

A TIME OF CHANGE: ACCELERATING THE RESPONSE TO TB TUBERCULOSIS REPORT TO CONGRESS

FEBRUARY 2019



U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT REPORT TO CONGRESS ON TUBERCULOSIS (TB) PROGRAMMING DURING FISCAL YEAR (FY) 2017 A TIME OF CHANGE: ACCELERATING THE RESPONSE TO TB
The U.S. Agency for International Development (USAID) submits this report to Congress pursuant to Section 302(g) Public Law 110-293, the Tom Lantos and Henry J. Hyde U.S. Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Authorization Act of 2008.

On the Cover: Cover Your Cough Training, Burma. Photo Credit: Hein Htet, Challenge TB.

GLOBAL CONTEXT

Tuberculosis (TB) is a curable disease, yet it remains the leading infectious-disease killer worldwide, and takes the lives of almost 4,600 people each day. The ambitious global goal of ending TB by 2030 requires accelerated action and additional investments by the governments of the highest-burden countries, donors, the private sector, and other local and global stakeholders.

Despite recent progress in reducing new cases, of and mortality from, TB, millions still suffer and die each year as a result of delayed diagnosis, weak health systems, the ongoing challenges of drug-resistant TB (DR-TB) and high-risk co-morbidities. In Calendar Year (CY) 2017, the most-recent year for which data are available, an estimated 10 million people became ill with TB, and 1.6 million died.² Finding individuals with TB, and supporting them to get effective TB treatment early in their illness, is critical to interrupting transmission, and remains a major challenge. In CY 2017, only 64 percent of new and relapsed cases were detected and notified to National Tuberculosis Programmes (NTPs), which left many people without access to high-quality care. Of those individuals detected with TB and started on treatment, almost 50 percent were not diagnosed with the mostaccurate point-of-care technology.3

The emergence and transmission of DR-TB threatens the progress made so far. In CY 2017, an estimated 560,000 people developed a form of TB that is resistant to the most-effective first-line antibiotic, rifampicin. DR-TB, including also multi-drug-resistant TB (MDR-TB) and extensively resistant TB (XDR-TB), has become a global problem and a challenge for Ministries of Health in every region. Only one in five individuals with DR-TB starts treatment, and just over half of those on treatment are cured. High-risk co-morbidities are strongly associated with TB. People who are living with HIV are 20-to-30 times more likely to develop active TB disease than people without HIV. More than 6.5 million of the total estimated active TB cases globally have a connection to undernourishment, smoking, diabetes, HIV, and/or the consumption of alcohol.4

The economic and social consequences of TB on individuals, families and communities are devastating. This includes the difficulties people face in gaining access to correct diagnosis and treatment. TB has a tremendous negative impact on development and exacerbates poverty. A systematic review by the World Health Organization (WHO) concluded that, on average, TB patients and their households lose 50 percent of their annual incomes from missed work because of illness from TB and the costs of seeking care for the illness, even where care for TB is free-of-charge. With support from Congress and the American taxpayer, USAID is working with governments, civil-society, faith-based organizations, and the private sector in partner countries to further their progress on the Journey to Self-Reliance and combating TB to create healthy, resilient, and productive citizens.

World Health Organization Global Tuberculosis Report 2018

² Ibid.

³ Ibid.

⁴ Ibio

⁵ National TB Patient Cost Survey to monitor progress toward the target to eliminate catastrophic costs and help design social protection and universal health coverage, accessed at http://www.who.int/tb/areas-of-work/tb-hiv/garciai patient cost survey rationale and method.pdf

USAID'S GLOBAL TB PROGRAM

USAID shares a vision of a world free of TB, and works to achieve this goal through the U.S. Government's (USG) Global TB Strategy, the <u>National Action Plan for Combating Multidrug-Resistant Tuberculosis</u> (<u>National Action Plan</u>), and the WHO <u>End TB Strategy</u>. The Agency is working with partners around the world to support the strategy to reach every person with TB, cure those in need of treatment, and prevent the spread of disease and new infections.

USAID'S FOCUS ON RESULTS

USAID leads the global TB efforts of the U.S.

Government (USG) to provide bilateral financial and technical assistance in 22 countries that have high burdens of TB, in cooperation with Ministries of Health. In addition, USAID also leverages the USG's investment in the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund) by providing targeted technical assistance to support the implementation of the Global Fund's TB grants in 32 countries.

USAID plays a critical coordination role in each country, by working closely with a wide range of multi-sectoral TB stakeholders, including Ministries of Health, the Global Fund Secretariat and Principal Recipients, other U.S. Government Departments and Agencies, the WHO, the Stop TB Partnership, civil society, faith-based organizations, communities, and the private sector. Further, USAID ensures that the Agency coordinates with other donors and host-country governments to avoid duplication of effort.

USAID's implementation focuses on a person-centered approach to improve access to high-quality TB care and efforts to increase the correct detection of all those with TB. These efforts consist of interventions that include funding community and facility-based screening; building diagnostic networks; providing appropriate treatment, including new drugs and regimens; expanding prevention strategies; and leveraging commitment from governments and other stakeholders. By improving the capacity of Ministries of Health to make high-quality TB care available, USAID's partners reach the people in greatest

need, particularly the most-vulnerable populations. In FY 2017, the Agency funded training for more than 36,000 health workers to increase staffing capacity in 22 countries.

USAID made significant progress in FY 2017 towards reaching the targets set forth in the USG's Global TB Strategy and the National Action Plan. On average, in the 22 countries with bilateral U.S. funding, since FY 2000, the incidence of TB decreased 25 percent, mortality from the disease fell by 41 percent, and TB case-notifications increased by 88 percent.

