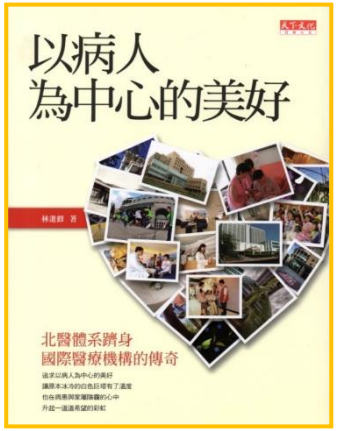

多剤耐性結核に対する患者中心の治療

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呼吸器内科部門
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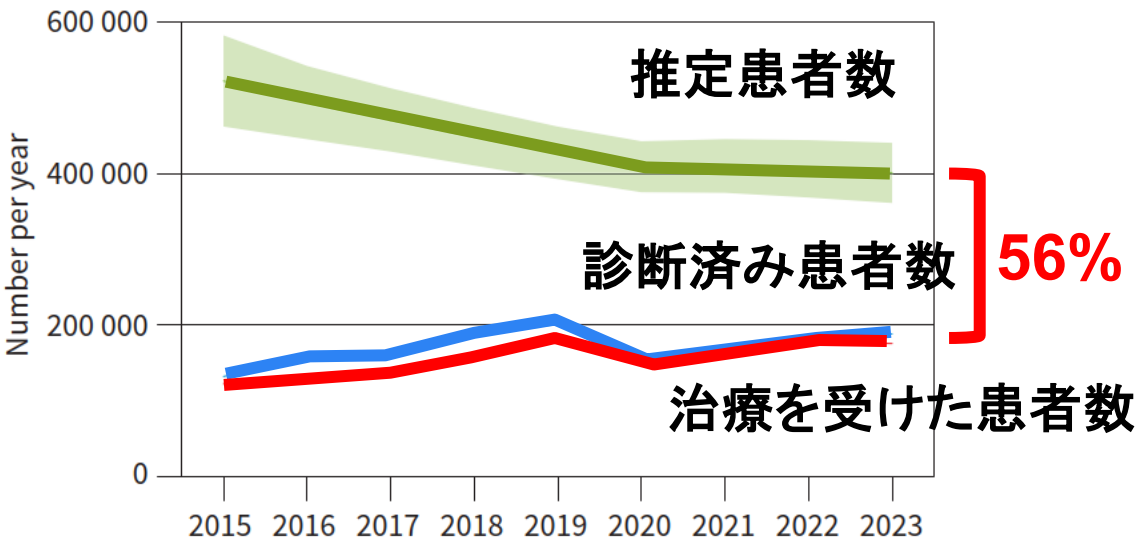
概要

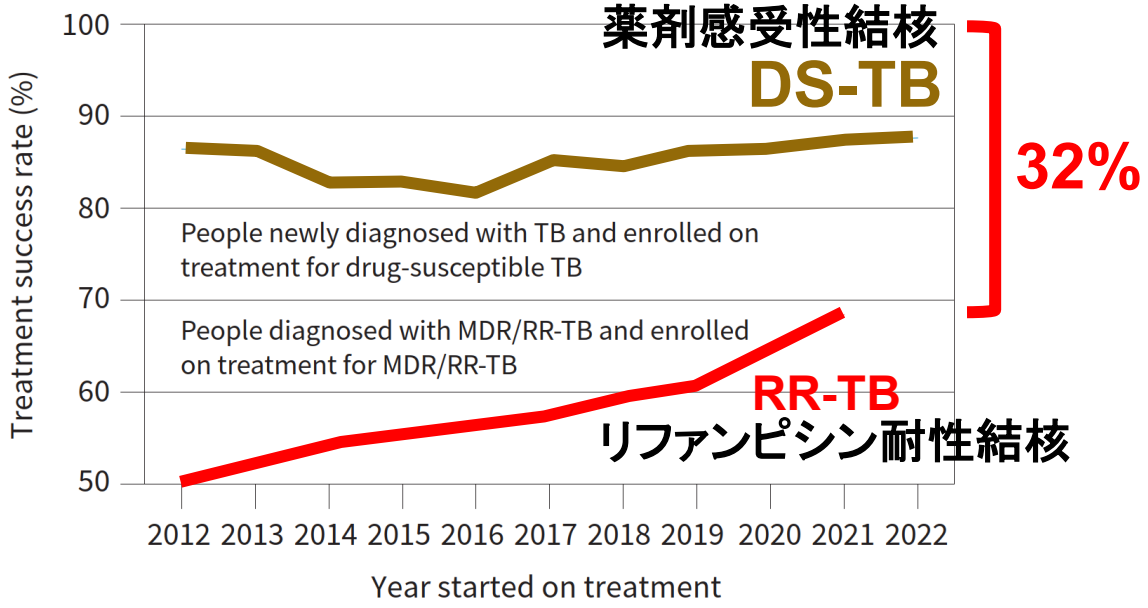
1. 背景
2. 多剤耐性結核（DR-TB）に対する包括的ケア
3. 積極的な薬剤安全性モニタリング
4. 治療薬モニタリング

