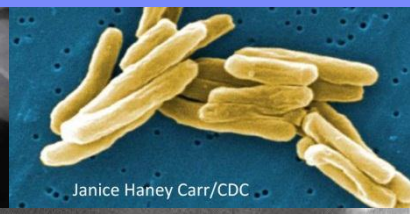


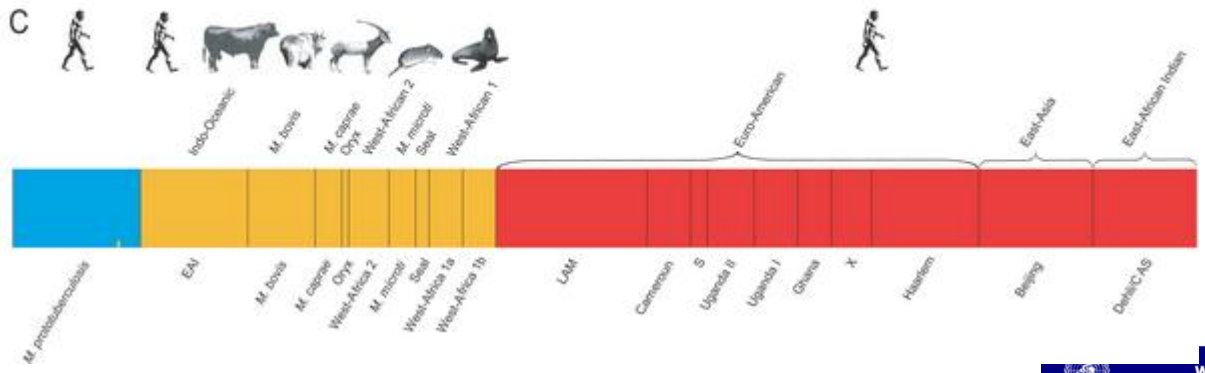



结核病的历史和防控

王伟炳
wwb@fudan.edu.cn
复旦大学公共卫生学院

TB is an old disease with old management tools

- 30年无新药物
- 80年无新疫苗
- 120年无新的现场诊断试验



2000关键数据

- 8百万以上结核病发病
- 近2百万人口死于结核病
- 世界三分之一人口感染结核杆菌
- 结核病导致青壮年死亡比其他任何传染病都多
- 每四秒即有一人患结核病
- 每十秒即有一人死于结核病
- 如果不治疗,活动性结核病人每年可感染10-15人

2010十大数据

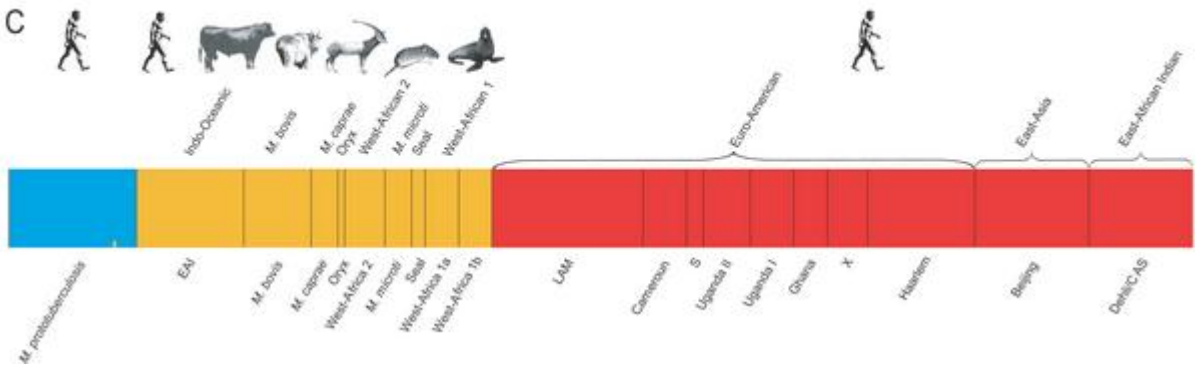
- 近9百万人发病
- 1百40万人死于TB
- 七万儿童死于TB
- 是HIV阳性患者的首要杀手
- 1990年开始，TB死亡率下降了40%
- 80% 的结核病报告患者在22个高负担国家
- 标准疗法治疗MDR-TB患者无效
- 65万人患有MDR-TB
- 四千六百万TB 被治愈
- 正处于实现两个2015全球目标的轨道上

白色瘟疫

- “面色苍白、身体消瘦、一阵阵撕心裂肺的咳嗽……”
- “痨病”
- “白色瘟疫”（The White Plague, 美国作家哈尔姆斯）
  - 肖邦，帕格尼尼（小提琴家），夏洛特·布朗蒂（简爱），艾米莉·布朗蒂（呼啸山庄），契可夫，劳伦斯….

历史

- 历史悠久的疾病：最早明确记载18000年前：野牛
- 从牛 ⇒ 人，或人直接感染？
- 并非直接来自于*M. bovis*，近代才进化
- 中东新石器时代骨骼（7000 BC）：史前人类具有TB
- 古埃及木乃伊的脊椎骨中(3000–2400 BC)



历史

- Egypt, 5,000 years ago
- India, 3,300and
- China 2,300

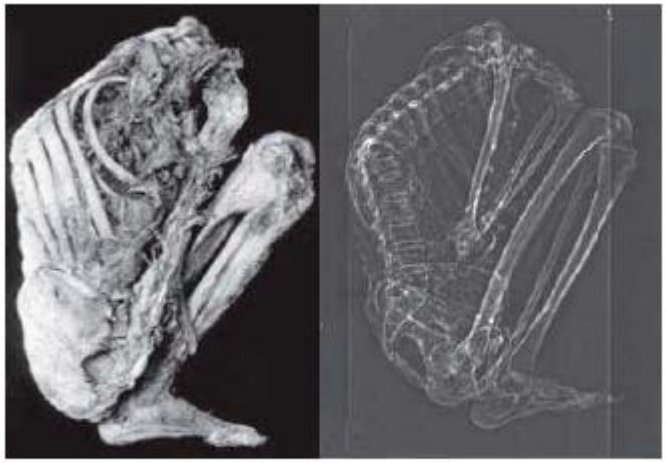


Figure 1-1: Left: Mummy 003, Museo Arqueológico de la Casa del Marqués de San Jorge, Bogota, Colombia. Right: Computerized tomography showing lesions in the vertebral bodies of T10/T11 (reproduced from Sotomayor 2004 with permission).

历史

- 希腊：希波克拉底在公元前460发现TB(phthisis)是该时代传播最快的疾病
- 南美洲：公元前750， Paracas-Caverna 文明
- 北美洲：后哥伦布

Royal Touch

- It was believed that Royal Touch, the touch of the sovereign of England or France, could cure diseases due to the divine right of sovereigns

Henri IV touching for scrofula

研究和治疗- 1020年

- 认为TB是一种传染病
- 接触土壤和水传播
- 隔离
- 食物疗法

"wolf's liver taken in thin wine, the lard of a sow that has been fed upon grass, or the flesh of a she-ass taken in broth".

- Pliny the Elder

1838 – 1845

- Dr. John Croghan将TB病人带到山洞治疗
- 温度和山洞中流通的空气
- 病人在一年内死去

1854

- 德国Görbersdorf开设了第一家TB疗养院

Figure 1-3: Sanatorio Pineta del Carso, Trieste, Italy.

Figure 1-4: Sanatorio Pineta del Carso. Bed-rest, fresh air and good nutrition were the hall-marks of sanatorium cure.

18-19世纪- 民间传说

- 工业革命之前（18世纪）：吸血病，消耗病
  - 一名患者死去，家庭内其他成员会得病
  - 抽取生命
  - 眼-红、浮肿，皮肤苍白，低热，咯血-吸血需要
- 罗曼蒂克化(19世纪)：TB产生欣快感(*Spes phthisica*) ("hope of the consumptive")
  - 在疾病的进程中获得创作的灵感
  - 死前获得灵感的爆发

肖邦、契诃夫、勃朗宁、史蒂文生、勃朗特姐妹、拜伦、劳伦斯郁达夫、萧红、鲁迅……

A romantic disease

Figure 1-5: Romantic view of TB: "The Lady of the Camellias" represented by Brazilian actres
Cacilda Becker under Italian director Luciano Salce, in São Paulo, Brazil (1952).

结核病对人类社会发展的影响

- 工业革命与结核病的传播
  - 大规模城市化
  - 拥挤的工厂
  - 营养不良
  - 大气污染

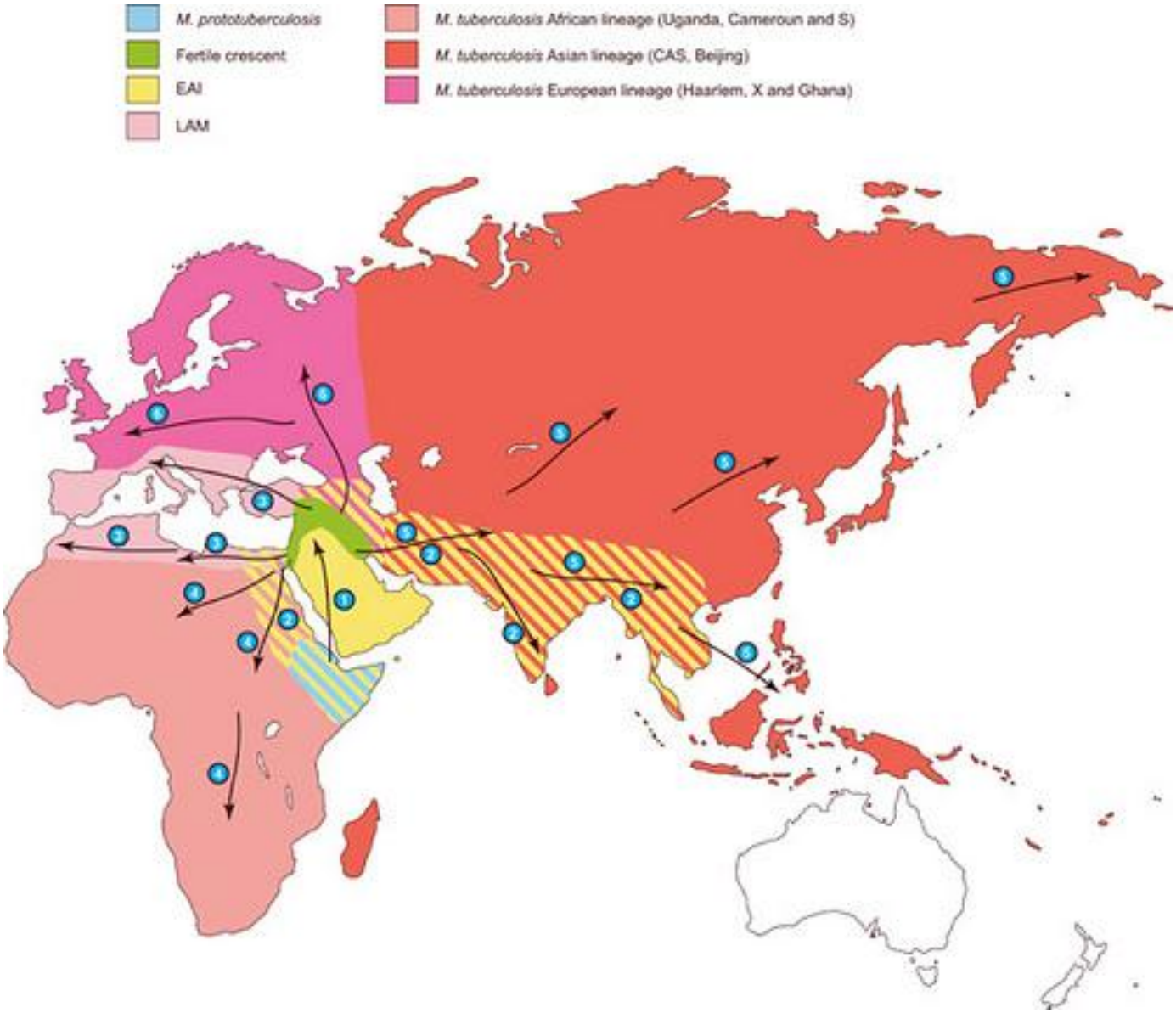
首次爆发在英国-第一个工业化国家（18世纪中期，19世纪中期）

19世纪晚期放缓

法国、德国、意大利、俄罗斯

20世纪晚期放缓

结核病与工业革命

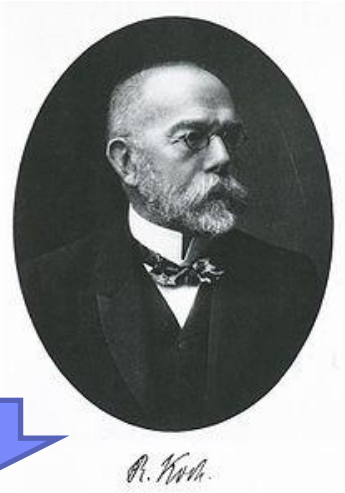

M. prototuberculosis
Fertile crescent
EAI
LAM
M. tuberculosis African lineage (Uganda, Cameroun and S)
M. tuberculosis Asian lineage (CAS, Beijing)
M. tuberculosis European lineage (Haarlem, X and Ghana)

1882-结核分枝杆菌

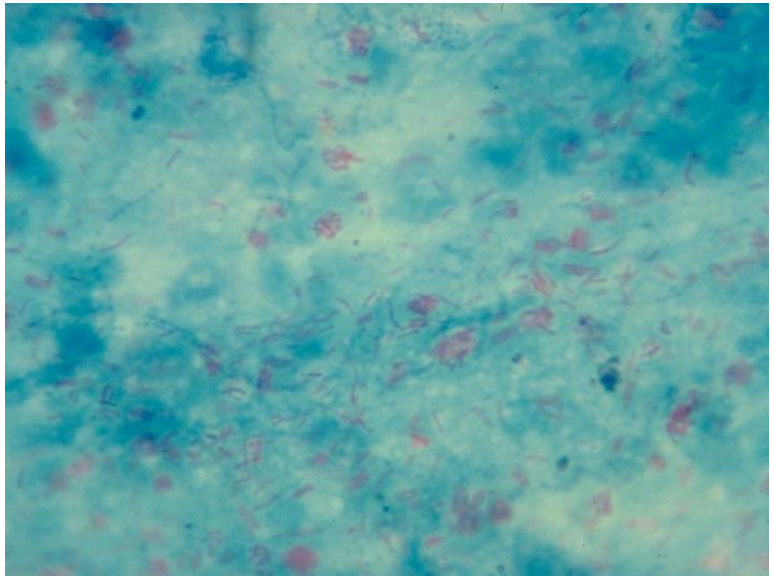
消耗病
162年后

- 1882年Koch首先由肺结核病人痰中发现了结核杆菌，并且证实结核病的病原是结核杆菌。
- 但他不承认牛结核和人结核的相似性，延迟了感染牛奶作为传染源的认识

巴斯消毒法



1905年诺贝尔生理和医学奖

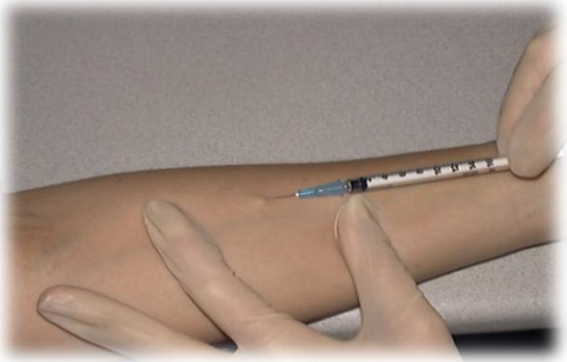


Patients with cavitary disease usually excrete such large numbers of tubercle bacilli that they can be readily seen with a microscopic examination of a sputum smear under the Ziehl-Neelsen staining method