Overall, USAID is on track to meet the FY 2019 treatment targets described in the USG Global TB Strategy: To treat successfully more than nine million people with TB, and start 290,000 individuals with DR-TB on second-line drug therapy. Among those individuals with TB who test positive for HIV, 87 percent began antiretroviral therapy. Please see the Appendix to this report for additional details on these targets and indicators.

In FY 2017, a total of nearly \$244 million, appropriated through USAID's Global Health Programs (GHP) and Economic Support Fund accounts, funded international TB programming, including through bilateral assistance to high-burden countries, regional platforms, and centrally managed mechanisms.



Gopal. Sylhet, Bangladesh. Photo Credit: Tristan Bayly, Challenge TB.

TB AND DIABETES: THE NEW EPIDEMIC

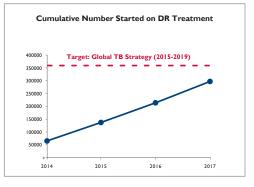
Weakened immune systems from diabetes can triple the risk of developing TB, and can worsen the effects of TB on the body. At the same time, TB can make controlling blood-sugar levels in people who have diabetes problematic. The number of people with diabetes is increasing, with the most-dramatic increases in low- and middle-income countries that are undergoing rapid economic, social, and lifestyle changes, a group that overlaps with those nations with the highest burden of TB.

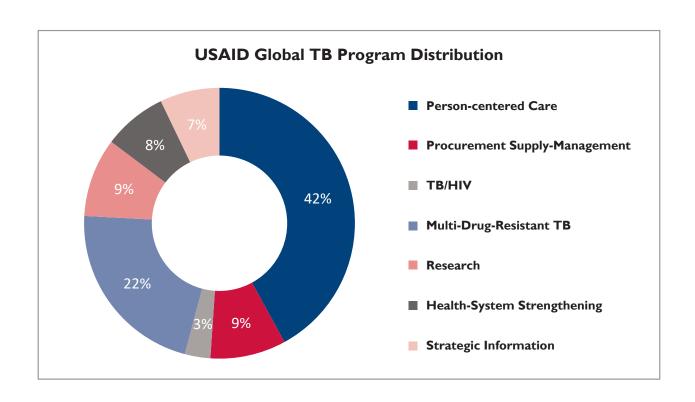
Approximately 10 percent of the 165 million people in Bangladesh suffer from diabetes. In CY 2017, the country diagnosed an estimated 364,000 cases of TB. USAID is working with the Diabetes Association of Bangladesh to address the growing burden of diabetes-associated TB that threatens the progress made in the global fight to end both diseases. This effort includes improving the early and correct detection of TB in people with diabetes, strengthening the systems and skills to diagnosis and manage individuals with the two diseases, and increasing awareness about both diseases in the community.

After seeing an advertisement on television that described his symptoms, 35-year-old Gopal traveled to Sylhet Diabetic Hospital, founded by the Diabetes Association of Bangladesh, to confirm his suspicions. Clinicians ultimately diagnosed him with both diabetes and TB, and he had to stop working for a few months until the TB treatment took effect. Following his treatment, he was able to return to selling fish in the market to support his wife and young child. People with TB often face stigma and discrimination that lead to isolation, as they withdraw from society and keep their disease a secret. Media campaigns are educating Bangladeshis on the challenges of these co-morbidities, which increases the likelihood that people will be more aware of their health situation and seek care early.









2017 ACHIEVEMENTS IN USAID TB PRIORITY COUNTRIES

22	Countries with bilateral programs
54	Countries received technical assistance
4,000,000	TB cases detected
3 percent	Increase in case-notifications ⁶
88 percent	Treatment success rate
83,000	Individuals with DR-TB started on appropriate treatment ⁷
27,600,000	GeneXpert cartridges procured under concessional pricing (cumulative)
62	Countries that used the Bedaquiline Donation Program (cumulative)
36,000	Health workers trained
19	Countries completed drug-resistance surveys (cumulative)
20	Countries completed TB prevalence surveys (cumulative)
5	Research studies supported that focused on new treatment regimens

⁶ The TB treatment-success rate for CY 2017 is affected by increases in TB notification by private-sector providers in India in FY 2016 that were unaccounted for in the country's analysis of treatment outcomes in CY 2017. Using the data provided to the WHO with these additional notified cases, the treatment success rate for India is 72 percent. For this report, the actual number of TB patients for whom treatment outcomes were reported in India helped determine the overall treatment-success rate in USAID TB priority countries, which yielded a result of 88 percent. In subsequent years, all notified patients in the treatment cohort for all priority countries will contribute to the overall treatment success rate.

⁷ Since FY 2014, USAID has calculated the total number of DR-TB patients who initiated second-line treatment by adding together three values reported to the WHO on an annual basis: Number of confirmed rifampicin-resistant (RR)/MDR-TB patients who started treatment (individuals with a laboratory test result to indicate either RR or MDR-TB); Number of unconfirmed RR/MDR-TB patients who started treatment (individuals without laboratory test result, but clinical diagnosis of RR or MDR-TB); and the number of confirmed XDR-TB patients who started treatment (patients with a laboratory test results to indicate XDR-TB). We are working with NTPs and the WHO to address the variation among NTPs reporting confirmed XDR-TB cases.

UNHLM ON TB KEY TARGETS

FOR 2022

'WE, HEADS OF STATE AND GOVERNMENT AND REPRESENTATIVES OF STATES AND GOVERNMENTS ASSEMBLED AT THE UNITED NATIONS IN NEW YORK ON 26 SEPTEMBER 2018':



1. COMMIT TO PROVIDE DIAGNOSIS AND TREATMENT

with the aim of successfully treating 40 million people with tuberculosis by 2022.

2. COMMIT TO PROVIDE DIAGNOSIS AND TREATMENT

with the aim of successfully treating 3.5 million children with tuberculosis by 2022.