RR-TB（リファンピシン耐性結核）の管理における未解決の課題

世界的に、RR-TBの56%が未治療のまま放置されている。



治療は32%が成功していない。



MDR-TB治療におけるフォローアップ喪失

- 2000年以前、台湾における治療成功率はわずか 51.2% だった。
- フルオロキノロンを治療に含めたにもかかわらず、治療成功率は依然として不十分（59.2%）。
- フォローアップ喪失率（治療中断率）は最大29.1%に達する。
- 治療レジメン（治療計画）だけでなく、管理（マネジメント）も重要である。

Eur Respir J 2006; 28: 980–985
DOI: 10.1183/09031936.06.00125705

Outcome of pulmonary multidrug-resistant tuberculosis: a 6-yr follow-up study

C-Y. Chiang*, D.A. Enarson*, M-C. Yu#, K-J. Bai#, R-M. Huang", C-J. Hsu", J. Suo" and T-P. Lin"

ABSTRACT: A retrospective study was performed to determine factors associated with the outcome of pulmonary multidrug-resistant tuberculosis (MDR-TB) in Taipei, Taiwan.

All patients newly diagnosed with pulmonary MDR-TB in a referral centre from 1992–1996 were enrolled and their outcome over the subsequent 6 yrs was determined.

A total of 299 patients were identified, comprising 215 (71.9%) males and 84 (28.1%) females with a mean age of 47.3 yrs. The patients received a mean of 3.7 effective drugs. Out of the 299 patients, 153 (51.2%) were cured, 31 (10.4%) failed, 28 (9.4%) died and 87 (29.1%) defaulted. Of the 125 patients receiving second-line drugs with ofloxacin, 74 (59.2%) were cured. Those who received ofloxacin had a lower risk of relapse than those receiving only first-line drugs (hazard ratio (HR) 0.16, 95% confidence interval (CI) 0.03–0.81) and a lower risk of TB-related death than those receiving second-line drugs but not ofloxacin (adjusted HR 0.50, 95% CI 0.31–0.82).

In conclusion, multidrug-resistant tuberculosis patients who received ofloxacin were more likely to be cured, and were less likely to die, fail or relapse. The utility of new-generation fluoroquinolones, such as moxifloxacin, in the treatment of multidrug-resistant tuberculosis needs to be evaluated. Default from treatment is a major challenge in the treatment of multidrug-resistant tuberculosis.

KEYWORDS: Death, follow-up, multidrug resistant, relapse, tuberculosis

Multidrug-resistant tuberculosis (MDR-TB), which is defined as a disease with isolates resistant to at least isoniazid and rifampin, compromises response to anti-TB treatment [1–3]. MDR-TB is prevalent in a number of countries [4].

Recommended treatment of MDR-TB includes the use of second-line anti-TB drugs [5]. To date, there have been no randomised controlled trials to evaluate the treatment of MDR-TB. Treatment regimens are determined individually for each patient, taking into account the results of susceptibility testing [6–12], or are standardised regimens [13–15] depending on the local situation.

The management of MDR-TB in Taipei, northern Taiwan, has been highly specialised in a referral centre, the Chronic Disease Control Bureau (CDCB), which was the headquarters of a TB control system functioning for >40 yrs (until 2002), with a network of public health nurses distributed in all townships and villages, responsible for TB services [16]. The majority of MDR-TB patients identified in general hospitals were referred to the CDCB for further management. Treatment of MDR-TB has increasingly included the use of ofloxacin in the second-line treatment regimen [17]. To understand the long-term outcome of MDR-TB, a consecutive series of MDR-TB cases were reviewed and followed up over time, with specific attention paid to the results of the use of ofloxacin for treatment. The results of this follow-up study are reported here.

