艾滋病合并结核病患者长期疗效分析：

一项多中心前瞻性队列研究

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Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
Total	37.9 million [32.7 million – 44.0 million]	1.7 million [1.4 million – 2.3 million]	770 000 [570 000 – 1.1 million]
Adults	36.2 million [31.3 million – 42.0 million]	1.6 million [1.2 million – 2.1 million]	670 000 [500 000 – 920 000]
Women	18.8 million [16.4 million – 21.7 million]	–	–
Men	17.4 million [14.8 million – 20.5 million]	–	–
Children (<15 years)	1.7 million [1.3 million – 2.2 million]	160 000 [110 000 – 260 000]	100 000 [64 000 – 160 000]

Source: UNAIDS/WHO estimates

World Health Organization

GLOBAL TUBERCULOSIS REPORT

2018

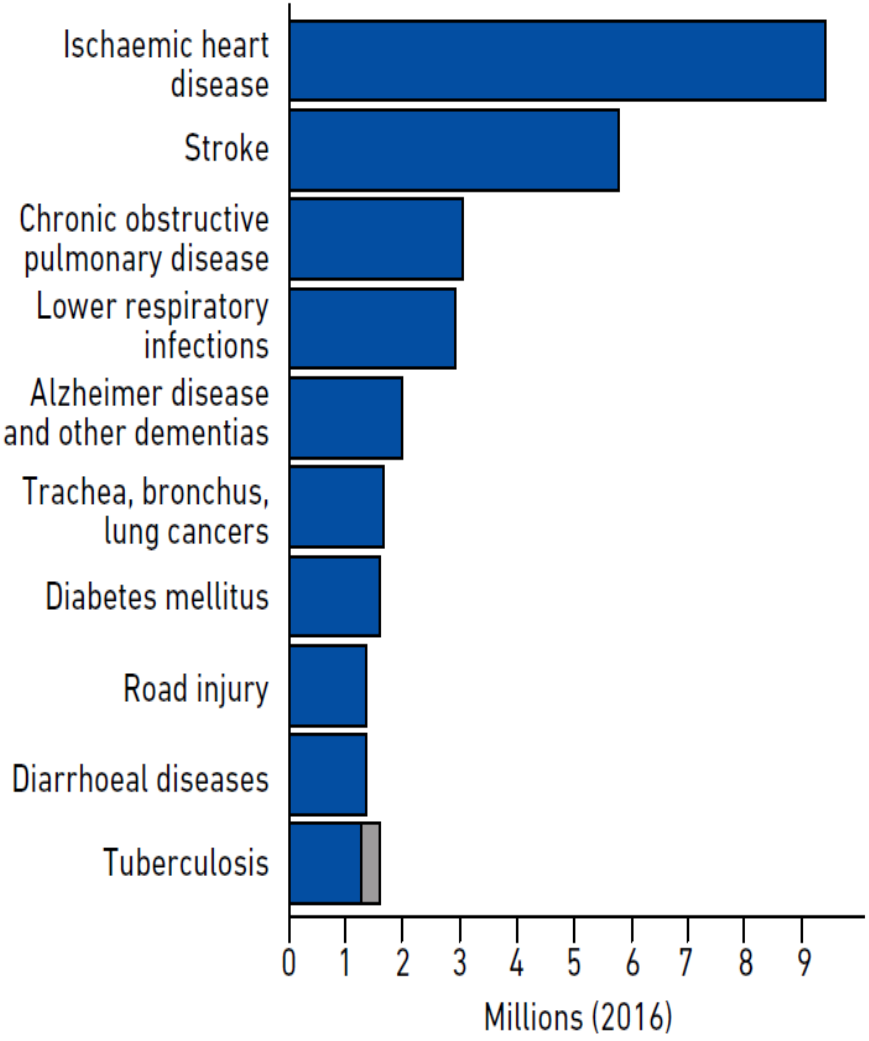
World Health Organization

END TB

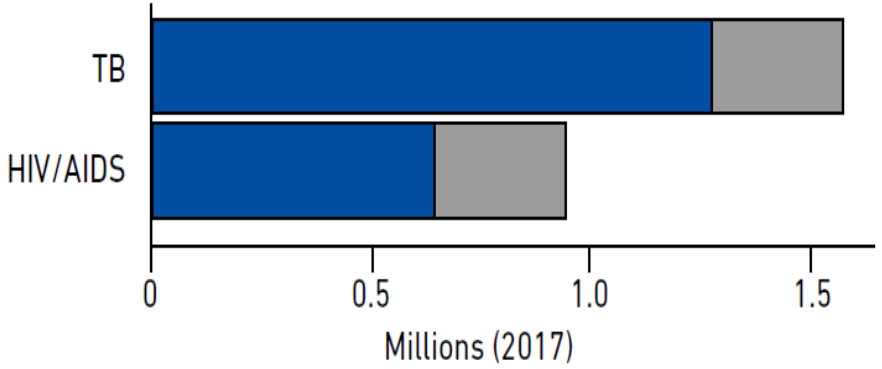
GLOBAL TUBERCULOSIS REPORT 2018

World Health Organization

Top causes of death worldwide in 2016.[a,b]
Deaths from TB among HIV-positive people are shown in grey.



Estimated number of deaths from HIV/AIDS and TB in 2017. Deaths from TB among HIV-positive people are shown in grey.[a,b]

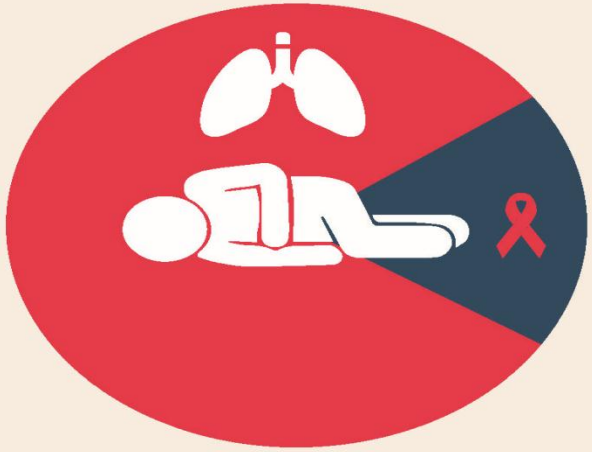


[a] For HIV/AIDS, the latest estimates of the number of deaths in 2017 that have been published by UNAIDS are available at http://www.unaids.org/en/resources/publications/all (accessed 15 August 2018). For TB, the estimates for 2017 are those published in this report.

[b] Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International classification of diseases.

TB IS THE TOP INFECTIOUS KILLER IN THE WORLD

IN 2017



1.6 MILLION PEOPLE DIED FROM TB

INCLUDING
300 000 PEOPLE
WITH **HIV**

TB is the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance

World Health Organization

TBHIV

World Health Organization

HIV-Associated Tuberculosis

ACHIEVEMENTS IN 2017

6.6 million lives saved of people with HIV through scale-up of collaborative TB/HIV activities since 2005

86% known HIV status among notified TB cases in the Africa, up from 14% in 2005

84% ART coverage among notified TB cases living with HIV, up from 36% in 2005

Close to 1 million PLHIV started TB preventive Treatment up from 26,000 in 2005

KEY CHALLENGES

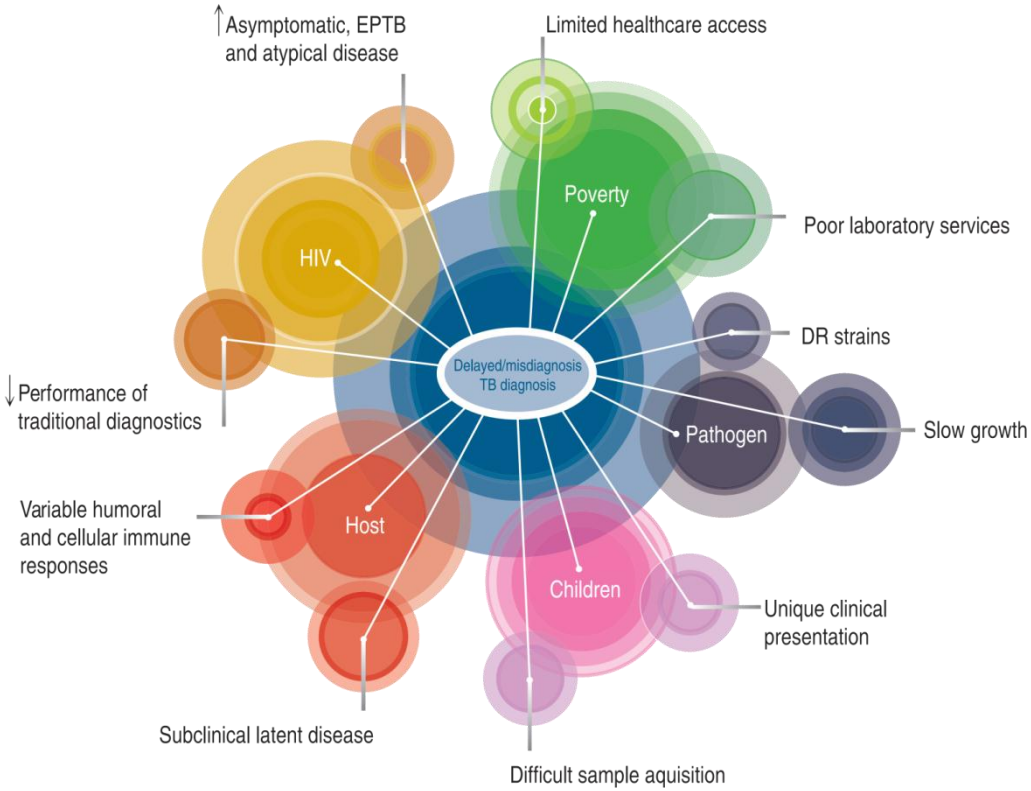
32% of AIDS deaths were from TB

49%

of all people with HIV-associated TB did not reach care
according to reported data

15/30 countries with high burden of HIV-associated TB reported IPT for PLHIV attending HIV care

GLOBAL BURDEN IN 2017

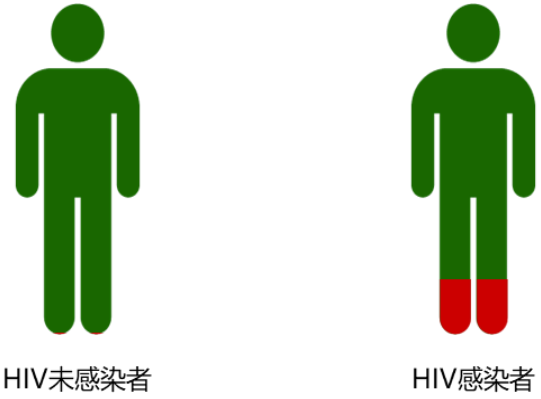


Reproduced from: Jonathan G. Peter et al. Diagnosis of TB: state of the art.

TB incidence estimates, 2017

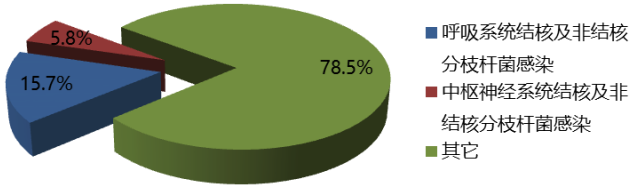
	Population (millions)	Incidence (including HIV)		Incidence (HIV-positive)		Incidence (MDR/RR-TB)	
		Number (thousands)	Rate	Number (thousands)	Rate	Number (thousands)	Rate
China	1 410	889 (761–1 030)	63 (54–73)	12 (6.3–18)	0.82 (0.45–1.3)	73 (55–94)	5.2 (3.9–6.6)
China, Hong Kong SAR	7	5 (4.2–5.7)	67 (58–78)	0.047 (0.039–0.055)	0.63 (0.53–0.74)	5.2 (3.9–6.6)	5.2 (3.9–6.6)
China, Macao SAR	<1	0.44 (0.37–0.50)	0.44 (0.37–0.50)	<0.01 (<0.01–<0.01)	0.12 (<0.1–0.15)	0.014 (<0.01–0.028)	2.3 (0.82–4.5)

NOTE: Rates are per 100 000 population.