3. COMMIT TO PROVIDE DIAGNOSIS AND TREATMENT

with the aim of successfully treating 1.5 million people with drug-resistant tuberculosis, including 115 000 children with drug-resistant tuberculosis, by 2022.



4. COMMIT TO PREVENT TUBERCULOSIS

for those most at risk of falling ill so that at least 30 million people, including 4 million children under five years of age, 20 million other household contacts of people affected by tuberculosis, and 6 million people living with HIV and AIDS, receive preventive treatment by 2022.



5. COMMIT TO MOBILIZE SUFFICIENT AND SUSTAINABLE FINANCING

for universal access to quality prevention, diagnosis, treatment and care of tuberculosis, from all sources, with the aim of increasing overall global investments for ending tuberculosis reaching at least US\$13 billion a year by 2022.

6. COMMIT TO MOBILIZE SUFFICIENT AND SUSTAINABLE FINANCING FOR R&D

with the aim of increasing overall global investments to US\$2 billion, in order to close the estimated US\$1.3 billion gap in funding annually for tuberculosis research, ensuring all countries contribute appropriately to research and development.







including by removing discriminatory laws, policies and programmes against people with tuberculosis, and through the protection and promotion of human rights and dignity.

Recognize the various sociocultural barriers to tuberculosis prevention, diagnosis and treatment services, especially for those who are vulnerable or in vulnerable situations, and the need to develop integrated, people-centred, community-based and gender-responsive health services based on human rights.



8.
COMMIT TO DELIVERING,
AS SOON AS POSSIBLE,
NEW, SAFE, EFFECTIVE,
EQUITABLE, AFFORDABLE,
AVAILABLE VACCINES,

point-of-care and child-friendly diagnostics, drug susceptibility tests and safer and more effective drugs and shorter treatment regimens for adults, adolescents and children for all forms of tuberculosis and infection, as well as innovation to strengthen health systems such as information and communication tools and delivery systems for new and existing technologies, to enable integrated people-centred prevention, diagnosis, treatment and care of tuberculosis.



9.
REQUEST THE DIRECTORGENERAL OF THE WORLD
HEALTH ORGANIZATION TO
CONTINUE TO DEVELOP
THE MULTISECTORAL
ACCOUNTABILITY
FRAMEWORK

and ensure its timely implementation no later than 2019.



10.
FURTHER REQUEST THE
SECRETARY GENERAL,
WITH THE SUPPORT OF
THE WORLD HEALTH
ORGANIZATION, TO
PROVIDE A PROGRESS
REPORT IN 2020

on global and national progress, across sectors, in accelerating efforts to achieve agreed tuberculosis goals, which will serve to inform preparations for a comprehensive review by Heads of State and Government at a high-level meeting in 2023.

USAID'S COMMITMENT TO ENDING TB

In late 2016, Member States of the United Nations General Assembly (UNGA), including the United States, agreed to hold the third disease-specific meeting of the UN as a High Level Meeting (UNHLM) on TB in September 2018. USAID strongly supported the UNHLM as the event set the stage for high-level attention and action on TB, including targets and positioning as the USG looks towards ending TB and achieving the goals laid out in the USG Global TB Strategy and the National Action Plan for Combating Multidrug-Resistant TB.

USAID'S GLOBAL ACCELERATOR TO END TUBERCULOSIS

During the UNHLM on TB, USAID Administrator
Mark Green announced the Agency's new TB business
model — the Global Accelerator to End Tuberculosis
to catalyze investments across multiple countries and
sectors to end the epidemic while building self-reliance.
The Accelerator is a new business model for combating
TB designed to increase investments from the public
and private sectors to end the TB epidemic, while
simultaneously building local commitment and capacity
and accelerating action to achieve the ambitious goals of
the UNHLM.

The Declaration that emerged from the UNHLM calls for diagnosing and enrolling an additional 40 million people on TB treatment by 2022, focused on countries with the highest burden of the disease. The Accelerator is USAID's contribution to these targets, and has these specific lines of effort: expanded targeted technical expertise to increase the diagnosis and treatment of cases of TB and MDR-TB including advisors in Ministries of Health; strengthened involvement of local organizations in the TB response, including community and faith-based groups; accelerated transition of sustainable funding and management of TB programs to governments and their partners; and improved coordination with other health programs, particularly addressing co-morbidities such as diabetes, HIV and undernourishment.

This change in approach will ensure USAID is fighting to end TB effectively and efficiently. The Accelerator will focus on locally generated solutions that will tailor USAID's TB response to patients and communities to address their diagnosis, treatment and prevention needs, while addressing stigma and discrimination. In addition, it will be used to coordinate multi-sectoral accountability mechanisms in USAID TB priority countries and engage and leverage civil society, private sector, community and faith-based organizations.

INCREASING COORDINATION WITH NATIONAL GOVERNMENTS

In a move towards ensuring greater accountability towards program implementation, the Government of Uganda signed a Partnership Statement with the U.S. government in October 2018. The agreement supports the Government of Uganda's efforts towards ending the TB epidemic and charges the Ministry of Finance, Planning and Economic Development of Uganda to create a TB-focused inter-ministerial taskforce. Targeted joint planning resulted in an action plan focused on achieving the objectives outlined in the Partnership Statement, in-line with TB National Strategic Plan.

