SARIMA and SARIMA-ETS-hybrid mode by output exponation data following pre-logarithm input

(A)




(Erratum: Y label is TB incidence rate(log))

(B)


Forecasts from ETS(A,A,A)
TB incidence (log)
-9.5
-10.0
-10.5
-11.0
-11.5
testData
ETS prediction
2005
2010
2015
2020
2025
2030
2035

(C)

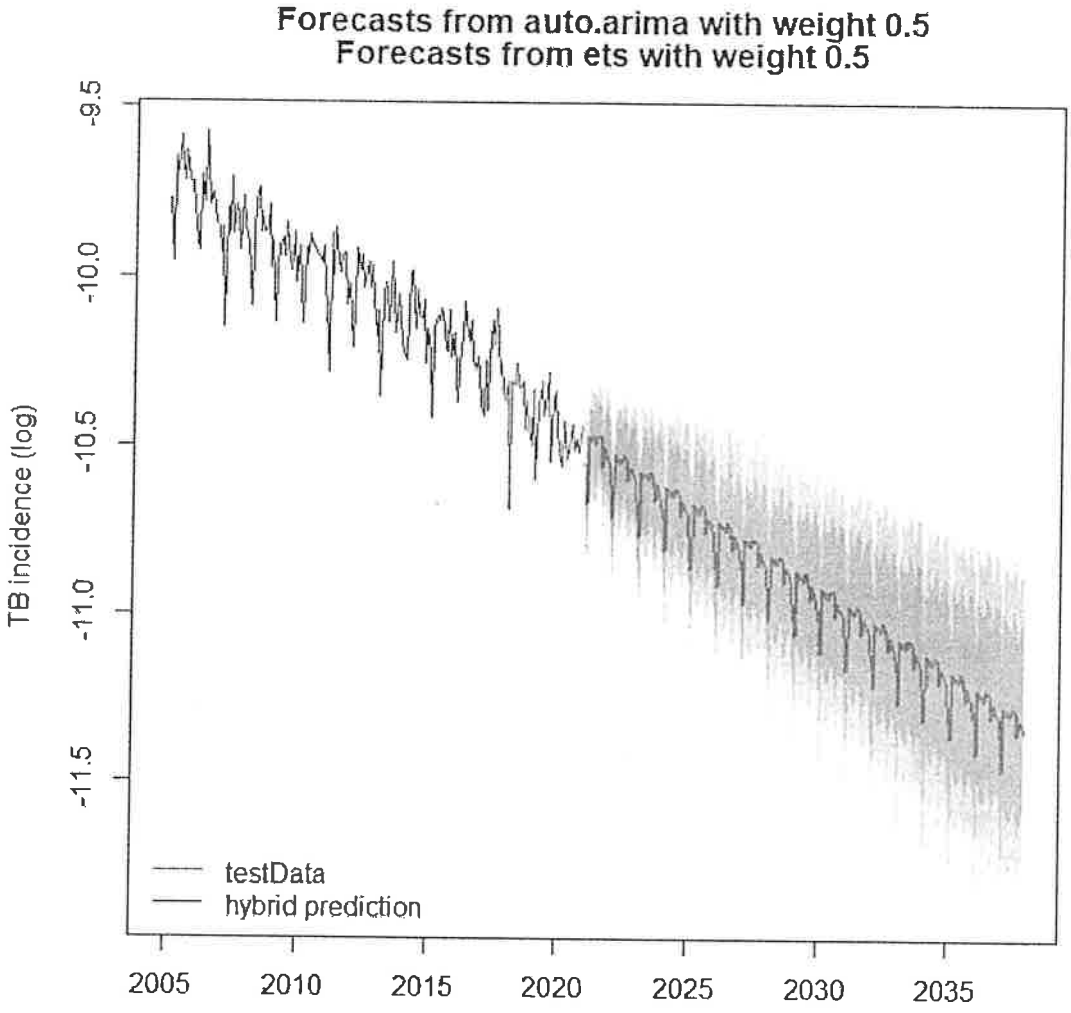
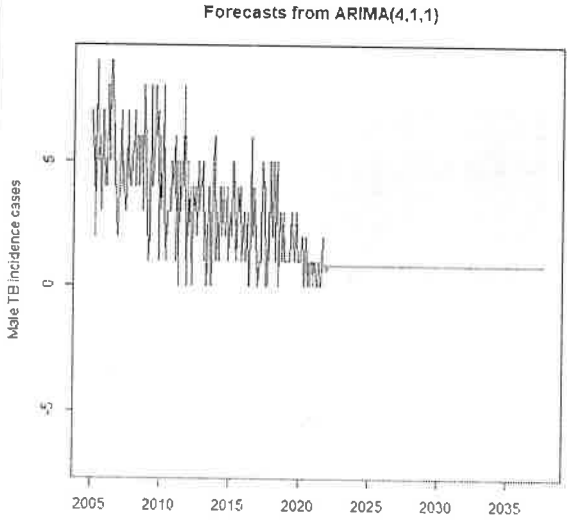
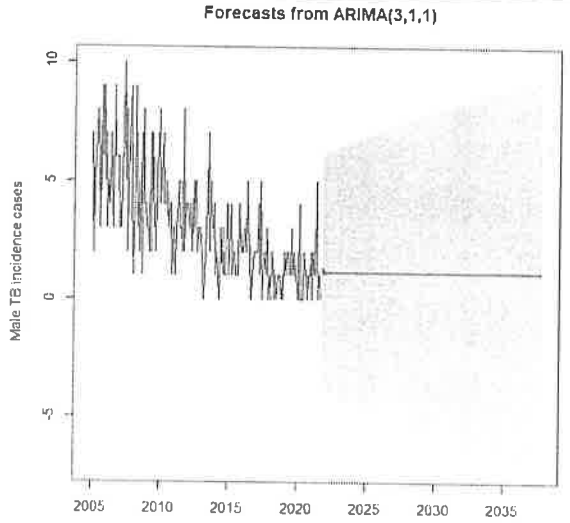

Forecasts from auto.arima with weight 0.5
Forecasts from ets with weight 0.5
TB incidence (log)
-9.5
-10.0
-10.5
-11.0
-11.5
testData
hybrid prediction
2005
2010
2015
2020
2025
2030
2035

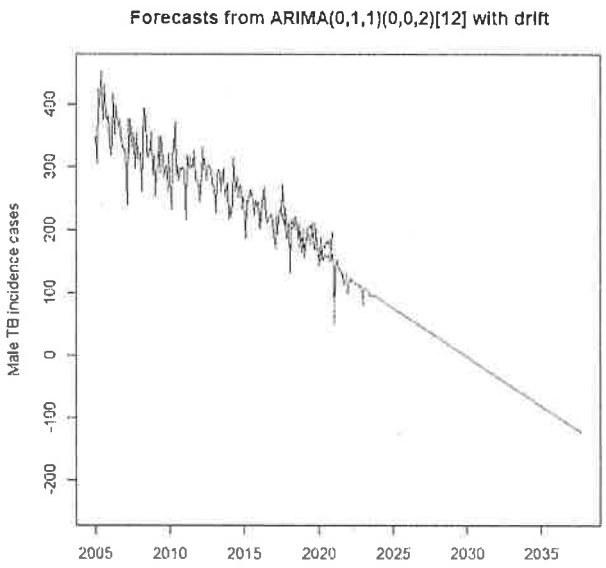
Fig 2 A、B、C: 綠線代表預測測試值(自提前1個月至提前30個月預測)，黑線代表實際值，藍線代表未來預測至2035年 。D:紅線SARINA分析及預測模型、綠線ETS分析及預測模型、藍線SARIMA-ETS Hybrid 預測模型