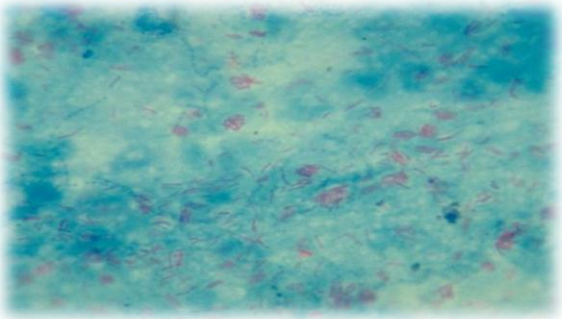
诊 断

- 细菌培养

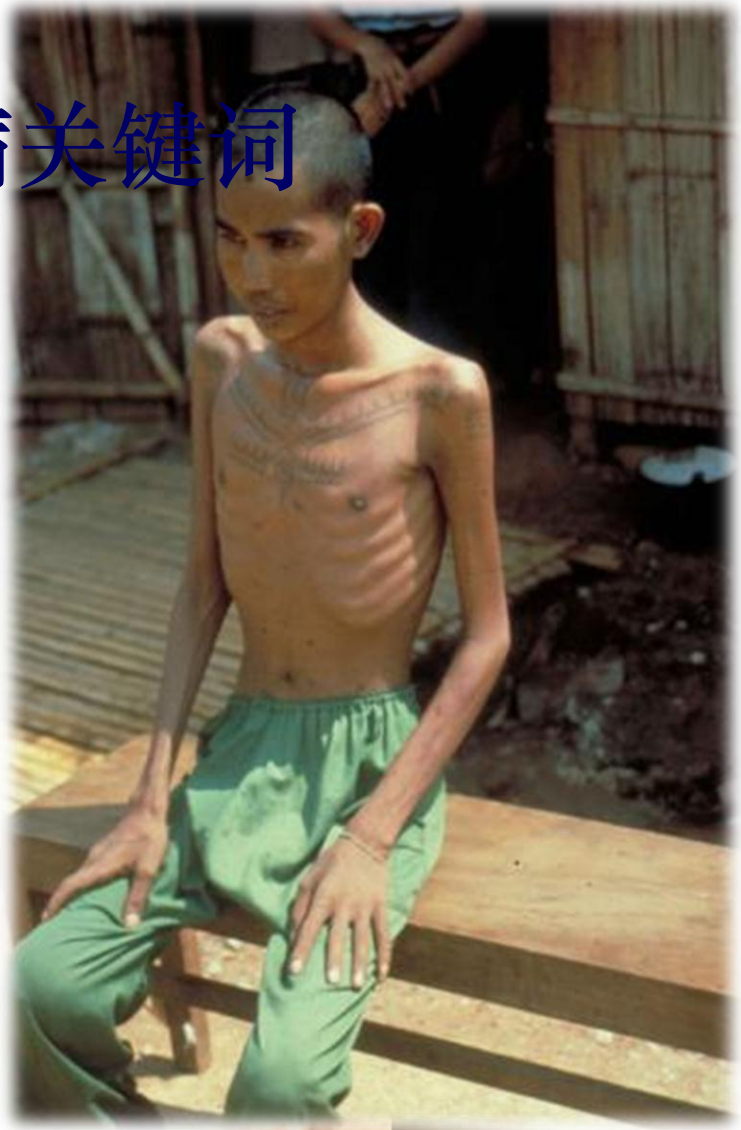
- 结核菌素皮试

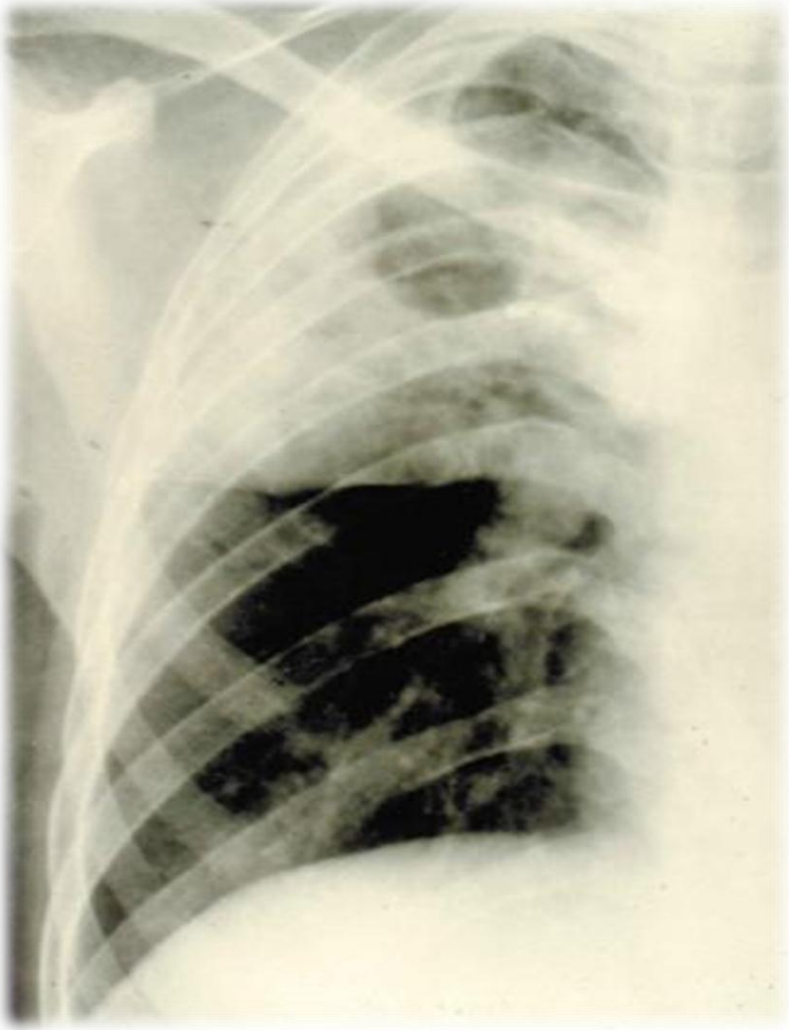


- 抗酸染色镜检



现代结核病关键词





This patient has rapidly progressing, cavitary tuberculosis pneumonia.

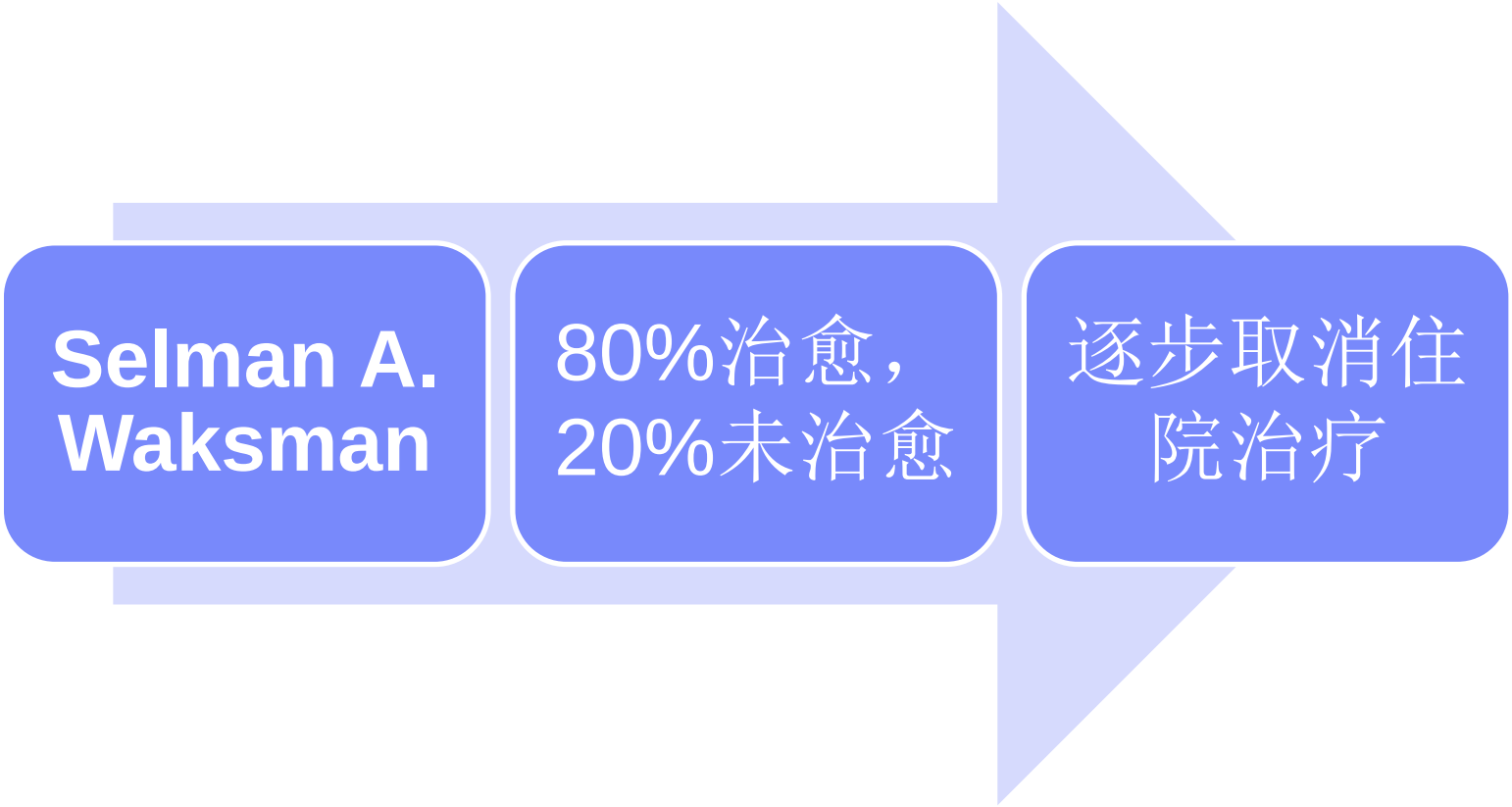
The most common presentation of tuberculosis is pulmonary. Pulmonary tuberculosis is also the epidemiologically most important form.