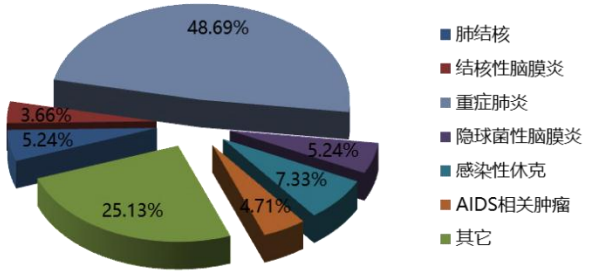


HIV感染者TB的患病率为HIV未感染者的16~27倍

191 例 AIDS 死亡患者疾病谱

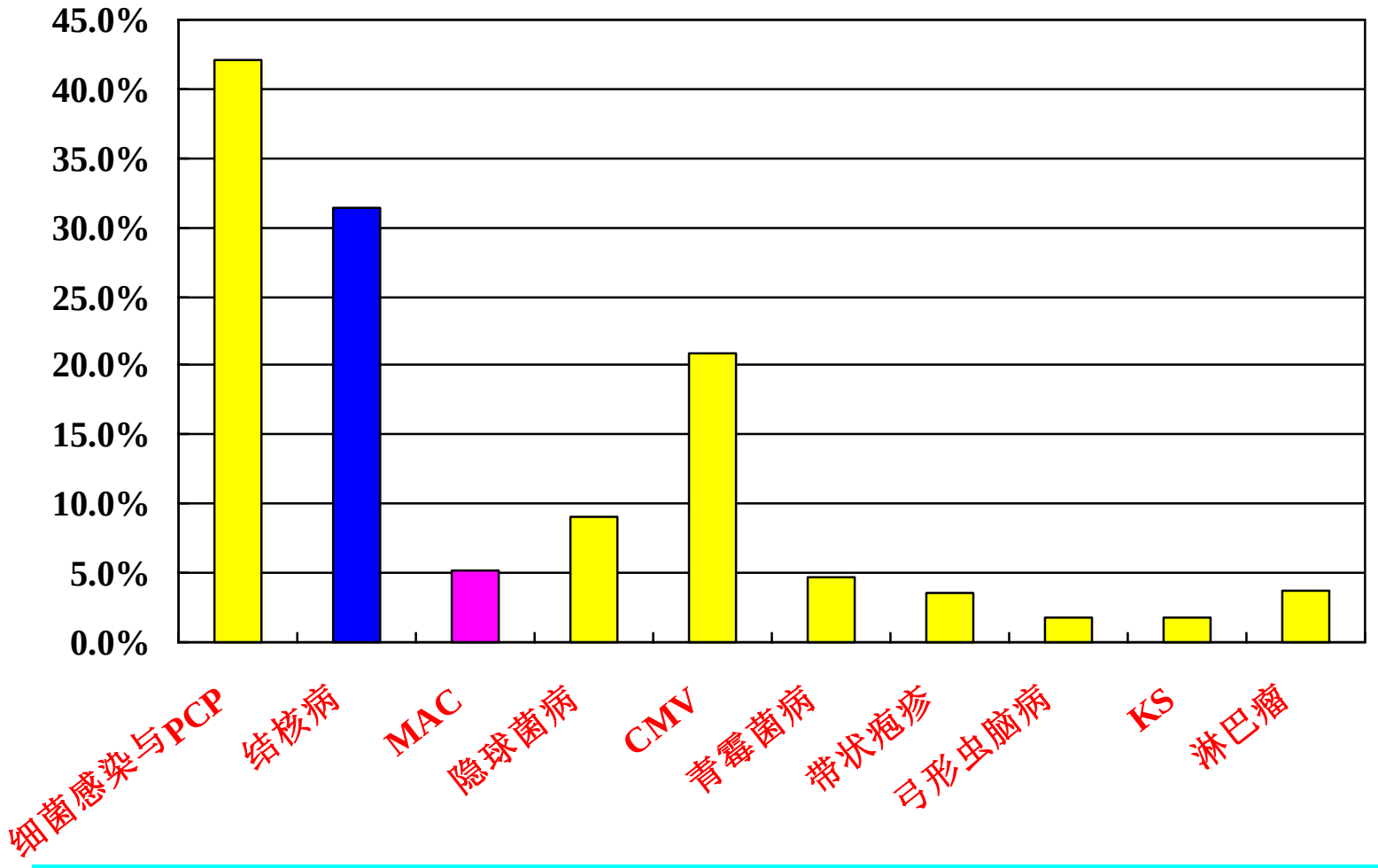


191 例 AIDS直接死亡原因



Reproduced from: WHO Global Tuberculosis Report 2018

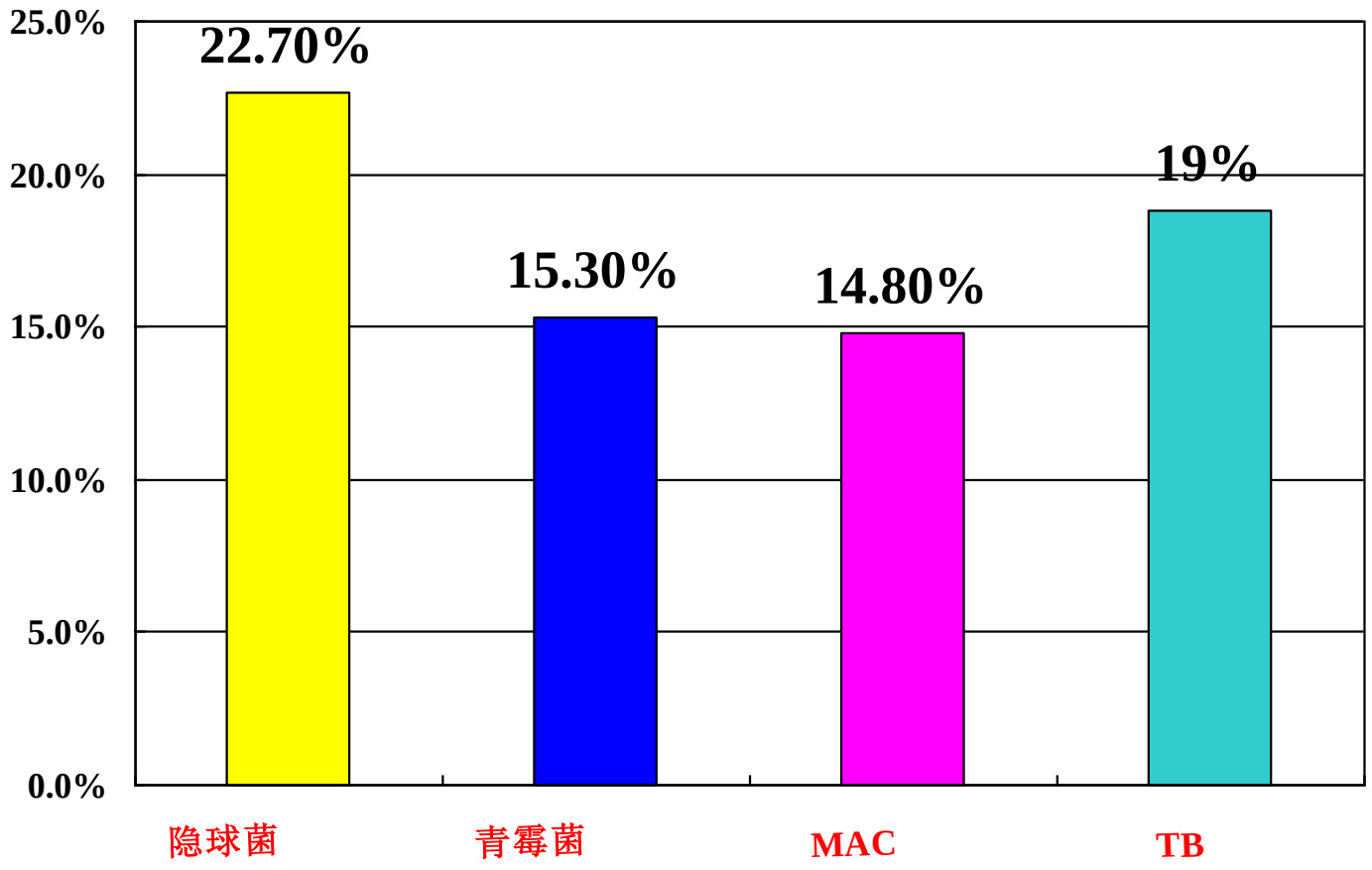
HIV住院患者的疾病谱（上海）



Luo B, et al. Medicine (Baltimore). 2016 May;95(21):e3802

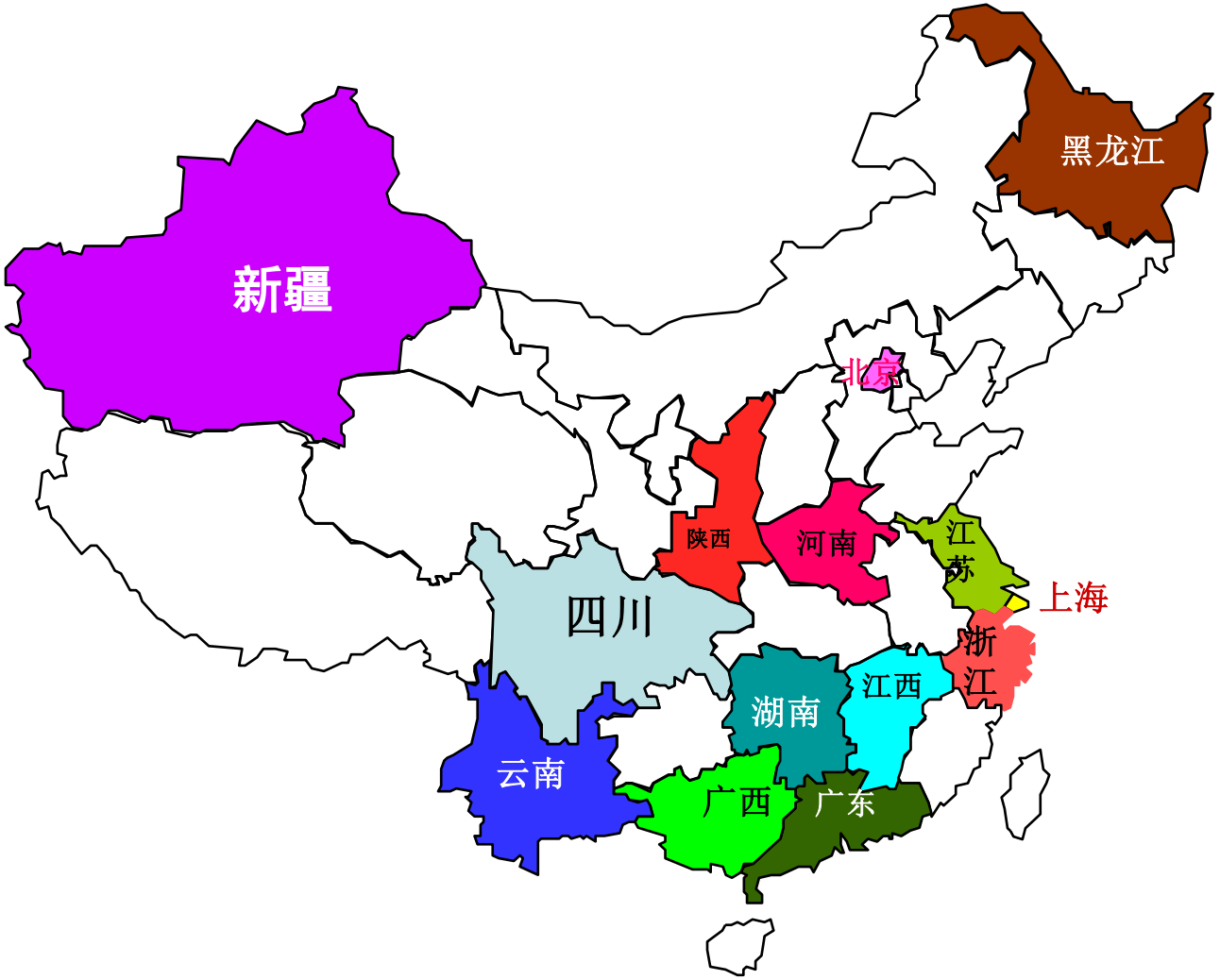
MTB是HIV患者血流感染的重要病原体

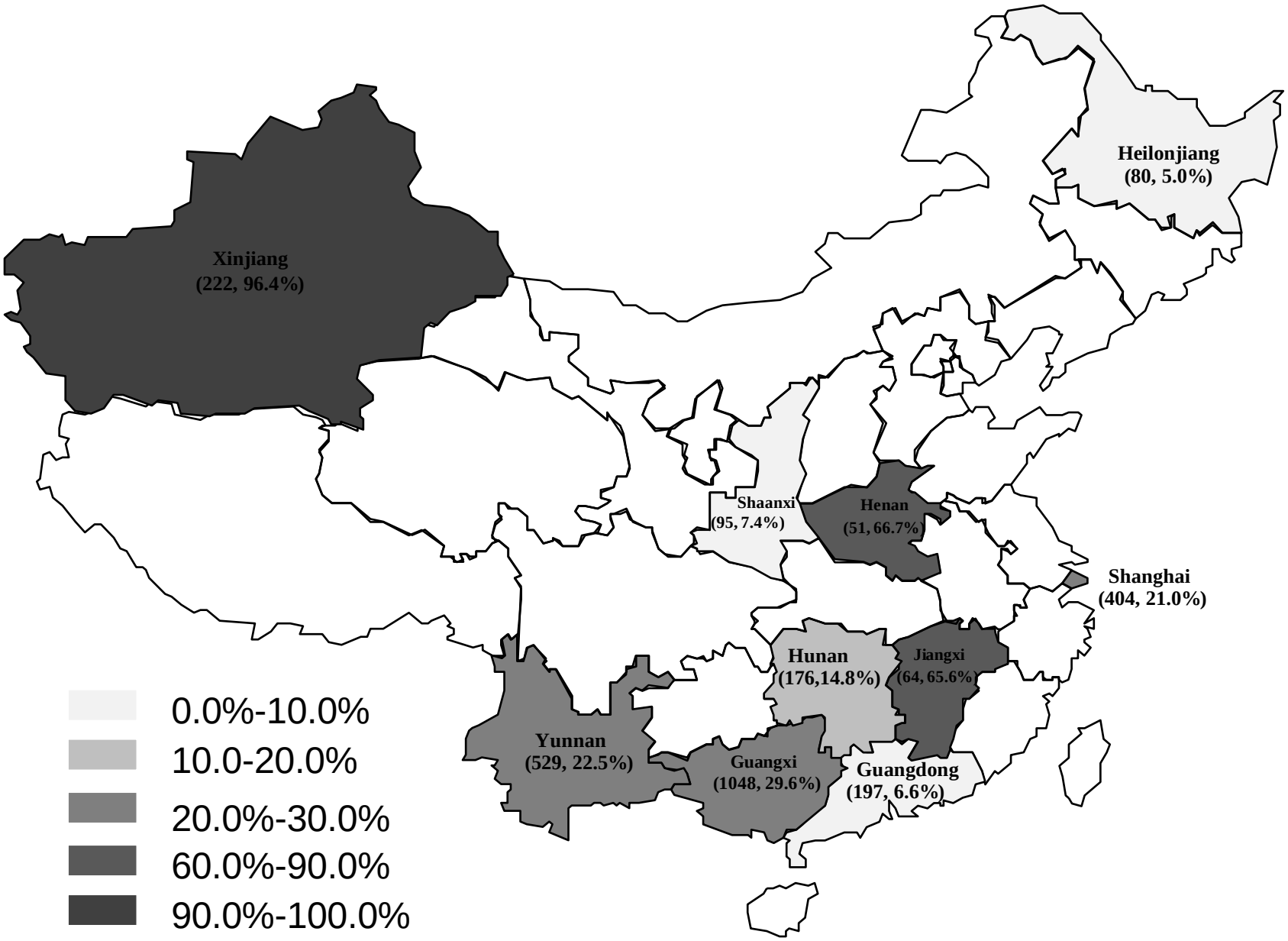
- **Among 2442 Chinese HIV inpatients, 229 (9.38 %) experienced BSIs.**



Qi T, Zhang R, Shen Y, et al. Eur J Clin Microbiol Infect Dis. 2016 Nov;35(11):1767-1770.

