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# HIV and tuberculosis co-infection in East Asia and the Pacific from 1990 to 2017: results from the Global Burden of Disease Study 2017

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**Background:** Periodic surveillance is crucial to provide information for resource allocation to control HIV/AIDS, tuberculosis (TB), and their co-infection, especially in areas with high morbidity and mortality like East Asia and the Pacific. Therefore, we examined the morbidity and mortality of HIV/AIDS and TB co-infection in this region from 1990 to 2017.

**Methods:** Utilizing the Global Burden of Disease (GBD) Study 2017, we obtained incidence, prevalence, and mortality numbers and rates of HIV/AIDS and TB co-infection, including HIV and drug-susceptible TB (DS-TB), multidrug-resistant TB without extensive drug resistance (MDR-TB without XDR), and extensive drug-resistant TB (XDR-TB). The trends in incidence, prevalence, and mortality from 1990 to 2017 for each co-infection type were analyzed using join-point regression modelling.

**Results:** In 2017, there were 238,372, 4,294, and 392 new cases of HIV-infected DS-TB, HIV-infected MDR-TB without XDR, and HIV-infected XDR-TB, respectively. The number of prevalent cases and deaths were 383,809 and 12,197 of HIV-infected DS-TB, 7,811 and 1,168 of HIV-infected MDR-TB without XDR, and 713 and 282 of HIV-infected XDR-TB. From 1990 to 2017, the age-standardized incidence rate and prevalence rate of HIV-infected DS-TB, and the prevalence rate of HIV-infected XDR-TB continuously increased; the incidence rate of HIV-infected XDR-TB increased from 1990 to 2005 before stabilizing. However, the incidence and prevalence rates of HIV-infected MDR-TB without XDR—as well as the mortality rates of all co-infection types—have decreased in the last 5 years.

**Conclusions:** Even though the mortality rates of all HIV and TB co-infection types have decreased recently, the overall trends in both incidence and prevalence rates of HIV-infected DS-TB and XDR-TB have been increasing since 1990. Efforts to control co-infection across drug resistance types should be continued and further strengthened.

**Keywords:** HIV; acquired immunodeficiency syndrome; tuberculosis; coinfection; East Asia and Pacific

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## Introduction

Both HIV/AIDS and tuberculosis (TB) are leading causes of morbidity and mortality globally (1,2). In 2017, there

were 8,965,800 new cases, 1,929,208,600 prevalent cases, and 1,183,700 deaths of TB, as well as 1,942,100 new cases, 36,822,200 prevalent cases, and 954,500 deaths of HIV/AIDS. Among all HIV/AIDS deaths, nearly 23% are related

to TB (1,2). HIV/AIDS, TB, and their co-infection are major global health concerns and have drawn the focus of the United Nations which made Sustainable Development Goal 3.3 to end HIV/AIDS epidemics by 2030. Continued surveillance is crucial in monitoring disease control efforts for both HIV/AIDS and TB. However, there has been insufficient attention placed on HIV/AIDS and TB co-infection in previous disease-specific research such as the Global Burden of Disease (GBD) Study (3-5).

When implementing control efforts for HIV/AIDS and TB, the East Asia and Pacific World Bank region plays an important role due to its high disease burden, particularly of TB (1-5). China and Indonesia, for example, are among the top ten countries in the world with the most prevalent cases of HIV/AIDS and are both top three countries worldwide with the most prevalent cases of TB in 2017 (6). As a region with high disease burdens of both HIV/AIDS and TB, the East Asia and Pacific region is also a high-risk region for their co-infection. In this article, we examined morbidity and mortality of HIV and TB co-infection in the East Asia and Pacific region from 1990 to 2017.

## Methods

This study is based on the data and measures of the GBD Study 2017. In brief, the GBD Study series provide comprehensive global disease information by quantifying geographically-specific disease measures such as incidence, prevalence, and mortality, as well as disease burden attributable to risk factors by age, sex, and geography over time. The current study includes data collected from 195 countries and territories from 1990 to 2017. Detailed information about the conception, design, data collection, and data synthesis of the GBD Study 2017 has been published elsewhere (1,2,7-11), and related information for HIV/AIDS, TB, and their co-infection has been described previously as well (3-5).

In this study, HIV and TB co-infection includes: HIV-infected drug-susceptible tuberculosis (HIV-infected DS-TB), HIV-infected multidrug-resistant tuberculosis without extensive drug resistance (HIV-infected MDR-TB without XDR), and HIV-infected extensively drug-resistant tuberculosis (HIV-infected XDR-TB). We examined both-sex incidence, prevalence, and deaths of HIV and TB co-infection based on all-age number and age-standardized rate by three co-infection types from the GBD Study 2017 data. We analyzed the trend of the three above measures for the period between 1990 and 2017 by using a join-

point regression model (version 4.6.0.0); a significant trend is indicated when the P value is lower than 0.05 (12,13). For HIV-infected DS-TB, the co-infection type with the highest burden, we conducted trend analysis for each measure (prevalence, incidence, and mortality) in the three countries with the highest number and the highest rate of that measure in 2017 (e.g., trend analysis for HIV-infected DS-TB incidence rate was conducted in Indonesia, Laos, and Myanmar, because their incidence rates of HIV-infected DS-TB were highest among all countries in the East Asia and Pacific region in 2017).

## Results

### *Incidence, prevalence, and mortality of HIV and tuberculosis co-infection in 2017*

Both-sex, all-age new cases, prevalent cases, and deaths of HIV-infected DS-TB, HIV-infected MDR-TB without XDR, and HIV-infected XDR-TB by countries in East Asia and the Pacific in 2017 are summarized in *Table 1*. In 2017, there were 238,372, 4,294, and 392 new cases of HIV-infected DS-TB, HIV-infected MDR-TB without XDR, and HIV-infected XDR-TB, respectively. The number of prevalent cases and deaths were 383,809 and 12,197 of HIV-infected DS-TB, 7,811 and 1,168 of HIV-infected MDR-TB without XDR, and 713 and 282 of HIV-infected XDR-TB.

For HIV-infected DS-TB in 2017, the countries with the highest number of new cases were Indonesia (168,147 cases), China (26,388 cases), and Myanmar (13,178 cases). The countries with the highest number of prevalent cases were Indonesia (246,729 cases), China (68,607 cases), and Vietnam (20,275 cases); and those with the highest number of deaths were Indonesia (2,994 deaths), Vietnam (2,485 deaths), and China (2,212 deaths).

Both-sex, age-standardized incidence rate, prevalence rate and mortality rate (per 100,000 population) of the three HIV and TB co-infection types by countries in East Asia and the Pacific are summarized in *Table 2*. The age distribution of these three rates are shown for both-sex, male-only, and female-only in *Figure 1*. For HIV-infected DS-TB in 2017, the top three countries with the highest incidence rate were Indonesia (61.27 new cases per 100,000), Laos (25.55 new cases per 100,000), and Myanmar (23.95 new cases per 100,000); those with the highest prevalence rate were also Indonesia (89.76 prevalent cases per 100,000), Laos (39.00 prevalent cases per 100,000), and Myanmar (33.88 prevalent cases per 100,000); and those

**Table 1** Both-sex, all-age, new cases, prevalent cases, and deaths (2017) of HIV and tuberculosis co-infection in East Asia and the Pacific