BCG疫苗发现和使用-1921年

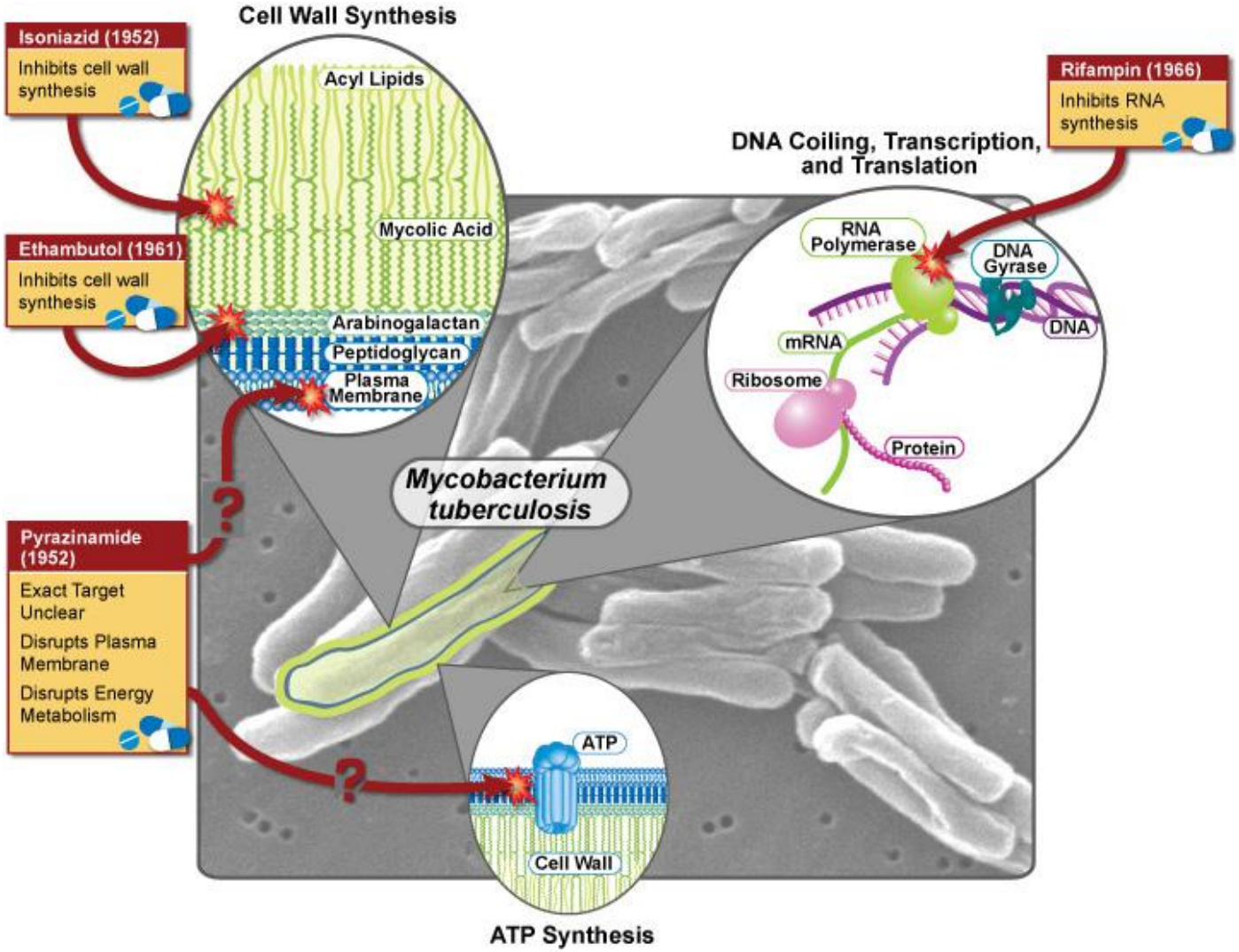
1921年，BCG疫苗首次在法国使用

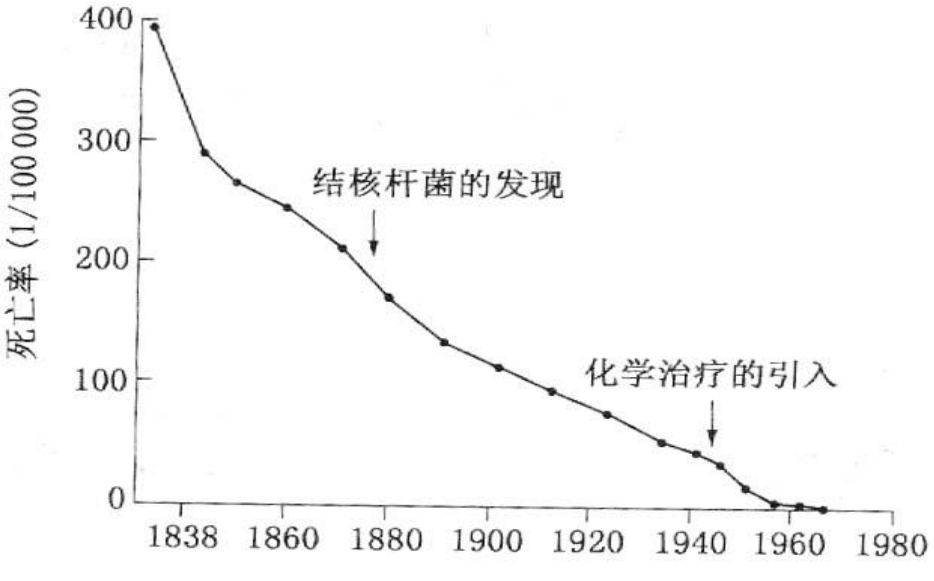
但直到二战时，才被美国/英国/德国广泛接受

链霉素的发现-1943年

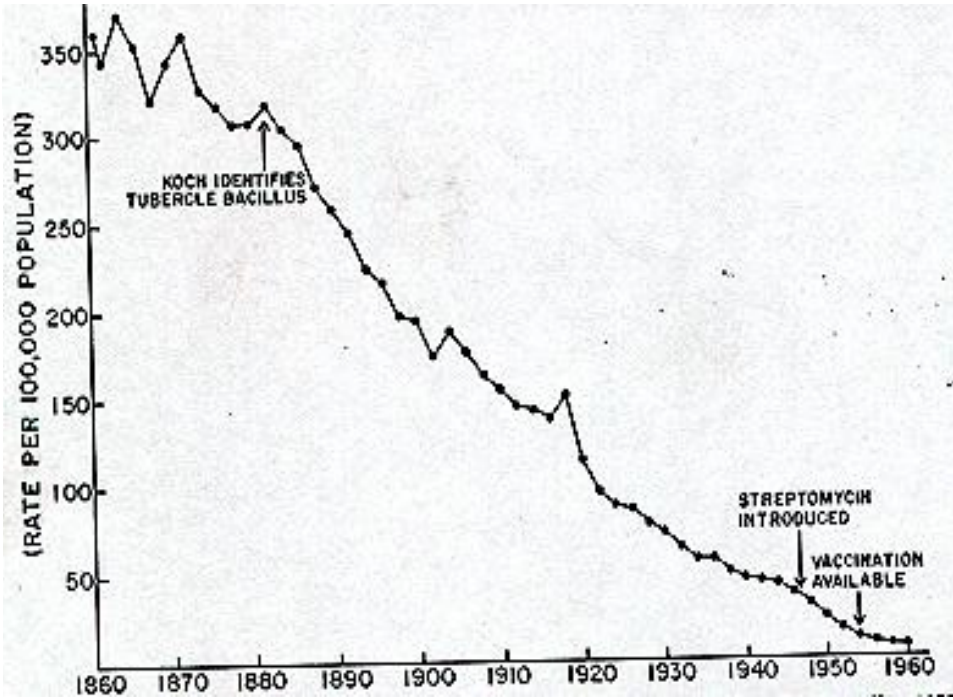


治疗


Cell Wall Synthesis
Isoniazid (1952)
Inhibits cell wall synthesis
Acyl Lipids
Mycolic Acid
Ethambutol (1961)
Inhibits cell wall synthesis
Arabinogalactan
Peptidoglycan
Plasma Membrane
Rifampin (1966)
Inhibits RNA synthesis
DNA Coiling, Transcription, and Translation
RNA Polymerase
DNA Gyrase
DNA
mRNA
Ribosome
Protein
Mycobacterium tuberculosis
Pyrazinamide (1952)
Exact Target Unclear
Disrupts Plasma Membrane
Disrupts Energy Metabolism
?
?
ATP
Cell Wall
ATP Synthesis

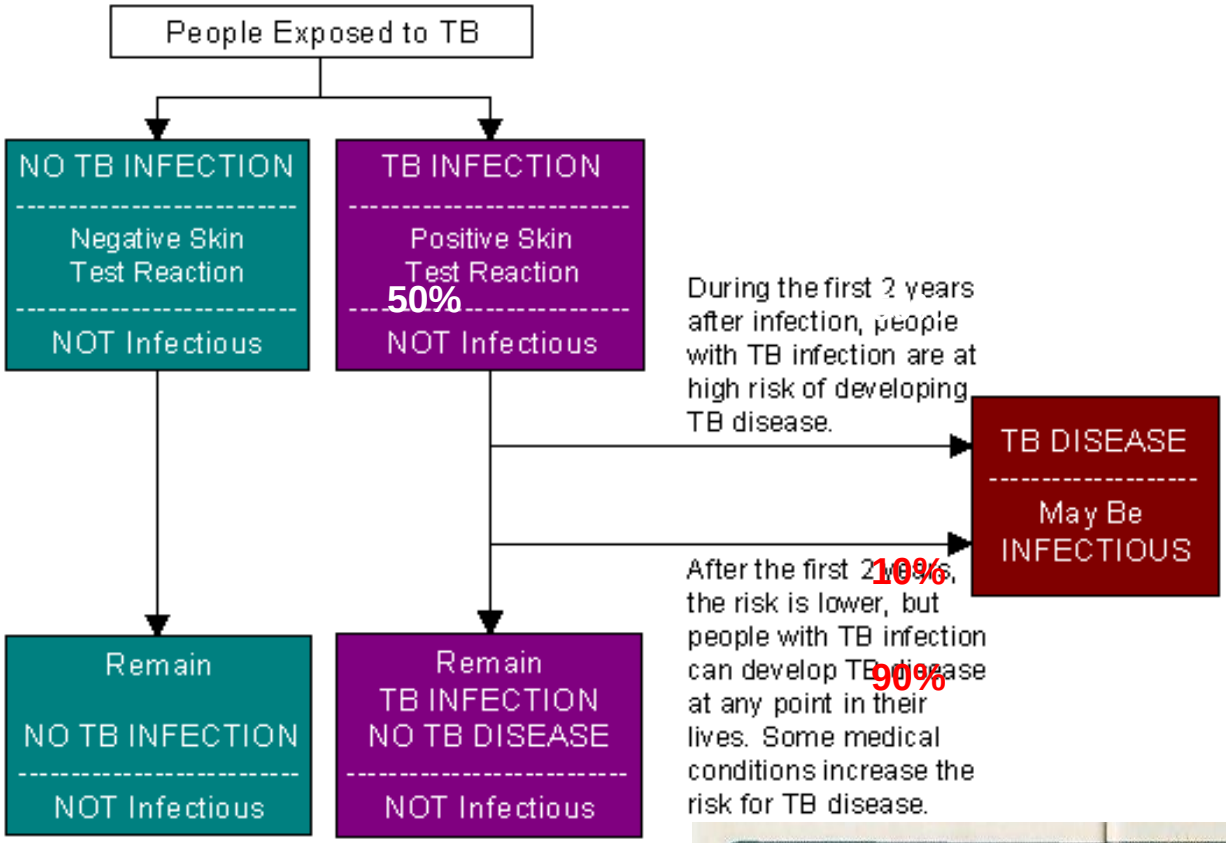


英国不同时期肺结核死亡率



美国结核病的死亡率

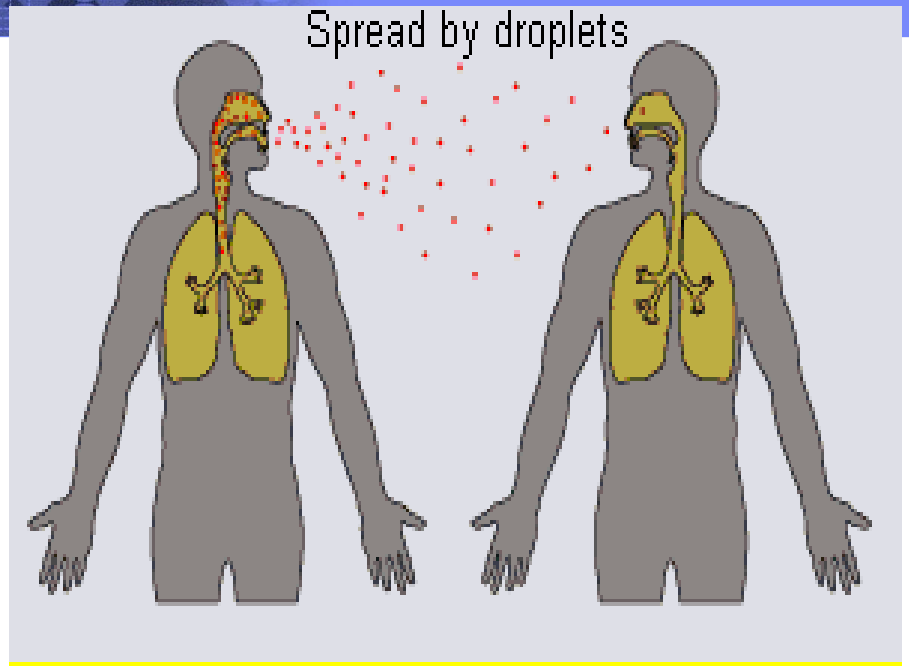
自然史
(in the absence of HIV infection)

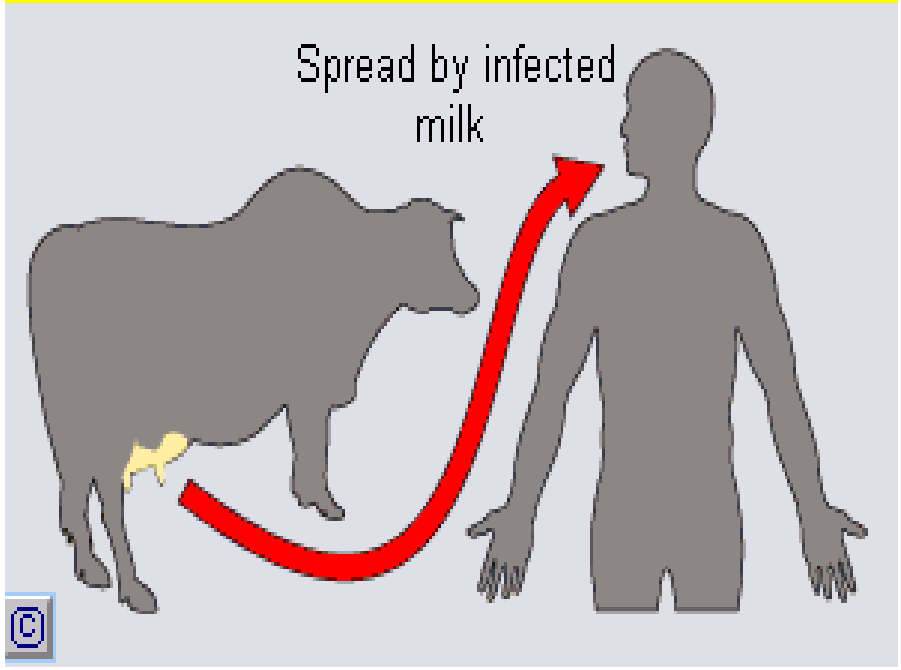


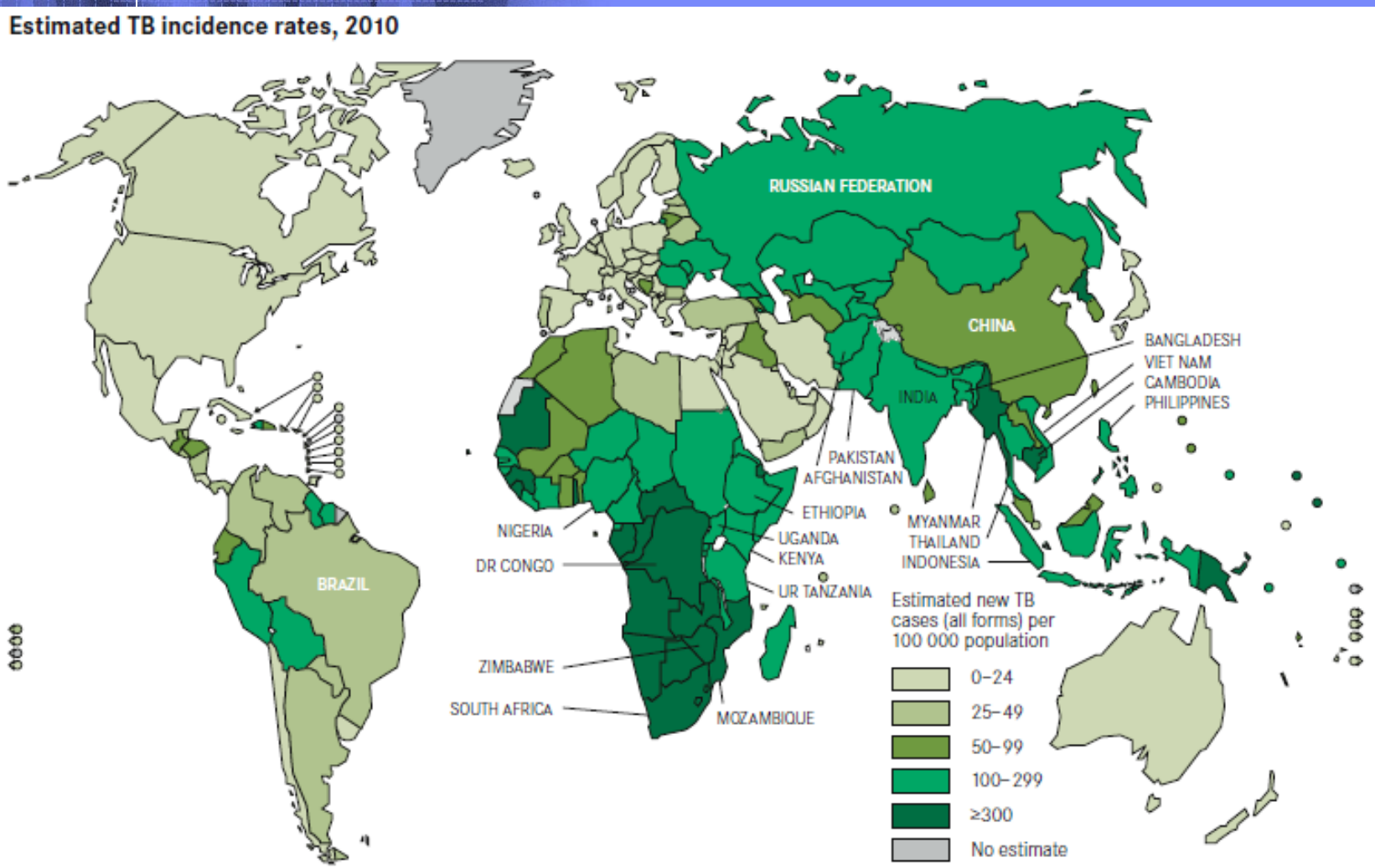
传染性

- 不是所有类型的结核病都具有传染性,也不是任何一个结核病人在其患病期间的住何时候都具有传染性
- 肺结核病中的一些类型常常具有传染性，而肺外结核病则不具有传染性
- 传染性肺结核传染性最强的时间是在发现及治疗之前 -早期发现和正确、及时治疗