Fig 3

利用 SARIMA模型推估各人口群之結核病新發生個案數，
依性別及人口年齡特徵分群(以原型病例數作未來性別病例數預測模型)

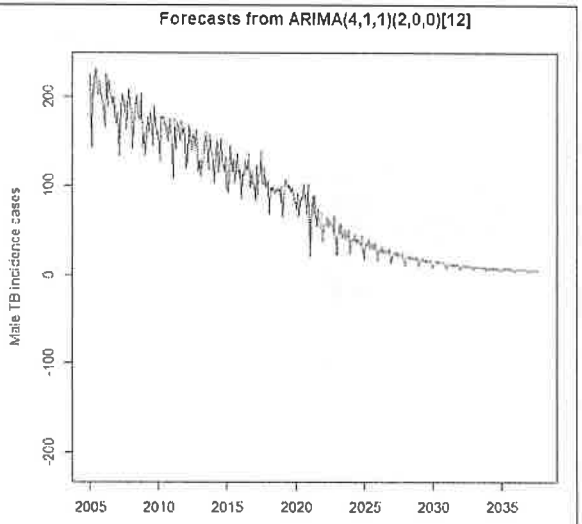
| | 男性 | 女性 |
|---|---|---|
| 0-14歲 |  <br>Performance metrics<br>ME RMSE MAE MPE MAPE MASE<br>-0.279 1.744 1.424 -Inf 0.739 -0.0290 |  <br>Performance metrics<br>ME RMSE MAE MPE MAPE MASE<br>-0.279 1.744 1.424 -Inf Inf 0.739<br>(Erratum: Y label is Female TB incidence cases ) |

15-64歳




Performance metrics

| ME | RMSE | MAE | MPE | MAPE | MASE |
|---|---|---|---|---|---|
| 0.632 | 26.018 | 19.073 | -1.621 | 8.223 | 0.746 |

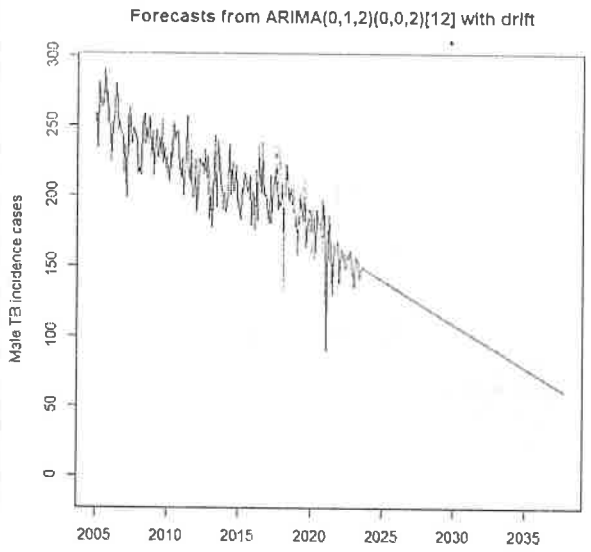



Performance metrics

| ME | RMSE | MAE | MPE | MAPE | MASE |
|---|---|---|---|---|---|
| -1.992 | 15.260 | 11.852 | -3.789 | 10.474 | 62 0.7380492 |

(Erratum: Y label is Female TB incidence cases )

65歳以上



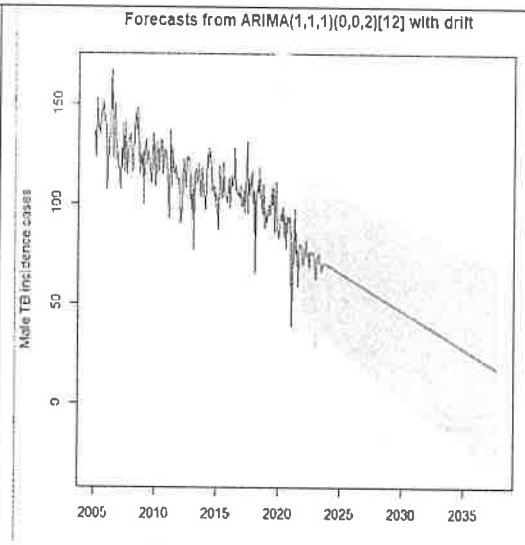

Performance metrics

(男) ME RMSE MAE MPE

0.0692 15.597 11.934 -0.685

MAPE MASE ACF1

Training set 5.899755 0.7655434 -0.0010197




Performance metrics

ME RMSE MAE MPE

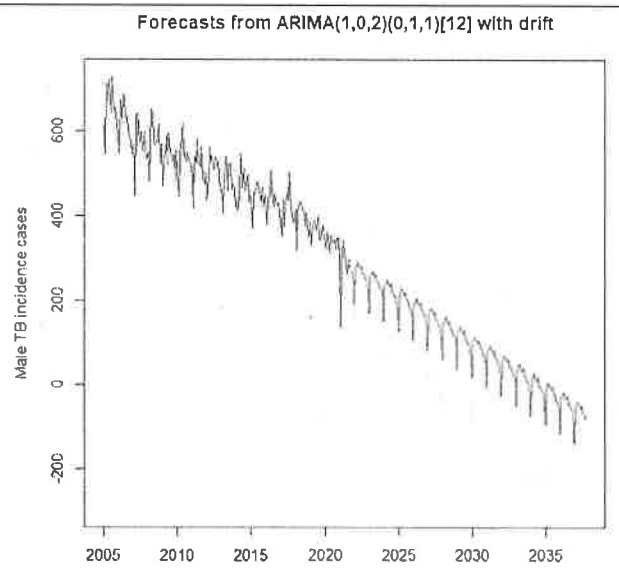
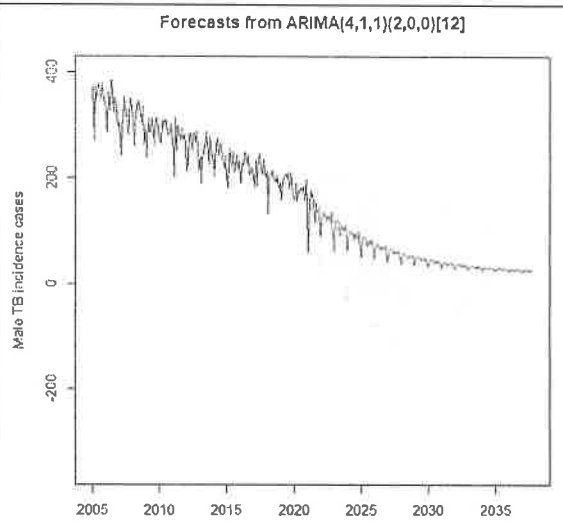
MAPE MASE :