Country/territories	HIV-infected DS-TB				HIV-infected MDR-TB without XDR				HIV-infected XDR-TB			
	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths
Global	1,321,568 [1,203,108–1,454,824]	1,049,482 [956,624–1,149,602]	194,617 [137,732–252,971]	52,006 [37,490–71,163]	37,614 [25,235–54,483]	22,601 [13,425–34,496]	1,689 [1,236–2,302]	1,413 [930–2,296]	1,232 [754–1,833]			
East Asia & Pacific	238,372 [216,240–263,359]	383,809 [348,722–420,741]	12,197 [8,889–16,235]	4,294 [2,293–8,611]	7,811 [3,853–16,470]	1,168 [632–1,957]	392 [210–786]	713 [352–1,502]	282 [153–470]			
American Samoa	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Australia	34 [30–37]	29 [26–32]	4 [2–6]	1 [1–2]	1 [1–2]	0 [0–1]	0 [0–0]	0 [0–0]	0 [0–0]			
Brunei	4 [3–4]	1 [1–2]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Cambodia	2,283 [2,063–2,531]	3,774 [3,374–4,177]	273 [168–414]	20 [3–69]	33 [5–114]	6 [1–22]	2 [0–6]	3 [0–10]	2 [0–5]			
China	26,388 [22,509–29,474]	68,607 [58,447–76,386]	2,212 [1,303–3,480]	1,355 [241–4,597]	3,502 [624–11,453]	262 [49–747]	124 [22–419]	319 [57–1,044]	63 [12–177]			
Federated States of Micronesia	12 [11–13]	11 [10–13]	1 [0–2]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Fiji	7 [6–8]	11 [10–12]	1 [1–2]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Guam	2 [2–3]	3 [3–3]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Indonesia	166,147 [152,129–186,153]	246,729 [221,597–272,148]	2,994 [2,664–3,408]	853 [88–3,639]	1,239 [129–5,161]	41 [4–178]	78 [8–332]	113 [12–471]	10 [1–44]			
Japan	158 [143–174]	100 [90–110]	54 [32–81]	2 [0–6]	1 [0–4]	1 [0–5]	0 [0–1]	0 [0–0]	0 [0–2]			
Kiribati	2 [2–3]	2 [2–3]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Laos	1,690 [1,444–1,961]	2,579 [2,203–3,008]	119 [1–520]	9 [1–37]	14 [1–54]	2 [0–11]	1 [0–3]	1 [0–5]	0 [0–3]			
Malaysia	1,238 [1,121–1,365]	2,137 [1,955–2,326]	162 [98–252]	12 [5–23]	20 [9–39]	4 [2–9]	1 [0–2]	2 [1–4]	1 [0–2]			
Marshall Islands	2 [1–2]	1 [1–1]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]			
Mongolia	8 [6–10]	3 [3–4]	1 [0–1]	1 [0–2]	0 [0–1]	0 [0–0]	0 [0–1]	0 [0–0]	0 [0–0]			

Table 1 (continued)

Table 1 (continued)

Country/territories	HIV-infected DS-TB				HIV-infected MDR-TB without XDR				HIV-infected XDR-TB			
	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths	New cases	Prevalent cases	Deaths
Myanmar	13,178 [1,857-14,567]	18,640 [16,701-20,696]	1,702 [1,199-2,200]	990 [451-1,873]	1,364 [613-2,598]	340 [156-612]	90 [41-171]	124 [56-237]	82 [37-146]			
New Zealand	11 [10-12]	6 [5-7]	1 [0-1]	0 [0-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
North Korea	1,679 [1,502-1,871]	2,078 [1,857-2,291]	85 [5-172]	89 [38-168]	103 [43-204]	12 [1-29]	8 [3-15]	9 [4-19]	3 [0-7]			
Northern Mariana Islands	0 [0-0]	1 [1-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Papua New Guinea	1,275 [1,132-1,430]	1,199 [1,072-1,332]	128 [78-200]	63 [31-114]	55 [27-97]	16 [7-33]	6 [3-10]	5 [2-9]	4 [2-8]			
Philippines	446 [398-498]	788 [695-890]	82 [49-128]	16 [5-40]	28 [8-68]	8 [2-19]	2 [0-4]	3 [1-6]	2 [1-4]			
Samoa	3 [3-3]	5 [5-6]	0 [0-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Singapore	75 [68-83]	33 [29-36]	1 [1-2]	1 [1-2]	0 [0-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Solomon Islands	19 [17-21]	22 [20-25]	3 [0-5]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
South Korea	753 [686-822]	510 [456-565]	62 [51-68]	16 [2-51]	10 [1-32]	3 [0-10]	2 [0-6]	1 [0-4]	1 [0-3]			
Thailand	9,013 [8,186-9,928]	15,798 [14,268-17,270]	1,797 [1,083-2,844]	279 [101-620]	461 [169-1,016]	144 [49-308]	25 [9-56]	42 [15-93]	35 [12-75]			
Timor-Leste	23 [21-26]	32 [29-35]	3 [1-5]	0 [0-1]	0 [0-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Tonga	1 [1-1]	1 [1-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Vanuatu	8 [7-9]	10 [9-11]	1 [0-1]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]			
Vietnam	11,708 [10,097-13,595]	20,275 [17,325-23,624]	2,485 [1,509-3,792]	580 [205-1,196]	969 [334-1,981]	326 [108-716]	53 [19-109]	88 [31-181]	78 [26-170]			

Data in parentheses are 95% uncertainty intervals. DS-TB, drug-susceptible tuberculosis; MDR-TB without XDR, multidrug-resistant tuberculosis without extensive drug resistance; XDR-TB, extensively drug-resistant tuberculosis.

**Table 2** Both-sex, age-standardized, incidence rate, prevalence rate, and mortality rate (2017) of HIV and tuberculosis co-infection per 100,000 population in East Asia and the Pacific