APPENDIX

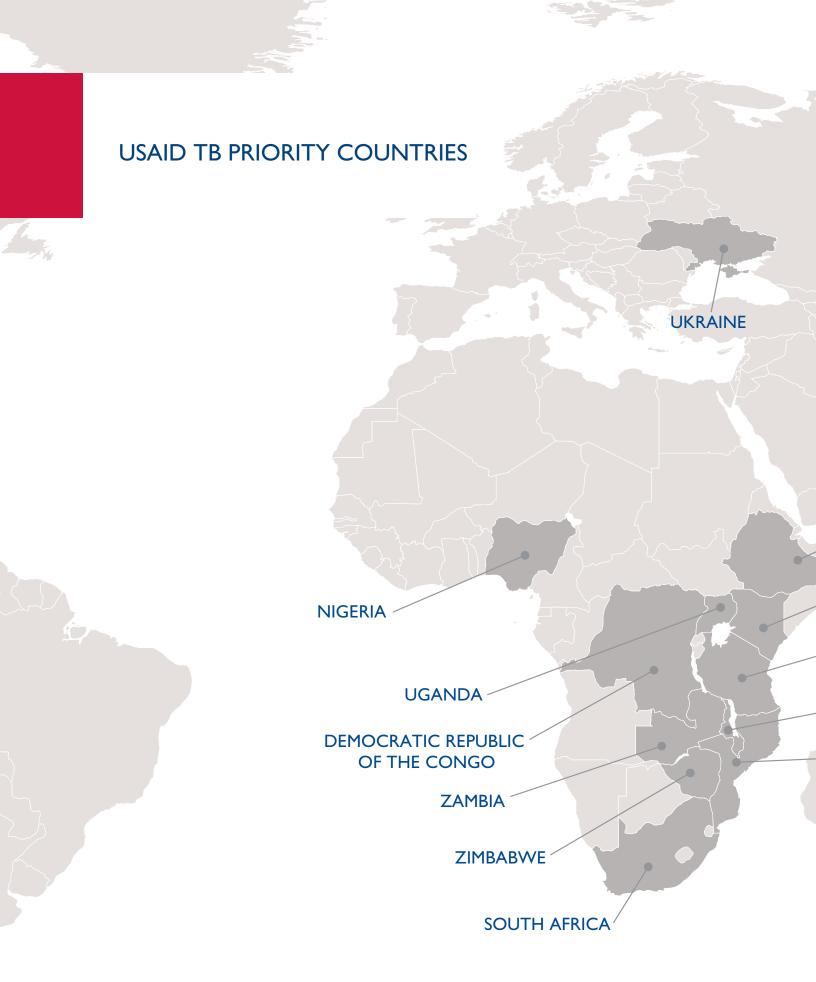
This appendix provides a snapshot of the achievements within each of the 22 countries where USAID provided bilateral assistance to end TB during FY 2017.

NOTES

- The charts present the distribution of program funding in broad categories.
- Unless otherwise noted, notification data are a proxy for persons diagnosed and started on treatment for active TB.
- The estimated burden uses data from FY 2017.
- The "40x22" and "30x22" targets were calculated using the latest data from the World Health Organization (WHO) on incidence estimates and notifications available publicly. With the exception of India and the Philippines, all projections were calculated using the TB Impact Model and Estimates Model supported by USAID. To reflect the ambition of National Governments, targets were adjusted upwards for TB treatment in India and Philippines based on their announcements at the United Nations High-Level Meeting (UNHLM) in September 2018. Targets may be adjusted in the coming months based on more in-depth discussions with governments.
- For the purpose of this appendix, "drug-resistant TB" (DR-TB) means disease that shows resistance to at least isoniazid and rifampicin.
- Bedaquiline (BDQ) is a recently developed anti-TB medication, prescribed for patients with advanced forms of multi-drug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB). Data on cumulative BDQ treatments received came from the Stop TB Partnership's Global Drug Facility, which supports the USAID-Johnson and Johnson Bedaquiline-Donation Program. BDQ data on South Africa came from the National Tuberculosis Programme (NTP) of the South African Ministry of Health.
- Complete FY 2017 TB preventive treatment data were unavailable for Bangladesh, the Democratic Republic of the Congo, Malawi, Uganda, and Tanzania.
- Data on the number of TB cases attributable to top risk factors were not available for Tajikistan. Other
 missing data related to these graphs are noted directly on the graphs.
- GeneXpert (Xpert) is a near-point-of-care diagnostic tool that tests sputum samples for the presence of TB. It is highly accurate and detects difficult-to-diagnose forms of TB, such as DR-TB and HIV-associated TB, in less than two hours, at more-accessible decentralized facilities. Concessional pricing data for Xpert cartridges in USAID TB priority countries include all purchases made by the public sector.

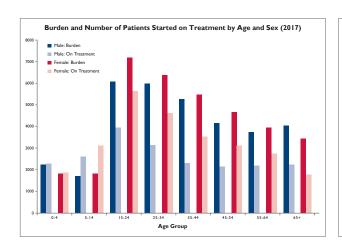
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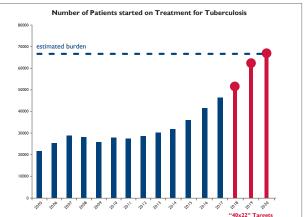
Data for all of the following pages come from USAID; the WHO; Cepheid, Inc.; the Stop TB Partnership's Global Drug Facility; and NTPs.