METHODS

Case ascertainment

Patients with MDR-TB were identified from the Mycobacteriology Laboratory of the CDCB (Taipei, Taiwan). Patients who were newly diagnosed with pulmonary MDR-TB from 1992–1996 were enrolled in this study in 2000, and their outcome over the subsequent 6 yrs after commencing treatment determined. All drug-susceptibility testing was performed in the CDCB [18]. Medical records were reviewed and information was collected on age, sex, history of TB treatment, drug susceptibility, HIV status, medications used for treatment, adverse reactions occurring during treatment for which medications had to be stopped, and outcome of treatment.

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"Chest Hospital, Dept of Health, Tainan, Taiwan, and
"National Tuberculosis Association, Taipei, China.

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June 23 2006

SUPPORT STATEMENT
C-Y. Chiang and D.A. Enarson proposed the original idea and designed the study. C-Y. Chiang, M-C. Yu, K-J. Bai, R-M Huang, C-J. Hsu, J. Suo, and T-P. Lin collected information and followed up patients. C-Y. Chiang and D.A. Enarson analysed and interpreted the data. All authors were involved in drafting the manuscript and gave final approval of the manuscript

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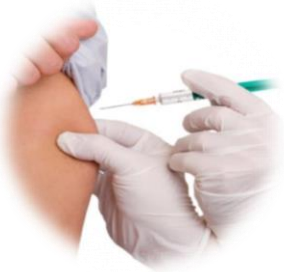
CY Chiang, 2006 ERJ