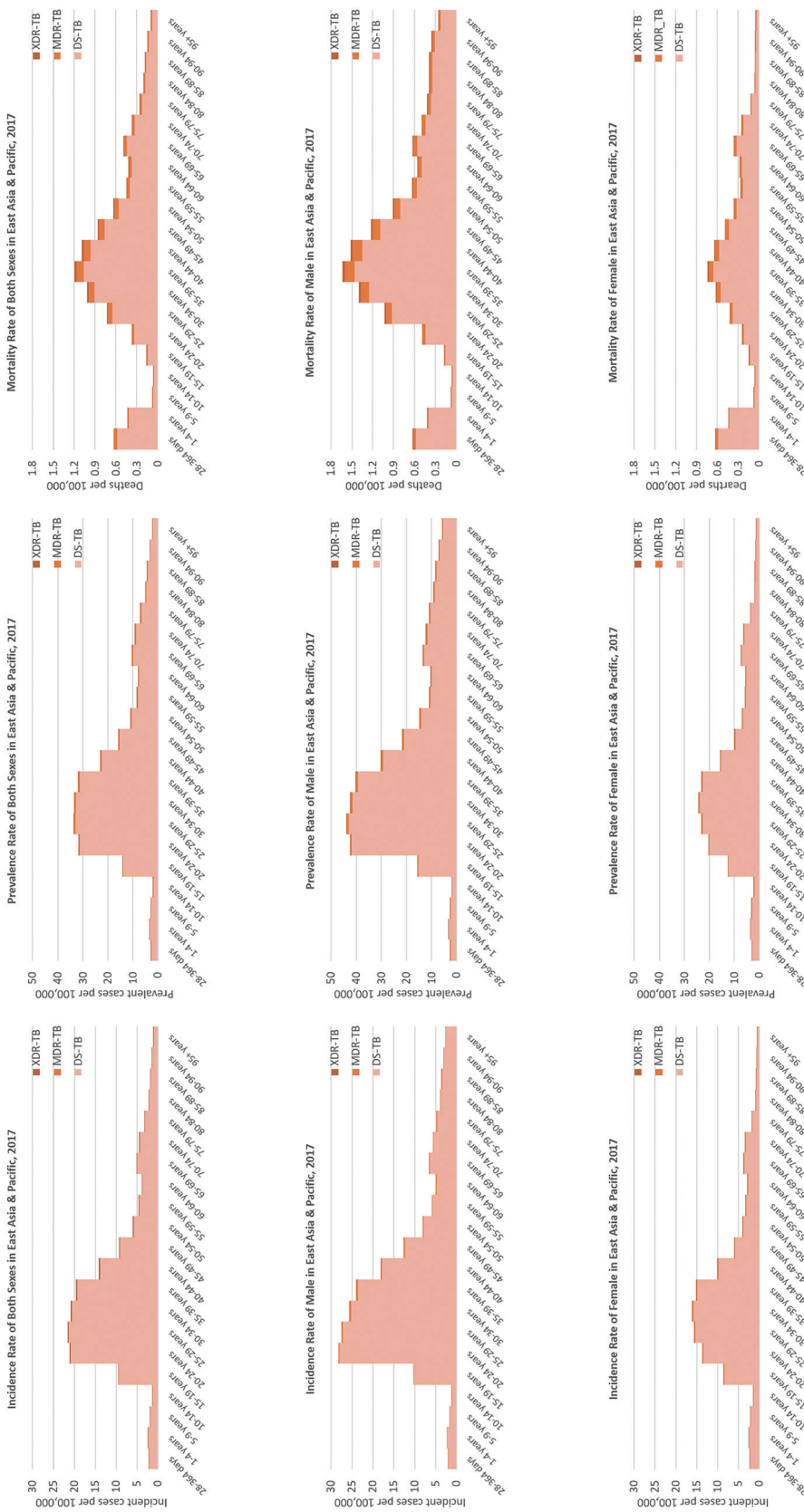
Country/territories	HIV-infected DS-TB			HIV-infected MDR-TB without XDR			HIV-infected XDR-TB		
	Incidence rate	Prevalence rate	Mortality rate	Incidence rate	Prevalence rate	Mortality rate	Incidence rate	Prevalence rate	Mortality rate
Global	16.71 (15.20–18.39)	13.25 (12.08–14.51)	2.50 (1.77–3.24)	0.66 (0.47–0.90)	0.47 (0.32–0.69)	0.29 (0.17–0.44)	0.02 (0.02–0.03)	0.02 (0.01–0.03)	0.02 (0.01–0.02)
East Asia & Pacific	9.72 (8.81–10.73)	15.45 (14.05–16.93)	0.47 (0.35–0.62)	0.16 (0.09–0.33)	0.29 (0.15–0.63)	0.04 (0.02–0.07)	0.02 (0.01–0.03)	0.03 (0.01–0.06)	0.01 (0.01–0.02)
American Samoa	0.24 (0.22–0.27)	0.50 (0.44–0.55)	0.02 (0.01–0.03)	0 (0–0)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Australia	0.11 (0.10–0.12)	0.10 (0.09–0.11)	0.01 (0.01–0.02)	0 (0–0.01)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Brunei	0.76 (0.69–0.85)	0.28 (0.25–0.31)	0.06 (0.03–0.09)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Cambodia	15.48 (13.98–17.16)	25.59 (22.88–28.32)	1.79 (1.10–2.71)	0.14 (0.02–0.47)	0.22 (0.03–0.77)	0.04 (0.01–0.14)	0.01 (0–0.04)	0.02 (0–0.07)	0.01 (0–0.04)
China	1.50 (1.28–1.67)	3.88 (3.31–4.32)	0.12 (0.07–0.20)	0.08 (0.01–0.26)	0.20 (0.04–0.65)	0.01 (0–0.04)	0.01 (0–0.02)	0.02 (0–0.06)	0 (0–0.01)
Federated States of Micronesia	12.66 (11.29–14.07)	11.98 (10.77–13.18)	0.98 (0.22–1.71)	0.05 (0–0.22)	0.05 (0–0.20)	0.01 (0–0.05)	0 (0–0.02)	0 (0–0.02)	0 (0–0.01)
Fiji	0.75 (0.68–0.83)	1.21 (1.10–1.32)	0.12 (0.07–0.18)	0 (0–0.01)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Guam	1.40 (1.27–1.54)	1.69 (1.54–1.84)	0.08 (0.05–0.13)	0.01 (0–0.04)	0.01 (0–0.05)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)
Indonesia	61.27 (55.32–67.99)	89.76 (80.62–99.03)	1.12 (0.99–1.27)	0.31 (0.03–1.32)	0.45 (0.05–1.88)	0.02 (0–0.07)	0.03 (0–0.12)	0.04 (0–0.17)	0 (0–0.02)
Japan	0.09 (0.08–0.10)	0.06 (0.05–0.06)	0.03 (0.02–0.05)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Kiribati	2.04 (1.84–2.27)	1.91 (1.74–2.11)	0.19 (0.15–0.23)	0.01 (0–0.04)	0.01 (0–0.04)	0 (0–0.01)	0 (0–0)	0 (0–0)	0 (0–0)
Laos	25.55 (21.83–29.65)	39.00 (33.30–45.47)	1.81 (0.01–7.94)	0.14 (0.01–0.56)	0.21 (0.02–0.82)	0.03 (0–0.17)	0.01 (0–0.05)	0.02 (0–0.07)	0.01 (0–0.04)
Malaysia	3.78 (3.43–4.17)	6.53 (5.97–7.11)	0.54 (0.33–0.84)	0.04 (0.02–0.07)	0.06 (0.03–0.12)	0.01 (0.01–0.03)	0 (0–0.01)	0.01 (0–0.01)	0 (0–0.01)
Marshall Islands	2.82 (2.54–3.14)	2.15 (1.94–2.37)	0.15 (0.03–0.26)	0.04 (0.01–0.11)	0.03 (0.01–0.08)	0.01 (0–0.02)	0 (0–0.01)	0 (0–0.01)	0 (0–0)

**Table 2** (continued)

Table 2 (continued)