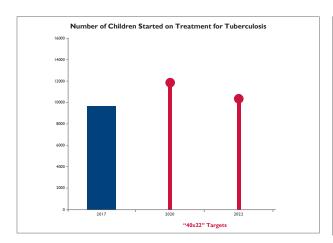


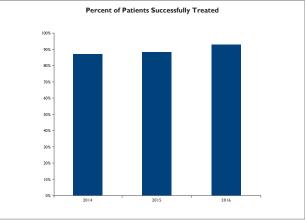


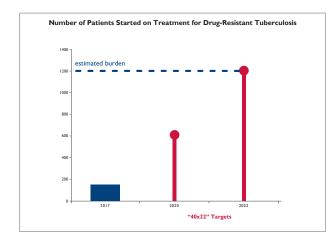
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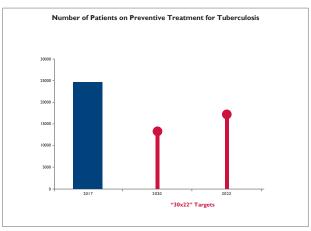




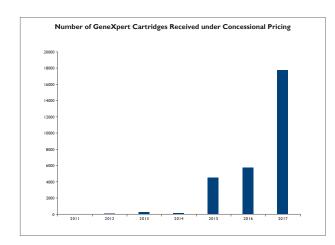


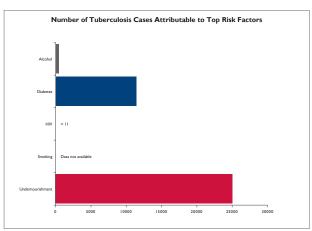


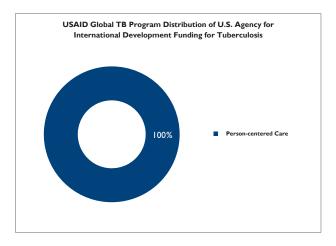




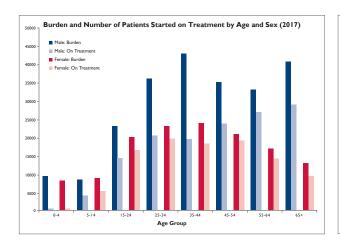
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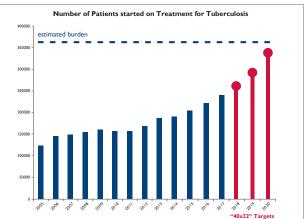


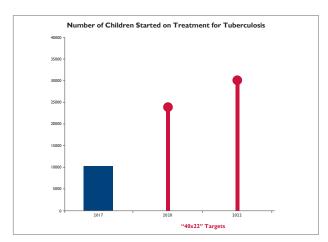


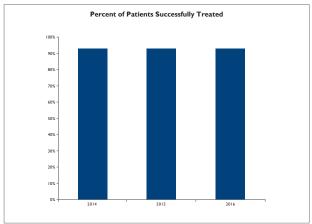


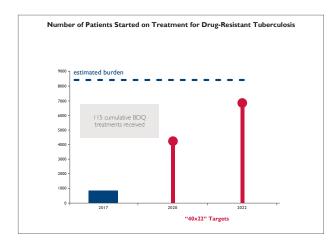
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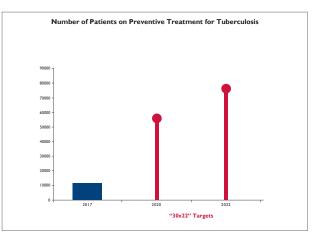




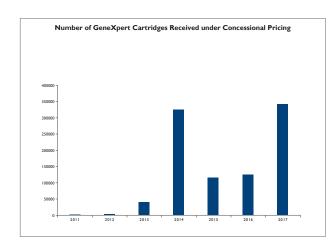


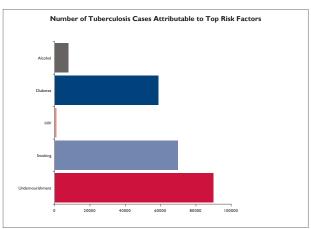


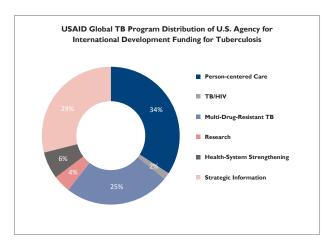




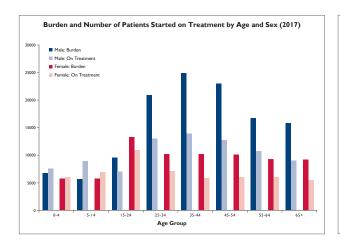
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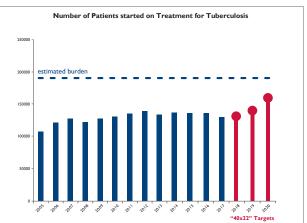


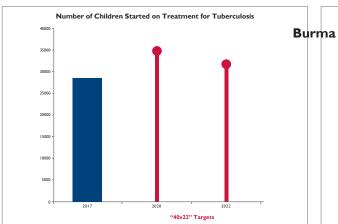


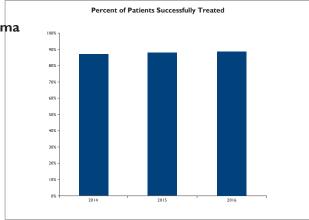


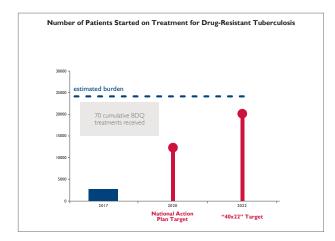
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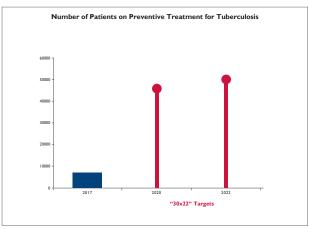