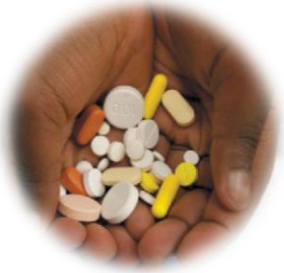
MDR-TB治療の成功を阻む要因

身体的・精神的・経済的困難

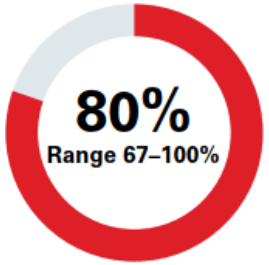
•注射治療（6～8か月）



•大量の服薬負担



•80%が壊滅的な経済的困難に直面



WHO, 2020, Global TB Report

有害事象（副作用）

•永久的な難聴

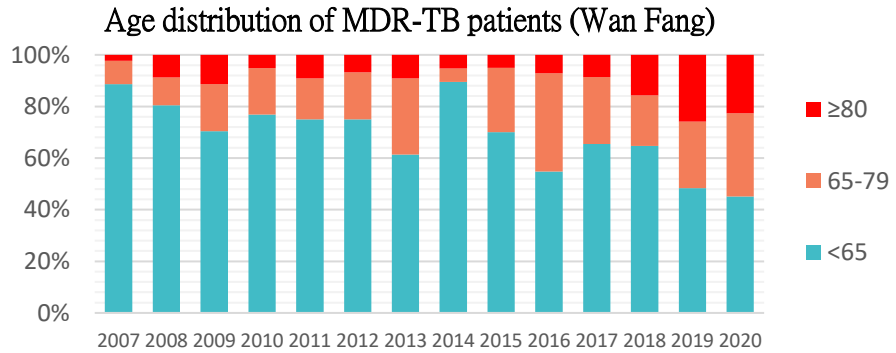
•永久的なしびれ

•80%の症例で治療計画の調整が必要

•50%が入院または生命を脅かす状態に

加齢と併存疾患

併存疾患あり 69.3%
糖尿病 27.2%
がん 6.7%



社会的スティグマ（偏見）

DR-TB（薬剤耐性結核）の包括的ケア
積極的な薬剤安全性モニタリング

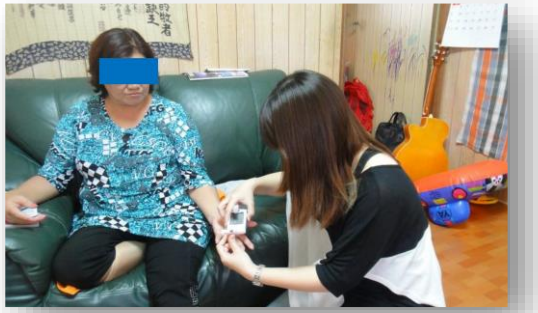
DR-TB（薬剤耐性結核）の包括的ケア

教育 → 身体評価 → 心理評価 → 家族および社会経済的支援

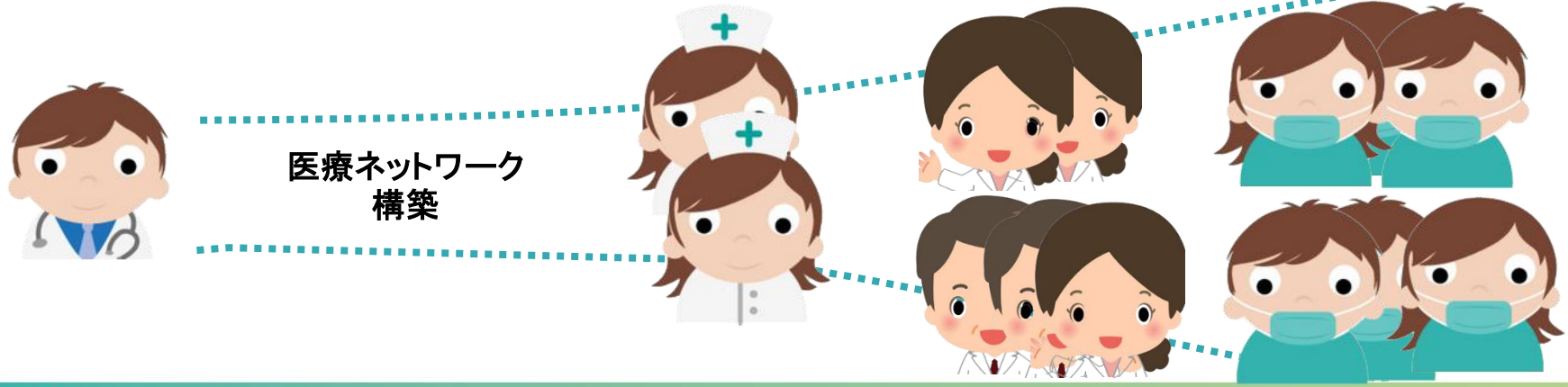
- 呼吸療法士
- 管理栄養士
- 看護師
- マネージャーおよび支援者
- ソーシャルワーカー
- 心理カウンセラー
- 患者と家族
- 臨床検査技師
- 臨床薬剤師
- 医師

台湾におけるMDR-TB（多剤耐性結核）治療コンソーシアム（2007年より）

地域社会に向けた患者中心のケアの展開
有害事象の迅速な管理を可能にする基盤構築



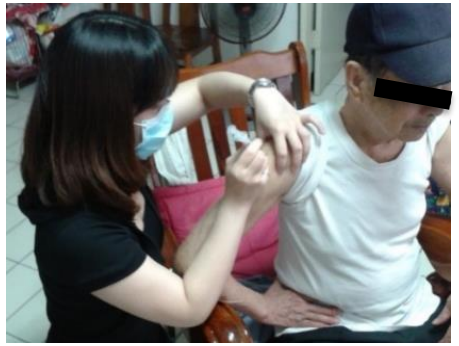
主治医　看護専門職　DOTS支援者　患者

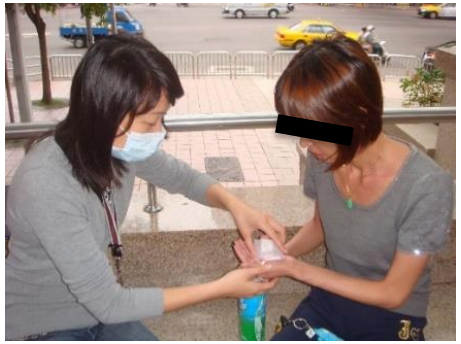
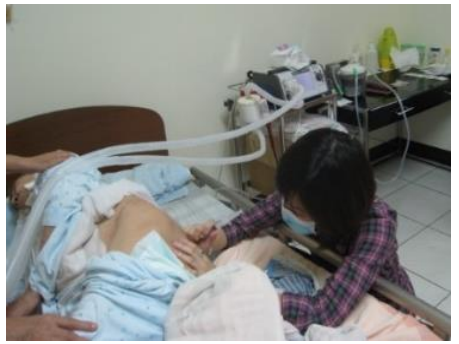