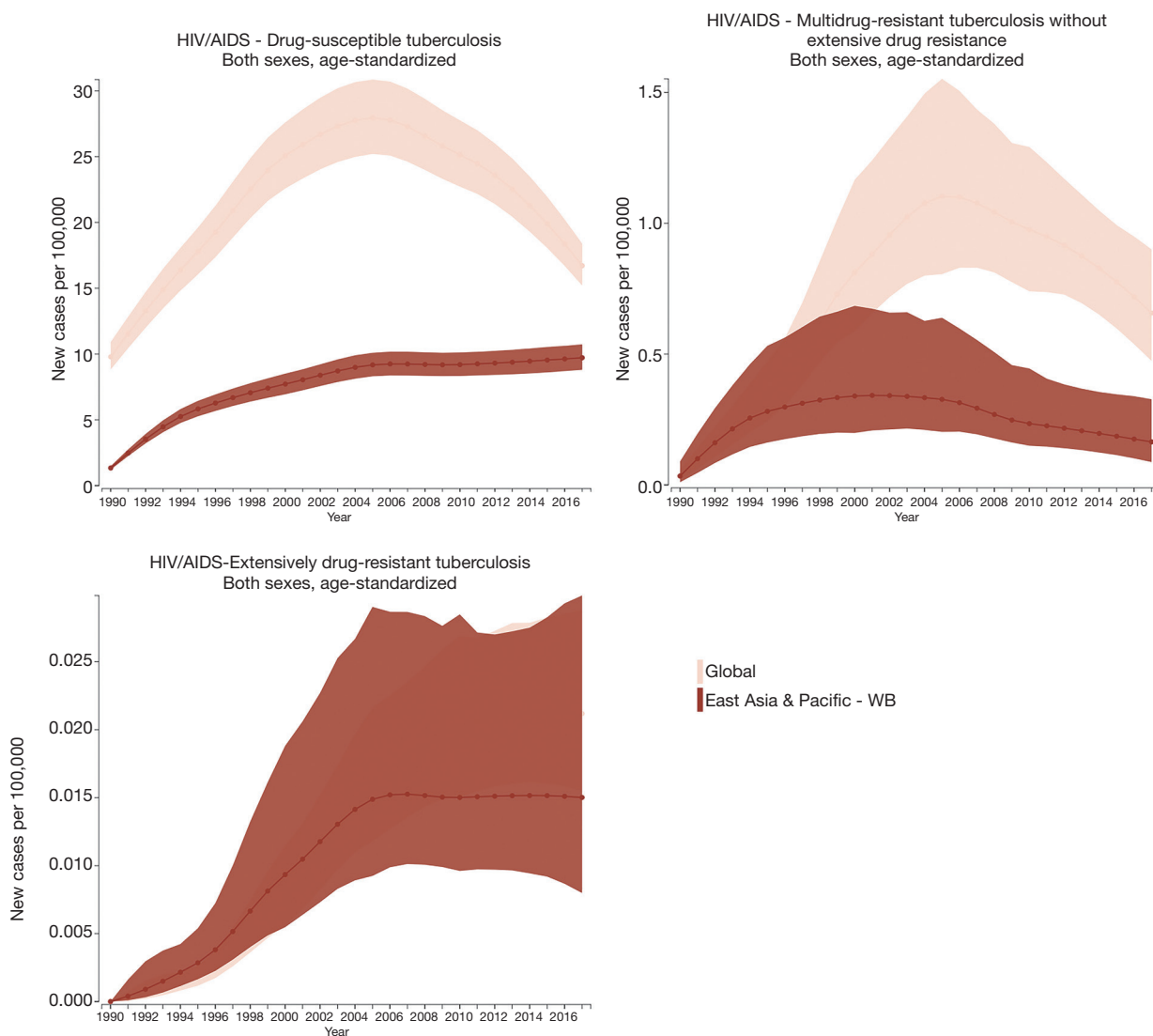
Country/territories	HIV-infected DS-TB			HIV-infected MDR-TB without XDR			HIV-infected XDR-TB		
	Incidence rate	Prevalence rate	Mortality rate	Incidence rate	Prevalence rate	Mortality rate	Incidence rate	Prevalence rate	Mortality rate
Mongolia	0.26 (0.20-0.31)	0.10 (0.08-0.12)	0.02 (0.01-0.04)	0.03 (0.01-0.08)	0.01 (0-0.03)	0.01 (0-0.01)	0.01 (0-0.02)	0 (0-0.01)	0 (0-0.01)
Myanmar	23.95 (21.55-26.48)	33.88 (30.35-37.62)	3.08 (2.16-3.99)	1.80 (0.82-3.41)	2.48 (1.11-4.73)	0.61 (0.28-1.11)	0.16 (0.07-0.31)	0.23 (0.10-0.43)	0.15 (0.07-0.26)
New Zealand	0.22 (0.20-0.24)	0.12 (0.11-0.13)	0.02 (0.01-0.02)	0.01 (0-0.01)	0 (0-0.01)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
North Korea	5.63 (5.03-6.27)	6.96 (6.22-7.68)	0.30 (0.02-0.59)	0.30 (0.13-0.56)	0.35 (0.14-0.68)	0.04 (0-0.10)	0.03 (0.01-0.05)	0.03 (0.01-0.06)	0.01 (0-0.02)
Northern Mariana Islands	1.00 (0.89-1.11)	1.31 (1.17-1.44)	0.04 (0.02-0.06)	0.02 (0-0.06)	0.02 (0-0.08)	0 (0-0.01)	0 (0-0.01)	0 (0-0.01)	0 (0-0)
Papua New Guinea	15.54 (13.80-17.43)	14.62 (13.07-16.23)	1.50 (0.92-2.36)	0.77 (0.38-1.39)	0.67 (0.33-1.19)	0.19 (0.08-0.39)	0.07 (0.04-0.13)	0.06 (0.03-0.11)	0.05 (0.02-0.09)
Philippines	0.41 (0.37-0.46)	0.73 (0.64-0.83)	0.08 (0.05-0.12)	0.02 (0-0.04)	0.03 (0.01-0.06)	0.01 (0-0.02)	0 (0-0)	0 (0-0.01)	0 (0-0)
Samoa	1.72 (1.55-1.90)	2.88 (2.64-3.15)	0.23 (0.03-0.40)	0 (0-0.01)	0 (0-0.01)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Singapore	1.06 (0.96-1.17)	0.46 (0.41-0.50)	0.01 (0.01-0.02)	0.01 (0.01-0.02)	0.01 (0-0.01)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Solomon Islands	3.27 (2.95-3.62)	3.85 (3.49-4.25)	0.48 (0.03-0.94)	0.01 (0-0.05)	0.01 (0-0.06)	0 (0-0.02)	0 (0-0)	0 (0-0.01)	0 (0-0.01)
South Korea	1.04 (0.95-1.14)	0.71 (0.63-0.78)	0.09 (0.07-0.10)	0.02 (0-0.07)	0.01 (0-0.04)	0 (0-0.01)	0 (0-0.01)	0 (0-0.01)	0 (0-0)
Thailand	10.42 (9.47-11.48)	18.27 (16.50-19.97)	1.97 (1.19-3.11)	0.32 (0.12-0.72)	0.53 (0.19-1.18)	0.16 (0.05-0.34)	0.03 (0.01-0.07)	0.05 (0.02-0.11)	0.04 (0.01-0.08)
Timor-Leste	2.11 (1.91-2.35)	2.90 (2.63-3.19)	0.29 (0.14-0.47)	0.01 (0-0.05)	0.02 (0-0.07)	0 (0-0.02)	0 (0-0)	0 (0-0.01)	0 (0-0)
Tonga	0.72 (0.65-0.80)	1.21 (1.10-1.33)	0.12 (0.08-0.20)	0 (0-0.01)	0 (0-0.02)	0 (0-0.01)	0 (0-0)	0 (0-0)	0 (0-0)
Vanuatu	3.11 (2.82-3.46)	3.89 (3.51-4.27)	0.32 (0.04-0.57)	0.01 (0-0.03)	0.01 (0-0.04)	0 (0-0.01)	0 (0-0)	0 (0-0)	0 (0-0)
Vietnam	10.78 (9.29-12.51)	18.66 (15.95-21.74)	2.23 (1.36-3.40)	0.53 (0.19-1.10)	0.89 (0.31-1.83)	0.29 (0.10-0.65)	0.05 (0.02-0.10)	0.08 (0.03-0.17)	0.07 (0.02-0.15)

DS-TB, drug-susceptible tuberculosis; MDR-TB without XDR, multidrug-resistant tuberculosis without extensive drug resistance; XDR-TB, extensive drug-resistant tuberculosis.



**Figure 1** The age distribution (2017) of incidence rate, prevalence rate, and mortality rate (per 100,000 population) of HIV and tuberculosis co-infection in East Asia and the Pacific. XDR-TB, extensive drug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis without extensive drug resistance; DS-TB, drug-susceptible tuberculosis.





**Figure 2** The trend (1990–2017) of both-sex, age-standardized incidence rate (per 100,000 population) of HIV and tuberculosis co-infection in East Asia and the Pacific.

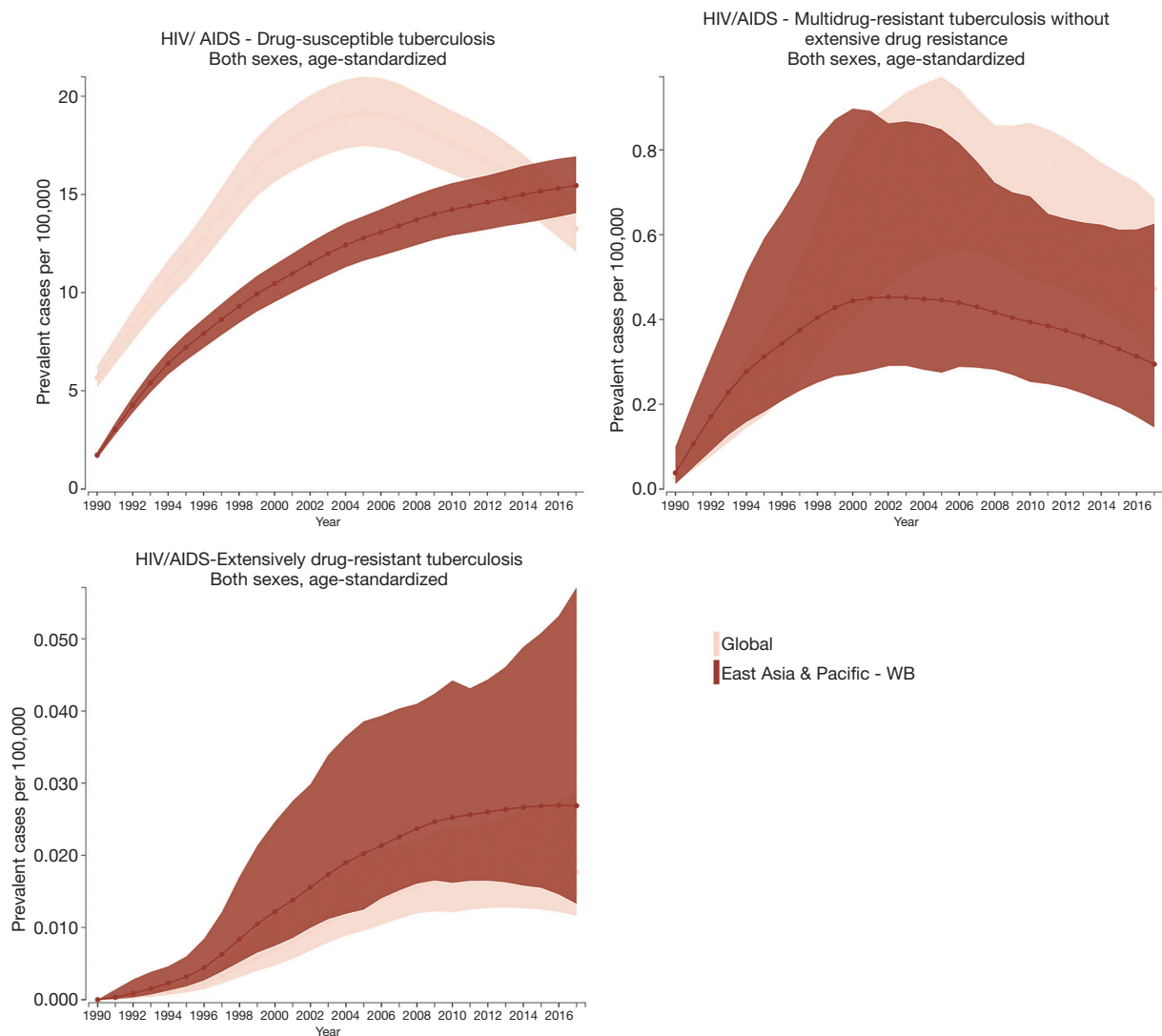
with the highest mortality rate were Myanmar (3.08 deaths per 100,000), Vietnam (2.23 deaths per 100,000), and Thailand (1.97 deaths per 100,000).