0.105 10.956 8.255 -1.287 8.007 0.754

ACF1

-0.010099

(Erratum: Y label is Female TB incidence cases )

| | | |
|---|---|---|
| All Age |  <br>Performance metrics<br>ME RMSE MAE MPE MAPE MASE:<br>-0.1201 29.606 22.573 -0.599 5.249 0.629 |  <br>Performance metrics<br>ME RMSE MAE MPE MAPE MASE:<br>-2.531 21.728 16.535 -2.369 7.568 0.704<br>(Erratum: Y label is Female TB incidence cases ) |

# 附錄

附件A 結核病確定病例統計

(附件A，略)

110 年發表 SCI 期刊論文

# Surveillance of tuberculosis and treatment outcomes following screening and therapy interventions among marriage-migrants and labor-migrants from high TB endemic countries in Taiwan

Mei-Mei Kuan

Chief Secretary Office, Taiwan Centers for Disease Control, Ministry of Health and Welfare, Taipei, Taiwan

## ABSTRACT

**Background:** Tuberculosis (TB) among migrants from high-risk countries and underling interventions were concerned for disease control. This study aimed to assess the TB trends among marriage-migrants with the 1–2-round vs. labor-migrants with the four-round TB screenings in the period of the first four post-entry years; pre-entry screenings by an initial chest X-ray (CXR) were conducted during 2012–2015, and a friendly treatment policy was introduced in 2014.

**Methods:** TB data of migrants during 2012–2015 were obtained from the National TB Registry Database and analyzed. The incidences, clinical characteristics, and treatment outcomes were assessed to explore the impact of underlying interventions.

**Results:** During post-entry 0–4 years, the TB incidence rates among marriage-migrants ranged 11–90 per 100,000 person-years, with 60.8% bacteria-positive and 28.2% smear-positive cases. Whereas among labor migrants, the incidence rates ranged 67–120 per 100,000 person-years, with 43.6% bacteria-positive and 13.7% smear-positive cases. All migrants originated from Southeast Asia following pre-entry health screening in 2012–2015. The TB cases among marriage-migrants were with a higher proportion of sputum-smear-positivity (SS+) (OR: 4.82, 95% CI [3.7–6.34]) and CXR cavitation (OR: 2.90, 95% CI [2.10–4.01]). Marriage-migrants with TB had treatment completion rate of >90%, which was above the WHO target. For labor-migrants with TB, when compared the period of post- vs. pre-implementation of the friendly therapy policy that eliminated compulsory repatriation, the overall treatment completion rate of those who stayed in Taiwan improved by 30.9% (95% CI [24.3–37.6]) vs. 6.7% (95% CI [3.8–9.7]), which exceeded a 4.88-fold (95% CI: 3.83–6.22) improvement. Additionally, the treatment initiation rate within 30 days of diagnosis for SS- TB and B- TB cases during post- vs. pre-implementation of the therapy policy was increased, that is, 77.1% vs. 70.9% (OR: 1.38, 95% CI [1.12–1.70]) and 78% vs. 77% (OR: 1.64, 95% CI [1.38–1.95]).

**Conclusion:** Multiple CXR screenings could identify more TB cases with sputum-smear-negativity (SS-) TB at the early-stage, introducing latent tuberculosis infection (LTBI) screening might save underlying efforts. For those labor-migrants with TB

Submitted 24 April 2020
Accepted 19 October 2020
Published 16 March 2021

Corresponding author
Mei-Mei Kuan, kuan@cdc.gov.tw

Academic editor
Maria Cristina Albertini

Additional Information and Declarations can be found on page 12

DOI 10.7717/peerj.10332



How to cite this article Kuan M-M. 2021. Surveillance of tuberculosis and treatment outcomes following screening and therapy interventions among marriage-migrants and labor-migrants from high TB endemic countries in Taiwan. PeerJ 9:e10332 DOI 10.7717/peerj.10332

who stayed in the receiving country, the friendly TB therapy policy not only significantly improved the treatment completion but also the early treatment initiation.

Subjects Epidemiology, Infectious Diseases, Public Health
Keywords Friendly therapy policy, Tuberculosis treatment, Migrants

## INTRODUCTION

Taiwan, with a population of approximately 23.4 million, is a country with moderate TB incidence ranged 46–53 per 100,000 population in 2012–2015 (*Taiwan Centers for Disease Control, 2018*) and has gradually decreased over time. Nevertheless, TB disproportionately affects the foreign-born population from TB high-risk countries, with an incidence in this population that is several times higher than that among the Taiwanese-born population (*Global Tuberculosis Report, 2018*; *The World Bank, 2018*; *Taiwan Centers for Disease Control, 2018*). The reasons for the TB burden in the migrant population are likely to be the reactivation of remotely acquired LTBI following migration from high TB burden countries to lower TB burden countries (*Global Tuberculosis Report, 2018*; *The World Bank, 2018*; *Taiwan Centers for Disease Control, 2018*). TB control measures for the foreign-born population from high endemic countries in Taiwan occur within the scopes of the TB medical surveillance program. All newly arriving residents and temporary residents with high risk undergo an immigration medical examination before arrival. This examination consists of a physical examination which includes chest X-ray (CXR), syphilis test, HIV serology and other routine tests. If there is a radiographic evidence of TB, three sputum smears and mycobacterial cultures are examined (*Taiwan Centers for Disease Control, 2018*). Following the pre-entry screening, mandatory TB screening of either four rounds during the first 3 years (*Kuan, 2018*) or 1–2 rounds during the first 4 years (*Kuan, Yang & Wu, 2014*) are required post-entry for labor migrants or marriage migrants, respectively, who come from Southeast Asian (including Indonesia, Vietnam, Philippines, and Thailand) or China. Applicants with active TB are required to complete treatment before entering Taiwan. Before 2013, migrant workers with TB were repatriated; since 2014, these individuals are allowed to stay in Taiwan for treatment except multiple drug-resistant TB (MDR-TB) patients. A study showed that TB case with smear-positive sputum was more infectious than those with smear-negative sputum (*Kuan, 2018*). Our previous studies revealed that a 30.2% (*Kuan, Yang & Wu, 2014*) and 14.3% (*Kuan, 2018*) smear-positive sputum among marriage migrants vs. labor migrants in Taiwan. In term of TB control targeting high TB incidence migrants, it should be taken into consideration along with screening the differences in pathogen exposure due to their origins, the ethnic socio-economic disparities and the experience of migration itself (*Hayward et al., 2018*); moreover, to overcome the cultural and structural barriers to accessing healthcare (*Hayward et al., 2018*) is also critical. Thus, a friendly TB therapy policy may prompt access to treatment for a migrant in the new residing country.
This study retrospectively analyzed a cohort from 2012–2015 aimed to analyze the impact

on TB incidence and clinical characteristics following the enhanced screening interventions among these high-risk migrants. Also, the treatment outcomes following the concurrent TB intervention programs as well as the effectiveness of introducing a friendly TB therapy policy in 2014 targeting labor migrants was assessed.

# MATERIALS AND METHODS

## Data Collection

TB data on migrants were retrieved from the following sources similar to previous studies (*Kuan, 2018*; *Kuan, Yang & Wu, 2014*): (1) the national TB registry database, which was updated regularly by clinicians and local health divisions; (2) The populations of marriage migrants and labor migrants were obtained from the official publications of the Ministry of the Interior (*Ministry of Interior Taiwan, 2016*).