DOTS-Plus、DOT以上の支援

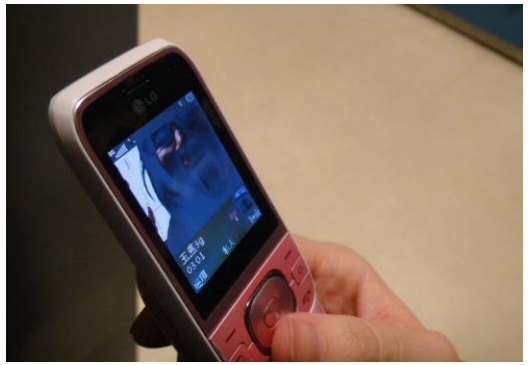
Anywhere（どこでも）: 農村部でも都市部でも、山奥の遠隔地でも対応可能
Omnipotent（多機能）: 創傷ケア、注射、積極的な薬剤安全性モニタリング
Nonstop（途切れなく）: 治療期間中、毎日継続的に提供





賢明な 直接監視下治療（DOT）



Application of Third-Generation (3G) Mobile Videophone to the DOTS-Plus Program in Multidrug-Resistant Tuberculosis in Taiwan: Case Report

Veng-Kai Tang, Kuan-Jen Bai, Chin-Yun Wang*, Ming-Chih Yu, Taipei-MDRTB Group

Multidrug-resistant tuberculosis (MDR-TB), caused by the bacterium, *Mycobacterium tuberculosis*, is resistant to both isoniazid and rifampicin and is a phenomenon threatening to destabilize global tuberculosis control. Taiwan's Centers for Disease Control implemented a patient-centered DOTS (directly observed treatment, short-course)-Plus program for MDR-TB patients in May 2007. We report the case of a 71-year-old MDR-TB patient who successfully completed 18 months of MDR-TB treatment under the DOTS-Plus program, beginning October 2007. A third-generation (3G) mobile videophone was used to watch the patient take medicine throughout his course of treatment. His acceptance of the program and compliance with monitoring by videophone DOT (V-DOT) were excellent. We conclude that V-DOT can be an effective approach to case management for MDR-TB patients and can achieve a high level of adherence in selected cooperative cases in Taiwan. ***(Thorac Med 2010; 25: 7-12)***

2007年、3G携帯電話を活用した革新的なビデオDOT

訪問監視 → **遠隔ビデオ監視**

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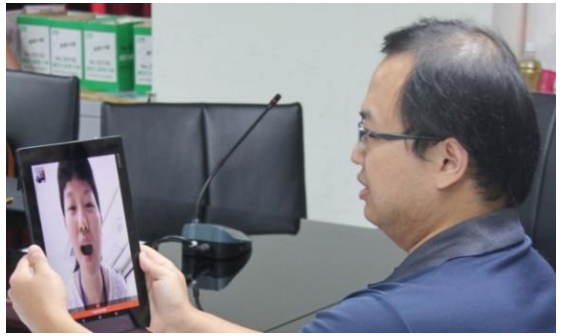
Original Article

Advantage in privacy protection by using synchronous video observed treatment enhances treatment adherence among patients with latent tuberculosis infection

Szu-Hsuan Chen[a,1], Irene Wang[b,c,1], Han-Lin Hsu[c,d], Chi-Ching Huang[a], Yi-Jun Liu[c], Denise Utami Putri[c], Chih-Hsin Lee[b,c,*]

[a] Department of Health, Taipei City Government, Taipei 11008, Taiwan
[b] Division of Pulmonary Medicine, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei 11031, Taiwan
[c] Pulmonary Research Center, Wan Fang Hospital, Taipei Medical University, Taipei 11696, Taiwan
[d] School of Respiratory Therapy, College of Medicine, Taipei Medical University, Taipei 11031, Taiwan