#### ***Incidence, prevalence, and mortality trends of HIV and tuberculosis co-infection from 1990 to 2017***

The incidence, prevalence, and mortality trends of HIV and tuberculosis co-infection are shown based on number (Figures S1-S3) and rate (per 100,000 population; Figures 2-4) for the period between 1990 and 2017. These figures show both of global trends and trends in the East

Asia and Pacific region. The results from trend analysis are summarized in Table S1. Overall, the incidence rates of HIV-infected DS-TB and HIV-infected MDR-TB without XDR (Figure 2), the prevalence rate of HIV-infected MDR-TB without XDR (Figure 3), and the mortality rate of all three co-infection types (Figure 4) in East Asia and the Pacific were lower than the global rates for the past decade.

For HIV-infected DS-TB, the overall number and rate for incidence and prevalence have increased from 1990 to 2017 (Table S1). More specifically, the prevalence rate of HIV-infected DS-TB was higher than the global level in recent years (2015–2017) (Figure 3). As for mortality, a



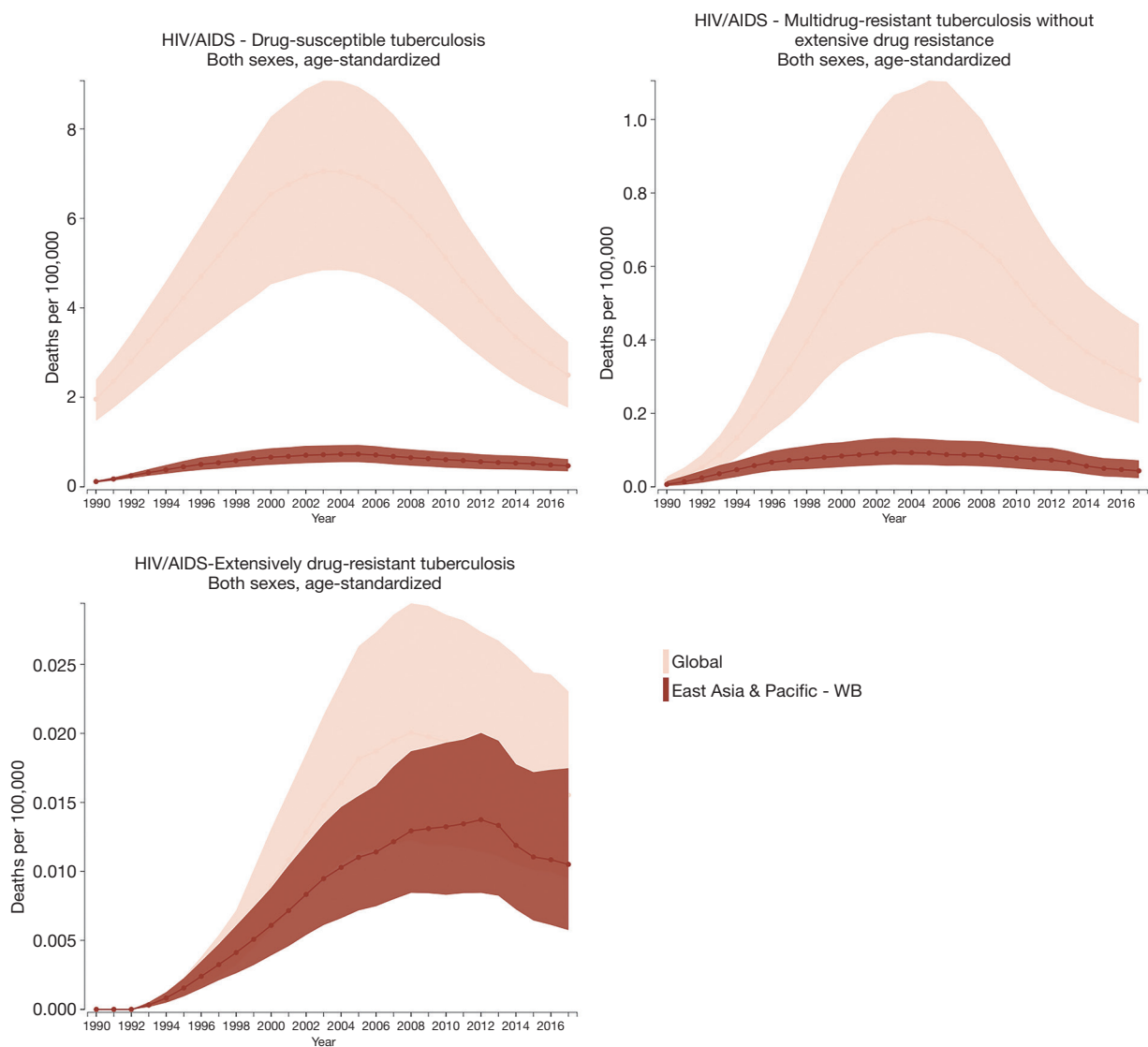
**Figure 3** The trend (1990–2017) of both-sex, age-standardized prevalence rate (per 100,000 population) of HIV and tuberculosis co-infection in East Asia and the Pacific.

significant increase began in 1990 (number: 2,156 deaths; rate: 0.12 deaths per 100,000) and reached its peak in 2005 (number: 17,284 deaths; rate: 0.73 deaths per 100,000); since 2005, mortality has significantly decreased (number in 2017: 12,197 deaths; rate in 2017: 0.47 deaths per 100,000) (*Table S1*). The countries with the highest value of each disease measure (number and rate) in 2017 are shown in *Table S2*; most demonstrated a decreasing trend in the three most recent years.

Each measure for HIV-infected MDR-TB without XDR showed a significant increase followed by a significant decrease after reaching a peak (*Table S1*). For example,

the mortality rate of HIV-infected MDR-TB significantly increased from 0.0067 deaths per 100,000 in 1990, reached its peak (0.09 deaths per 100,000) in 2003, and then significantly decreased to 0.04 deaths per 100,000 in 2017.

The number of HIV-infected XDR-TB incident and prevalent cases as well as prevalence rate presented a continuous increase throughout the period (1990–2017); the incidence rate increased significantly from 1990 to 2005 and then became steady (2005–2017). The mortality rate showed a continuous significant increase and then a significant decrease after reaching a peak in 2012 (*Table S1*).



**Figure 4** The trend (1990–2017) of both-sex, age-standardized mortality rate (per 100,000 population) of HIV and tuberculosis co-infection in East Asia and the Pacific.

## Discussion

Complete, timely, reliable, and valid surveillance is important to quantify the morbidity and mortality of HIV/AIDS and TB co-infection for disease control (14–17). This study provides up-to-date measure information including tendency of the co-infection in East Asia and Pacific by utilizing data and measures compiled by the GBD Study 2017. We found that both-sex, age-standardized mortality rates of the three HIV/AIDS and TB co-infection types in East Asia and the Pacific were lower than global rates over the past decade. In addition, the trend in mortality (number

and rate) in all co-infection types significantly decreased over the five most recent years of data. However, both the number and rate for incidence and prevalence of HIV-infected DS-TB and HIV-infected XDR-TB have been increasing throughout the period (1990–2017).