## Definition of migrants with TB

Two strategies of post-entry TB screenings were targeted towards foreign migrants from highly endemic Southeast Asian countries (including Vietnam, Philippines, Thailand, and Malaysia) during the first 4 post-entry years following pre-entry screenings in Taiwan: (1) For labor migrants (foreign workers), 4 screenings at 0–3 days as well as at 6, 12, 18 and 30 months are conducted (*Kuan, 2018*). (2) For marriage migrants (foreign spouses), one to two mandatory TB screenings are conducted (*Kuan, Yang & Wu, 2014*). The definition of marriage migrants with TB (*Kuan, Yang & Wu, 2014*) or labor migrants with TB (*Kuan, 2018*) was described as previously (*Kuan, 2018*; *Kuan, Yang & Wu, 2014*). Treatment completion, according to the WHO guidelines, is defined as accomplished by a standard regimen, that is, a 6–9-month regimen, or complete treatment by a longer regimen. The TB treatment completion rate was obtained as the number of TB patients who achieved treatment completion by the standard or longer therapy regimen divided by the number of TB patients staying in Taiwan.

## Statistics and analysis

The TB incidence (per 100,000 population) was calculated as the number of newly detected labor migrants with TB during the study period (2012–2015) divided by the population per year. The yearly fluctuating trends in the TB incidence rates among labor migrants ($X_1$) and marriage migrants ($X_2$) vs. the WHO estimated TB incidence rates (*Taiwan Centers for Disease Control, 2018*) (Y), as well as the TB incidences ($X_1$) of the labor migrants vs. the marriage migrants ($X_2$), were detected with linear regression analysis. Furthermore, several odds ratio tests were performed: the studied TB case population was divided into two exposure categories: marriage migrants vs. labor migrants or post-implementation (2014–2015) vs. pre-implementation (2012–2013) of the friendly therapy policy. Categorical variables were subjected to binary analysis using a $2 \times 2$ table to compute odds ratios (ORs) and 95% confidence intervals (CIs) by using R Programming or OpenEpi (*Dean, Sullivan & Soe, 2006*) for assessment of the difference between paired binary variable determinants; the control (i.e., reference) for each variable was the total number in each stratified category, excluding the detected items (i.e., independent

variables). The TB treatment outcome was estimated by calculating the transferred-out rate and the treatment completion rate. To assess the impact of implementing the friendly therapy policy with no compulsory repatriation, the post-implementation (2014–2015) vs. pre-implementation (2012–2013) TB treatment completion rate, the percentage of sputum smear positivity of the transferred out cases vs. the cases staying in Taiwan for therapy, and the initiation of treatment within 30 days of diagnosis, that is, the delay (in days) of treatment initiation (standard or longer regimen) following diagnosis among labor migrants during post vs. pre-implementation of the therapy policy, were estimated by *t*-tests (2-sides) or Chi-squared tests.

### Ethics statement

This study was approved by the Institutional Review Board of the Taiwanese CDC under identification number TwCDCIRB106135.

## RESULTS

### TB incidence trends among migrants and TB screening impact

The TB surveillance strategy in Taiwan implemented a mandatory screening post-entry for immigrants at risk. This is either an 1–2 rounds or four rounds of screenings targeted to marriage migrants or labor migrants who come from high-burden countries, during the first 0–4 years or the first 0–3 years, respectively, following an initial pre-entry screening with CXR detection. For migrants from the same area of origin (Indonesia, Vietnam, Thailand, and the Philippines), the TB incidence rates of labor migrants were higher than those of marriage migrants, $P < 0.001$ (Table 1). Briefly, the TB incidence ranged 67.71–143.78 (per 100,000) among labor migrants, 11.3–99.74 among marriage migrants from Southeast Asia, and 11.4–15.66 among those from China during their first post-entry 0–4 years in 2012–2015 (Table 1). Relationships among the fluctuation trends during the first 0–4 years of the post-entry period were detected. The TB incidence rates of the labor migrants ($X_1$) or of the marriage migrants ($X_2$) were positively correlated with those of WHO estimated (Y) for their countries of origin (*The World Bank, 2018*) based on yearly surveillance by the Pearson's correlation or liner association in the manner of significant ($n = 16$, Pearson's correlation $R_{X1:Y}$: 0.74, linear association $R^2_{X1:Y}$: 0.55, $P < 0.0001$) or of less significant ($n = 14$, Pearson's correlation $R_{X2:Y}$: 0.65, linear association $R^2_{X2:Y}$: 0.42, $P = 0.0125$). Furthermore, the TB incidence rates of the labor migrants ($X_1$) vs. those of the marriage migrants ($X_2$) identified were higher, but the association between these fluctuation trends appeared insignificant (i.e., $n = 14$, Pearson's correlation $R$:0.248; linear association: $R^2_{X2:X1}$: 0.061, $P = 0.393$).

### Comparison of TB screening impact on clinical characteristics among TB cases

TB cases identified among marriage migrants were similar to those identified among labor migrants in terms of nationality, but the marriage migrants were more likely to be women (OR: 25.37, 95% CI [13.47–47.81]), were more likely to be older than 45 years old (OR: 3.89, 95% CI [2.61–5.78]) and had more severe infections (Table 2) at diagnosis.

Table 1 **Tuberculosis notification and treatment outcomes among labor and marriage migrants.**