プライバシー保護



治療薬モニタリング

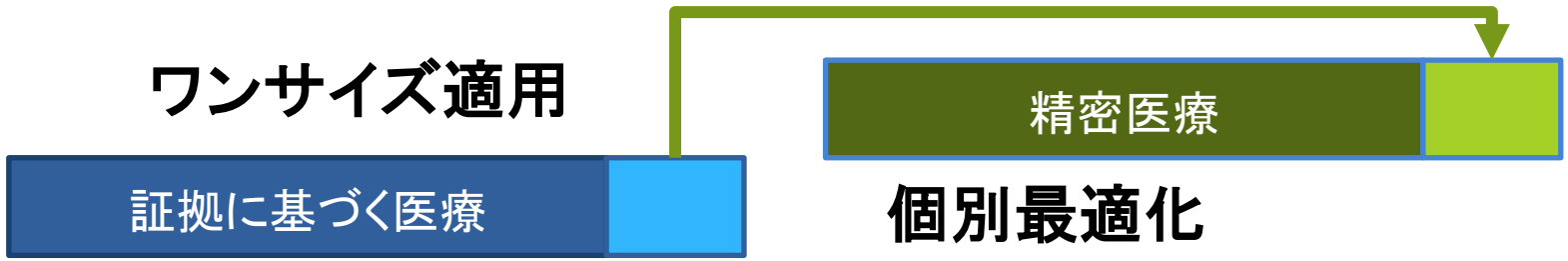
最適な有効性、最小限の毒性

- 有効性、および/または、毒性の評価が容易な PD マーカーが存在しない。

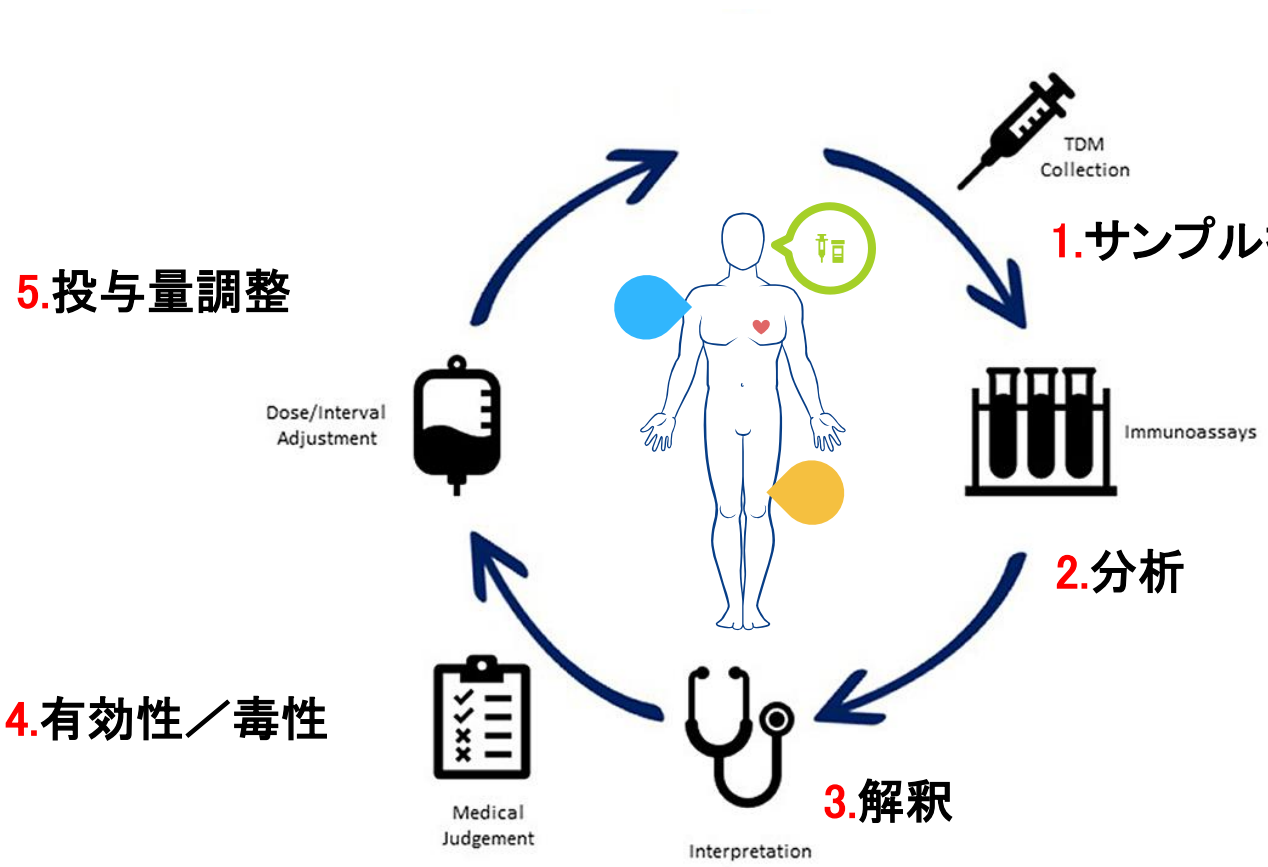
  （ワルファリン）
- **PD 関係**（**PD relationships**）が薬物曝露と有効性、および/または、毒性の間で一貫している
- **狭い治療域**（**narrow therapeutic margin**）のため、非常に高い標準用量をすべての患者に適用することは許されず、全体的な有効性を確保する必要がある