The decreasing tendency of mortality demonstrates a remarkable progress in disease treatment. Since the introduction of antiretroviral therapy (ART), a lower mortality rate has been successfully achieved in HIV patients with and without TB (18–25). However, considering the co-infection of both diseases, especially

HIV-infected MDR-TB (including HIV-infected XDR-TB), treatment management is more complicated compared to the management of either disease on its own. The complication includes drug interactions, overlapping toxicity, and the possibility of immune reconstitution inflammatory syndrome (IRIS), which may potentially lead to drug resistance, nonadherence to therapy, and/or virological failure (26). To some extent, this complication explains why both the incidence rate and prevalence rate of HIV-infected XDR-TB have not declined over the last decade.

The increasing numbers and rates of incidence and prevalence of HIV-infected DS-TB and HIV-infected XDR-TB reflect the difficulty of prevention efforts. For example, the breakthrough discovery of highly active ART is able to reduce the size of the immunocompromised population and decrease the life-time risk of developing active TB (14). As a result, the World Health Organization (WHO) recommends an earlier initiation of ART to prevent active tuberculosis in people with HIV (27). However, the availability and distribution of these therapies vary—not all HIV patients receive the therapy, regardless of TB status (14,28). According to the GBD Study 2015, the global ART coverage per 100 people living with HIV in 2015 was 40.6%, and the coverage in the high sociodemographic index (SDI) countries was 51.5%. However, the coverage in Southeast Asia, East Asia, and Oceania (major parts of the East Asia and Pacific region) was only 25.9%, lower than not only global coverage but also lower than coverage in low SDI countries (37.9%) (4).

To eliminate both HIV/AIDS and TB, as well as their co-infection, further efforts for treatment are needed. Main strategies should be: early use of ART, early testing to detect drug resistance, sustained adherence to appropriate drug-resistant TB regimens, and proper monitoring for treatment response and adverse effects (17). Early use of ART has been difficult to implement due to low ART coverage, reflecting the limited available resources globally (28,29) and in East Asia and the Pacific, especially in regions with the highest disease morbidity and mortality such as Myanmar (30) and some regions of China (e.g., Xinjiang Province) (31). As for early detection of drug resistance, although a rapid detection of TB and drug resistance in patients living with HIV has been well established (e.g., Xpert MTB/RIF) (32), one major barrier for a broader implementation is the cost (33,34). To achieve sustained adherence to TB regimens and proper monitoring for treatment response and adverse effects, programmatic management is recommended. The Cambodian National MDR-TB program is one example of

a successful program that achieved treatment success based on a community-based effort (35).

To achieve the above treatment strategies, main barriers to disease control should be targeted. In addition to limited resources (e.g., ART coverage, cost, well-established programmatic management), efforts should also focus on stigma. Stigma is a substantial challenge for HIV diagnosis and treatment (36-39). This increases the risk of developing TB, and the risk of new HIV/AIDS (and, consequentially, TB) cases through infection. Reducing stigma requires respectful and targeted engagement, especially for marginalized populations [sex workers, men who have sex with men (MSM), transgender people, people who inject drugs, and people in prison] (40). For this, legal and social environments play an important role, especially those involving health professionals (40,41). Incarceration is another major obstacle. According to a systematic review and meta-analysis, the prevalence of HIV/AIDS and TB co-infection among incarcerated individuals is high worldwide: 32.6% globally, and 35% in Asia (42). One reason accounting for such a high prevalence is that incarceration is a main risk factor of developing TB, especially among those who contracted HIV/AIDS via drug injection (43,44). Other reasons include limited resources for diagnosis and treatment adherence, low treatment completion rate due to limited resources as well as movement by individuals into and out of the prison system (42,45). In addition to the above barriers, an evidence gap between research outputs and policy also exists. A study in Cambodia found that only a small proportion of TB research outputs addressed policy and program planning (46). This study indicates substantial room for improvement in alignment between researchers, funders, and policy makers.

This study has several limitations. First, we followed the GBD study methods using aggregated data from the GBD website. Detailed limitations on the GBD study's methods have been well discussed in previous publications (1-11). Second, the distribution of HIV/AIDS and TB co-infection is heterogeneous between local regions within each country and the present results using GBD Study measures only demonstrate a country-level picture of the co-infection in East Asia and the Pacific. Furthermore, we did not provide estimates of the co-infection by age and sex for each country. However, detailed estimates are available on the GBD website (<http://ghdx.healthdata.org/gbd-results-tool>). For further improvement of our future research, it is reasonable to consider those measures among more vulnerable populations, including incarcerated populations.

## Conclusions

HIV/AIDS, tuberculosis, and their co-infection constitute a substantial portion of global morbidity and mortality. Our study indicates that the trends in almost all measures of the three co-infection types examined here have been decreasing globally, and their trends in mortality have also been decreasing in East Asia and the Pacific. However, the overall trends in both incidence and prevalence of HIV-infected DS-TB and HIV-infected XDR-TB have been increasing since 1990. Continuous efforts should be kept in progress for disease control. For example, further development of treatments specifically for co-infection and management protocols, as well as cost containment, are needed to reverse the current increasing trends of these co-infection types.

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## Footnote

*Conflicts of Interest:* This study has been presented at the ATS 2019 International Conference (Dallas, USA).

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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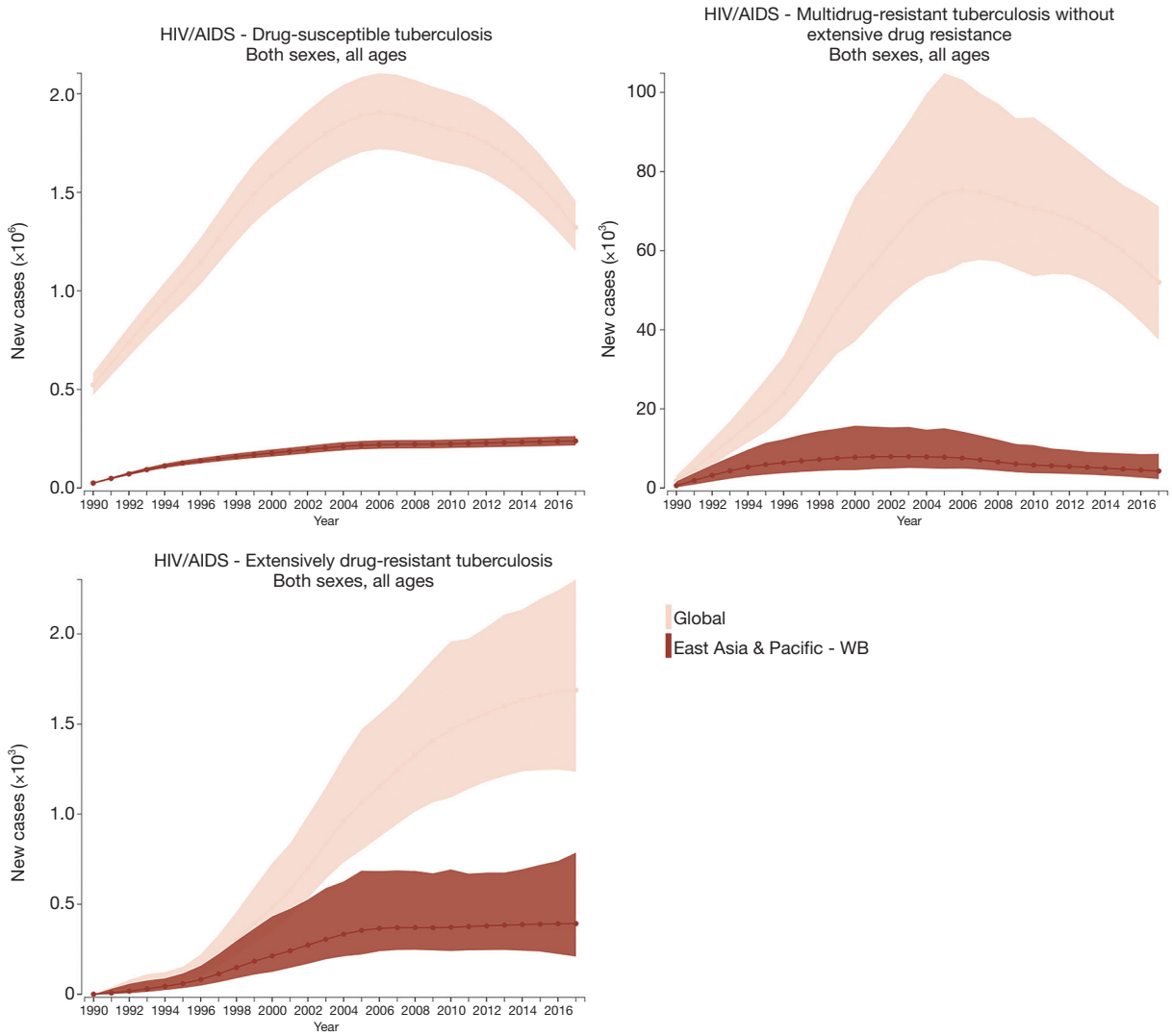


Figure S1 The trend (1990–2017) of both-sex, all-age new cases of HIV and tuberculosis co-infection in East Asia and the Pacific.