艾滋病合并结核病重大专项参与单位





Unpublished data

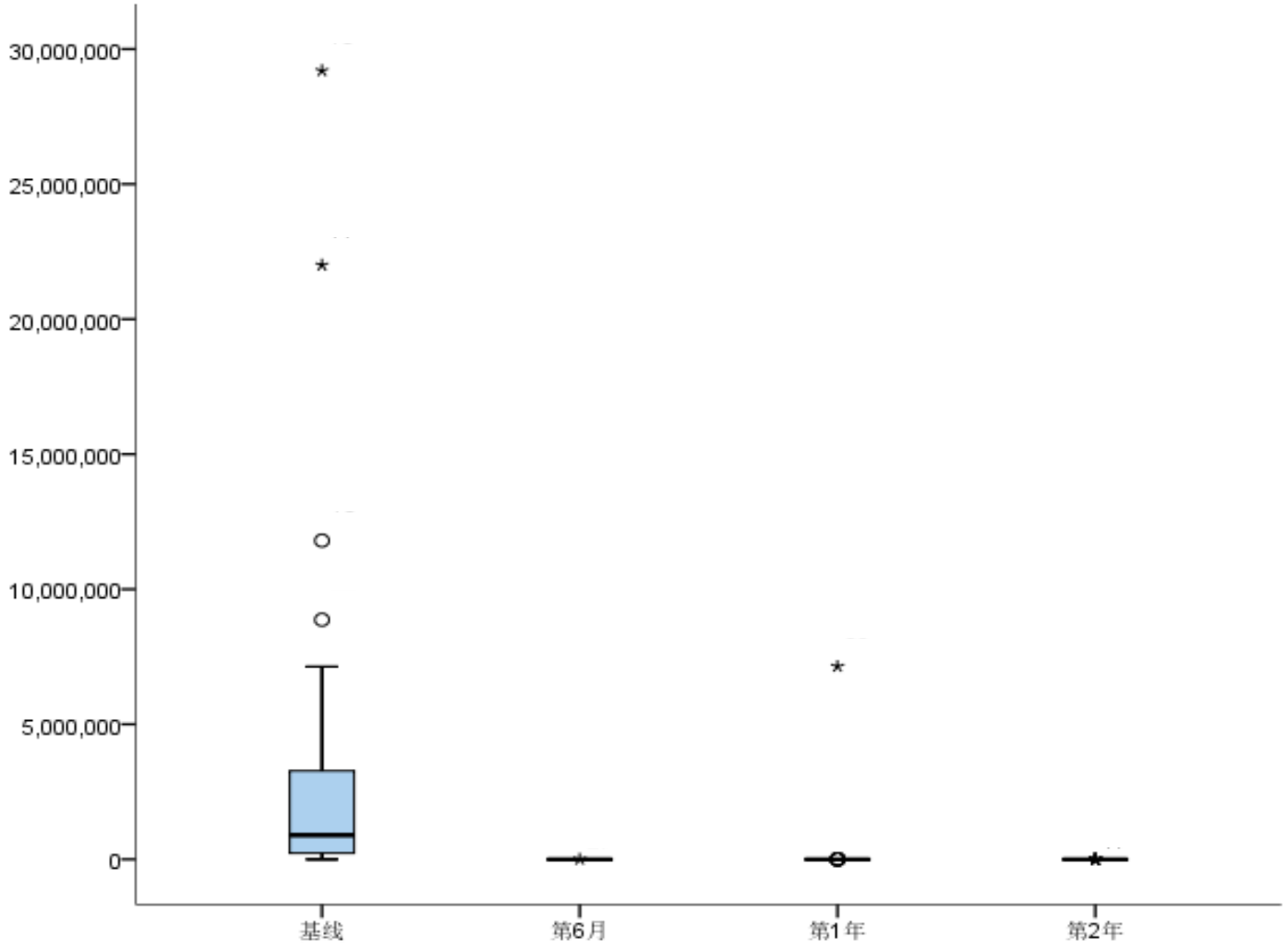
研究目的

- 分析艾滋病合并结核病患者长期疗效，明确HIV相关结核病长期随访的结局。
- 明确艾滋病合并结核病抗病毒和抗结核治疗的近期和远期疗效以及不良反应，为“双感”患者的管理提供实践依据。

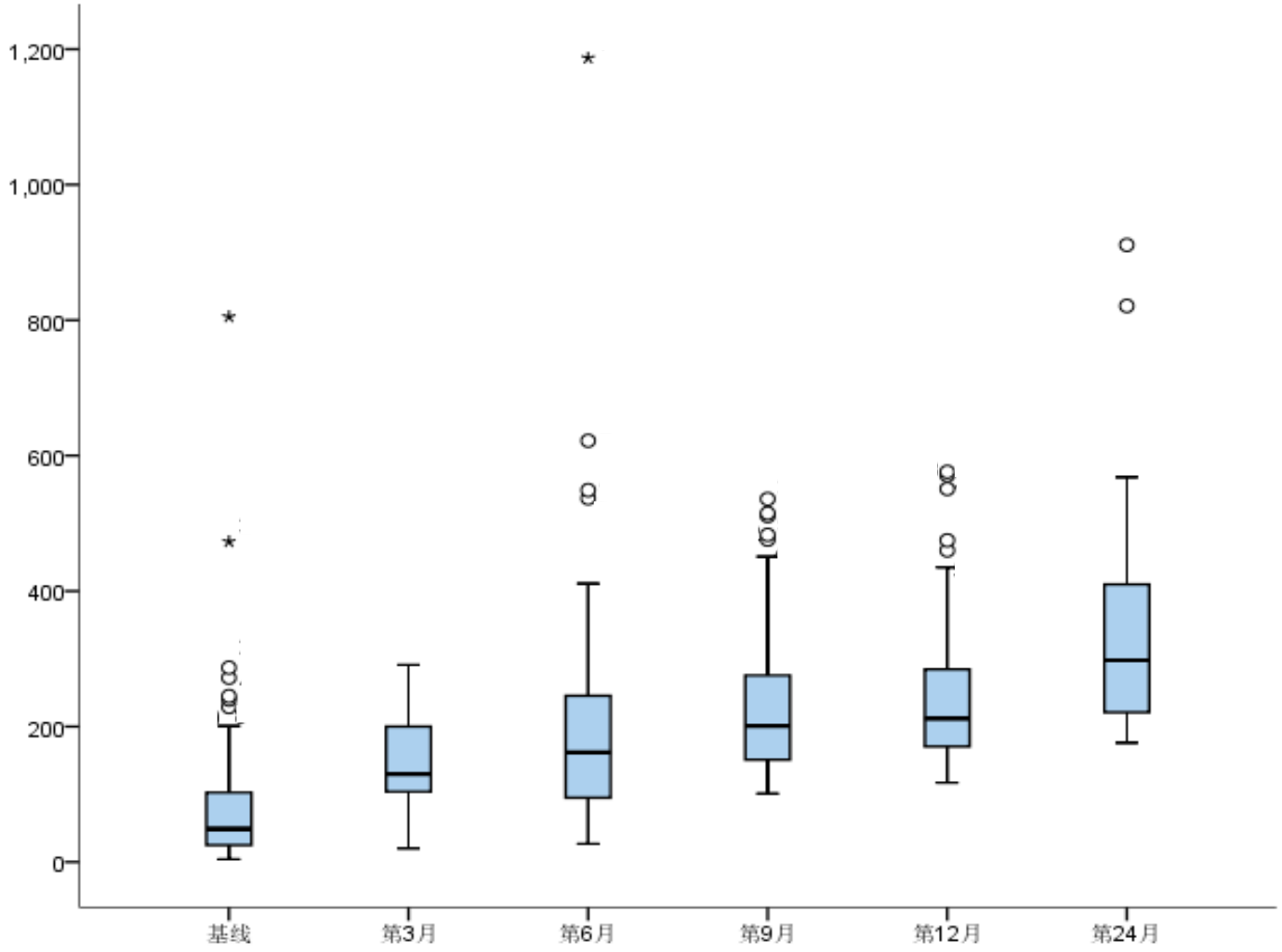
研究方法

- 对国家十二五艾滋病合并结核病重大科技专项入组的艾滋病合并结核病患者进行长期随访。
- 所有患者在知情同意后均给予2HREZ/4HR抗结核治疗，抗结核治疗2周开始启动ART，初始ART方案为TDF+3TC+EFV,治疗过程中按照研究方案进行随访和观察。
- 记录临床症状、伴随疾病、抗病毒和抗结核疗效并进行相应的实验室检测及影像学检查。
- 抗病毒疗效评价按照病毒抑制的比例，首次病载检测在ART治疗6月时进行，以后每年一次。
- 抗结核疗效按照WHO疗效评估标准进行（痰涂片和培养）。
- 使用SPSS 23.0 来输入和分析数据。

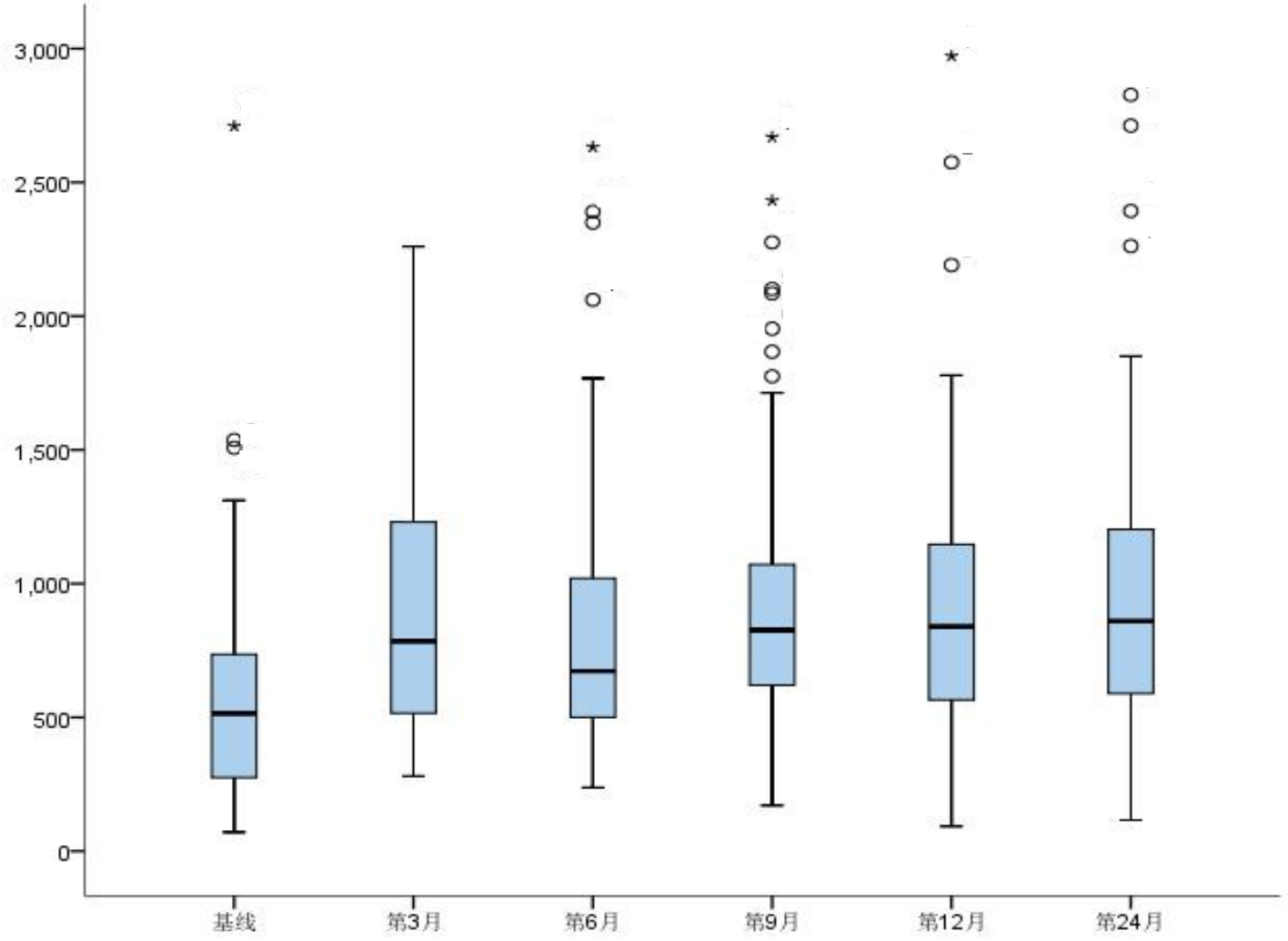
研究结果–病毒抑制情况


30,000,000
25,000,000
20,000,000
15,000,000
10,000,000
5,000,000
0
基线
第6月
第1年
第2年