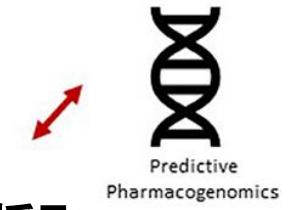
研究と実践の間の大きなギャップ

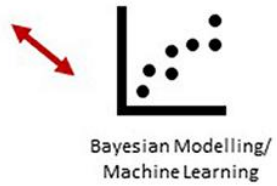
- 臨床試験の対象となるのはごく一部の被験者のみである
- 併存疾患、極端なBMI（体格指数）、妊娠、高齢、
  薬物相互作用のある患者は、通常、薬物動態データの開発
  （第I～III相試験）には含まれない。



個別化精密投薬







01 予測薬理ゲノミクス

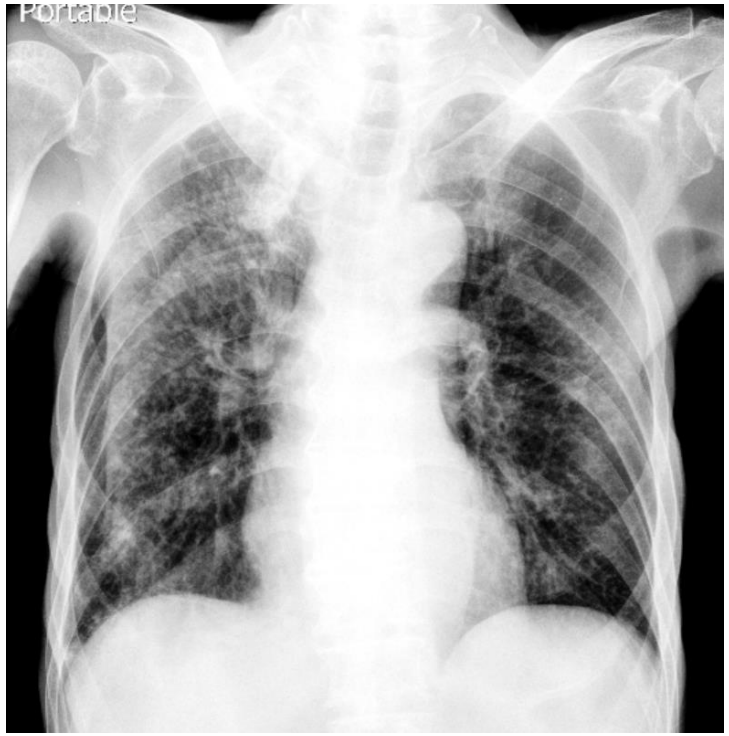
02 現場検査

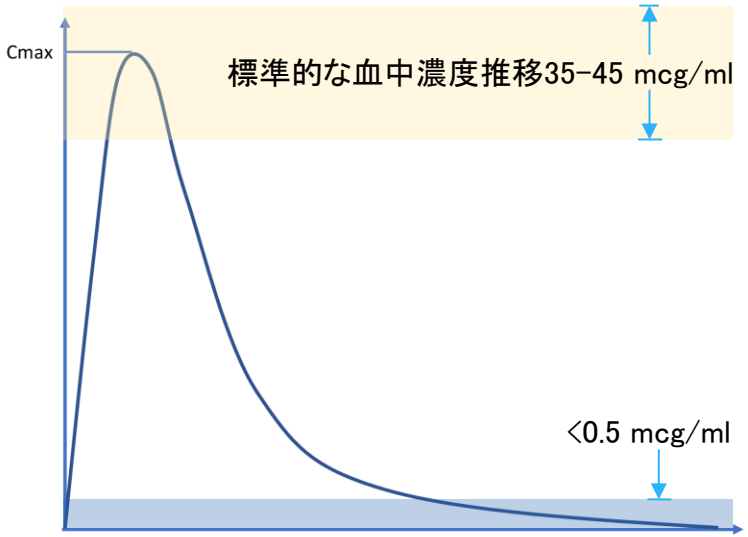
03 集団モデリング

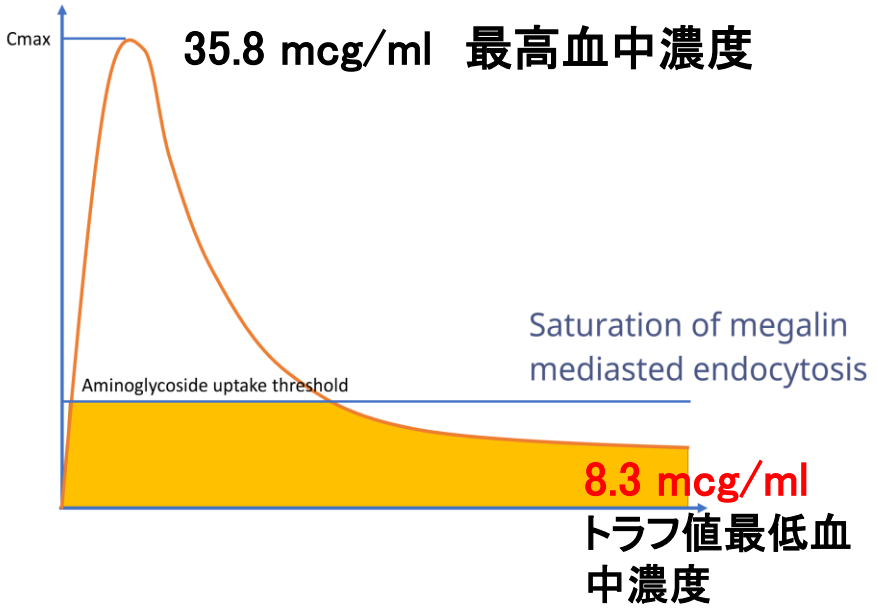
04 組織内薬物濃度測定

Kapoor A, Front. Pediatr. 2021. doi: 10.3389/fped.2021.661536

カナマイシンの治療薬物モニタリング



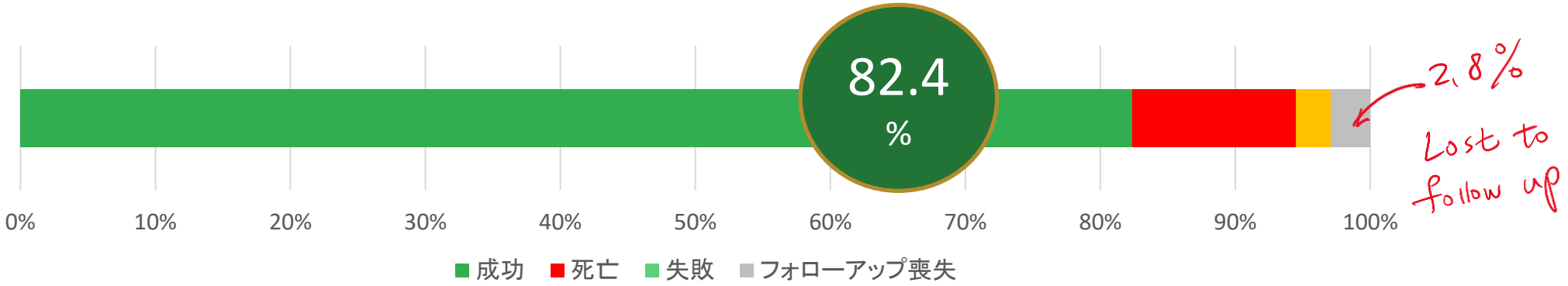




- **対象者**：74歳男性
- **クレアチニン値（Cr）**：0.83 mg/dl
- **体重**：35 kg

- **投与量**：カナマイシン 500 mg **qd**（1日1回）

台湾におけるMDR-TB：フォローアップ喪失への対応



予測因子	総数 No.	単変量解析 OR	(95% CI)	多変量解析 aOR	(95% CI)
年齢（年）					
<45	224	基準		基準	
45–64	294	0.55	(.31–.99)	0.71	(.37–1.35)
≥65	168	0.16	(.09–.28)	0.19	(.10–.35)
フルオロキノロン耐性	121	0.64	(.40–1.03)	0.49	(.29–.85)
がん	41	0.12	(.06–.23)	0.11	(.05–.24)
慢性腎疾患	46	0.25	(.14–.47)	0.28	(.14–.55)

Ming-Chih Yu. Clin Infect Dis. 2018 Jul 15; 67(2): 202–210.

まとめ

- 私たちは以下の戦略を通じて、MDR-TB（多剤耐性結核）患者が安全かつ効果的に抗結核治療を完了することをサポートしました。

1 地域における包括的なチームケア

2 治療に関連する有害事象の積極的な監視と管理

3 毒性を最小限に抑え、治療効果を確保するための個別化・精密な投与設計