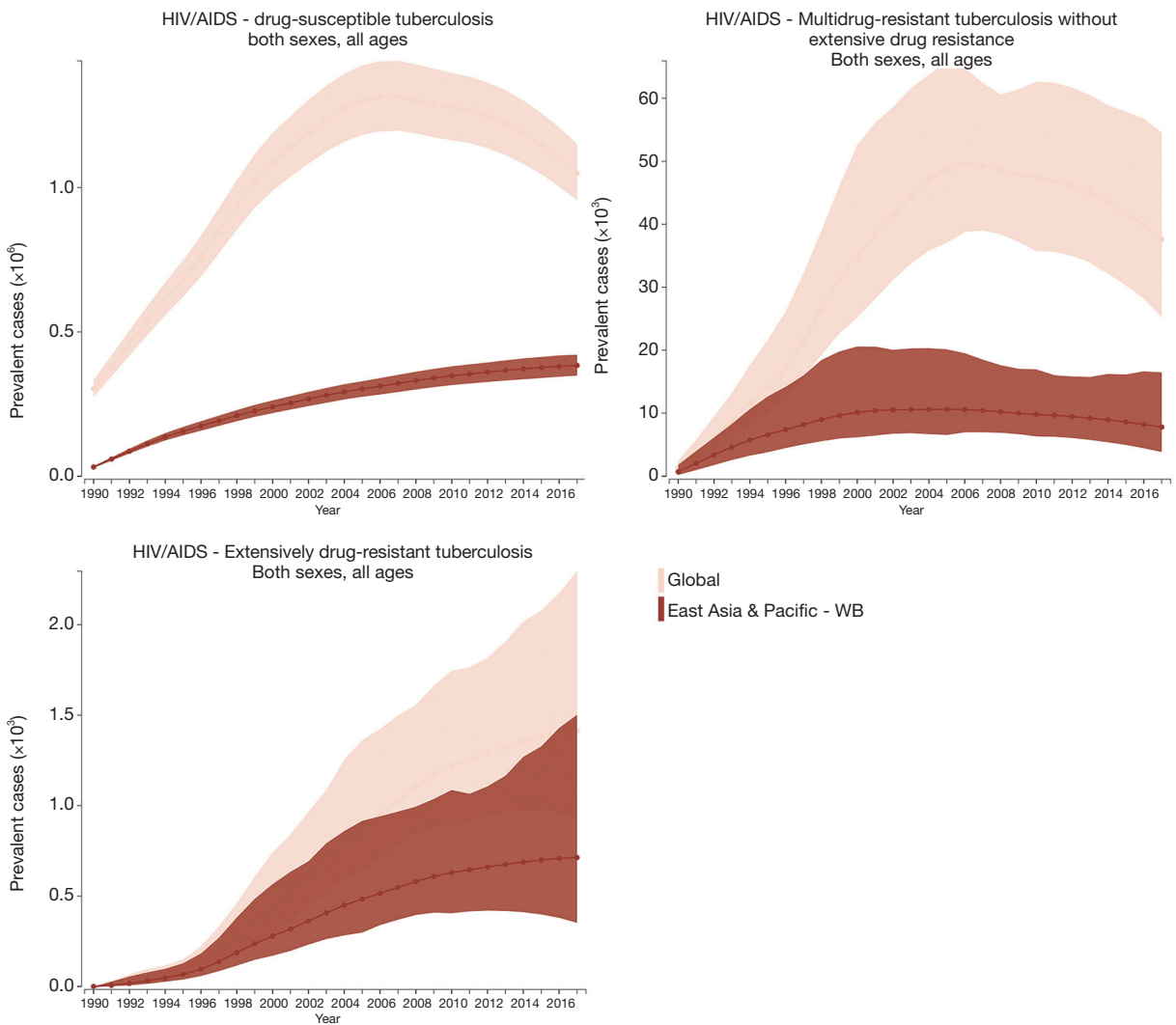
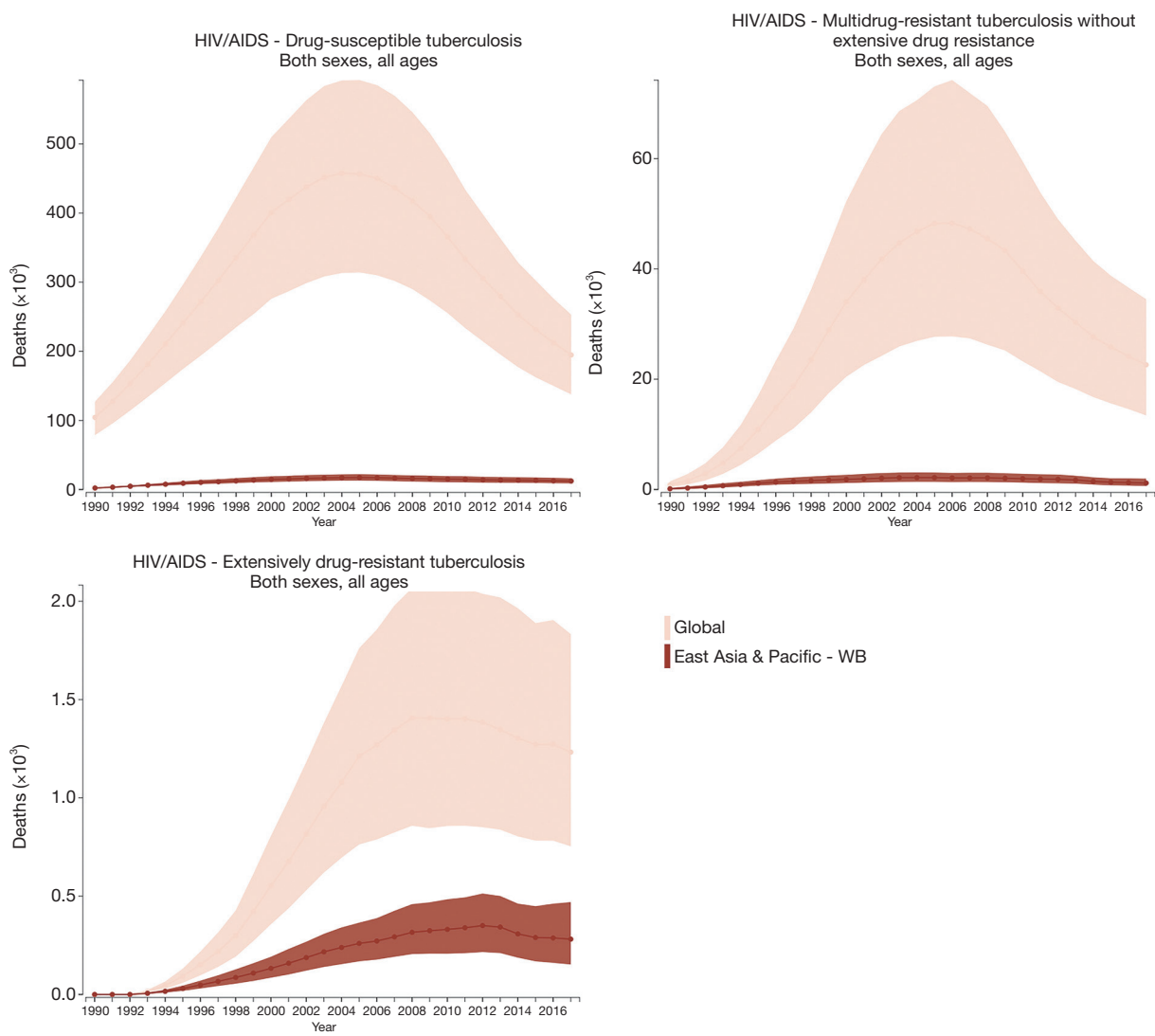


Figure S2 The trend (1990–2017) of both-sex, all-age prevalent cases of HIV and tuberculosis co-infection in East Asia and the Pacific.