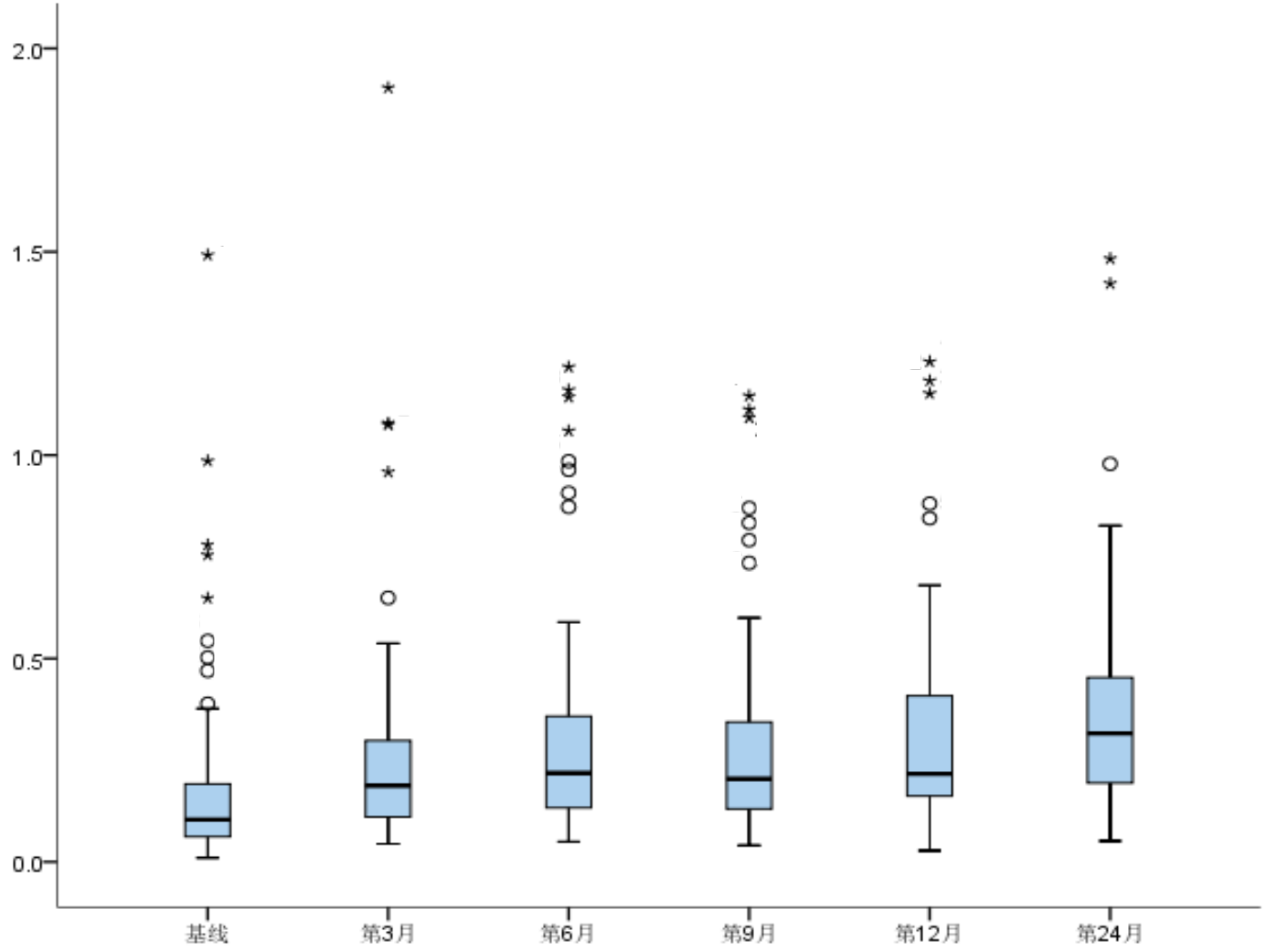
研究结果–$CD4^+$T细胞的动态变化



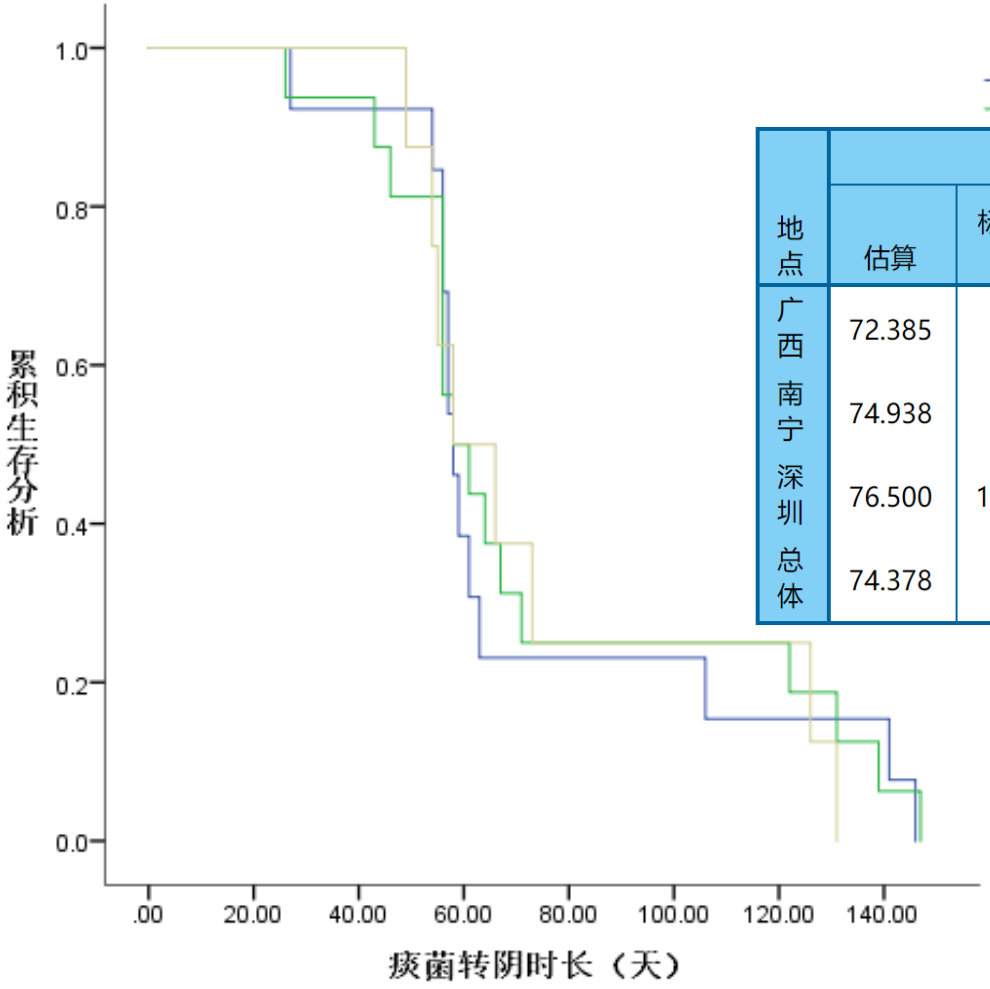
研究结果-$CD8^+$T细胞的动态变化



研究结果-CD4/CD8比值的变化

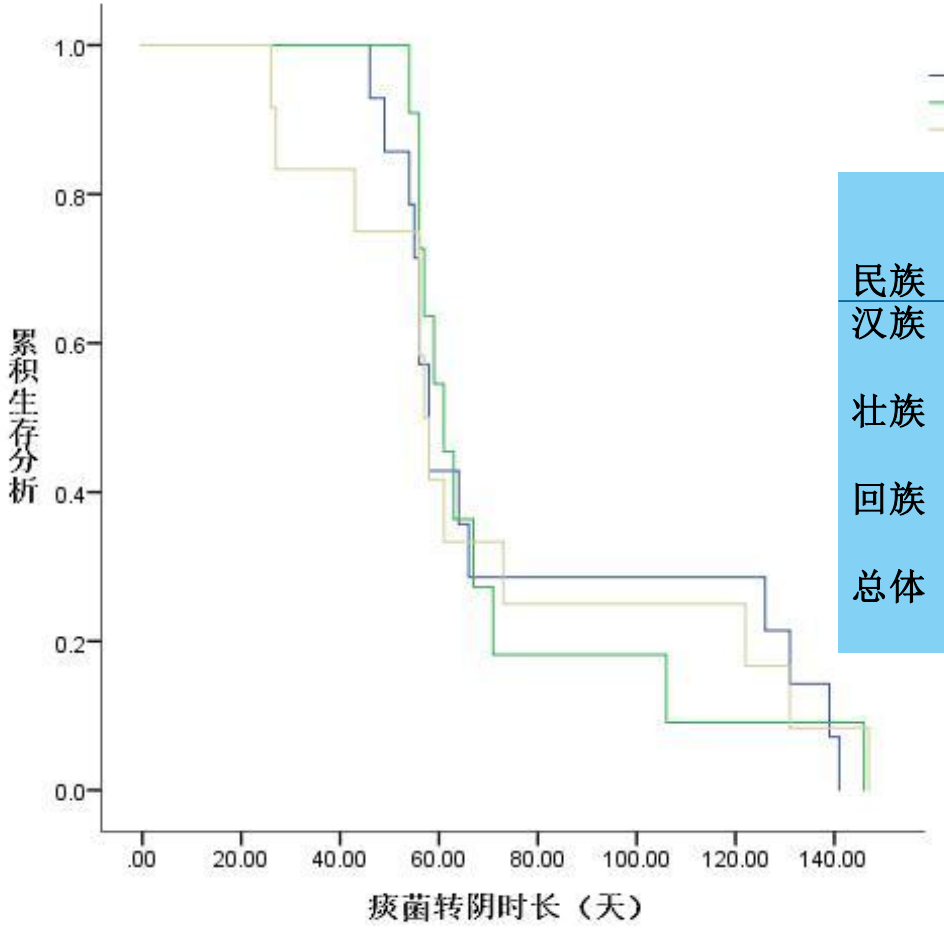


研究结果–痰菌转阴（1）



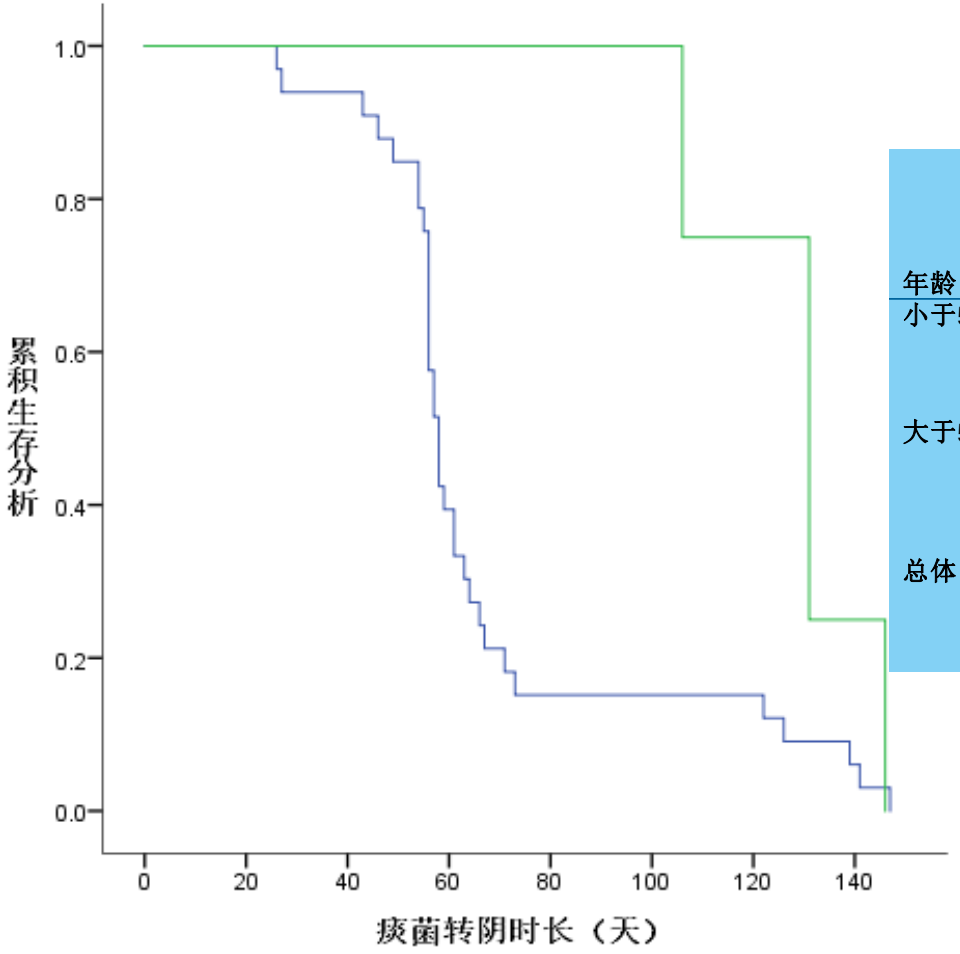
地点	平均值[a]				中位数			
	估算	标准误差	95% 置信区间		估算	标准误差	95% 置信区间	
			下限	上限			下限	上限
广西	72.385	9.893	52.994	91.776	58.000	1.348	55.358	60.642
南宁	74.938	9.359	56.594	93.281	58.000	5.000	48.200	67.800
深圳	76.500	11.657	53.652	99.348	58.000	7.778	42.755	73.245
总体	74.378	5.747	63.114	85.642	58.000	2.027	54.027	61.973