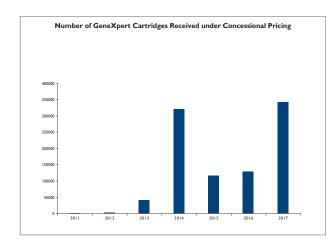


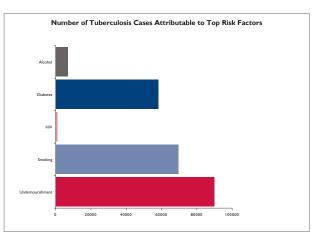


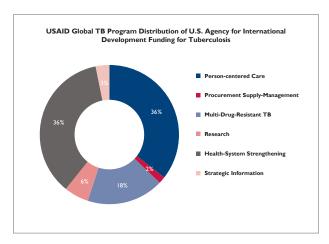




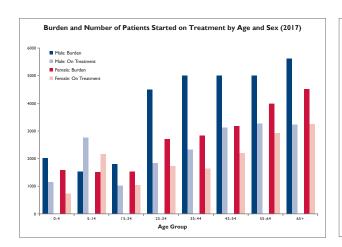
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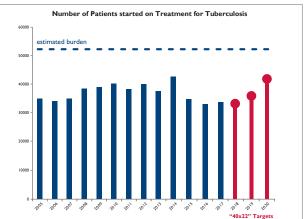


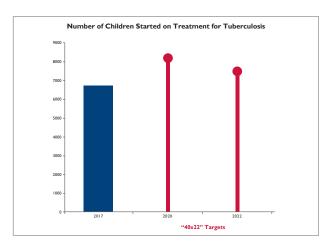


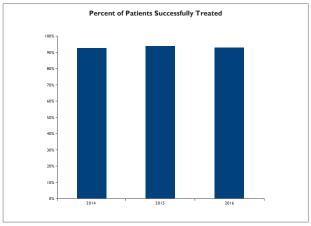


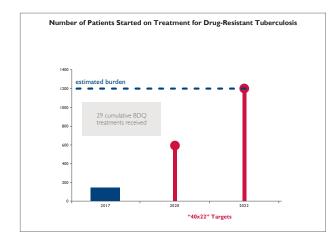
KINGDOM OF CAMBODIA

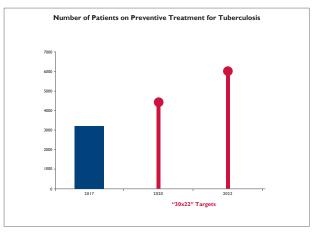




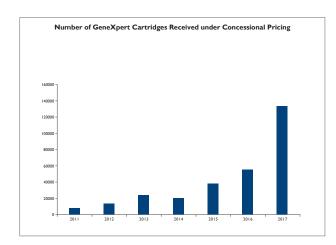


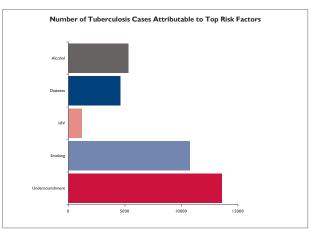


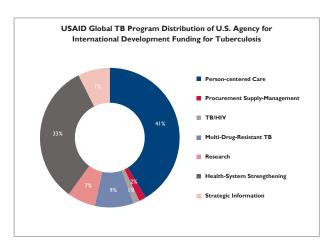




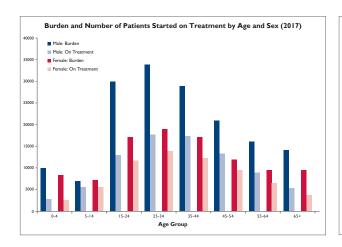
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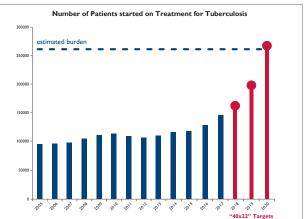


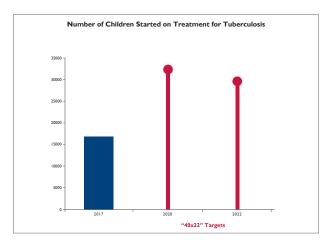


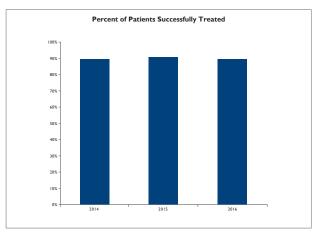


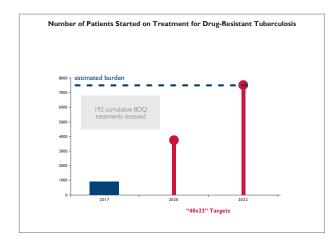
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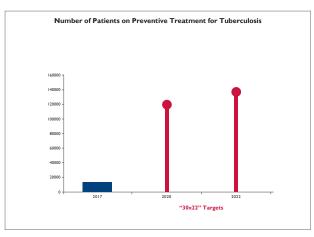




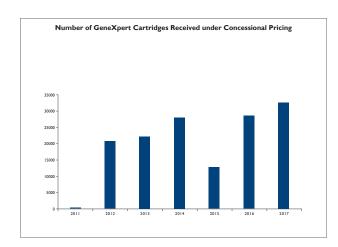


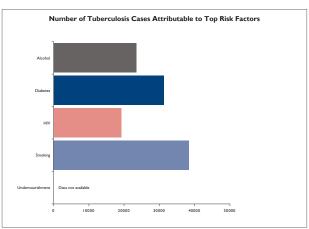


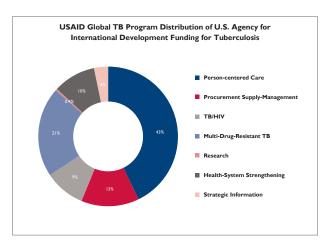




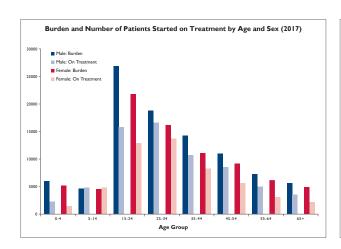
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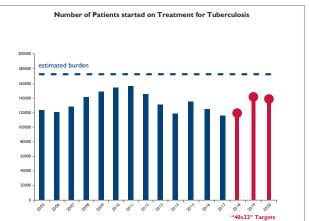