| | | Labor migrants | | | | | Marriage migrants | | | | Chi-sq[g] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | | 2012 | 2013 | 2014 | 2015 | Sum | 2012 | 2013 | 2014 | 2015 | Sum | *p*-value |
| | Notification TB cases | 472 | 581 | 646 | 624 | 2,323 | 109 | 92 | 95 | 84 | 380 | |
| Age | ≤24 | 101 | 102 | 129 | 120 | 452 | 6 | 9 | 4 | 4 | 23 | <0.001 |
| | 25–44 | 363 | 464 | 489 | 483 | 1,799 | 91 | 72 | 80 | 72 | 315 | |
| | ≤45 | 8 | 15 | 28 | 21 | 72 | 12 | 11 | 11 | 8 | 42 | |
| Sex | Female | 295 | 352 | 361 | 370 | 1,378 | 107 | 92 | 89 | 82 | 370 | <0.001 |
| | Male | 177 | 229 | 285 | 254 | 945 | 2 | 0 | 6 | 2 | 10 | |
| Country | Indonesia | 221 | 286 | 322 | 296 | 1,125 | 13 | 6 | 7 | 9 | 35 | <0.001 |
| | Vietnam | 77 | 98 | 102 | 123 | 400 | 44 | 44 | 34 | 30 | 152 | |
| | Philippines | 109 | 128 | 152 | 162 | 551 | 4 | 4 | 8 | 0 | 16 | |
| | Thailand | 65 | 69 | 68 | 43 | 245 | 0 | 2 | 3 | 1 | 6 | |
| | China | | | | | 0 | 48 | 36 | 42 | 44 | 170 | |
| Population | Indonesia | 191,127 | 213,234 | 229,491 | 236,526 | 870,378 | 27,684 | 27,943 | 28,287 | 28,699 | 112,613 | <0.001 |
| | Vietnam | 100,050 | 125,162 | 150,632 | 169,981 | 545,825 | 87,357 | 89,042 | 91,004 | 93,441 | 360,844 | |
| | Philippines | 86,786 | 89,024 | 111,533 | 123,058 | 410,401 | 7,465 | 7,707 | 8,021 | 8,326 | 31,519 | |
| | Thailand | 67,611 | 61,709 | 59,933 | 58,372 | 247,625 | 8,336 | 8,375 | 8,467 | 8,525 | 33,703 | |
| | China | | | | | 0 | 306,514 | 315,905 | 323,358 | 330,069 | 1,275,846 | |
| TB incidence | Indonesia | 115.63 | 134.13 | 140.31 | 125.14 | | 46.96 | 21.47 | 24.75 | 31.36 | | |
| | Vietnam | 76.96 | 78.3 | 67.71 | 72.36 | | 50.37 | 49.41 | 37.36 | 32.11 | | |
| | Philippines | 125.6 | 143.78 | 136.28 | 131.65 | | 53.58 | 51.9 | 99.74 | 0 | | |
| | Thailand | 96.14 | 111.82 | 113.46 | 73.67 | | 0 | 23.88 | 35.43 | 11.73 | | |
| | China | | | | | | 15.66 | 11.4 | 12.99 | 13.33 | | |
| Clinical characteristics | B+[a] | 205 | 260 | 271 | 276 | | 67 | 59 | 64 | 41 | | |
| | B−[b] | 234 | 290 | 349 | 325 | | 40 | 31 | 29 | 39 | | |
| | SS+[c] | 77 | 81 | 75 | 85 | | 31 | 32 | 31 | 23 | | |
| | MDR-TB | 1 | 6 | 2 | 3 | | 0 | 0 | 0 | 0 | | |
| TB treatment | DOST | 297 | 398 | 457 | 484 | | 101 | 92 | 92 | 80 | | |
| | Died | 1 | 2 | 2 | 3 | | 0 | 1 | 1 | 0 | | |
| | Transferred out | 426 | 526 | 457 | 380 | | 9 | 2 | 3 | 2 | | |
| | Transferred-out rate | 0.903 | 0.905 | 0.707 | 0.609 | 0.21 (0.16–0.26)[h] | 0.083 | 0.022 | 0.032 | 0.024 | | |
| | Lost to follow up | 8 | 9 | 11 | 15 | 1.27 (0.7–2.4)[h] | 0 | 1 | 1 | 1 | | |
| | Staying in Taiwan (ST)[d] | 46 | 55 | 189 | 244 | | 100 | 90 | 92 | 82 | | |
| | Treat. completion (TC)[e] | 46 | 48 | 178 | 233 | 4.88 (2.8–6.2)[h] | 99 | 89 | 90 | 80 | | |
| | TC = 6–9 months[e] | 42 | 48 | 174 | 232 | | 99 | 89 | 88 | 79 | | |
| | TC > 6–9 months[e] | 0 | 0 | 4 | 1 | | 0 | 0 | 2 | 1 | | |
| | STT-completion rate[f] | 0.913 | 0.873 | 0.92 | 0.95 | | 0.96 | 0.989 | 0.96 | 0.96 | | |

**Notes:**

[a] B+: bacterial positivity, with positivity among 3 sputum smears or sputum cultures.
[b] B−: bacterial negativity, with no positivity among 3 sputum smears or sputum cultures.
[c] SS+: positivity among 3 sputum smears.
[d] Staying in Taiwan cases = all TB cases—transferred-out cases, including compulsorily repatriated cases.
[e] Treatment completion using 6–9-month regimens, that is, a standard regimen or longer regimen.
[f] The treatment completion rate of cases staying in Taiwan = cases staying in Taiwan with treatment completion by a standard or longer therapy regimen/cases staying in Taiwan.
[g] Pearson's Chi-squared test.
[h] Odds ratio of TB cases during 2014–2015 vs. 2012–2013.

Table 2 **The impact of TB screening on clinical characteristics among migrants with TB.**

| | Marriage migrant | Labor migrant | Odds Ratio |
|---|---|---|---|
| Total | *N* = 380 | *N* = 2,323 | |
| Sex | | | |
| Female | 370 | 1,378 | 25.37 (13.47–47.81)* |
| Age at diagnosis, years | | | |
| ≥45 | 42 | 72 | 3.89 (2.61–5.78)* |
| 44≤ | 338 | 2,251 | 0.26 (0.17–0.38)* |
| CXR | | | |
| Normal | 40 | 238 | 1.03 (0.72–1.47) |
| Abnormal without cavitation | 270 | 1,922 | 0.51 (0.40–0.66)* |
| Abnormal with cavitation | 60 | 141 | 2.90 (2.10–4.01)* |
| No record | 10 | 260 | |
| Sputum smear | | | |
| SS− | 246 (64.7%) | 1,834 (78.9%) | 0.49 (0.39–0.62)* |
| SS+ | 107 (28.2%) | 318 (13.7%) | 4.82 (3.7–6.34)* |
| No record | 27 | 171 | |
| Sputum culture | | | |
| SC+ | 222 | 990 | 1.89 (1.52–2.39)* |
| SC− | 148 | 1,222 | 0.57 (0.46–0.71)* |
| No record | 10 | 824 | |
| Bacterial status | | | |
| B+ | 231 (60.8%) | 1,012 (43.6%) | 2.01 (1.61–2.51)* |
| B− | 149 (39.2%) | 1,311 (56.4%) | 0.50 (0.40–0.62)* |

**Notes:**
* Odds ratio: significant.
SS, sputum smear; SC, sputum culture.

The effect of TB screenings on clinical characteristics among migrants with TB after post-entry screenings were assessed and revealed 60.8% bacteria-positive and 58.4% smear-positive cases among marriage migrants; 43.6% bacteria-positive and 42.6% smear-positive cases among labor migrants (Table 1). The marriage migrants with 1–2 rounds vs. labor migrants with four rounds post-entry screenings had higher rates of sputum smear positivity (SS+) (OR: 4.82, 95% CI [3.7–6.34]), higher rates of CXR cavitation (OR: 2.90, 95% CI [2.10–4.01]) and higher rates of B+ (OR: 2.1, 95% CI [1.61–2.51]) (Table 2).

## Anti-TB treatment outcomes: post- vs. pre-implementation of the friendly therapy policy

The overall treatment completion rate was >90% among both the labor and marriage migrants who stayed in Taiwan and accepted TB treatment (Table 1), which was above the WHO target of >85% (*Dean, Sullivan & Soe, 2006*). Comparing outcome during post- (2014–2015) vs. pre- (2012–2013) implementation of the therapy policy with no compulsory repatriation for labor migrants, the treatment completion rate was increased by 4.88-fold (95% CI [3.83–6.22]), that is, 30.9% (95% CI [24.3–37.6]) vs. 6.7% (95% CI

[3.8–9.7]) (Table 1). Higher completion rates for SS– TB cases OR: 7.45 (95% CI [5.44–10.2]) or B– TB cases OR: 6.87 (95% CI [4.21–11.2]); SS+ TB cases, OR: 13.43 (95% CI [4.02–44.79]) (Table 3), or B+TB cases OR: 5.83 (95% CI [3.62–9.42]) were also observed.