传播





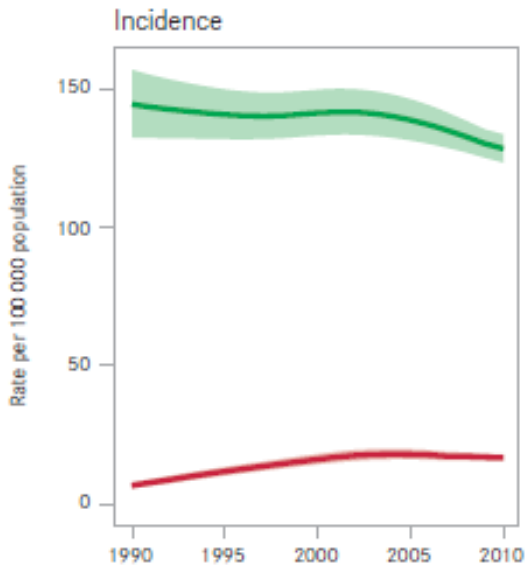


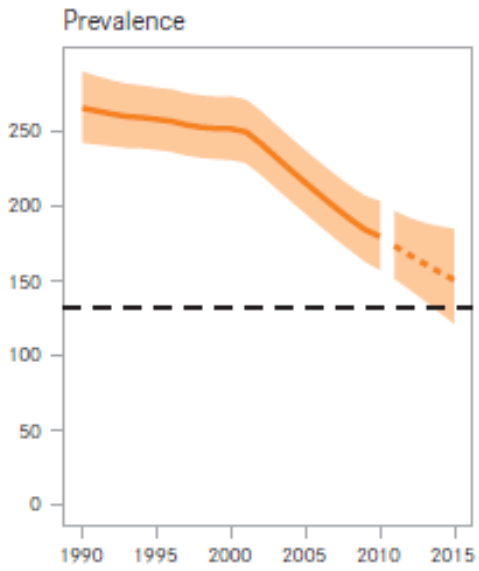
8.8 million new cases in 2010

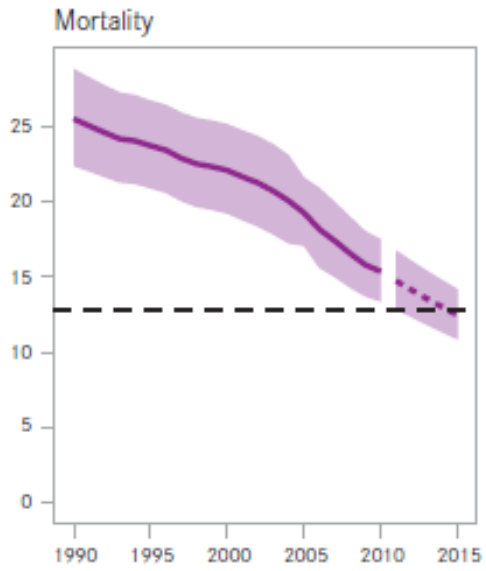
1.1 million TB deaths in 2010

12.0 million prevalent cases in 2010

WHO 2011 report


Incidence
Rate per 100 000 population
150
100
50
0
1990
1995
2000
2005
2010


Prevalence
250
200
150
100
50
0
1990
1995
2000
2005
2010
2015

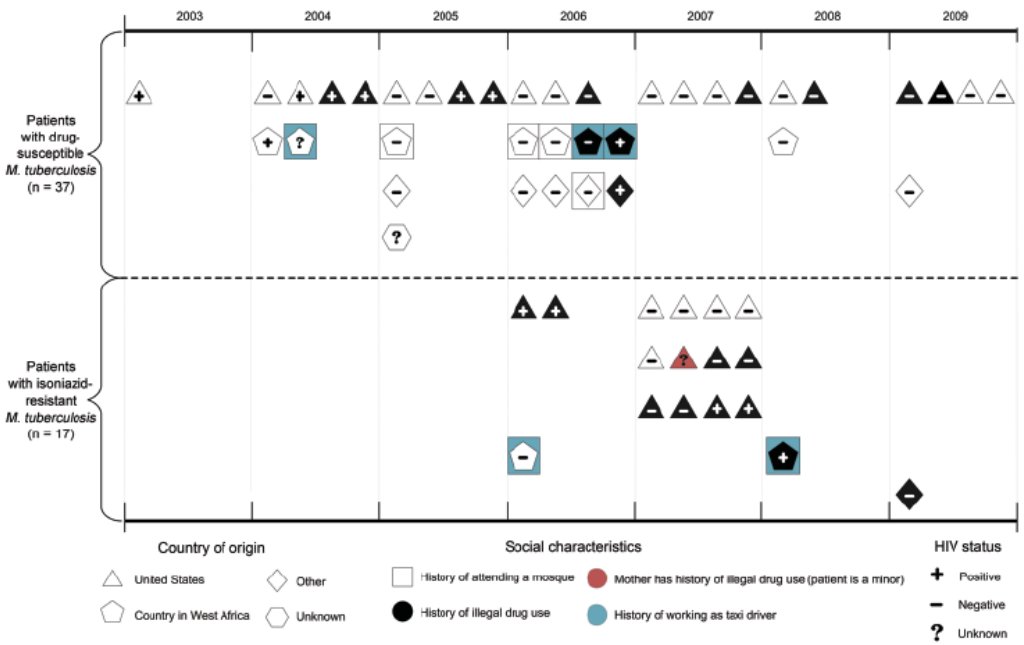

Mortality
25
20
15
10
5
0
1990
1995
2000
2005
2010
2015

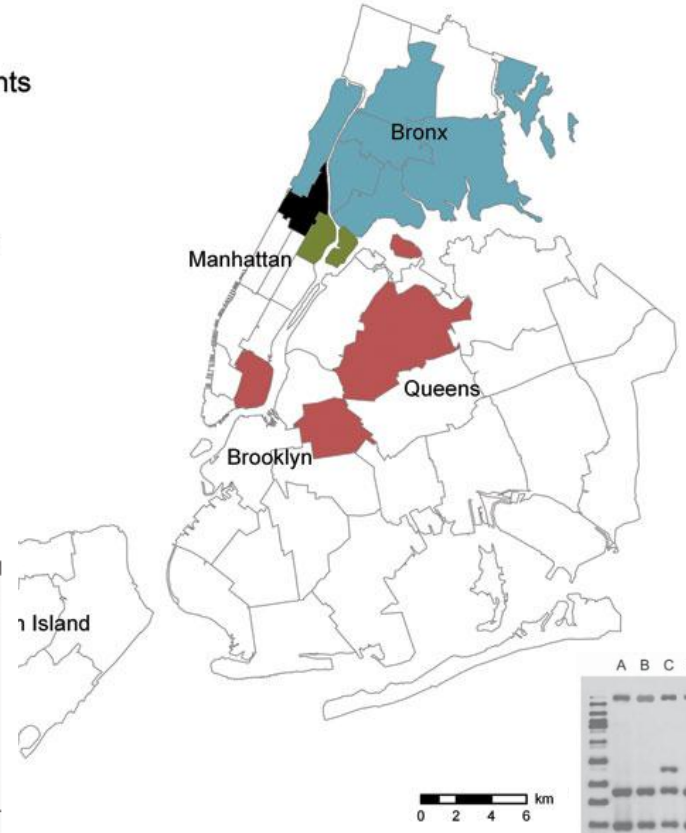
纽约TB爆发-90年代

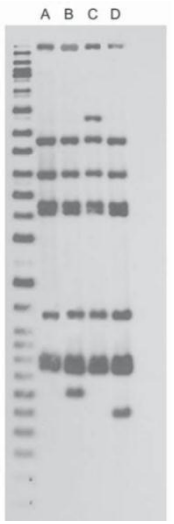
- >350病例
- 几乎耐所有一线药物
- 几乎都感染HIV
- HIV阳性患者和医务工作者

纽约结核病爆发调查

- Drug Susceptibility Testing
- RFLP
- Contact Investigation/Cluster Investigation







In 1993, WHO

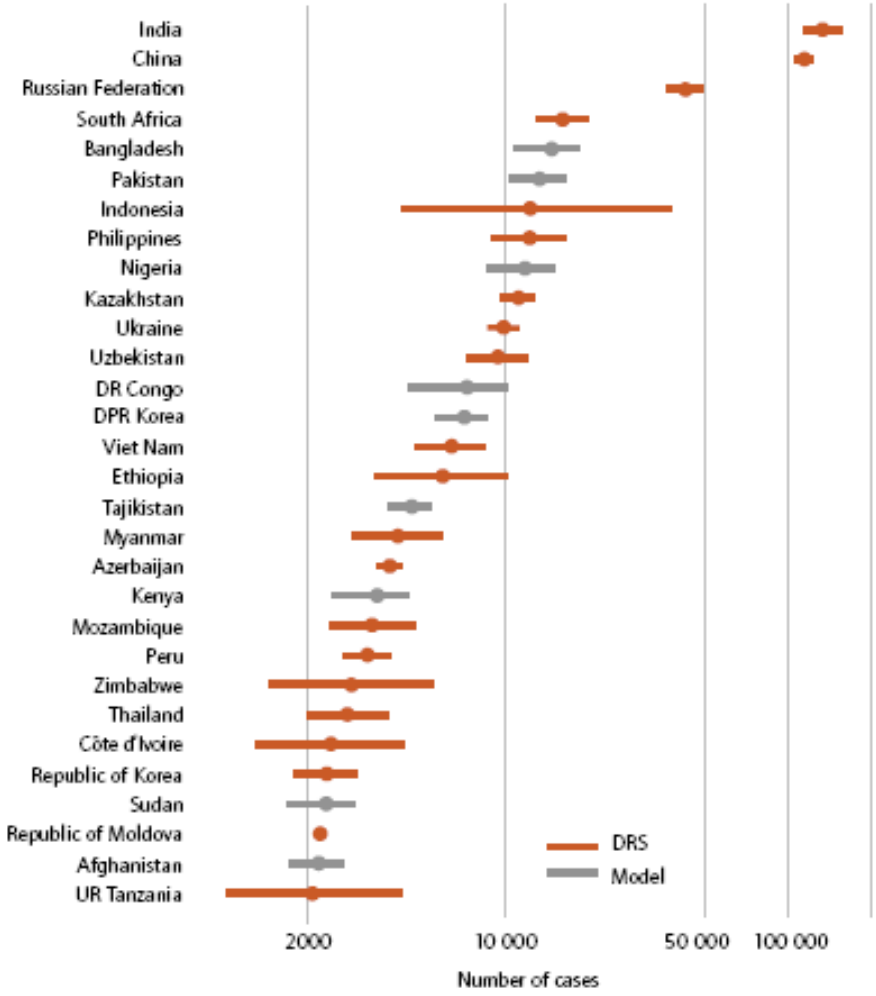
宣布

全球结核病紧急状态

面临的挑战/危险因素

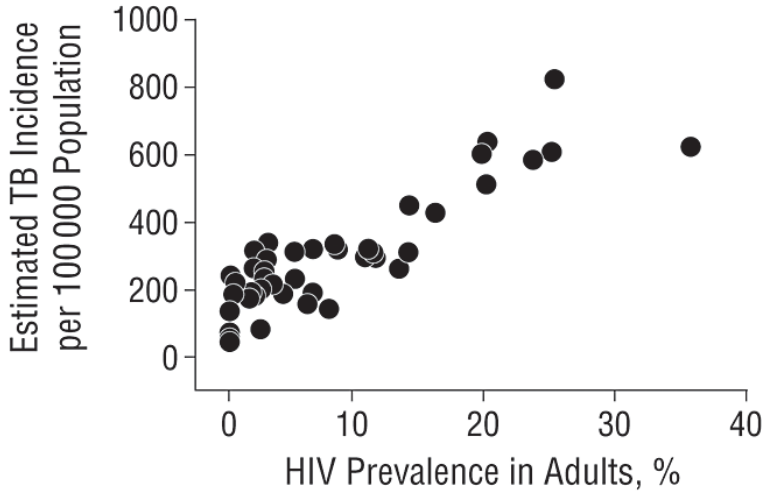
22 个高负担国家

Countries with the highest numbers of estimated MDR-TB cases, 2007. Horizontal lines denote 95% confidence intervals. The source of estimates is drug resistance surveillance or surveys (DRS, in red) or modelling (in grey).