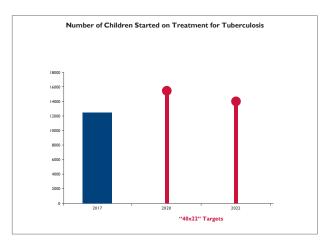


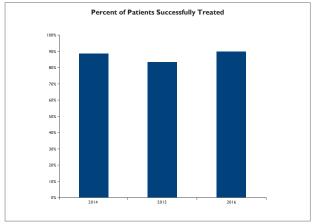


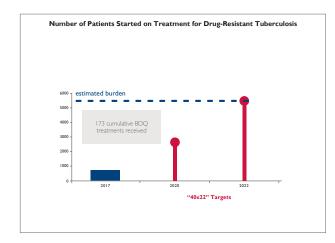
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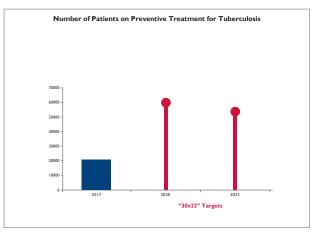






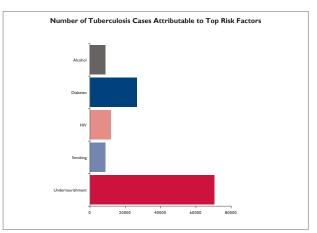


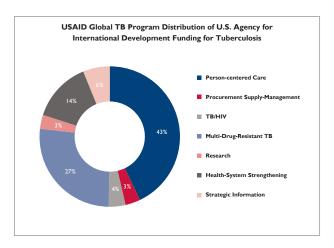




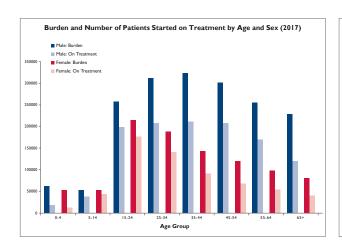
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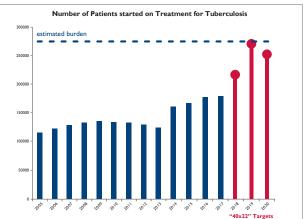


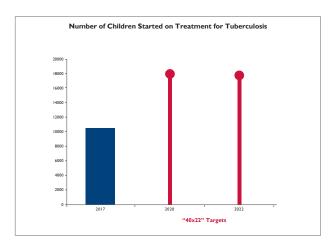


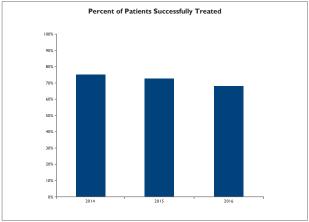


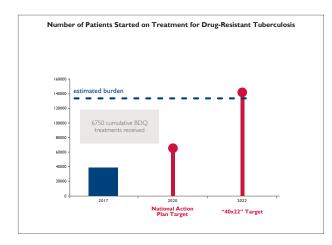
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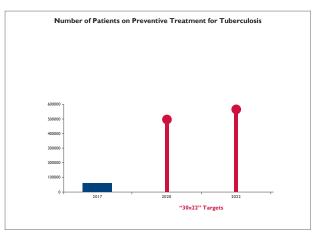




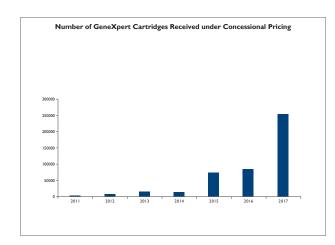


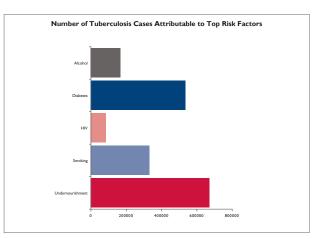


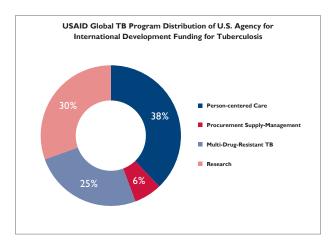




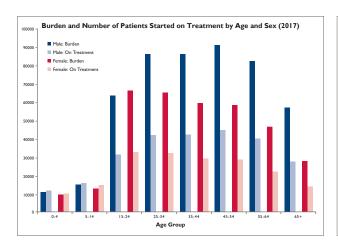
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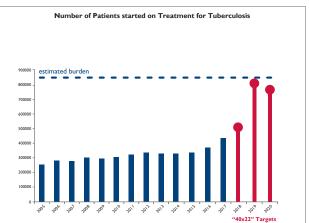


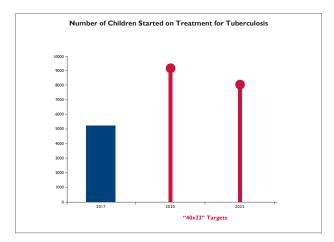


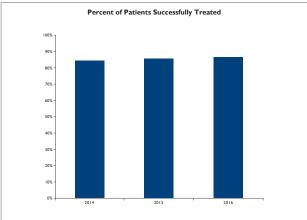


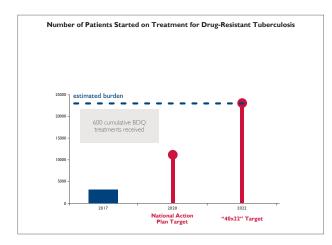
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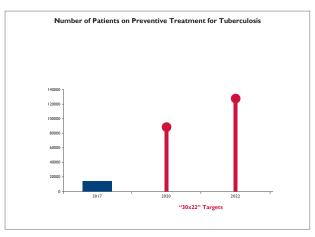