After 2014 (post-) vs. before 2013 (pre) implementing friendly therapy being less in transfer out TB cases of OR: 0.21 (95% CI [0.16–0.26]) (Table 1) which was detailed by less transfer out cases with both SS- TB cases of OR: 0.61 (95% CI [0.38–0.97]) or B– TB cases of OR: 0.58 (95% CI [0.49–0.69]) and SS+ TB cases of OR: 0.44 (95% CI [0.27–0.71]) or B+ TB cases of OR: 0.66 (95% CI [0.56–0.79]) (Table 3) as well as being no significant change in lost-to follow up TB cases of OR: 1.27 (95% CI [0.69–2.40]) among labor migrants were exhibited (Table 1).

In terms of overall TB treatment initiation within 30 days of diagnosis, in both migrants with SS+ TB (96.7% (188/194) vs. 91.2% (290/318)) and SS– TB (81.8% (301/368) vs. 74.3% (1,364/1,834)), the marriage migrants were more compliant than labor migrants. Moreover, comparing the overall initiation rate of TB treatment among labor migrants with TB showed a significant increase of 73.7% vs. 68.2% (OR: 1.31, 95% CI [1.09–1.57]) during the post- vs. pre-implementation of the therapy policy. Furthermore, during the post- vs. pre-implementation of the therapy policy, the TB treatment initiation rate among labor migrants showed a significant increase of 77% vs. 71% (OR: 1.38, 95% CI [1.12–1.70]) with SS– TB and a non-significant change of 89.4% vs. 93.00% (OR: 0.63, 95% CI [0.29–0.39]) with SS+ TB. Meanwhile, a significant increasing of 78% vs. 77% (OR:1.64, 95% CI [1.38–1.95]) with B– TB and a non-significant change of 83% vs. 85% (OR: 0.84, 95% CI [0.70–1.01]) with B+ TB was observed (Table 3).

## DISCUSSION

Multiple initial screenings with CXR could identify more SS– TB cases at an early stage with low infectivity and result in a higher incidence. For migrants who come from high TB burden regions, a pre-entry initial screening with a CXR is required and follow by mandatory 1–2 rounds of post-entry screening for marriage migrants or four rounds for labor migrants in Taiwan, respectively. This initiative resulted in a higher incidence with more SS– TB among labor migrants and a lower incidence but more SS+ TB or more CXR cavitation TB cases among marriage-migrants (Tables 1 and 2). Moreover, the higher annual TB incidence rates in labor migrants were significantly ($R^2$: 0.55, $P$ <0.0001) associated with the WHO estimated TB incidence rates (*Taiwan Centers for Disease Control, 2018*) of their original countries and there were significantly fewer severe cases, that is, fewer SS+ TB cases or fewer CXR cavitation TB cases, among the labor migrants. On the other hand, relatively lower annual TB incidence rates among marriage migrants were less significantly associated with the WHO-estimated TB incidence rates (*Taiwan Centers for Disease Control, 2018*) of their original countries ($R^2$ = 0.42, $P$ = 0.0125), and there were significantly more severe cases, that is, more SS+ TB cases (OR: 4.82), or more CXR abnormal with cavitation TB (OR: 2.90) (Table 2). Thus, these results indicated that the greater number (four rounds) of mandatory post-entry screenings for labor migrants vs. the 1–2 rounds for marriage migrants could screen out more TB cases;

Table 3 **Tuberculosis treatment outcomes of labor migrants with TB during post- vs. pre- friendly therapy policy.**

| Anti-TB treatment | TB cases | Pre-FT $N$ = 1,053 | Post-FT $N$ = 1,270 | Odds ratio |
|---|---|---|---|---|
| Outcome by nationality | Indonesia | $n'$ = 507 | $n'$ = 618 | |
| | Transf. out | 450 | 394 | 0.22 (0.16–0.31)* |
| | Longer reg. | 0 | 4 | |
| | Stand. Reg. | 49 | 206 | 4.81 (3.43–6.75)*,^ |
| | No record | 8 | 14 | |
| | Vietnam | $n'$ = 175 | $n'$ = 225 | |
| | Transf. out | 158 | 153 | 0.23 (0.13–0.40)* |
| | Longer reg. | 0 | 0 | |
| | Stand. Reg. | 15 | 67 | 4.52 (2.48–8.25)^ |
| | No record | 98 | 5 | |
| | Philippines | $n'$ = 237 | $n'$ = 314 | |
| | Transf. out | 212 | 206 | 0.22 (0.14–0.36)* |
| | Longer reg. | 0 | 1 | |
| | Stand. Reg. | 24 | 106 | 4.52 (2.79–7.33)^ |
| | No record | 1 | 1 | |
| | Thailand | $n'$ = 134 | $n'$ = 111 | |
| | Transf. out | 132 | 84 | 0.05 (0.01–0.20)* |
| | Longer reg. | 0 | 0 | |
| | Stand Reg. | 2 | 26 | 19.88 (4.6–85.95)^ |
| | No record | 0 | 1 | |
| Outcome of DOST | SS-/DOST | $n$ = 537 | $n$ = 784 | 1.60 (1.3–1.96)* |
| | Completion | 50 | 334 | 7.45 (5.44–10.2)^ |
| | Refuse | 4 | 5 | |
| | Transfer out | 250 | 225 | 0.61 (0.38–0.97)* |
| | Lost to follow up | 14 | 22 | |
| | Side effect | 5 | 5 | |
| | Not bac | 33 | 16 | |
| | other | 170 | 175 | |
| | SS+/DOST | $n$ = 124 | $n$ = 117 | 0.75 (0.45–1.25) |
| | Completion | 3 | 33 | 13.43 (4.02–44.79)* |
| | Transfer out | 62 | 45 | 0.44 (0.27–0.71)^ |
| | Lost to follow up | 3 | 4 | |
| | Side effect | 3 | 0 | |
| | Not bac | 1 | 0 | |
| | other | 49 | 35 | |
| | B+/DOST | $n$ = 332 | $n$ = 382 | 0.93 (0.78–1.11) |
| | Refuse | 5 | 1 | |
| | Complete | 20 | 129 | 5.83 (3.62–9.42)* |
| | Side effect | 3 | 3 | |
| | Lost to follow up | 11 | 8 | |
| | Transfer out | 438 | 408 | 0.66 (0.56–0.79) |

Table 3 (continued)

| Anti-TB treatment | TB cases | Pre-FT $N$ = 1,053 | Post-FT $N$ = 1,270 | Odds ratio |
|---|---|---|---|---|
| | B-/DOST | $n$ = 346 | $n$ = 534 | 1.48 (1.25–1.76) |
| | Refuse | 8 | 4 | |
| | Complete | 33 | 240 | 6.87 (4.21–11.2)[a] |
| | Side effect | 5 | 2 | |
| | Lost to follow up | 6 | 18 | |
| | Transfer out | 458 | 392 | 0.58 (0.49–0.69)[a] |
| Treatment | SS– | $n$ = 805 | $n$ = 1,029 | |
| Initiation day of diagnosis | <30 day | 571 | 793 | 1.38 (1.12–1.70)[a] |
| | >30 day | 145 | 157 | 0.82 (0.64–1.05) |
| | No record | 89 | 79 | |
| | <$n$ 30 day rate[b,c] | 0.71 | 0.77 | |
| | SS+ | $n$ = 158 | $n$ = 160 | |
| | <30 day | 147 | 143 | 0.63 (0.29–1.39) |
| | >30 day | 2 | 3 | 2.99 (0.50–18.08) |
| | No record | 9 | 14 | |
| | <30 day rate | 0.93 | 0.89 | |
| | B– | $n$ = 399 | $n$ = 658 | |
| | <30 day | 307 | 512 | 1.64 (1.38–1.95)[a] |
| | >30 day | 92 | 146 | |
| | <30 day rate[c,d] | 0.77 | 0.78 | |
| | B+ | $n$ = 347 | $n$ = 379 | |
| | <30 day | 296 | 313 | 0.84 (0.70–1.01) |
| | >30 day | 51 | 66 | |
| | <30 day rate | 0.85 | 0.83 | |

**Notes:**

[a] Comparison of treatment outcomes post- vs. pre- implementation of friendly therapy, odds ratio test: significant; either $N$ or $n'$: calculate reference for odds ratio.