研究结果–痰菌转阴（2）



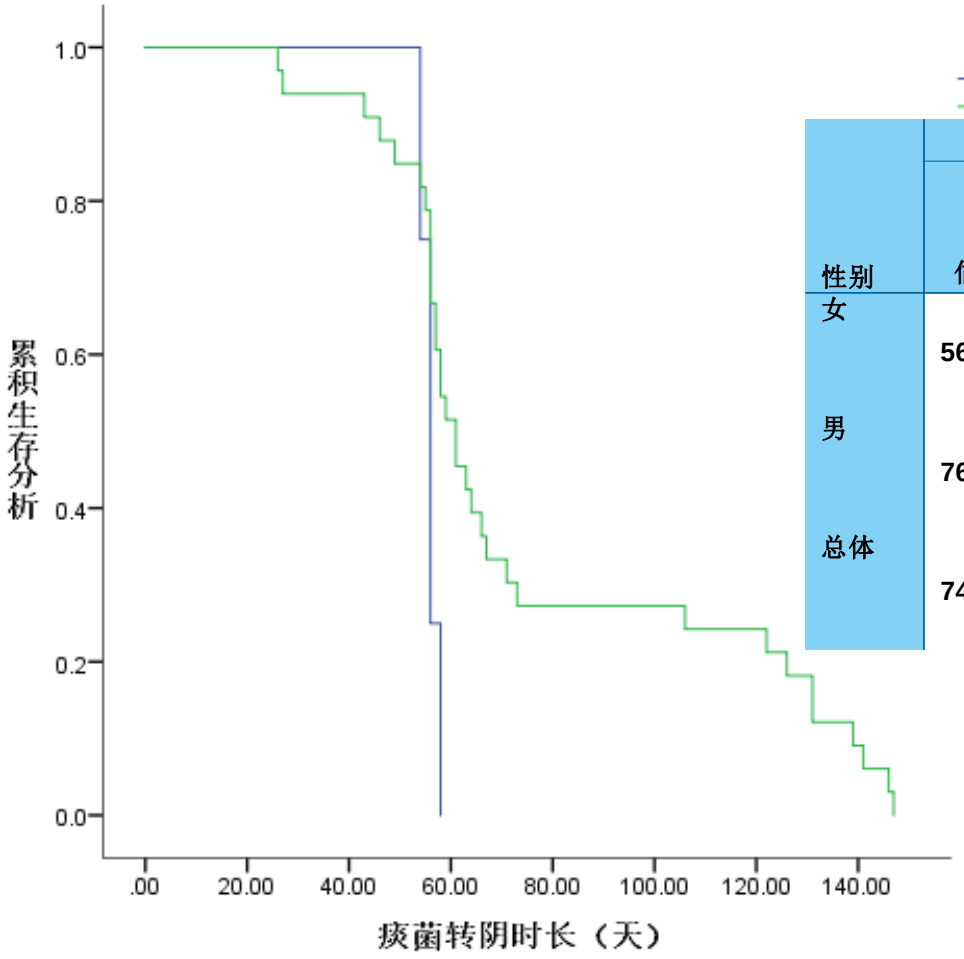
民族	平均值[a]				中位数			
	估算	标准误差	95% 置信区间		估算	标准误差	95% 置信区间	
			下限	上限			下限	上限
汉族	78.500	9.911	59.074	97.926	58.000	1.852	54.371	61.629
壮族	72.364	8.575	55.556	89.171	61.000	3.303	54.526	67.474
回族	71.417	11.560	48.760	94.074	57.000	1.732	53.605	60.395
总体	74.378	5.747	63.114	85.642	58.000	2.027	54.027	61.973

研究结果–痰菌转阴（3）



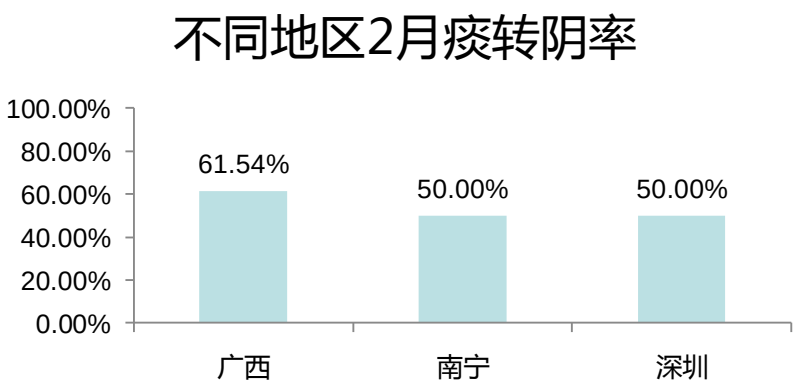
年龄	平均值[a]				中位数			
	估算	标准误差	95% 置信区间		估算	标准误差	95% 置信区间	
			下限	上限			下限	上限
小于50	67.818	5.333	57.366	78.270	58.000	1.136	55.774	60.226
大于50	128.500	8.292	112.249	144.751	131.000	10.825	109.782	152.218
总体	74.378	5.747	63.114	85.642	58.000	2.027	54.027	61.973

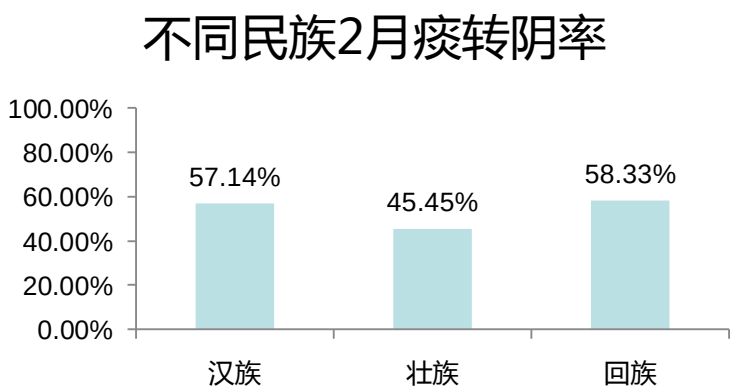
研究结果–痰菌转阴（4）

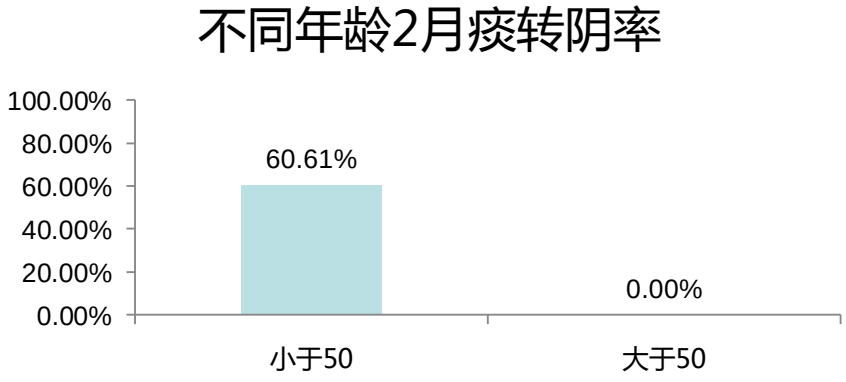


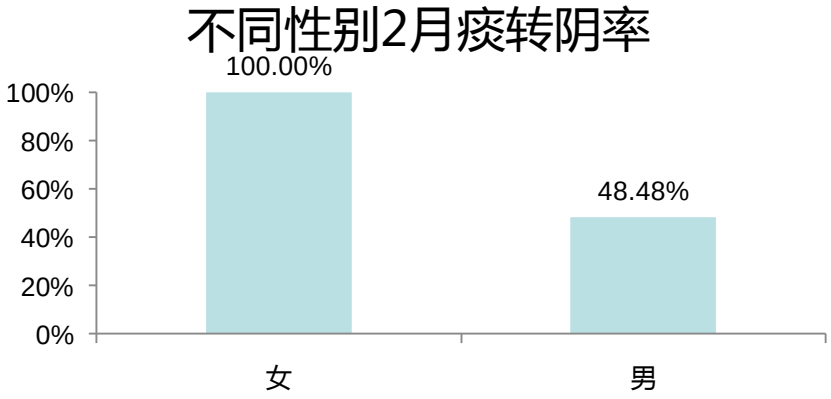
性别	平均值[a]				中位数			
	估算	标准误差	95% 置信区间		估算	标准误差	95% 置信区间	
			下限	上限			下限	上限
女	56.000	.816	54.400	57.600	56.000	.866	54.303	57.697
男	76.606	6.342	64.176	89.036	61.000	2.860	55.394	66.606
总体	74.378	5.747	63.114	85.642	58.000	2.027	54.027	61.973

研究结果–痰菌转阴（5）


不同地区2月痰转阴率
100.00%
80.00%
60.00%
40.00%
20.00%
0.00%
61.54%
50.00%
50.00%
广西
南宁
深圳


不同民族2月痰转阴率
100.00%
80.00%
60.00%
40.00%
20.00%
0.00%
57.14%
45.45%
58.33%
汉族
壮族
回族


不同年龄2月痰转阴率
100.00%
80.00%
60.00%
40.00%
20.00%
0.00%
60.61%
0.00%
小于50
大于50


不同性别2月痰转阴率
100%
80%
60%
40%
20%
0%
100.00%
48.48%
女
男

研究结果-抗结核治疗疗程

地区		实际强化期（天）	实际巩固期时长	实际总治疗时间
1.00	平均值	73.07	230.7381	303.8095
	中位数	70.00	194.0000	260.5000
	标准差	22.823	119.90567	125.53772
	个案数	42	42	42
2.00	平均值	128.97	320.6897	449.6552
	中位数	109.00	365.0000	444.0000
	标准差	71.311	132.49935	123.58984
	个案数	29	29	29
3.00	平均值	149.60	332.8000	482.4000
	中位数	135.50	363.0000	462.0000
	标准差	77.352	161.16506	143.82489
	个案数	10	10	10
总计	平均值	102.53	275.5432	378.0741
	中位数	76.00	246.0000	359.0000
	标准差	60.876	136.51997	147.86284
	个案数	81	81	81

ANOVA 表

			平方和	自由度	均方	F	显著性
实际强化期（天）*地区	组间	（组合）	78870.022	2	39435.011	14.136	.000
	组内		217596.151	78	2789.694		
	总计		296466.173	80			
实际巩固期时长*地区	组间	（组合）	176206.173	2	88103.086	5.227	.007
	组内		1314809.926	78	16856.538		
	总计		1491016.099	80			
实际总治疗时间*地区	组间	（组合）	489070.128	2	244535.064	15.138	.000
	组内		1260003.428	78	16153.890		
	总计		1749073.556	80			

研究结果–抗结核治疗疗程

			统计	标准误差
实际强化期（天）	平均值		102.53	6.764
	平均值的 95% 置信区间	下限	89.07	
		上限	115.99	
	5% 剪除后平均值		96.85	
	中位数		76.00	
	方差		3705.827	
	标准差		60.876	
	最小值		25	
	最大值		350	
	全距		325	
	四分位距		70	
	偏度		1.694	.267
	峰度		3.028	.529
实际巩固期时长	平均值		275.5432	15.16889
	平均值的 95% 置信区间	下限	245.3562	
		上限	305.7303	
	5% 剪除后平均值		272.8203	
	中位数		246.0000	
	方差		18637.701	
	标准差		136.51997	
	最小值		41.00	
	最大值		592.00	
	全距		551.00	
	四分位距		225.50	
	偏度		.332	.267
	峰度		-.986	.529

			统计	标准误差
实际总治疗时间	平均值		378.0741	16.42920
	平均值的 95% 置信区间	下限	345.3789	
		上限	410.7692	
	5% 剪除后平均值		371.8059	
	中位数		359.0000	
	方差		21863.419	
	标准差		147.86284	
	最小值		144.00	
	最大值		770.00	
	全距		626.00	
	四分位距		241.00	
	偏度		.472	.267
	峰度		-.608	.529

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END TB

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Epidemiology

Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). Millions of people continue to fall sick with TB each year.

In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million)[2] among HIV-negative people and there were an additional 300 000 deaths from TB (range, 266 000–335 000) among HIV-positive people.[3]

Drug-resistant TB continues to be a public health crisis. The best estimate is that, worldwide in 2017, 558 000 people (range, 483 000–639 000) developed TB that was resistant to rifampicin (RR-TB), the most effective first-line drug, and of these, 82% had multidrug-resistant TB (MDR-TB).[5] Three countries accounted for almost half of the world's cases of MDR/RR-TB: India (24%), China (13%) and the Russian Federation (10%).

Globally, 3.5% of new TB cases and 18% of previously treated cases had MDR/RR-TB.