**Figure S3** The trend (1990–2017) of both-sex, all-age deaths of HIV and tuberculosis co-infection in East Asia and the Pacific.

**Table S1** Trend analysis on the number and rate of incidence, prevalence and mortality (1990–2017) of HIV and tuberculosis co-infection in East Asia and the Pacific

Measures	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6	
	Years	Slope	Years	Slope	Years	Slope	Years	Slope	Years	Slope	Years	Slope
HIV-infected drug-susceptible tuberculosis (HIV-infected DS-TB)												
New cases	1990–1994	21,970**	1994–1998	11,595**	1998–2005	8,404**	2005–2009	758*	2009–2017	2,034**	–	–
Incidence rate	1990–1993	1.068**	1993–1996	0.593**	1996–2002	0.342**	2002–2005	0.276**	2005–2010	–0.012	2010–2017	0.074**
Prevalent cases	1990–1994	26,234**	1994–1999	17,888**	1999–2004	13,177**	2004–2009	9,472**	2009–2013	6,658**	2013–2017	4315**
Prevalence rate	1990–1993	1.248**	1993–1996	0.826**	1996–1999	0.660**	1999–2004	0.501**	2004–2009	0.315**	2009–2017	0.184**
Deaths	1990–1996	1,382**	1996–1999	1,120**	1999–2002	818**	2002–2005	408*	2005–2012	–462**	2012–2017	–368**
Mortality rate	1990–1995	0.068**	1995–1999	0.045**	1999–2002	0.026**	2002–2005	0.009	2005–2010	0.026**	2010–2017	–0.019**
HIV-infected multidrug-resistant tuberculosis without extensive drug resistance (HIV-infected MDR-TB without XDR)												
New cases	1990–1994	1,183**	1994–1998	464**	1998–2002	185**	2002–2006	–104**	2006–2009	–517**	2009–2017	–218**
Incidence rate	1990–1993	0.062**	1993–1996	0.027**	1996–2000	0.010**	2000–2005	–0.002**	2005–2009	–0.021**	2009–2017	–0.010**
Prevalent cases	1990–1994	1,268**	1994–1999	786**	1999–2002	282**	2002–2006	–3	2006–2013	–190**	2013–2017	–356**
Prevalence rate	1990–1993	0.065**	1993–1996	0.038**	1996–2000	0.025**	2000–2005	–0.0003	2005–2013	–0.011**	2013–2017	–0.017**
Deaths	1990–1996	215**	1996–2003	117**	2003–2008	–15	2008–2012	–61**	2012–2015	–178**	2015–2017	–73
Mortality rate	1990–1996	0.011**	1996–2003	0.004**	2003–2008	–0.002**	2008–2012	–0.003**	2012–2015	–0.007**	2015–2017	–0.003*
HIV-infected extensively drug-resistant tuberculosis (HIV-infected XDR-TB)												
New cases	1990–1993	10**	1993–1996	17**	1996–1999	35**	1999–2005	30**	2005–2017	3**	–	–
Incidence rate	1990–1995	0.001**	1995–2002	0.001**	2002–2005	0.001**	2005–2017	–0.001 to 0	–	–	–	–
Prevalent cases	1990–1993	9**	1993–1996	23**	1996–2004	44**	2004–2009	32**	2009–2014	16**	2014–2017	8**
Prevalence rate	1990–1995	0.001**	1995–2004	0.002**	2004–2009	0.001**	2009–2014	<0.001**	2014–2017	<0.001	–	–
Deaths	1990–1993	1	1993–1998	16**	1998–2005	26**	2005–2012	13**	2012–2015	–23**	2015–2017	–4
Mortality rate	1990–1994	<0.001	1994–2004	0.001**	2004–2008	0.001**	2008–2012	<0.001	2012–2015	–0.001**	2015–2017	–0.001 to 0

Incidence, prevalence and mortality rates are age-standardized, per 100,000 population. The slope in each time period represents a unit of change per year. The slope is significantly different from zero (\*,  $P < 0.05$ ; \*\*,  $P < 0.01$ ). DS-TB, drug-susceptible tuberculosis; MDR-TB without XDR, multidrug-resistant tuberculosis without extensive drug resistance; XDR-TB, extensive drug-resistant tuberculosis.

**Table S2** Trend analysis on the number and rate for incidence, prevalence and mortality (1990–2017) of HIV-infected drug-susceptible tuberculosis (HIV-infected DS-TB) in the top three countries of East Asia and the Pacific based on 2017

Measures	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6	
	Years	Slope	Years	Slope	Years	Slope	Years	Slope	Years	Slope	Years	Slope
New cases												
Indonesia	1990–1994	14,197**	1994–1997	6,956**	1997–2005	5,849**	2005–2009	4,355**	2009–2017	3,224**	–	–
China	1990–1994	1,845**	1994–2005	545**	2005–2010	–1,518**	2010–2014	284*	2014–2017	824**	–	–
Myanmar	1990–1994	2,401**	1994–1999	1,713**	1999–2004	1,328**	2004–2007	151	2007–2013	–941**	2013–2017	–1,972**
Incidence rate												
Indonesia	1990–1993	7.822**	1993–1996	3.796**	1996–2007	1.622**	2007–2017	0.857**	–	–	–	–
Laos	1990–1996	1.161**	1996–1999	1.874**	1999–2002	2.755**	2002–2005	0.844**	2005–2012	–0.258**	2012–2017	–1.172**
Myanmar	1990–1994	5.770**	1994–1999	3.355**	1999–2004	2.156**	2004–2007	–0.382**	2007–2013	–2.283**	2013–2017	–3.991**
Prevalent cases												
Indonesia	1990–1994	16,223**	1994–1997	10,013**	1997–2010	8,947**	2010–2007	5,130**	–	–	–	–
China	1990–1995	1,798**	1995–2000	2,069**	2000–2005	700**	2005–2013	1,838**	2013–2017	2,332**	–	–
Vietnam	1990–1998	902**	1998–2005	1,221**	2005–2011	–52	2011–2017	369**	–	–	–	–
Prevalence rate												
Indonesia	1990–1993	8.801**	1993–1996	5.054**	1996–2010	2.776**	2010–2017	1.363**	–	–	–	–
Laos	1990–1996	1.469**	1996–2000	2.485**	2000–2005	3.787**	2005–2009	1.819**	2009–2013	–0.043**	2013–2017	–1.318**
Myanmar	1990–1993	7.543**	1993–1998	5.201**	1998–2004	3.711**	2004–2007	0.047	2007–2012	–2.169**	2012–2017	–5.989**
Deaths												
Indonesia	1990–1995	42**	1995–2001	73**	2001–2010	124**	2010–2013	276**	2013–2017	98**	–	–
Vietnam	1990–1996	144**	1996–2003	257**	2003–2006	78*	2006–2009	–139**	2009–2014	4	2014–2017	–67**
China	1990–1993	177**	1993–2003	85**	2003–2012	–96**	2012–2017	99**	–	–	–	–
Mortality rate												
Myanmar	1990–1992	0.213	1992–1997	0.757**	1997–2005	1.085**	2005–2009	–0.279**	2009–2014	–1.203**	2014–2017	–0.925**
Vietnam	1990–1997	0.218**	1997–2002	0.281**	2002–2005	0.104**	2005–2009	–0.192**	2009–2014	–0.048**	2014–2017	–0.095**
Thailand	1990–1993	1.216**	1993–1996	0.660**	1996–1999	–0.049	1999–2007	–0.462**	2007–2011	–0.138**	2011–2017	–0.009

\*, P<0.05; \*\*, P<0.01.