[b, c] The proportions of cases of initiate treatment between post-FT and pre-FT was significantly different which was approved by a Fisher's exact test, $P$ = 0.0296 ($P$ < 0.05) that is, to reject the null hypothesis; $n$, denominator for rate.

although the incidence rate appeared higher, but more cases had early-stage disease with SS– TB. Also, these results corroborate previous findings that multiple TB screenings in individuals with initial abnormal CXRs result in the detection and identification of more SS– TB cases at an early disease stage (*Kuan, 2018*), which might benefit for timely therapy initiation; thus, might increase the success of treatment and reduce disease burden including blocking the potential disease dissemination. However, the high proportion of bacteriological negativity that is, of >35% with B- TB in both groups, for example, 56.4% in labor migrants vs. 39.2% in marriage migrants (Table 1), has suggested the multiple TB screenings might be of over-detection (*Kuehne et al., 2018*; *Aldridge et al., 2016*). While the reasons for the high TB burden in the migrant population are likely to be the reactivation of remotely acquired LTBI following migration from high TB burden countries to lower TB burden countries (*Global Tuberculosis Report, 2018*; *The World Bank, 2018*; *Taiwan Centers for Disease Control, 2018*). Therefore, it is important that

applying a LTBI screening combined with prevention treatment (PT) at a pre- or post-entry in the very beginning will save a lot of efforts in later stages, for example, multiple screenings (*The New York Times Editorial Board, 2018*) and might meet the core of an earlier TB mitigation strategy for TB control intervention targeting at high-risk migrants even including BCG-vaccinated individuals (*Olivieri et al., 2016*); for example, a 2-step LTBI screening: performing an expensive interferon-gamma release assay (IGRA) after positivity on the economical tuberculin skin test (TST), then combined with PT (*Olivieri et al., 2016*). Thus, antibiotics can effectively and economically eliminate tuberculosis, before they become contagious, that is, to treat individuals who are still invisibly sick. In several countries, such as the United States, Britain, and Canada, LTBI screenings combined with PT strategies have long since become public health norms for migrants (*The New York Times Editorial Board, 2018*).

The repatriated labor migrants with TB were not traced in this study if they received any treatment when they returned home country. Nonetheless, both marriage migrants and labor migrants with TB who stayed in Taiwan and accepted either the standard (6–9 months) or longer regimen of TB therapy achieved a TB treatment completion rate of 87–99% (Table 1), which was above the WHO target of >85% (*WHO, 2006–2015*) during 2012–2015. In terms of assessing the overall treatment outcome of TB cases, it was found that cases identified among labor migrants significantly had poorer treatment completion than those among marriage-migrants in Taiwan because of a higher percentage of transferred out cases in 2012–2015 (Table 1). The treatment completion rate in Taiwan was high in marriage migrants (96–99%; Table 1). As for labor migrants, after the implementation of the therapy policy which eliminated repatriation of TB cases and allowed for therapy in the host country, the completion rates raised to 24–37% from 3.8–9.7% (Tables 1 and 3) after the implementation of the therapy policy during 2012–2015.

Overall, the improvement of an increased 4.88-fold that is, 30.9% in 2014–2015 vs. 6.7% in 2012–2013 of the TB treatment completion among labor migrants during periods post-implementation (2014–2015). It was further observed that TB cases with more SS– (OR: 7.45) or B– 44(OR: 1.48) and more SS+ (OR: 13.43) or B+ (OR: 5.83) was treatment completed since 2014 (Table 3) among labor-migrants, which demonstrates the benefit of implementing the friendly therapy policy. Also, the reducing potential structural barriers to TB treatment completion (*Kourbatova et al., 2006*; *Datiko & Lindtjorn, 2010*; *Lambert et al., 2003*), limited access to care (*Kourbatova et al., 2006*), and relocations of labor-migrants were conducted by introducing the therapy policy since 2014. Moreover, after 2014, a significant decline in transfer out TB cases was observed in both of SS- TB cases (OR: 0.61) or B– TB cases (OR: 0.58) and SS+TB cases (OR: 0.44) or B+ TB cases (OR: 0.66) among labor migrants during this study period (Table 3).

Additionally, because the higher number of SS– or B– TB cases among labor migrants than among marriage migrants was also worried as a potential risk of being delayed or untreated and then, in turn, developing TB dissemination. Since very few bacilli are sufficient to cause infection (*Sepkowitz, 1996*; *Scandurra et al., 2020*), therapy should not be delayed in labor-migrants with SS– TB according to the WHO guidelines, especially those

who were to provide long-term care for vulnerable people or the elderly; therefore, initiation rate of anti-TB treatment within 30 days of diagnosis was concerned. Af introducing the friendly therapy policy, the overall treatment initiation rate within 30 days of diagnosis was significantly increasing (OR: 1.31) among labor migrants. Furthermore, the overall initiation rate of treatment exhibited higher among labor migrants with SS+ TB (93.0%) or B+ TB (83.9%) than those with SS− TB (70.9%) or B (77.4%) and implicated that relatively more TB cases with SS− or B− had somehow de treatment than those with SS+ or B+. Nevertheless, after introducing the therapy p for labor migrants, showed a significant increase in the initiation rate of treatment for SS− TB of 77% vs. 71% (OR: 1.38) or B− TB of 78% vs. 77% (OR:1.64) during t post vs. pre-implementation of the policy. Relatively, this implementation was not significantly impacted the treatment initiation rate among labor immigrants with SS of between 91–89% (OR: 0.63) or B+ (OR: 0.84) (Table 3). Thus, the friendly therap policy in Taiwan has resulted in an improved experience of reducing structural barrie TB mitigation since its implementation in 2014, which has successfully promoted th anti-TB treatment outcomes including improvement in treatment initiation especiall those who with S− TB or B− TB and increasing treatment completion for those migr with TB stayed in Taiwan. Therefore, based on our observations, there is a need for intensifying health education that promotes TB therapy includes delivering the information of the ongoing availability of free, accessible health services for vulnerab groups such as high-risk migrants; this health education could also be a critical elemen increasing treatment success (*Hayward et al., 2018*; *Scandurra et al., 2020*; *Dangisso, Datiko & Lindtjørn, 2015*) and early therapy for individuals with TB in receiving countr

### Limitations

The post-entry screening frequency of 1–2 rounds for marriage migrants was not the sa as that for labor migrants (four rounds), which might cause an underestimation of TI incidence in the former. The authentic treatment completion rate may have been underestimated among labor migrants who opted to return to their original countries for treatment, as they were not or enrolled in or followed by this study. The proportions migrants with TB who were due to TB reactivation or transmission were not defined by t molecular testing in this study.