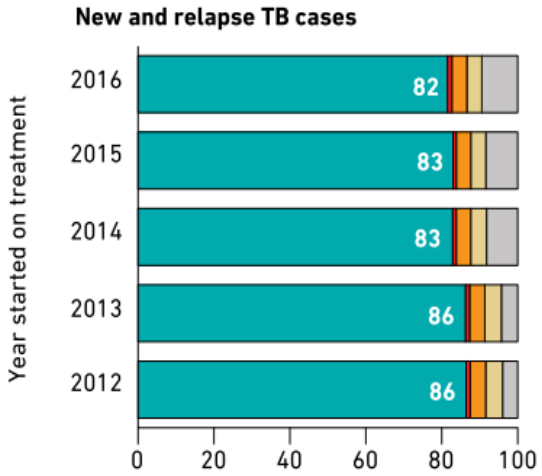
In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million)[2] among HIV-negative people and there were an additional 300 000 deaths from TB (range, 266 000–335 000) among HIV-positive people.[3]

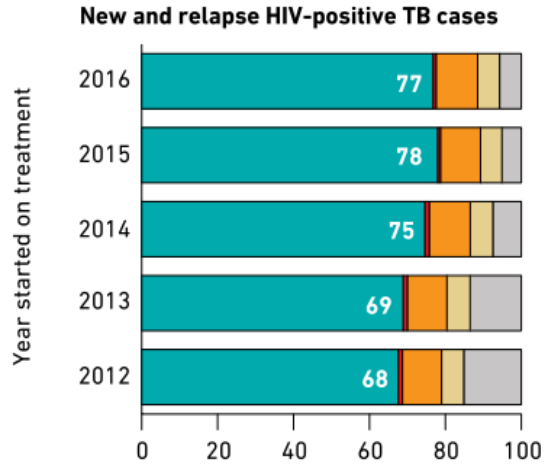
Globally, the best estimate is that 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017: 5.8 million men, 3.2 million women and 1.0 million children. There were cases in all countries and age groups, but overall 90% were adults (aged ≥15 years), 9% were people living with HIV (72% in Africa) and two thirds were in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). These and 22 other countries in WHO's list of 30 high TB burden countries accounted for 87% of the world's cases.[4] Only 6% of global cases were in the WHO European Region (3%) and WHO Region of the Americas (3%).

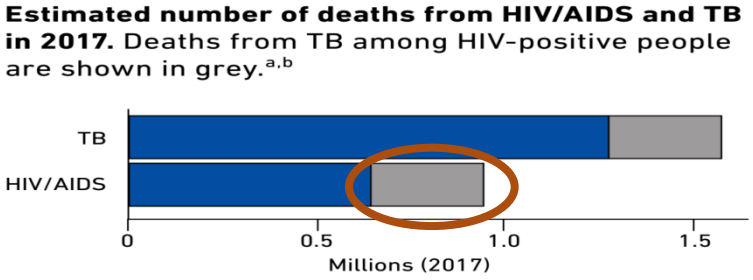
About 1.7 billion people, 23% of the world's population, are estimated to have a latent TB infection, and are thus at risk of developing active TB disease during their lifetime.

In 2016, 6.3 million new cases of TB were reported (up from 6.1 million in 2015), equivalent to 61% of the estimated incidence of 10.4 million; the latest treatment outcome data show a global treatment success rate of 83%, similar to recent years. There were 476 774 reported cases of HIV-positive TB (46% of the estimated incidence), of whom 85% were on antiretroviral therapy (ART). A total of 129 689 people were started on treatment for drug-resistant TB, a small increase from 125 629 in 2015 but only 22% of the estimated incidence; treatment success remains low, at 54% globally.

Globally, treatment success has increased slightly in recent years







[a] For HIV/AIDS, the latest estimates of the number of deaths in 2017 that have been published by UNAIDS are available at http://www.unaids.org/en/resources/publications/all (accessed 15 August 2018). For TB, the estimates for 2017 are those published in this report.

[b] Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International classification of diseases.

Treatment success | Failure | Died | Lost to follow-up | Not evaluated | No data reported

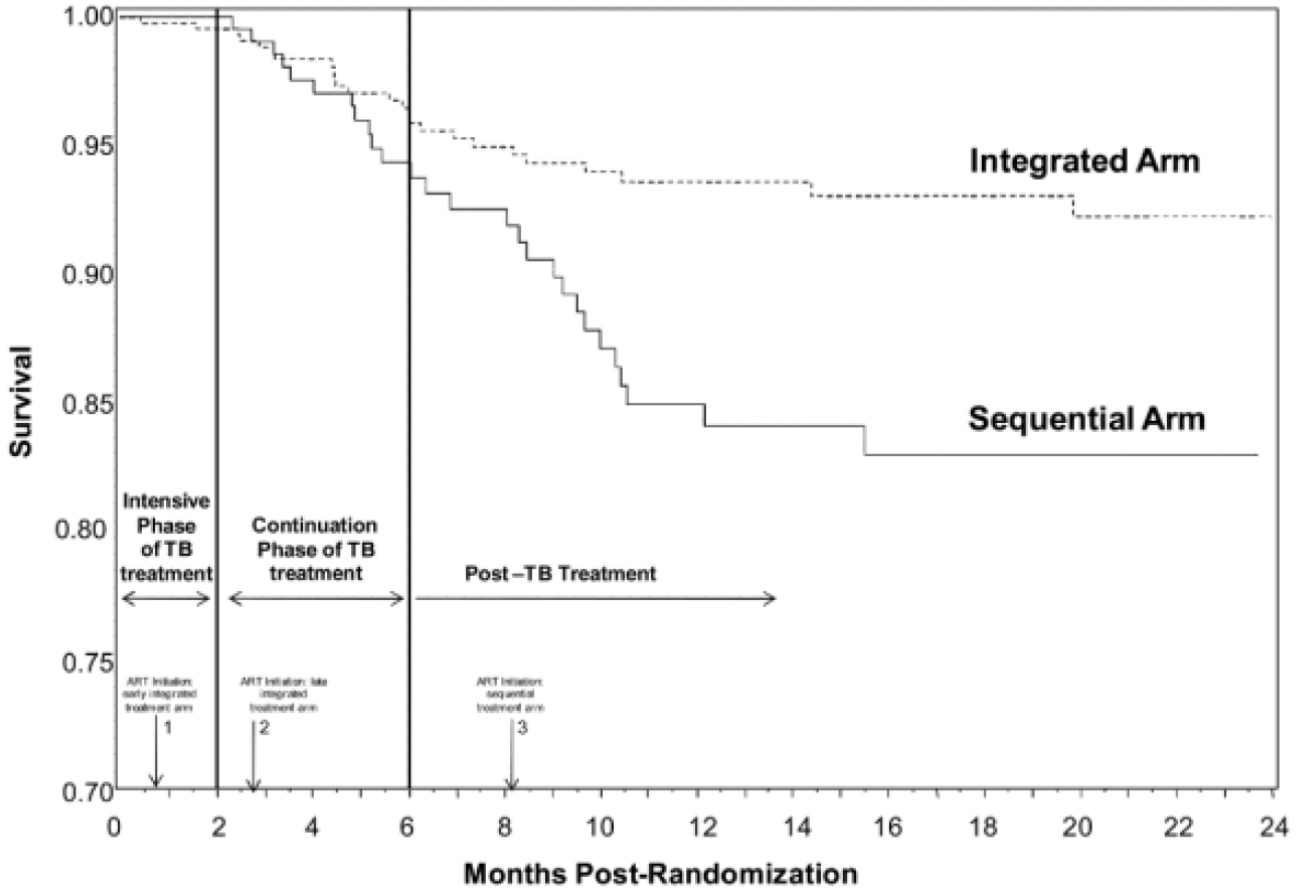
Global Tuberculosis Report 2018

Globally in 2016, 57% of notified TB patients had a documented HIV test result, up from 55% in 2015. In the WHO African Region, where the burden of HIV-associated TB is highest, 82% of TB patients had a documented HIV test result (up from 81% in 2015).

The treatment success rate for HIV-associated TB (2015 cohort) was 78% and for extensively drug-resistant TB (XDR-TB) (2014 cohort) it was 30%.

SAPiT Trial

- The median duration of follow-up in the trial was 12.1 months (interquartile range: 6.1–21.6 months).



Abdool Karim SS, et al. Timing of initiation of antiretroviral drugs during tuberculosis therapy. N Engl J Med. Feb 25 2010;362(8):697-706

SAPiT trial: Clinical outcomes from tuberculosis and HIV treatment

	Treatment arm				Integrated vs sequential treatment arm p-value
	Integrated n=343		Sequential n=171		
Tuberculosis treatment outcomes[1]	Retreatment tuberculosis	First episode tuberculosis	Retreatment tuberculosis	First epsode tuberculosis	
Tuberculosis cured[2]	67 (57.8%)	131 (57.7%)	31 (53.5%)	67 (59.3%)	1.00
Tuberculosis treatment successfully completed[3]	16 (13.8%)	42 (18.5%)	5 (8.6%)	16 (14.2%)	0.20
Treatment success (Tuberculosis cure + successful tuberculosis treatment completion)	83 (71.6%)	173 (76.2%)	36 (62.1%)	83 (73.5%)	0.07
Died prior to tuberculosis treatment completion	7 (6.0%)	12 (5.3%)	6 (10.3%)	9 (8.0%)	0.19
Treatment interruption	2 (1.7%)	3 (1.3%)	3 (5.2%)	7 (6.2%)	0.0096
Treatment failure	0	0	0	1 (0.9%)	0.33
Loss to follow-up prior to Tuberculosis treatment outcome	13 (11.2%)	13 (5.7%)	6 (10.3%)	6 (5.3%)	1.00
Transferred to other clinics - Tuberculosis treatment outcome not known	1 (0.9%	5 (2.2%)	2 (3.5%)	1 (0.9%)	1.00
Other outcome	1 (0.9%)	1 (0.4%)	0	0	
Tuberculosis treatment outcome pending (still on treatment at time of analysis)	9 (7.8%)	20 (8.8%)	5 (8.6%)	6 (5.3%)	0.49
HIV treatment outcomes					
At 12 months post-randomization:					
Proportion with viral load <400 copies/ml (95% CI)	90% (199/221) (85.1 to 93.5)		77.8% (70/90) (67.6 to 85.6)		0.006
Mean CD4 count increase from baseline cells/mm3 (95% CI)	148.7 (N=207) (130.5 to 166.9)		100.7 (N=84) (77.5 to 124.0)		0.004
At 6 months post-antiretroviral therapy initiation:					
Proportion with viral load <400 copies/ml (95% CI)	91.1% (174/191) (85.9 to 94.6)		86.7% (39/45) (72.5 to 94.5)		0.40
Mean CD4 count increase from baseline cells/mm3 (95% CI)	124.2 (N=187)(105.4 to 143.1)		116.3 (N=41) (88.0 to 144.6)		0.71

[1] This tuberculosis treatment outcome analysis only includes patients who were enrolled at least 7 months prior to the date of analysis

[2] Tuberculosis cure = acid-fast bacilli smear negative close to time of tuberculosis treatment completion

[3] Tuberculosis treatment successfully completed = consumed more than 85% of their prescribed tuberculosis medication

N Engl J Med. 2011 October 20; 365(16): 1471–1481. doi:10.1056/NEJMoa1013911.

Earlier versus Later Start of Antiretroviral Therapy in HIV-Infected Adults with Tuberculosis

TUBERCULOSIS OUTCOMES

The median duration of tuberculosis treatment was 26.0 weeks (interquartile range, 25.8 to 26.9) in the earlier-ART group and 26.0 weeks (interquartile range, 25.7 to 26.4) in the later-ART group (P = 0.13). When tuberculosis treatment ended, there was no significant difference between the two groups with regard to tuberculosis outcomes (see the Supplementary Appendix). Recurrence of tuberculosis was observed in 22 patients: 8 in the earlier-ART group and 14 in the later-ART group (P = 0.11).

VIROLOGIC RESPONSE AND IMMUNE RECONSTITUTION

ART was initiated in 319 of 332 patients (96%) in the earlier-ART group at a median of 14 days after the onset of tuberculosis treatment (interquartile range, 14 to 15) and in 300 of 329 patients (91%) in the later-ART group at a median time of 56 days (interquartile range, 56 to 57). At week 50, the viral load was undetectable in 96.5% of patients, with no difference between the two study groups (P = 0.82), whereas the median gain in the CD4+ T-cell count was 118 per cubic millimeter (interquartile range, 67 to 191) in the earlier-ART group and 112 per cubic millimeter (interquartile range, 53 to 175) in the later-ART group (P = 0.22). At all subsequent follow-up times, there was no difference between the groups in the percentage of patients with an undetectable viral load (which remained consistently above 95%) or in the median CD4+ T-cell count (Fig. 3).

The median duration of follow-up was 25 months

Clin Infect Dis. 2019 Mar 28. pii: ciz256. doi: 10.1093/cid/ciz256. [Epub ahead of print]

Dolutegravir-Based Antiretroviral Therapy for Patients Co-Infected with Tuberculosis and Hiv: A Multicenter, Noncomparative, Open-Label, Randomized Trial.