TB/HIV 合并感染

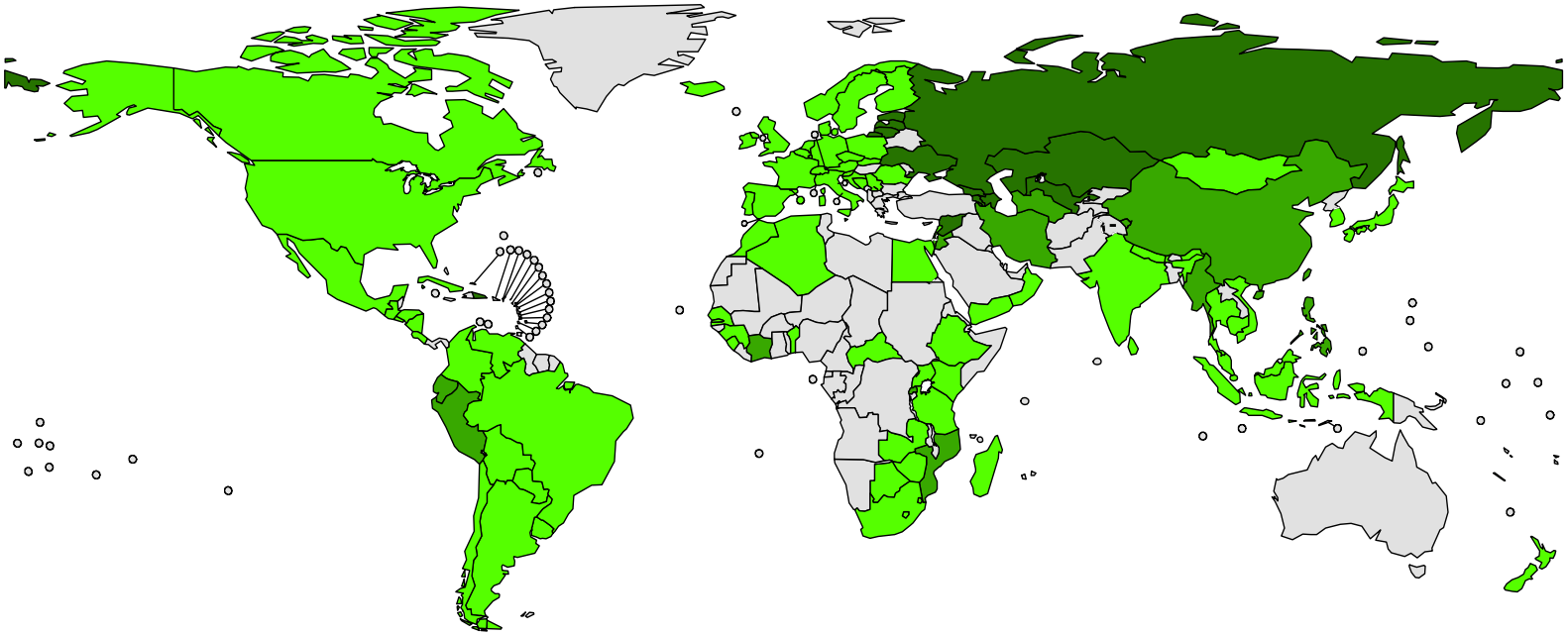
- TB/HIV 合并感染将加剧结核病在中国的流行程度
- 截至2009年底，估计中国现存活艾滋病病毒感染者和病人约74万人
- 其中半数最终会发生活动性肺结核



MDR-TB among new cases, 1994- 2007

World Health Organization

THE STOP TB DEPARTMENT



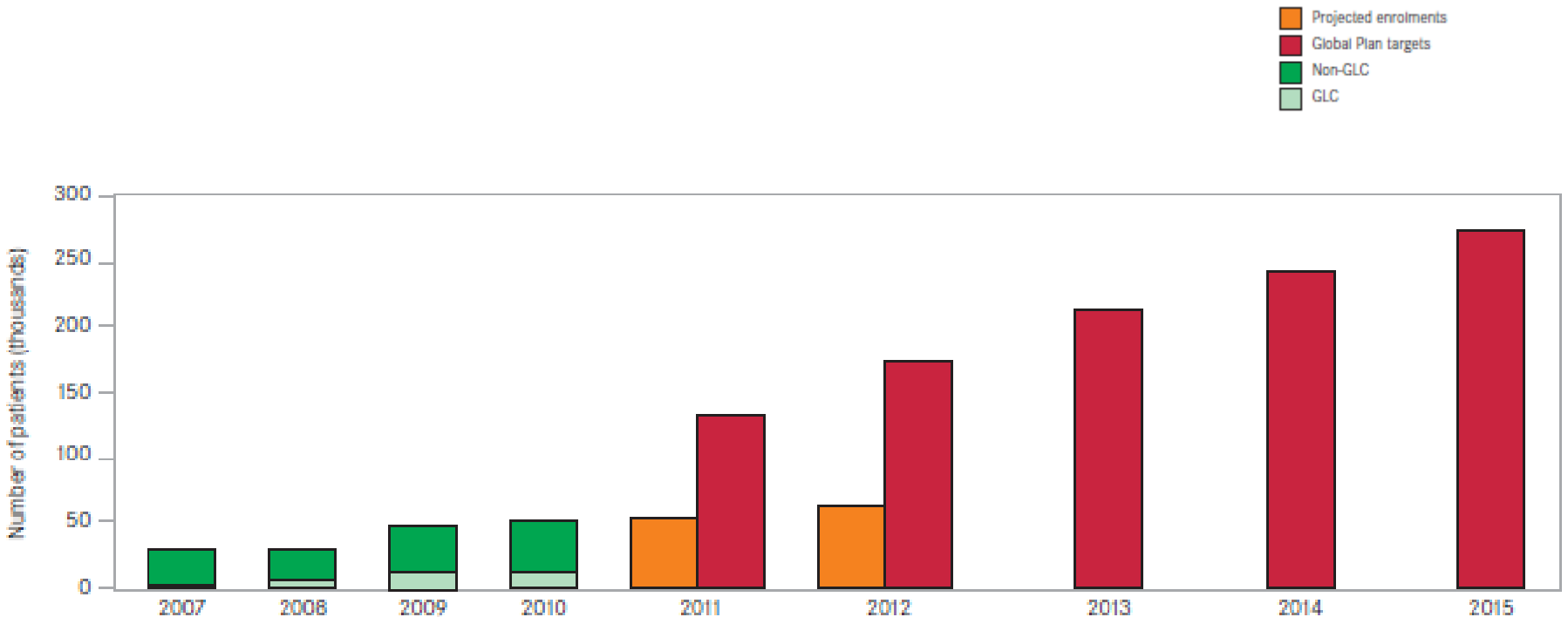
< 3%
3-6 %
> 6 %
No data

- There were an estimated **440 000 new MDR-TB cases** in 2008, and **150 000 deaths from MDR-TB**

- It was estimated that in 2009, **3.3% of all new TB cases had MDR-TB**

- **Detection & Diagnosis**
  - 7% of all estimated MDR-TB patients diagnosed and notified
- **Treatment Success** - 60% of people with MDR-TB, who were enrolled on treatment programmes, successfully treated

全球MDR患病人数


Projected enrolments
Global Plan targets
Non-GLC
GLC
Number of patients (thousands)
300
250
200
150
100
50
0
2007
2008
2009
2010
2011
2012
2013
2014
2015


诊断结果
耐多药性
肺结核

耐多药结核病（MDR-TB）

耐多药性结核病（MDR-TB）是指同时对异烟肼和利福平这两种最重要的抗结核药耐受

估计感染多耐药性结核病患者达到5千万

现在发展中国家承担不起某些耐多药菌株的治疗

治疗费用增加百倍

MDR-TB产生的原因

- 间断治疗或中断治疗所致
- 抗生素滥用

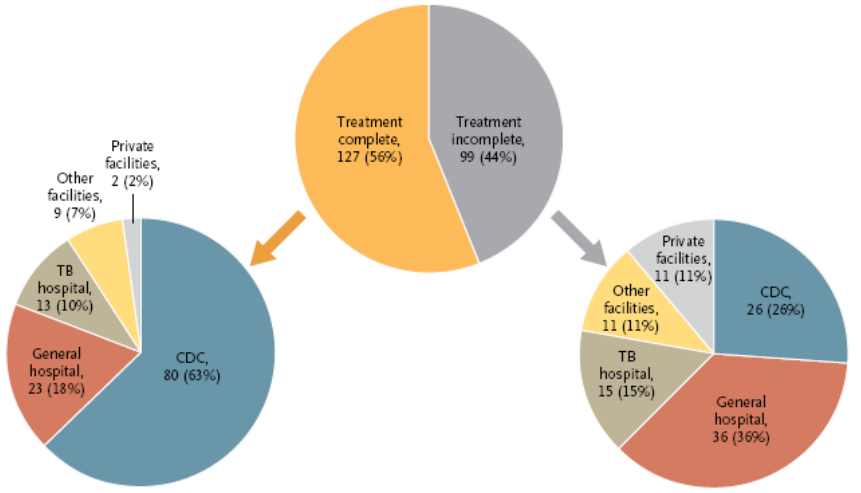


Figure 1. Patients with Previously Treated Tuberculosis in Whom Multidrug-Resistant Tuberculosis Was Detected, According to Completion or Noncompletion of Their Last Treatment Course and Location of Their Last Treatment.

In China, most patients with tuberculosis receive treatment either at the local tuberculosis clinic of the Chinese Center for Disease Control and Prevention (CDC) or in the hospital system. Patients receiving care in hospitals that specialize in the treatment of tuberculosis (TB hospitals) are more likely to be those with cases that are difficult to treat.

Map world-wide spread of Beijing genotype strains

Judith Glynn et al.: Review publications on Beijing strains (EID 2002, **8:**843-849.)

Estimated number of MDR-TB Cases, 2011

Russian Federation
44,000
(14% of global MDR burden)

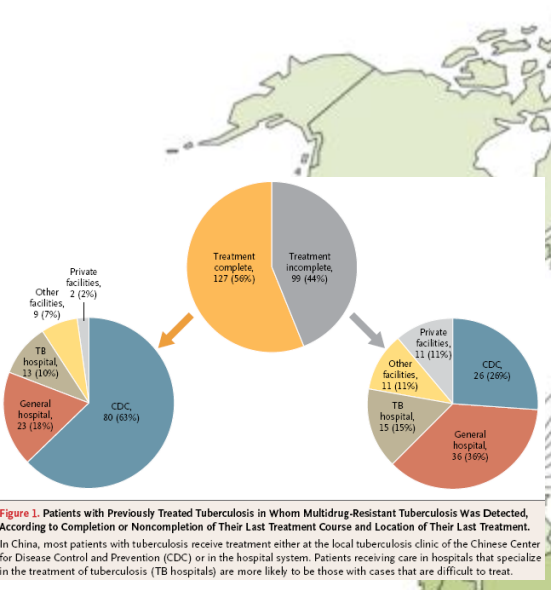
China
61,000
(20% of global MDR burden)

South Africa
8,100
Based on old survey data

Pakistan
10,000
(3% of global MDR burden)

India
66,000
(21% of global MDR burden)

Philippines
11,000
(4% of global MDR burden)

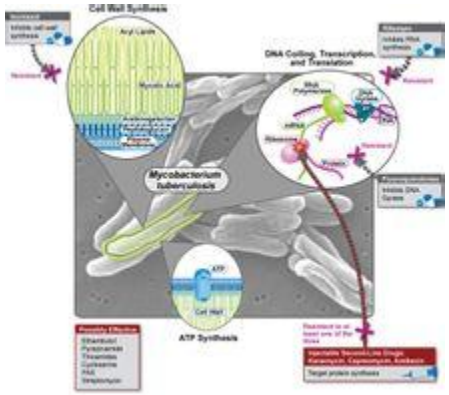


GLOBAL TB PROGRAMME

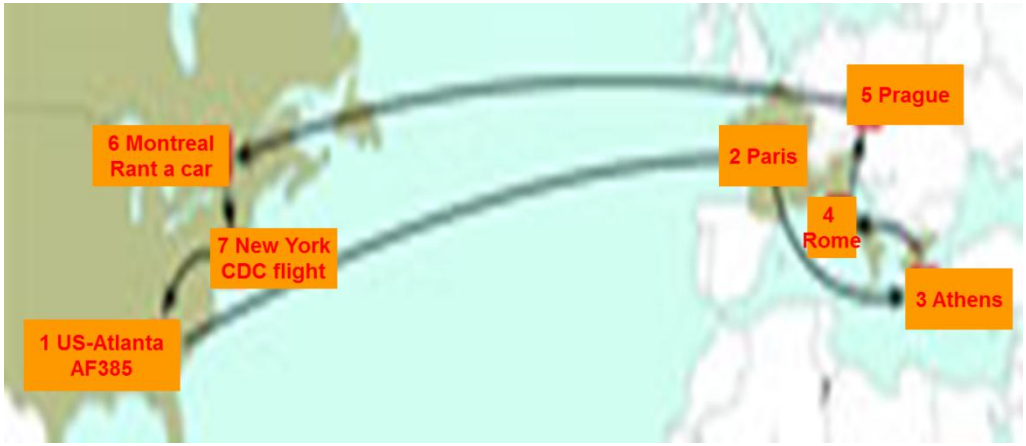
World Health Organization

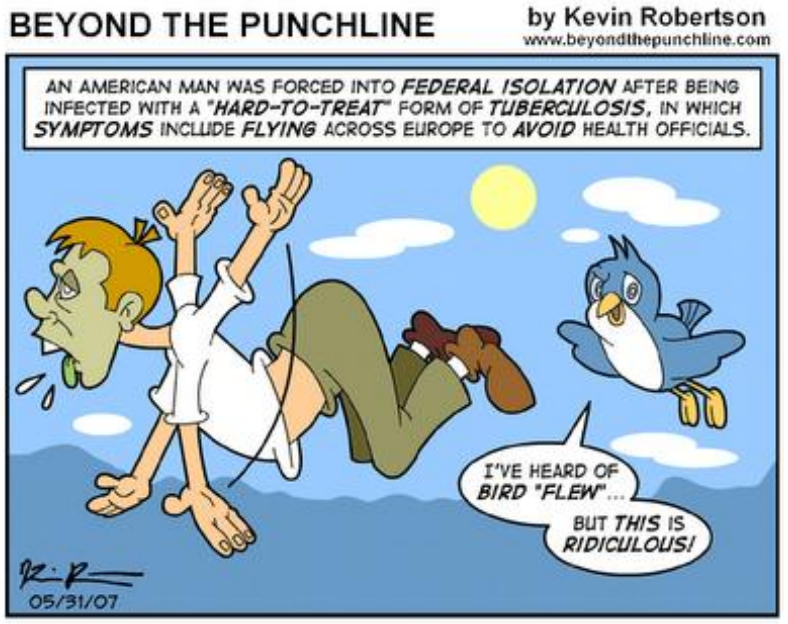
Drug-resistant TB

- 广泛耐药结核病（XDR-TB）严重耐药结核是除耐多药结核之外对任何氟喹诺酮类药物以及三种二线注射药物（硫酸卷曲霉素、卡那霉素和阿米卡星）中至少一种具耐药性的结核。