## CONCLUSIONS

Multiple screenings following an initial abnormal CXR in migrants could detect early-sta TB cases; nevertheless, an improved therapy completion is a substantial step for TB elimination. The relatively higher odds of SS+ TB and bacterial negativity >35% among migrants might be an index of persistent TB reactivation or over-diagnosis; therefore, it recommended that adding LTBI screening combined with preventive treatment as an alternative approach might save multiple screening effort for high-risk migrants. The friendly treatment policy for migrants, which eliminated repatriation for labor migrants with TB, could benefit in anti-TB treatment outcomes include increasing therap

initiation in SS– or B– TB cases and treatment completion for those who stayed in receiving countries.

## ACKNOWLEDGEMENTS

We thank all Taiwanese clinics for their routine data notification and the Taiwan CDC staff for disease control administration and data management. We would like to express deep gratitude and appreciation to Prof. Mesay Hailu Dangisso and Dr. Dustin C. Yang for reviewing the manuscript and offering expertise suggestions.

## ADDITIONAL INFORMATION AND DECLARATIONS

### Funding

The publication fee would be paid by Taiwan CDC. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

### Grant Disclosures

The following grant information was disclosed by the authors:
Taiwan CDC.

### Competing Interests

The author declares that they have no competing interests.

### Author Contributions

- Mei-Mei Kuan conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the paper, and approved the final draft.

### Ethics

The following information was supplied relating to ethical approvals (i.e., approving bo and any reference numbers):

This study was approved by the Institutional Review Board of the Taiwanese CDC (No. TwCDCIRB106115).

### Data Availability

The following information was supplied regarding data availability:

The raw data summary is available as a Supplemental File.

The raw data used in this study were acquired from the TCDC TB registry system which cannot be shared due to the individual information privacy protection policy. Interested readers can apply for access to the data resources: details of individual TB ca including "area, age, and gender".

Interested readers can access the TCDC Epidemic Intelligence Center data resource contacting gnnhuo@cdc.gov.tw to obtain access to the data presented here: https://da cdc.gov.tw/en/dataset/aagstable-tuberculosis (and graphed here: https://nidss.cdc.gov. en/nndss/Diagram?id=010).

## Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.10332#supplemental-information.

## REFERENCES


**Aldridge RW, Zenner D, White PJ, Williamson EJ, Muzyamba MC, Dhavan P, Mosca D, Thomas HL, Lalor MK, Abubakar I, Hayward AC. 2016.** Tuberculosis in migrants moving from high-incidence to low-incidence countries: a population-based cohort study of 519 955 migrants screened before entry to England, Wales, and Northern Ireland. *Lancet* **388(10059)**:2510–2518 DOI 10.1016/S0140-6736(16)31008-X.

**Dangisso MH, Datiko DG, Lindtjørn B. 2015.** Accessibility to tuberculosis control services and tuberculosis program performance in southern Ethiopia. *Global Health Action* **8(1)**:29443 DOI 10.3402/gha.v8.29443.

**Datiko DG, Lindtjorn B. 2010.** Mortality in successfully treated tuberculosis patients in southern Ethiopia: a retrospective follow-up study. *International Journal of Tuberculosis and Lung Disease* **14(7)**:866–871.

**Dean AG, Sullivan KM, Soe MM. 2006.** OpenEpi: open source epidemiologic statistics for Public health. *Available at www.OpenEpi.com* (accessed 18 January 2021).

**Global Tuberculosis Report. 2018.** Taiwan Centers for Disease Control, Department of Health. *https://www.who.int/tb/publications/global_report/en/*. Taiwan Tuberculosis Control Report. *Available at https://www.cdc.gov.tw/english/ infectionreport.aspx?treeid=384771910 4bc0678&nowtreeid=ffb51203f16bfe57.*

**Hayward S, Harding RM, McShane H, Tanner R. 2018.** Factors influencing the higher incidence of tuberculosis among migrants and ethnic minorities in the UK. *F1000Research* **7**:461.

**Kourbatova EV, Borodulin BE, Borodulina EA, Rio CD, Blumberg HM, Leonard MKJ. 2006.** Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. *International Journal of Tuberculosis and Lung Disease* **10(11)**:1224–1230.

**Kuan M-M. 2018.** Nationwide surveillance algorithms for tuberculosis among immigrant workers from highly endemic countries following the pre-entry screening in Taiwan. *BMC Public Health* **18(1)**:1151 DOI 10.1186/s12889-018-6029-x.

**Kuan MM, Yang HL, Wu HS. 2014.** Tuberculosis among newly arrived foreign spouses before obtaining citizenship, Taiwan, 2006–2011. *International Journal of Tuberculosis and Lung Disease* **18(8)**:931–938 DOI 10.5588/ijtld.13.0809.

**Kuehne A, Hauer B, Brodhun B, Haas W, Fiebig L. 2018.** Find and treat or find and lose? Tuberculosis treatment outcomes among screened newly arrived asylum seekers in Germany from 2002 to 2014. *Euro Surveill* **23**:11 DOI 10.2807/1560-7917.ES.2018.23.11.17-00042.

**Lambert ML, Hasker E, Van-Deun A, Roberfroid D, Boelaert M, Van-der-Stuyft P. 2003.** Recurrence in tuberculosis: relapse or reinfection? *Lancet Infectious Diseases* **3(5)**:282–287 DOI 10.1016/S1473-3099(03)00607-8.

**Ministry of Interior Taiwan. 2016.** Statistics: annual report of the Ministry of the Interior. *Available at https://www.moi.gov.tw/files/site_stuff/321/1/month/month_en.html.*

**Olivieri R, Scarnera S, Ciabattini A, De Vuono G, Manzi P, Pozzi G, Battista G, Medaglini D. 2016.** Using IFN-gamma release assay to confirm tuberculin skin test improves the screening of latent tuberculosis infection in Italian healthcare workers. *Journal of Occupational Medicine and Toxicology* **11(1)**:29 DOI 10.1186/s12995-016-0117-6.

**Scandurra G, Degeling C, Douglas P, Dobler CC, Marais B. 2020.** Tuberculosis in migrants—screening, surveillance and ethics. *BMC Pneumonia* **12**:9 DOI 10.1186/s41479-020-00072-5.

**Sepkowitz KA. 1996.** How contagious is tuberculosis? *Clinical Infectious Diseases* **23**(5):954–962 DOI 10.1093/clinids/23.5.954.

**Taiwan Centers for Disease Control. 2018.** Ministry of Health and Welfare, R.O.C. (Taiwan). Statistics of communicable diseases and surveillance report 2018. *Available at https://www.cdc.gov.tw/InfectionReport/Info/DRiONFTwYxu8T162Hnt6yFw?infoId=qQSzJI0i1S8Xv8hATYLx4A.*

**The New York Times Editorial Board. 2018.** We know how to conquer tuberculosis. Why aren't outbreaks in poor countries treated the same way as those in rich ones? New York Times. Sept. 26. *Available at https://www.nytimes.com/2018/09/26/opinion/we-knowhow-to-conquer-tuberculosis.html.*

**The World Bank. 2018.** Incidence of tuberculosis (per 100,000 people). *Available at http://data.worldbank.org/indicator/SH.TBS.INCD.*

**WHO. 2006–2015.** *Global plan to stop TB.* Geneva: WHO.