Abstract

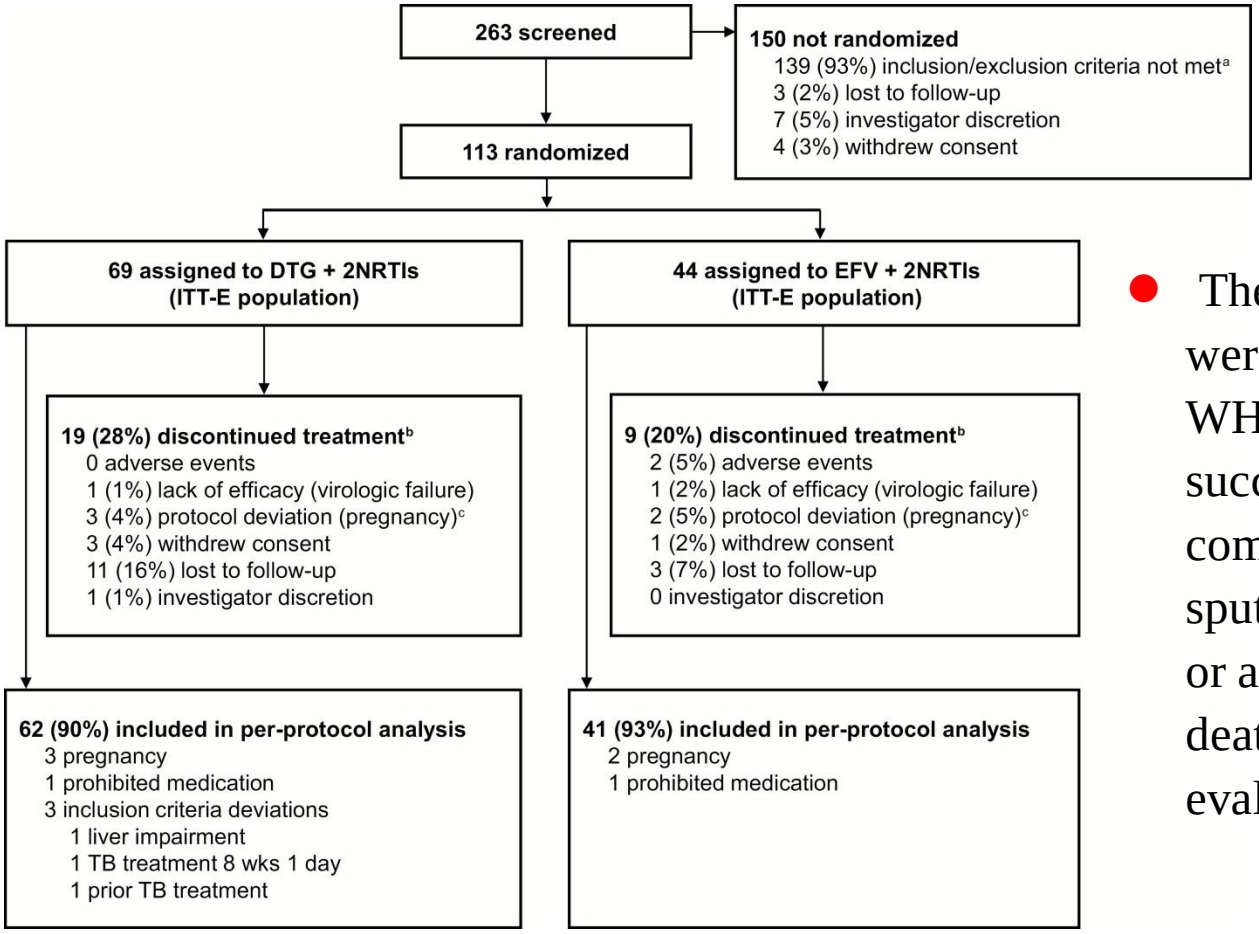
BACKGROUND: Concurrent treatment of tuberculosis and HIV is challenging owing to drug interactions, overlapping toxicities, and immune reconstitution inflammatory syndrome (IRIS). The efficacy and safety of dolutegravir were assessed in adults with HIV and drug-susceptible tuberculosis.

METHODS: INSPIRING (NCT02178592) is a non-comparative, active-control, randomised, open-label study in HIV-1-infected ART-naïve adults (CD4+ 50 cells/mm3). Participants on rifampicin-based tuberculosis treatment ≤8 weeks were randomised (3:2) to receive dolutegravir (50 mg twice-daily during and 2 weeks post-tuberculosis therapy, then 50 mg once-daily) or efavirenz (600 mg daily), with two NRTIs for 52 weeks. The primary endpoint was the proportion of dolutegravir-arm participants with plasma HIV-1-RNA <50 copies/mL (responders) by FDA Snapshot algorithm (intent-to-treat exposed population) at Week 48. The study was not powered to compare arms.

RESULTS: For dolutegravir (N=69), Baseline HIV-1-RNA was >100,000 copies/mL in 64%, with median CD4+ 208 cells/mm3; for efavirenz (N=44), 55% had HIV-1-RNA >100,000 copies/mL, median CD4+ count was 202 cells/mm3. Week 48 response rate was 75% (52/69) (95% CI: 65%, 86%) for dolutegravir and 82% (36/44) (95% CI: 70%, 93%) for efavirenz. Dolutegravir non-response was driven by non-treatment-related discontinuations (n=10 lost-to-follow-up). There were no deaths or study drug switches. There were two discontinuations for toxicity (efavirenz). There were three protocol-defined virological failures (2 dolutegravir, no acquired resistance; 1 efavirenz, NRTI and NNRTI emergent resistance). Tuberculosis treatment success was high. TB-associated IRIS was uncommon (4/arm), with no discontinuations for IRIS.

CONCLUSIONS: Among adults with HIV receiving rifampicin-based tuberculosis treatment, twice-daily dolutegravir was effective and well-tolerated.

Figure 1. Trial profile. Abbreviations: DTG, dolutegravir; EFV, efavirenz; HIV-1, human immunodeficiency virus–1; ...



- The TB treatment outcomes were defined, in accordance with WHO guidelines, as treatment success (cure or treatment completion), failure (positive sputum acid-fast bacilli smear at or after 5 months of treatment), death, loss to follow-up, or not evaluated (eg, transferred out).

Clinical Infectious Diseases, ciz256, https://doi.org/10.1093/cid/ciz256

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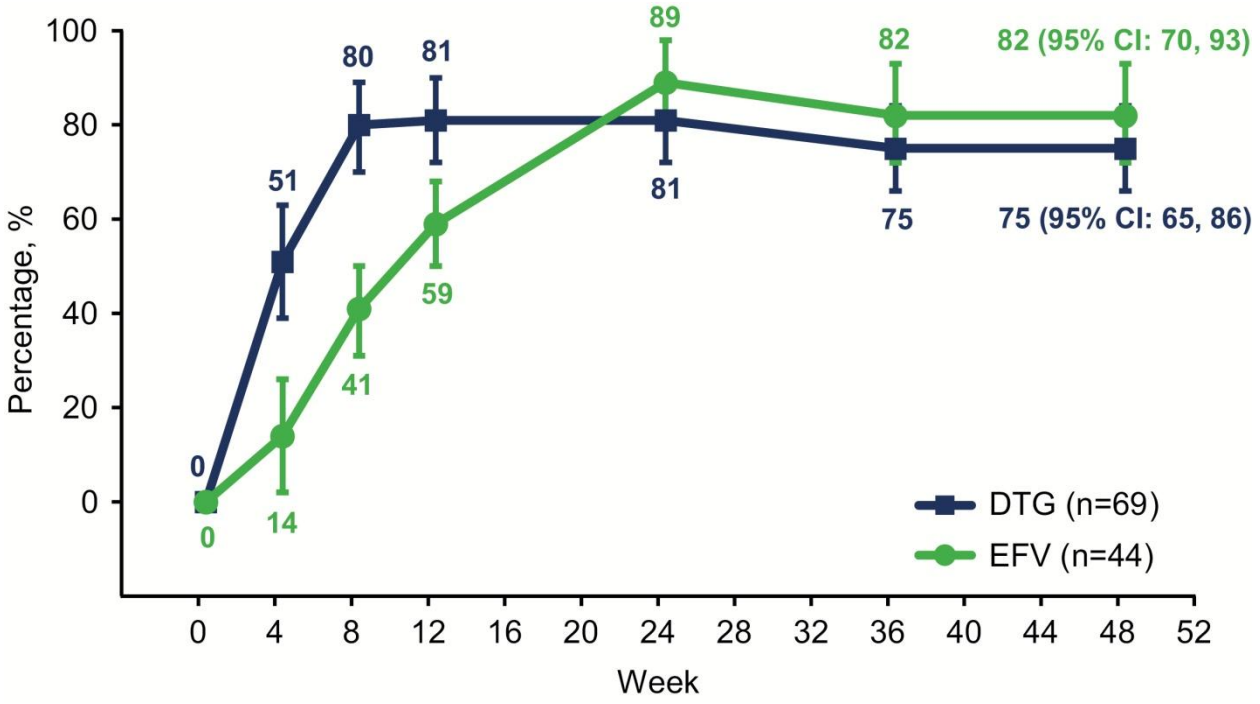
Figure 2. Proportion of participants in the ITT-E population with Snapshot HIV-1 RNA ≤50 copies/mL, by week following ...



- In the DTG arm, 88% of participants achieved TB treatment success, with no treatment failures. In the EFV arm, 91% of participants had treatment success and 1 patient had a treatment failure (positive cultures at months 4 and 6 and a negative culture at 9 months).
- Adverse events were common (75% in the DTG arm and 91% in the EFV arm). Grade 3 or 4 adverse events and serious adverse events were rare.

Clinical Infectious Diseases, ciz256, https://doi.org/10.1093/cid/ciz256

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Efficacy and Safety of Once-Daily Nevirapine- or Efavirenz-Based Antiretroviral Therapy in HIV-Associated Tuberculosis: A Randomized Clinical Trial

Results. A total of 116 patients (75% [87 patients] of whom had pulmonary TB), with a mean age of 36 years, a median CD4+ cell count of 84 cells/mm^3, and a median viral load of 310 000 copies/mL, were randomized. At 24 weeks, 50 of 59 patients in the EFV group and 37 of 57 patients in the NVP group had virological suppression ($P = .024$). There were no deaths, 1 SAE, and 5 treatment failures in the EFV arm, compared with 5 deaths, 2 SAEs, and 10 treatment failures in the NVP arm. The trial was halted by the data and safety monitoring board at the second interim analysis. Favorable TB treatment outcomes were observed in 93% of the patients in the EFV arm and 84% of the patients in the NVP arm ($P = .058$).

Study Endpoints

The primary composite study endpoint was related to the efficacy of the ART regimen at 24 weeks: death, HIV-1 RNA level >400 copies/mL, default, or termination of study drug as a result of toxicity were considered unfavorable. With respect to pulmonary TB, the response was considered favorable if all sputum cultures were negative in the last 2 months of treatment. Unfavorable responses to ATT included failure (clinical or bacteriological), default, or death due to TB. For extra pulmonary TB, favorable response was defined as improvement of symptoms, regression of lymph nodes, and/or radiographic improvement.

Clinical Infectious Diseases 2011;53(7):716–724

TB Relapse in HIV

TABLE 2. TREATMENT OUTCOMES OF PATIENTS ACCORDING TO HIV STATUS

Outcomes	HIV Infected (*n*) (%)	HIV Uninfected/Unknown (*n*) (%)	Relative Risk (*95% CI*)	p Value
No. of subjects	264	436		
Treatment duration				
Months on treatment, mean ± SD	10.2 ± 4.9	8.4 ± 3.5		< 0.001
Received 6 mo of treatment (vs. > 6 mo)	33/196 (16.8)	133/362 (36.7)	0.46 (0.33–0.64)	< 0.001
Bacteriologic outcomes				
Weeks to sputum smear negative, mean ± SD	5.5 ± 5.6	5.6 ± 5.4		0.85
Weeks to sputum culture negative, mean ± SD	8.2 ± 12.4	8.0 ± 7.3		0.86
Converted cultures in 8 wk	129/174 (74.1)	197/303 (65.0)	1.14 (1.01–1.29)	0.04
Outcomes				
All failures	15/202 (7.4)	15/365 (4.1)	1.81 (0.90–3.62)	0.09
All relapses (rate per 100 person-years)	13 (9.31)	3 (0.97)	9.64 (2.75–33.8)	< 0.001
Acquired drug resistance	11 (4.2)	2 (0.5)	9.08 (2.03–40.7)	< 0.001
Adverse drug reaction to treatment	55/258 (21.3)	54/434 (12.4)	1.71 (1.22–2.41)	0.002
Received therapy intermittently	56/255 (22.0)	109/431 (25.3)	0.87 (0.65–1.15)	0.32
Months of follow-up after treatment completion				
Mean ± SD	8.4 ± 6.8	10.1 ± 5.7		0.005
Median (range)	8.5 (0–34.5)	12.0 (0–26.0)		
Died during treatment or follow-up (rate per 100 person-years)	85 (23.5)	27 (4.5)	5.19 (3.37–8.00)	< 0.001
Death due to tuberculosis	13/85 (15.3)	2/27 (7.4)	2.06 (0.50–8.58)	0.52

Nahid P, et al. Treatment outcomes of patients with HIV and tuberculosis. Am J Respir Crit Care Med. Jun 1 2007;175(11):1199-1206

TABLE 3. TREATMENT OUTCOMES OF HIV-INFECTED PATIENTS ACCORDING TO TREATMENT DURATION

Outcomes	Completed in 6 mo (*n*) (%)	Completed in > 6 mo (*n*) (%)	Relative Risk (*95% CI*)	p Value
No. of subjects	33	163		
Characteristics				
$CD4^+$ T lymphocyte count ⩾ 200 cells/mm^3 (28 missing)	19/31 (61.3)	97/137 (70.8)	0.87 (0.64–1.17)	0.30
Received ART during tuberculosis therapy				
HAART	2 (6.1)	28 (17.2)	0.33 (0.07–1.55)	0.16
Single- or dual-drug ART	16 (48.5)	65 (39.9)	1.15 (0.53–2.51)	0.73
None	15 (45.5)	70 (42.9)	(Reference)	1.00
Opportunistic infection	24 (72.7)	84 (51.5)	1.41 (1.09–1.82)	0.03
Cavitary disease	2 (6.1)	16 (9.8)	0.62 (0.15–2.56)	0.74
Received any directly observed therapy	21 (63.6)	128 (78.5)	0.81 (0.62–1.06)	0.07
Adherent to drug regimen	32 (97.0)	70 (42.9)	2.26 (1.87–2.72)	< 0.001
Substance abuse	12 (36.4)	85 (52.2)	0.70 (0.43–1.12)	0.10
Bacteriologic outcomes				
Weeks to sputum smear negative, mean ± SD	5.4 ± 4.2	5.5 ± 5.7		0.93
Weeks to sputum culture negative, mean ± SD	5.8 ± 2.5	8.9 ± 14.5		0.03
Converted cultures in 8 wk	21/25 (84.0)	86/121 (71.1)	1.18 (0.96–1.45)	0.18
Outcomes				
All failures	0	9 (5.5)	0.25 (0.02–4.26)*	0.36
All relapses (rate per 100 person-years)	5 (23.4)	8 (7.04)	3.32 (1.09–10.2)	0.04
Acquired drug resistance	1 (3.0)	4 (2.5)	1.23 (0.14–10.7)	1.00
Adverse drug reaction to treatment	1 (3.0)	36 (22.1)	0.14 (0.02–0.97)	0.01
Received therapy intermittently	7 (21.2)	43 (26.4)	0.80 (0.40–1.63)	0.53
Months of follow-up after treatment completion				
Mean ± SD	7.8 ± 5.4	8.6 ± 7.1		0.55
Median (range)	7.6 (0–16.6)	8.6 (0–34.5)		
Died during follow-up† (rate per 100 person-years)	9 (38.0)	37 (30.3)	1.25 (0.60–2.59)	0.55
Death due to tuberculosis	1/9 (11.1)	2/37 (5.4)	2.06 (0.21–20.2)	0.49

Nahid P, et al. Treatment outcomes of patients with HIV and tuberculosis. Am J Respir Crit Care Med. Jun 1 2007;175(11):1199-1206

Efficacy of a 6-month versus 9-month Intermittent Treatment Regimen in HIV-infected Patients with Tuberculosis

A Randomized Clinical Trial

The outcome of treatment was considered "favorable" if all available (n = 6) sputum cultures were negative during the last 2 months of treatment, for culture-positive pulmonary TB. For extrapulmonary and culture-negative pulmonary TB, outcome was based on resolution of symptoms and signs and regression of lymph nodes and/or radiographic clearance, respectively.