XDR-TB警示了我们什么？





Case of Atlanta lawyer with presumed XDR-TB caused international concern

The case of Mumbai and the "TDR-TB outbreak"


THE TIMES OF INDIA | India

Search

Home City India World Business Tech Sports Entertainment Life & Style Women Hot on the Web NRI Photos Times Now Videos LIVE TV

New, deadlier form of TB hits India

Malathy Iyer, TNN

Tags: World Health Organization | Tuberculosis | TB

33 928

Tweet Recommend

MUMBAI: Tuberculosis, which kills around 1,000 people a

w entity-

DR-TB)-has been isolated in the fluid samples

e at Hinduja Hospital at Mahim . The hospital's

th Organization (WHO) to test TB patients for


Correspondence

Totally Drug-Resistant Tuberculosis in India

To the Editor—Three years after extensively drug-resistant (XDR) tuberculosis was first described in 2006, Velayati et al [1] drew attention to the emergence of totally drug-resistant (TDR) tuberculosis in a cohort of 15 patients from Iran, resistant to all first- and second-line drugs. Since the first cases of XDR tuberculosis

individually and often in incorrect doses, from multiple private practition

4 physicians during a 18-mor

in an attempt to cure their

resistant (MDR) tuberculosis

The latest WHO global resista

estimated 110 132 cases of M

culosis from India in 2006,

counts for 20% of the wor

tuberculosis load [3]. Althou

RNTCP has been a tremendo

Note


EMERGING INFECTIOUS DISEASES®

EID Journal

November 2012

Challenges and Controversies in Defining Totally Drug-Resistant Tuberculosis

About the Journal

Subscribe

Ahead of Print / In Press

Author Resource Center

Medscape CME

More Content

Social Media

Announcement Calendar

Contact Us

Related Articles

EID Journal > November 2012

Recommend 1 Tweet 4 Share

Online Report

Challenges and Controversies in Defining Totally Drug-Resistant Tuberculosis

Peter Cegielski ✉, Paul Nunn, Ekaterina V. Kurbatova, Karin Weyer, Tracy L. Dalton, Douglas F. Wares, Michael F. Iademarco, Kenneth G. Castro, and Mario Raviglione

Author affiliations: Author affiliations: Centers for Disease Control and Prevention, Atlanta, Georgia, USA (P. Cegielski, E.V. Kurbatova, T.L. Dalton, M.F. Iademarco, K.G. Castro); World Health Organization, Geneva, Switzerland (P. Nunn, K. Weyer, D.F. Wares, M. Raviglione)

Suggested citation for this article

Article Contents

- Online Report
- References
- Suggested Citation

Abstract

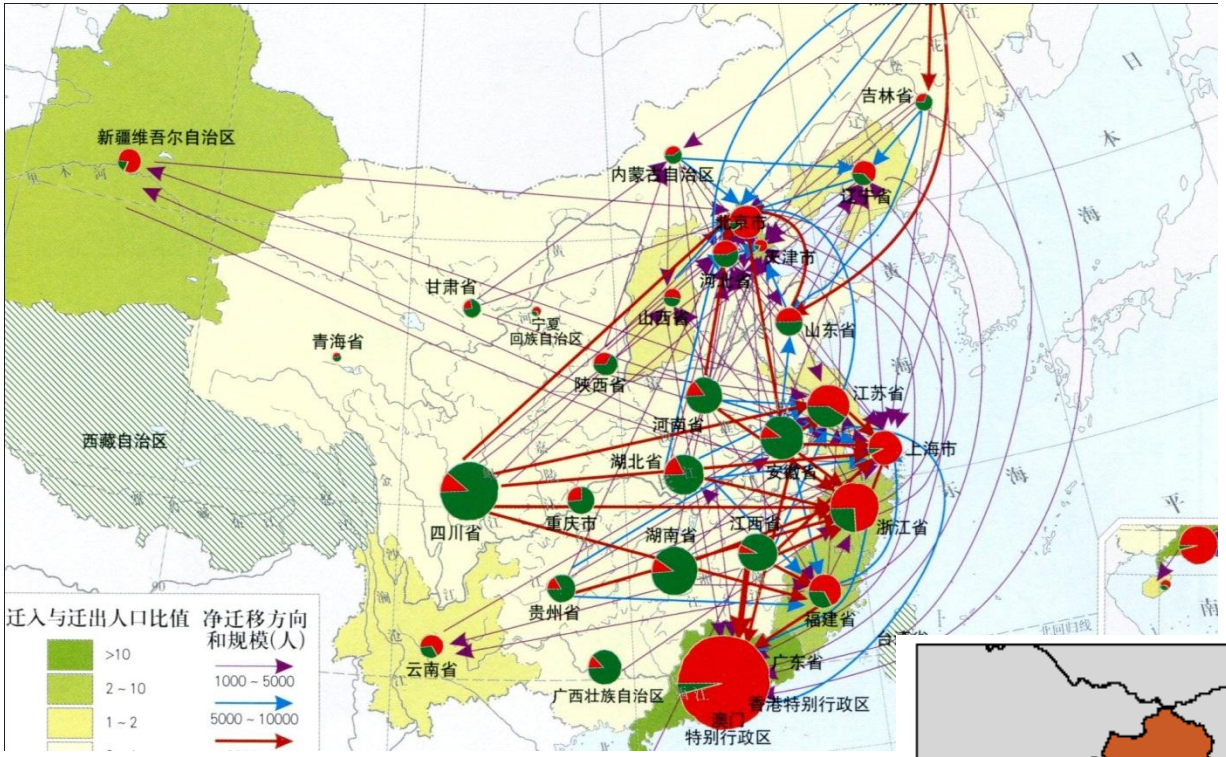
In March 2012, in response to reports of tuberculosis (TB) resistant to all anti-TB drugs, the World Health Organization convened an expert consultation that identified issues to be reso

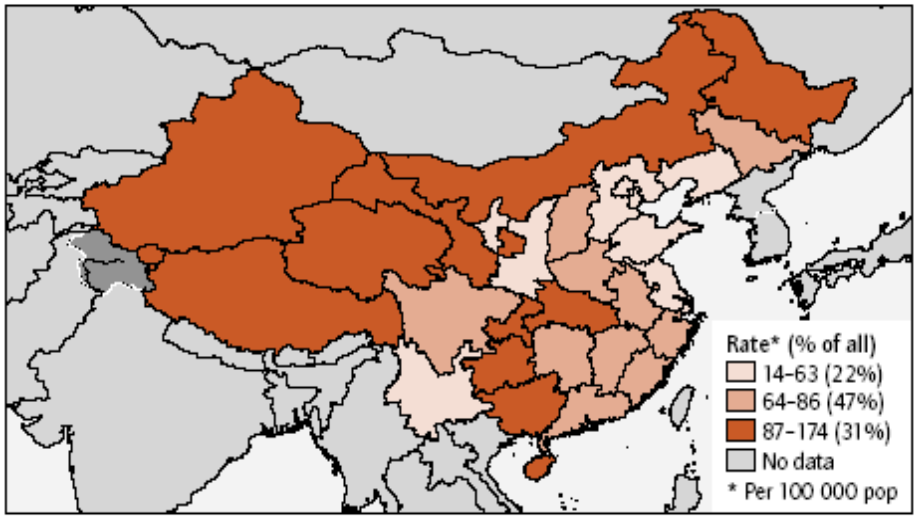
结核病与流动人口

- 观光旅游、国际旅行及移民都有助于TB的传播
- 在很多发达国家结核病患者中至少有一半是来自外来人口
- 美国结核病患者中有三分之一人口是外来人员
- 发达国家中其他流动人口，如流浪者，他们感染结核病的危险性还在上升

WHO告诫：一旦流动人口问题进入紧急状态，结核病将成为首要公共卫生问题 。

人口移动与疫情


新疆维吾尔自治区
内蒙古自治区
吉林省
辽宁省
北京市
天津市
河北省
甘肃省
宁夏
回族自治区
山西省
山东省
青海省
陕西省
江苏省
河南省
上海市
西藏自治区
湖北省
安徽省
四川省
重庆市
江西省
浙江省
湖南省
贵州省
福建省
云南省
广东省
广西壮族自治区
香港特别行政区
澳门
特别行政区
迁入与迁出人口比值
>10
2 ~ 10
1 ~ 2
净迁移方向
和规模(人)
1000 ~ 5000
5000 ~ 10000


Rate* (% of all)
14-63 (22%)
64-86 (47%)
87-174 (31%)
No data
* Per 100 000 pop

行动和策略

Partnership for Global Action

控制对策

DOTS

(Directly observed treatment, short course)

- 政治承诺
- 痰涂片显微镜检查
- 药品供应
- 监测系统
- 直接督导下有效化疗方案的应用

全球采取的行动

2001年10月22日华盛顿部长级会议：号召各国及合作伙伴将采取特别行动，并提出4个未来的目标：

1）50天（2001年底）：完成制订国家的规划，启动全球控制艾滋病、结核病、疟疾基金；

2）50周（2002年底）：发现率达35%，建立结核病控制机构间协调委员会,全球结核病药物基金提供每年治疗100万病人的药物；

3）50月（2005年底）：**发现率达70%，治愈率达85%**，开发MDR和TB-HIV双重感染的有效措施。制订2006-2010年全球计划；

4）50年（2050年底）：消除作为全球公共卫生的结核病。

WHO calls drug-resistant TB a time bomb as the Gates Foundation and Chinese government announce a $33 million initiative to fight it

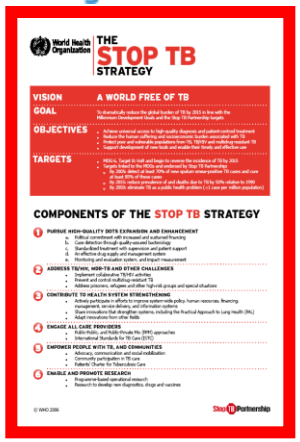
1 April 2009 - Beijing

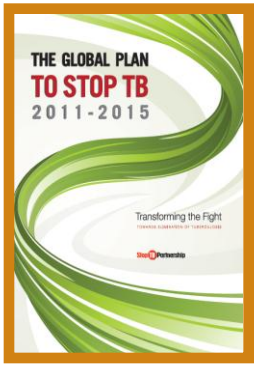
全球应对：目标、计划、策略

UN Millennium Development Goals

Goal 6: to have halted by 2015 and begun to reverse the incidence…

World Health Organization





2015: 50% reduction in TB prevalence and deaths compared to 1990

2050: elimination (<1 case per million population)

1. Pursue high-quality DOTS expansion
2. Address TB-HIV, MDR-TB, and needs of the poor and vulnerable
3. Contribute to health system strengthening
4. Engage all care providers
5. Empower people with TB and communities
6. Enable and promote research

Goals, targets and indicators for TB control

Millennium Development Goals set for 2015

Goal 6: Combat HIV/AIDS, malaria and other diseases

Target 6c: Halt and begin to reverse the incidence of malaria and other major diseases

Indicator 6.9: Incidence, prevalence and death rates associated with TB

Indicator 6.10: Proportion of TB cases detected and cured under DOTS

Stop TB Partnership targets set for 2015 and 2050

By 2015: Reduce prevalence and death rates by 50%, compared with their levels in 1990

By 2050: Reduce the global incidence of active TB cases to <1 case per 1 million population per year

绿灯委员会 (GLC)

- 对DOTS规划提供技术援助
- 促进全球二线抗结核药物的合理使用，并且帮助获得价格优惠、质量可靠的二线抗结核药物
- 对项目的持续监测和督导

新方法和技术

- 促进新药研究
- 诊断方法的进步也需要加速

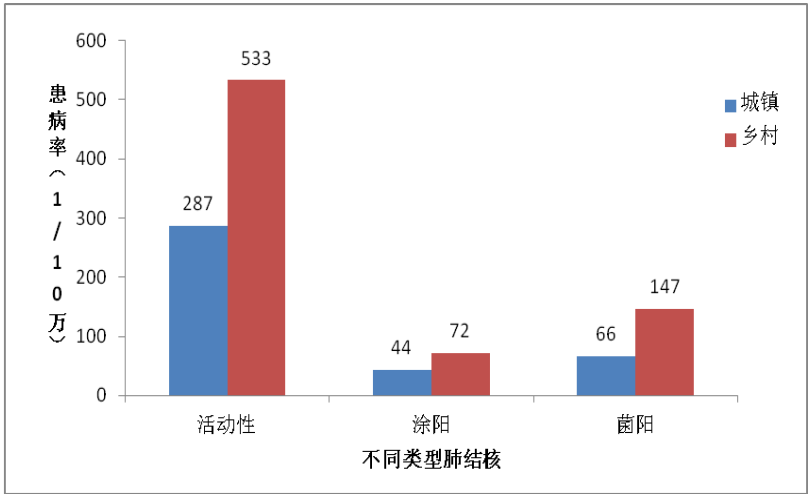
Xpert: evidence and operations

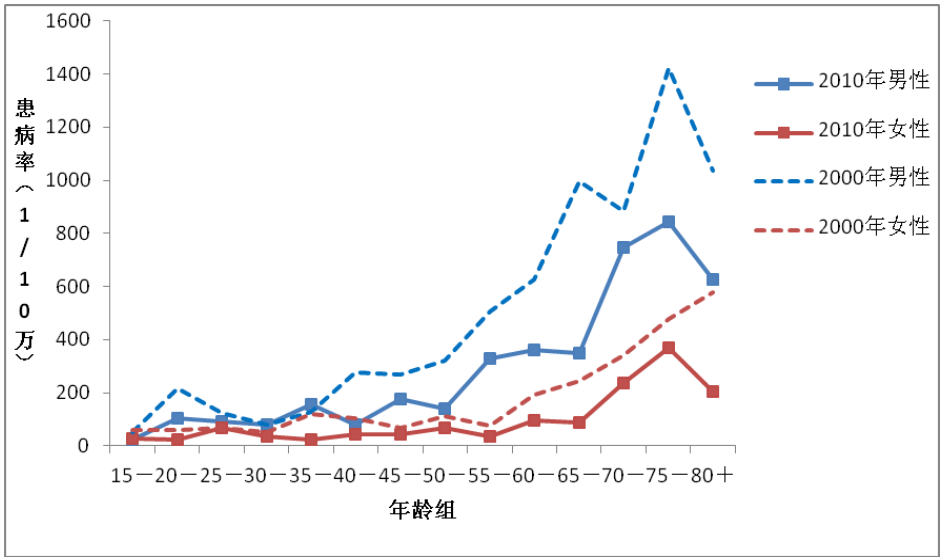
中国的结核病流行情况

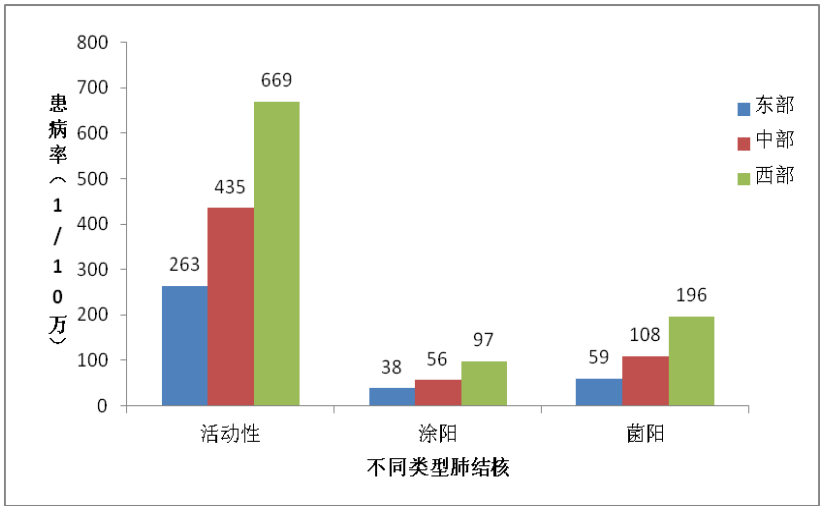
中国结核病患病率分布

第四、五次全国结核病流调患病率及递降率

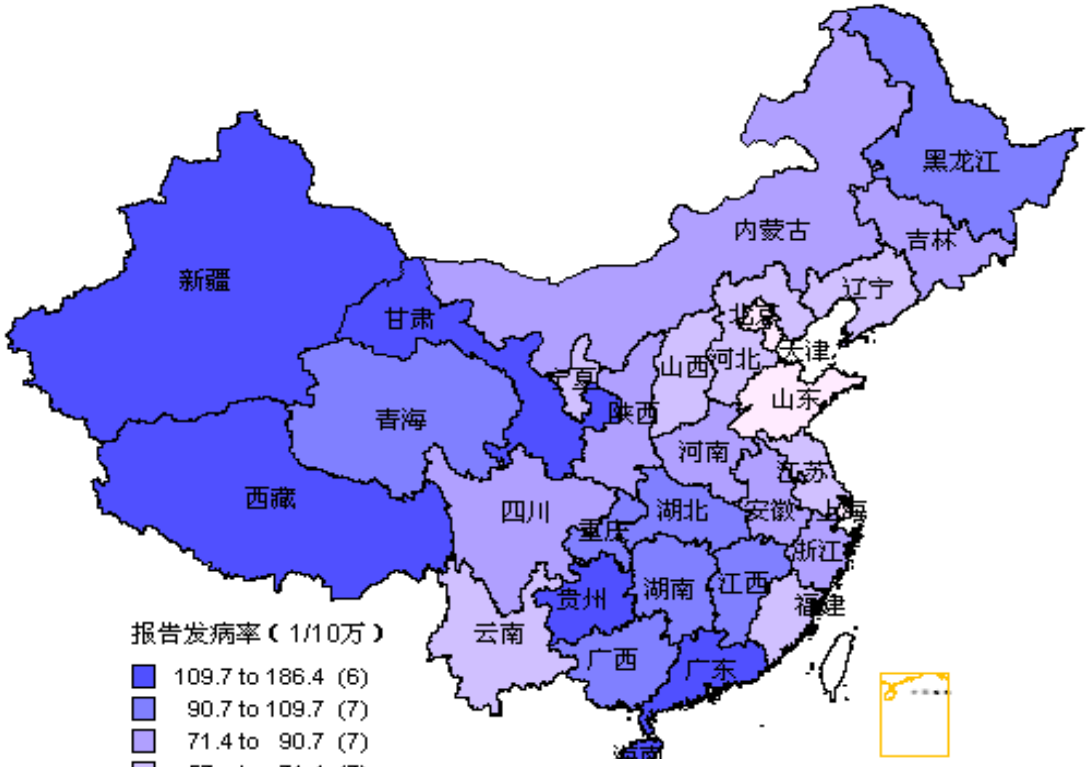
病人分类	患病率(1/10 万)		2000 年—2010 年
	2000	2010	递降率(%)
活动性肺结核	459	429	0.7
涂阳肺结核	167	60	9.7
菌阳肺结核	213	112	6.2

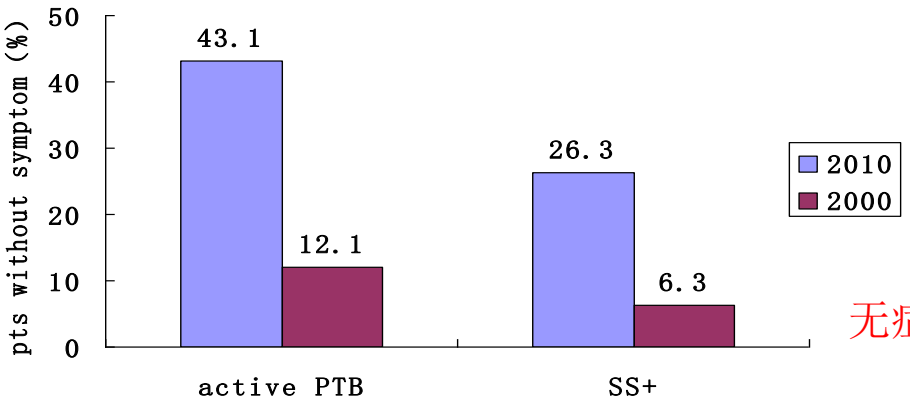






2011年全国肺结核患者报告发病率分布





无症状患者的比例

来源：姜世闻，中国CDC

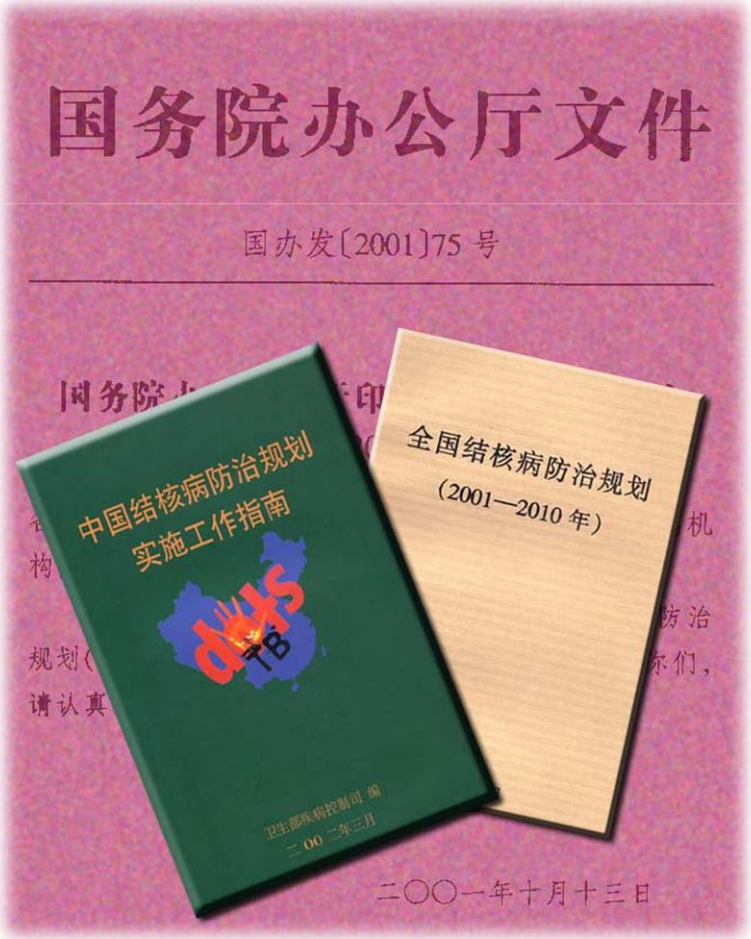
耐药情况

Table 1. Drug Susceptibility and Resistance to First-Line and Second-Line Antituberculosis Drugs.*

Susceptibility or Resistance	Patients with New Cases of Tuberculosis (N=3037)		Patients with Previously Treated Tuberculosis (N=892)	
	no.	*% (95% CI)†*	*no.*	*% (95% CI)†*
Susceptibility to all four first-line drugs‡	2009	65.8 (62.4–69.1)	417	45.5 (40.6–50.4)
Resistance to first-line drugs				
Any first-line drug	1028	34.2 (30.9–37.6)	475	54.5 (49.6–59.4)
Isoniazid	486	16.0 (13.9–18.1)	335	38.5 (33.7–43.3)
Rifampin	202	6.7 (5.3–8.0)	258	29.4 (24.8–34.0)
Ethambutol	153	4.9 (3.7–6.1)	157	17.2 (13.7–20.7)
Streptomycin	834	27.7 (24.4–31.0)	320	37.2 (32.5–42.0)
Isoniazid or rifampin (but not both)	338	11.2 (8.4–14.2)	141	16.1 (8.9–24.7)
Multidrug resistance§	175	5.7 (4.5–7.0)	226	25.6 (21.5–29.8)
Susceptibility to ofloxacin and kanamycin	2906	95.8 (94.7–96.9)	797	88.6 (85.3–91.8)
Resistance to ofloxacin and kanamycin				
Ofloxacin or kanamycin	131	4.2 (3.1–5.3)	95	11.4 (8.2–14.7)
Ofloxacin	88	2.7 (1.8–3.6)	76	8.7 (6.1–11.2)
Kanamycin	59	2.0 (1.4–2.6)	33	4.8 (2.5–7.2)
Multidrug resistance plus resistance to ofloxacin or kanamycin	58	1.8 (1.0–2.6)	73	8.5 (6.4–10.6)
Extensive drug resistance¶	15	0.5 (0.2–0.8)	14	2.1 (0.6–3.5)