Measurements and Main Results: Of the patients, 70% had culture-positive pulmonary TB; the median viral load was 155,000 copies/ml and the $CD4^+$ cell count was 160 cells/mm^3. Favorable response to antituberculosis treatment was similar by intent to treat (Reg6M, 83% and Reg9M, 76%; P = not significant). Bacteriological recurrences occurred significantly more often in Reg6M than in Reg9M (15 vs. 7%; $P < 0.05$) although overall recurrences were not significantly different (Reg6M, 19% vs. Reg9M, 13%). By 36 months, 36% of patients undergoing Reg6M and 35% undergoing Reg9M had died, with no significant difference between regimens. All 19 patients who failed treatment developed acquired rifamycin resistance (ARR), the main risk factor being baseline isoniazid resistance.

Am J Respir Crit Care Med Vol 181. pp 743–751, 2010

Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

Recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America

- Despite these substantial clinical challenges, co-treatment of HIV-related TB improves survival(particularly for persons with CD4 cell counts <50 cells/μL), decreases the risk of additional opportunistic illnesses, can achieve high rates of viral suppression, may improve TB treatment outcomes, and, despite higher rates of IRIS at low CD4 cell counts, is not associated with higher rates of other treatment-related adverse events.

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Tuberculosis/HIV Coinfection (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

- Selection of a tuberculosis (TB)-preventive treatment for individuals living with HIV and coinfected with latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral therapy (ART) regimen as noted below:
  - Any ART regimen can be used when isoniazid alone is used for LTBI treatment **(AII)**.
  - Only efavirenz (EFV)- or raltegravir (RAL)-based regimens (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used with once-weekly isoniazid plus rifapentine **(AIII)**.
  - If rifampin or rifabutin is used to treat LTBI, clinicians should review Tables 19a through 19e to assess the potential for interactions among different antiretroviral (ARV) drugs and the rifamycins **(BIII)**.
- All patients with both HIV and active TB who are not on ART should be started on ART as described below:
  - **In patients with CD4 counts <50 cells/mm^3:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI)**.
  - **In patients with CD4 counts ≥50 cells/mm^3:** Initiate ART within 8 weeks of starting TB treatment **(AIII)**.
  - **In all pregnant women with HIV:** Initiate ART as early as feasible, for treatment of maternal HIV infection and to prevent mother-to-child transmission (MTCT) of HIV **(AIII)**.
  - **In patients with tuberculous meningitis:** Caution should be exercised when initiating ART early, as high rates of adverse events and deaths have been reported in a randomized trial **(AI)**.
- Rifamycins are critical components of TB treatment regimens and should be included for patients with both HIV and active TB, unless precluded because of TB resistance or toxicity. However, rifamycins have a considerable potential for drug-drug interactions. Clinicians should review Tables 19a through 19e to assess the potential for interactions among different ARV drugs and the rifamycins **(BIII)**.

Initial Characteristics to Consider in All Persons with HIV:

- Pretreatment HIV RNA level (viral load)
- Pretreatment CD4 count
- HIV genotypic drug resistance testing results (based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the reverse transcriptase [RT] and protease [PR] genes. If transmitted INSTI resistance is a concern, providers should consider also testing for resistance mutations to this class of drugs).
- HLA-B*5701 status
- Individual preferences
- Anticipated adherence to the regimen

Specific Comorbidities or Other Conditions:

- Cardiovascular disease, hyperlipidemia, renal disease, liver disease, osteopenia/osteoporosis or conditions associated with BMD loss, psychiatric illness, neurologic disease, drug abuse or dependency requiring narcotic replacement therapy
- Pregnancy or pregnancy potential. Clinicians should refer to the latest Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in The United States (Perinatal Guidelines) for more detailed recommendations on the safety and effectiveness of ARV drugs during pregnancy.
- Coinfections: HBV, hepatitis C virus (HCV), TB

Regimen-Specific Considerations:

- Regimen's genetic barrier to resistance
- Potential adverse effects
- Known or potential drug interactions with other medications (see Drug Interactions)
- Convenience (e.g., pill burden, dosing frequency, availability of fixed-dose combination formulations, food requirements)
- Cost (see Cost Considerations and Antiretroviral Therapy)

FDA Approval of HIV Medicines

1981: First AIDS cases are reported in the United States.

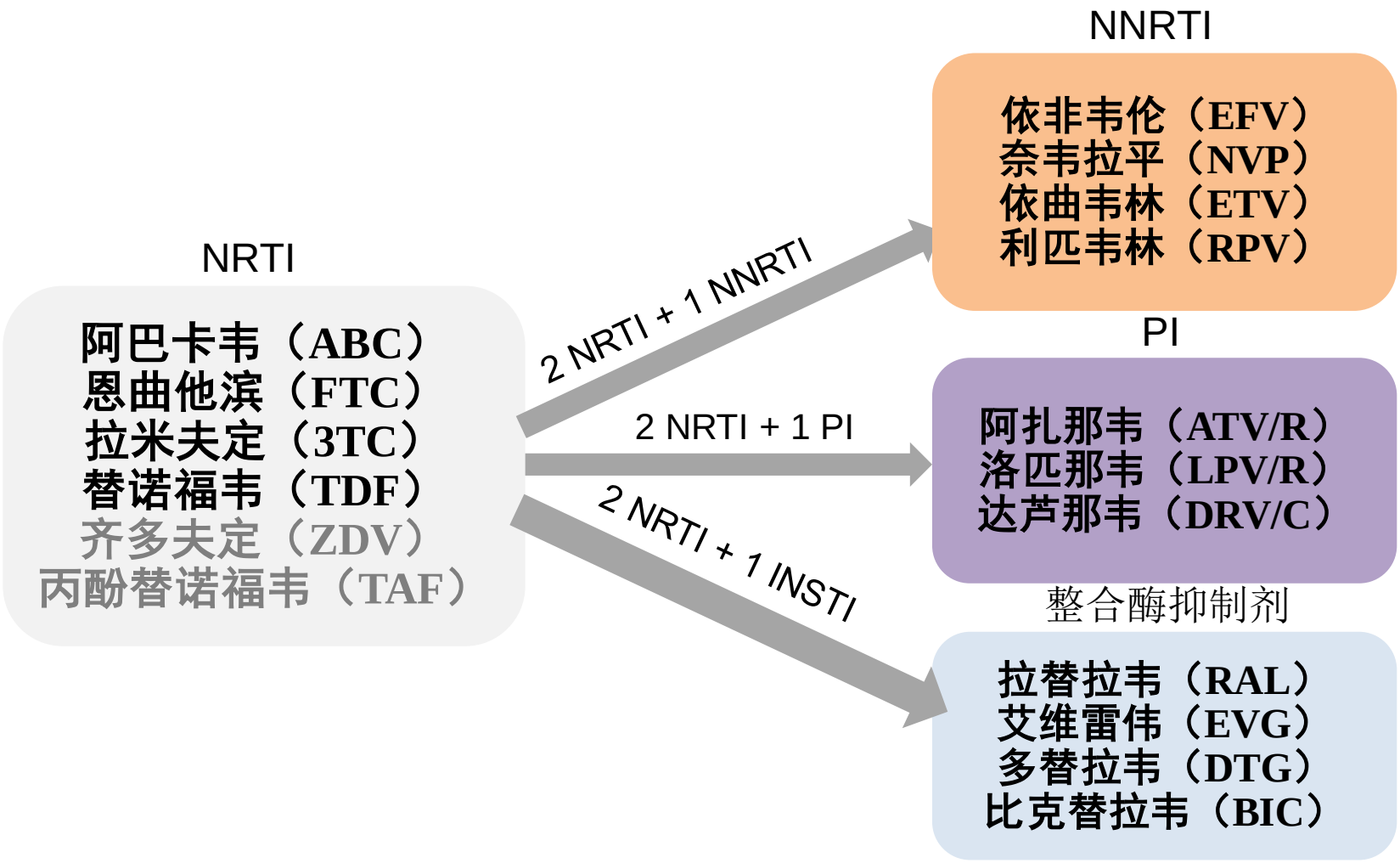
'85-'89	**1987** Zidovudine (NRTI)				
'90-'94	**1991** Didanosine (NRTI)	**1992** Zalcitabine (NRTI)	**1994** Stavudine (NRTI)		
'95-'99	**1995** Lamivudine (NRTI) Saquinavir (PI)	**1996** Indinavir (PI) Nevirapine (NNRTI) Ritonavir (PI)	**1997** Combivir (FDC) Delavirdine (NNRTI) Nelfinavir (PI)	**1998** Abacavir (NRTI) Efavirenz (NNRTI)	**1999** Amprenavir (PI)
'00-'04	**2000** Didanosine EC (NRTI) Kaletra (FDC) Trizivir (FDC)	**2001** Tenofovir DF (NRTI)	**2003** Atazanavir (PI) Emtricitabine (NRTI) Enfuvirtide (FI) Fosamprenavir (PI)	**2004** Epzicom (FDC) Truvada (FDC)	
'05-'09	**2005** Tipranavir (PI)	**2006** Atripla (FDC) Darunavir (PI)	**2007** Maraviroc (CA) Raltegravir (INSTI)	**2008** Etravirine (NNRTI)	
'10-'14	**2011** Complera (FDC) Nevirapine XR (NNRTI) Rilpivirine (NNRTI)	**2012** Stribild (FDC)	**2013** Dolutegravir (INSTI)	**2014** Cobicistat (PE) Elvitegravir (INSTI) Triumeq (FDC)	
'15-'19	**2015** Evotaz (FDC) Genvoya (FDC) Prezcobix (FDC)	**2016** Descovy (FDC) Odefsey (FDC)	**2017** Juluca (FDC)	**2018** Biktarvy (FDC) Cimduo (FDC) Delstrigo (FDC) Doravirine (NNRTI) Ibalizumab-uiyk (PAI) Symfi (FDC) Symfi Lo (FDC) Symtuza (FDC) Temixys (FDC)	**2019** Dovato (FDC)

Drug Class Abbreviations:
CA: CCR5 Antagonist; **FDC:** Fixed-Dose Combination; **FI:** Fusion Inhibitor; **INSTI:** Integrase Inhibitor; **NNRTI:** Non-Nucleoside Reverse Transcriptase Inhibitor; **NRTI:** Nucleoside Reverse Transcriptase Inhibitor; **PE:** Pharmacokinetic Enhancer; **PI:** Protease Inhibitor; **PAI:** Post-Attachment Inhibitor

Note: Drugs in gray are no longer available and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations.

AIDSinfo

初始治疗方案如何选择


NNRTI
依非韦伦（EFV）
奈韦拉平（NVP）
依曲韦林（ETV）
利匹韦林（RPV）
NRTI
阿巴卡韦（ABC）
恩曲他滨（FTC）
拉米夫定（3TC）
替诺福韦（TDF）
齐多夫定（ZDV）
丙酚替诺福韦（TAF）
2 NRTI + 1 NNRTI
2 NRTI + 1 PI
2 NRTI + 1 INSTI
PI
阿扎那韦（ATV/R）
洛匹那韦（LPV/R）
达芦那韦（DRV/C）
整合酶抑制剂
拉替拉韦（RAL）
艾维雷伟（EVG）
多替拉韦（DTG）
比克替拉韦（BIC）

ART-HIV合并结核病

- 推荐一线ART方案：AZT(TDF)+3TC(FTC)+EFV
- 可选择含INSTI的方案
  - 合并使用利福平，DTG需增量（50mg,2次/d），RAL增量（800mg,2次/d)或维持原剂量（400mg,2次/d)
  - 使用DTG或RAL者可考虑用利福布汀代替利福平，无需调整剂量
- 使用利福布汀方案者，可选择含PI类方案

中国艾滋病诊疗指南（2018年版）. 中华内科杂志,2018,57(12): 867-884

结　论

- HIV合并结核病患者抗病毒疗效与单纯感染者相当。
- HIV合并结核病患者抗结核治疗后痰2月转阴率低，治疗疗程偏长，老年患者抗结核疗效偏低。
- HIV合并结核病患者长期预后与单纯HIV感染相当。
- 早期启动ART对改善HIV合并结核病患者的预后至关重要。

The End

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Thank You!