我国采取的行动

- 2001年10月13日国务院颁布了《2001—2010年全国结核病防治规划》
  - 《全国结核病防治规划(2011—2015年)》



国际项目

◆世行贷款/DFID中国结核病控制项目

◆日本政府

◆加拿大政府支持苏、浙、鲁三省

◆荷兰皇家结核病协会

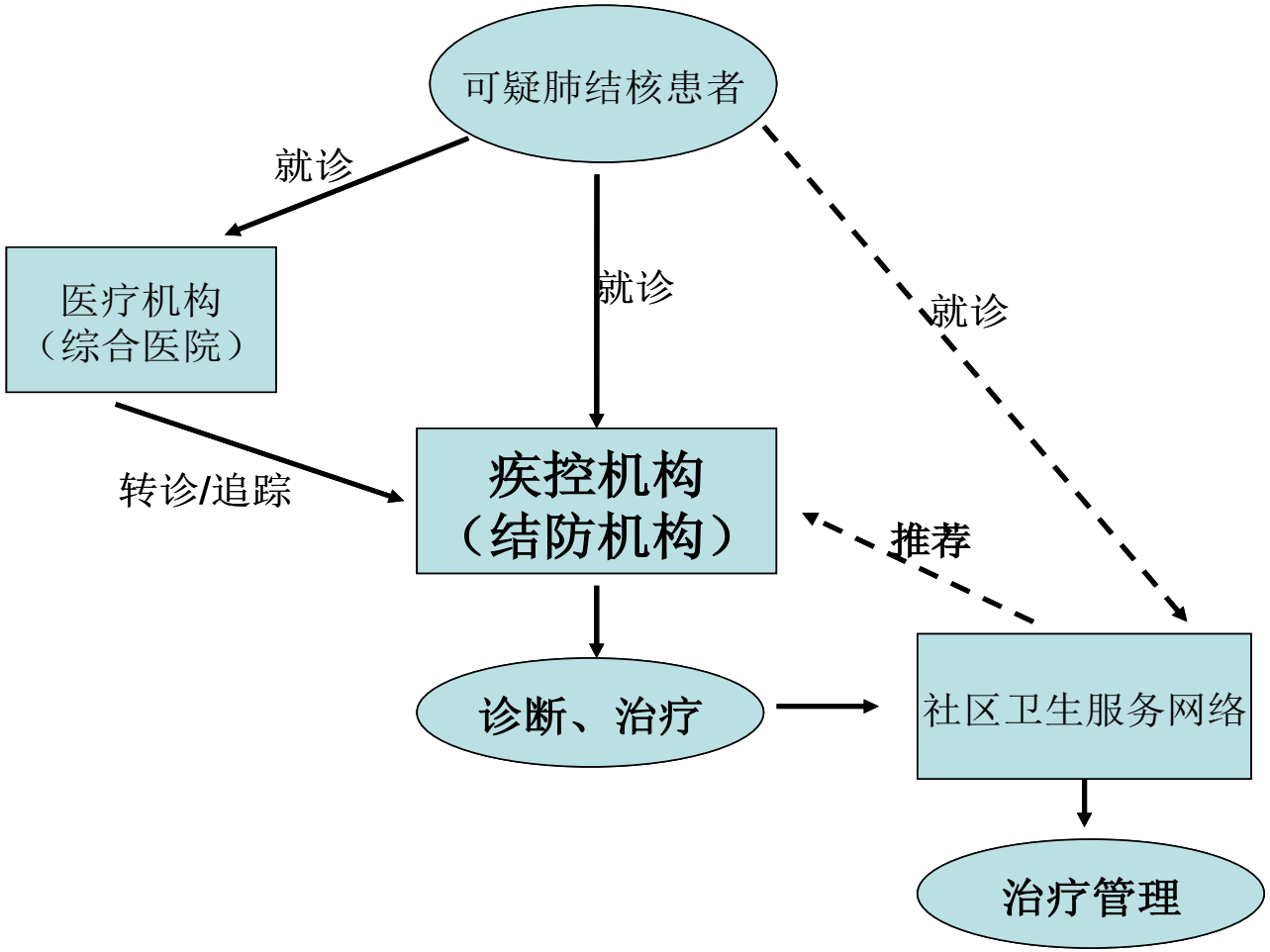
◆全球基金

◆比利时达米恩基金会

◆国际防痨和肺部疾病联合会FIDELIS

中国结核病防控系统

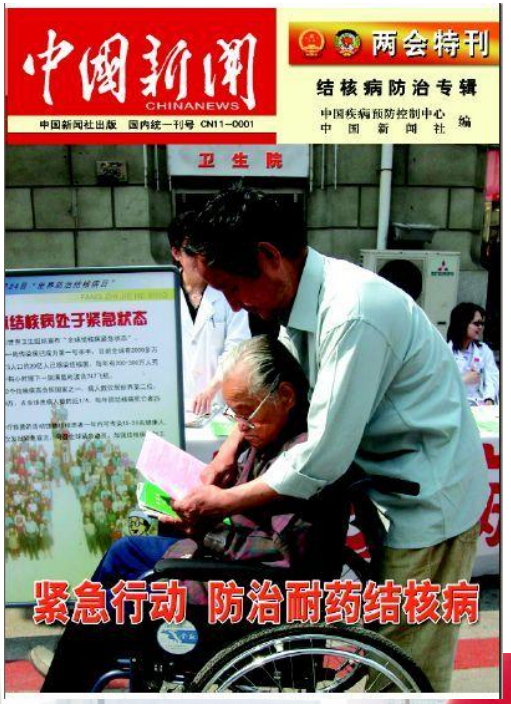
- 结核病防治所负责诊治
- 医院负责报告和推荐
- 社区卫生中心也有推荐责任

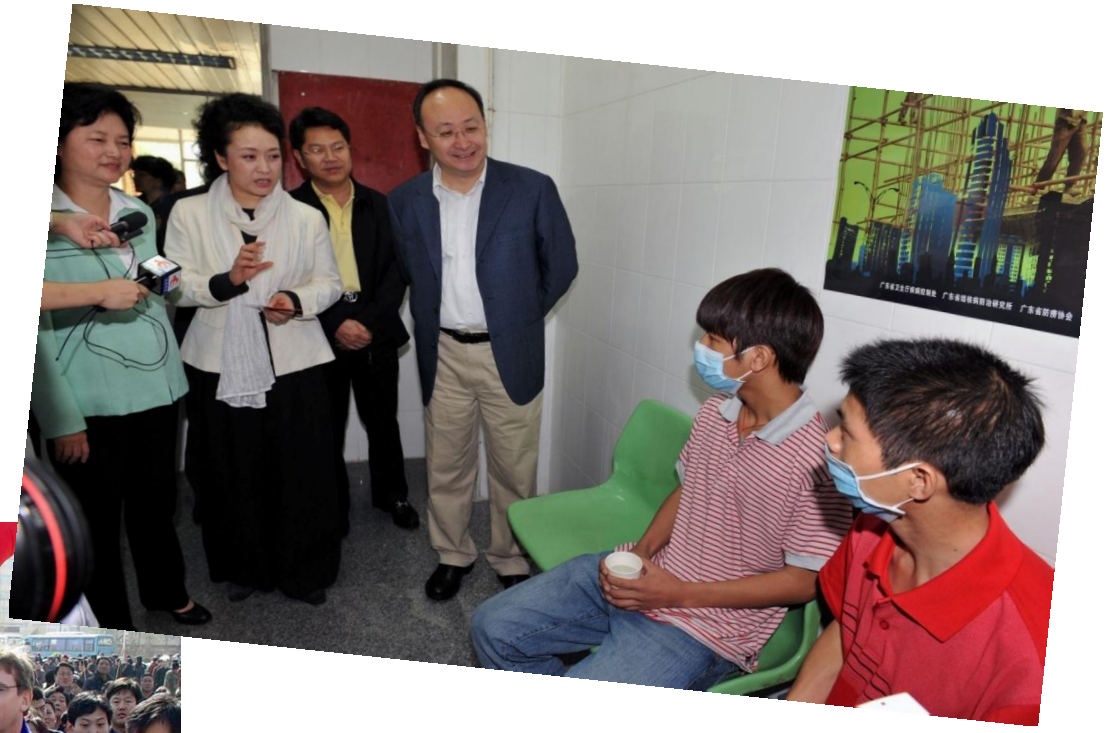


中国的经验

政府承诺 → 免费治疗 → 宣传教育

经 验


中国新闻
CHINANEWS
两会特刊
结核病防治专辑
中国疾病预防控制中心
中 国 新 闻 社 编
中国新闻社出版 国内统一刊号 CN11—0001
卫 生 院
紧急行动 防治耐药结核病




2003年3月24日世界防治结核病日
实施短程督导化疗
People with
TB


dots
TB
防治结核 造福人民


百千万志愿者
防治结核病知识传播行动

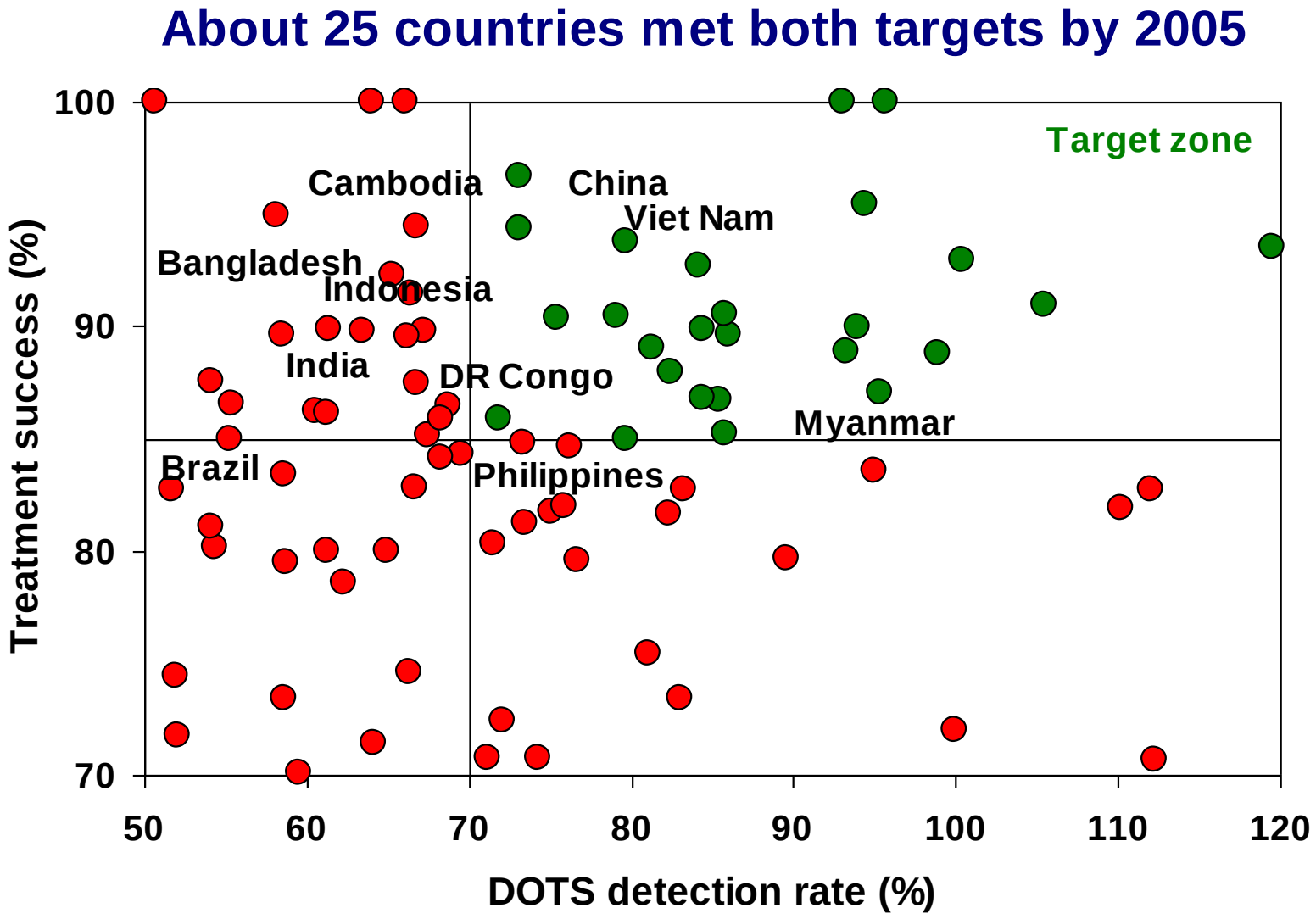

中新网图


咳嗽、咳痰超过三周，
可能得了肺结核

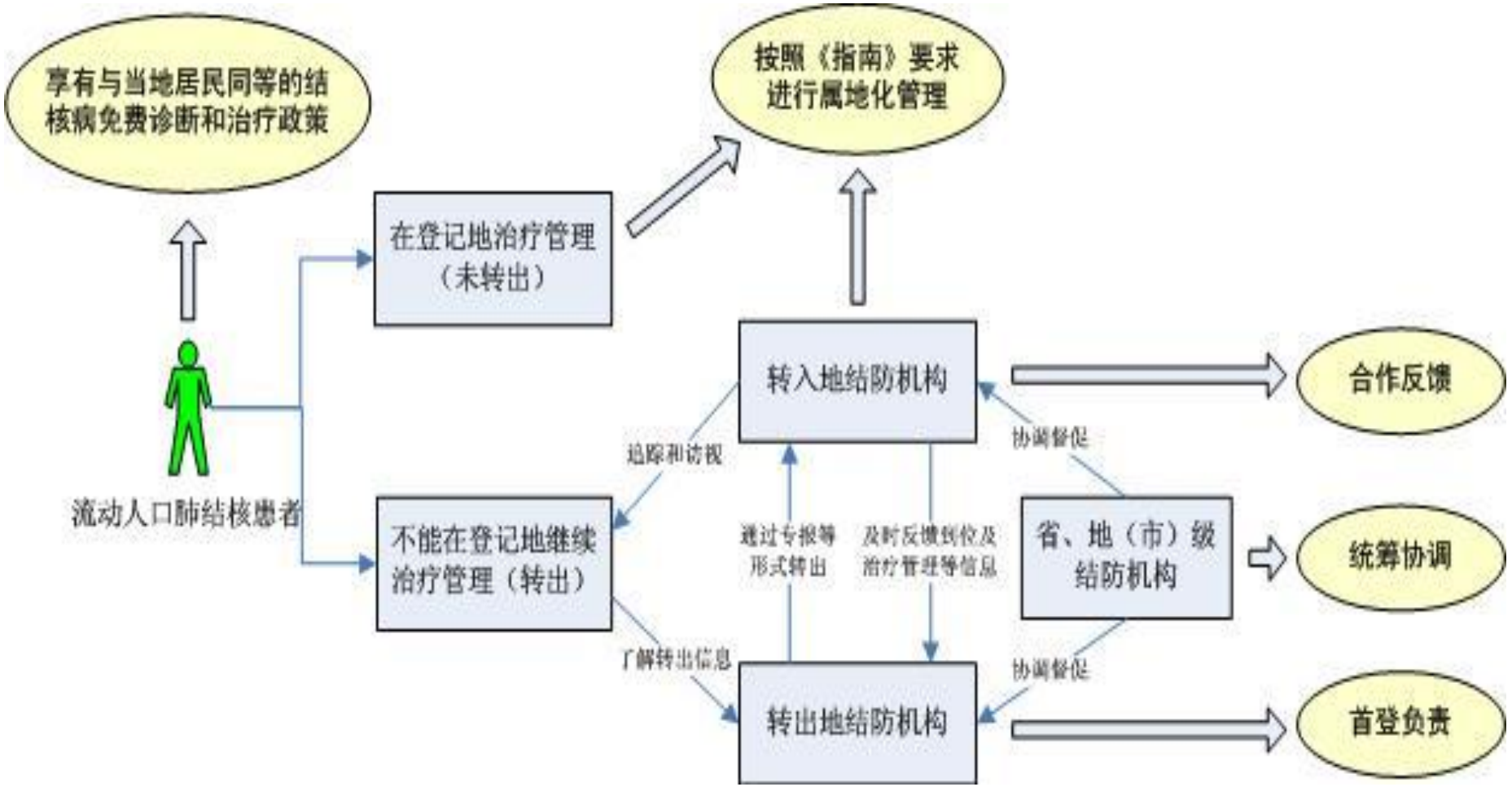
国家结核病信息网络


中国疾病预防控制信息系统 - Windows Internet Explorer
Function Menu
Search Area
Case list
结核病管理信息系统
报告卡管理
报告卡浏览
病案管理
患者病案登记
患者病案管理
耐多药可疑者
耐多药患者管理
患者转出管理
患者转入管理
项目管理
项目维护
项目启动情况统计表
季度录入报表
药品用量季度录入表
初诊患者检查情况
上季度结核病实验室工作情况
新登记涂阳患者家庭密切接触者
乡镇查痰点设置及患者发现情况
健康教育活动报表
患者病案管理
显示登记本
查重
审核标记
登记号
首诊断单位
姓名
性别
年龄
登记日期
登记分类
诊断结果
2月末痰检结果
重新登记病案号
病案来源
治疗状态
转诊状态
操作
2211-00256 顺德区慢性病防治中心 王家军 男 36 2011-04-18 新患者 涂阴患者 收治 在治 查看
2211-00255 顺德区慢性病防治中心 张利民 男 22 2011-04-18 新患者 涂阴患者 新生成 在治 查看
2211-00254 顺德区慢性病防治中心 陈水养 男 42 2011-04-18 新患者 涂阴患者 收治 在治 查看
2211-00253 顺德区慢性病防治中心 郭照遗 男 48 2011-04-18 新患者 涂阴患者 收治 在治 查看
2211-00252 顺德区慢性病防治中心 闭华勇 男 33 2011-04-18 新患者 涂阴患者 收治 在治 查看
2211-00251 顺德区慢性病防治中心 袁志春 男 45 2011-04-18 新患者 涂阴患者 新生成 在治 查看
完成
Internet | 保护模式: 启用
100%

数据的真实性？


About 25 countries met both targets by 2005
Target zone
Cambodia
China
Viet Nam
Bangladesh
Indonesia
India
DR Congo
Myanmar
Brazil
Philippines
Treatment success (%)
100
90
80
70
50
60
70
80
90
100
110
120
DOTS detection rate (%)

流动人口的管理程序


享有与当地居民同等的结核病免费诊断和治疗政策
按照《指南》要求进行属地化管理
在登记地治疗管理（未转出）
转入地结防机构
合作反馈
流动人口肺结核患者
追踪和访视
协调督促
不能在登记地继续治疗管理（转出）
通过专报等形式转出
及时反馈到位及治疗管理等信息
省、地（市）级结防机构
统筹协调
了解转出信息
协调督促
转出地结防机构
首登负责

I am stopping TB. I take all my anti-TB drugs as prescribed.

I am stopping TB. At the clinic where I work we provide prompt and accurate diagnosis of drug-resistant tuberculosis.

I am stopping TB. On my visits to check the health of the people in my community, I stay alert to the signs and symptoms of TB.

You can stop TB. Join us.

www.stoptb.org

World Health Organization

I AM Stopping TB

Thanks for your attention.