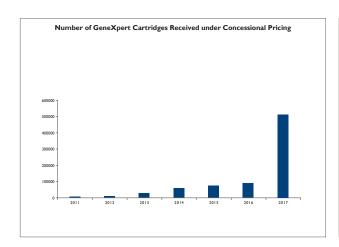


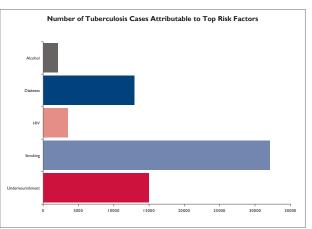


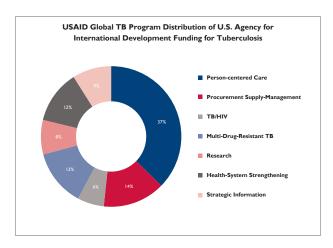




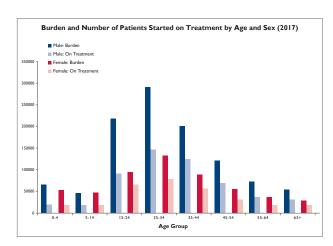
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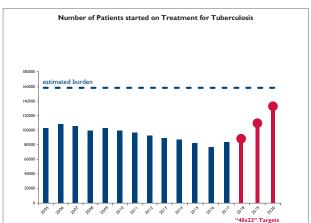


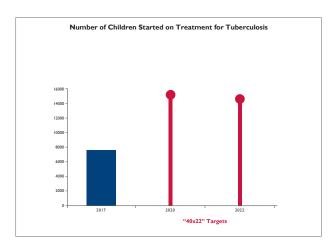


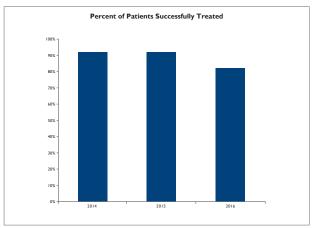


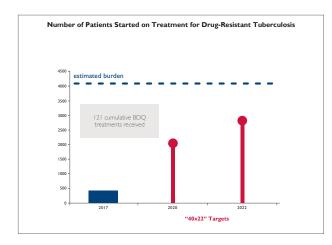
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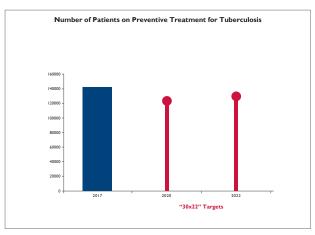




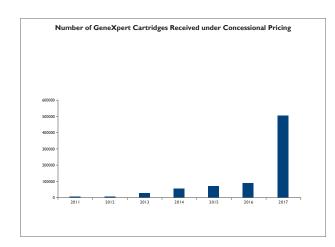


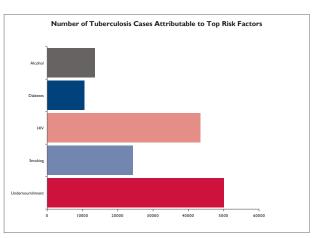


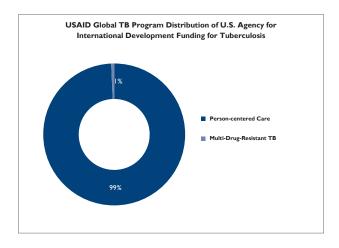




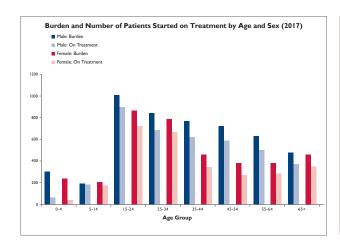
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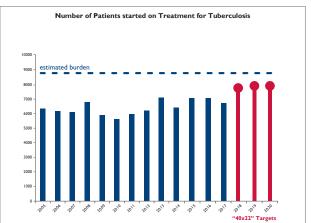


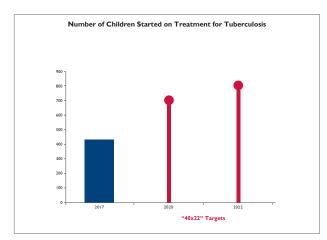


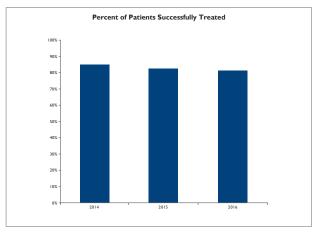


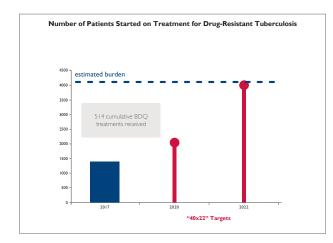
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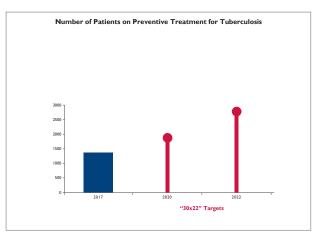




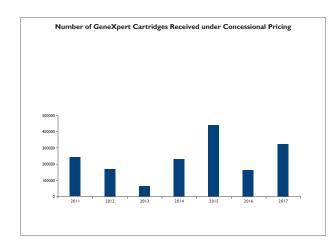


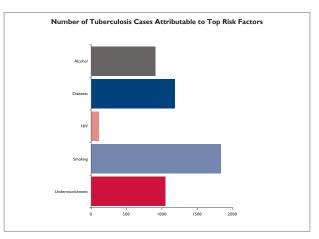


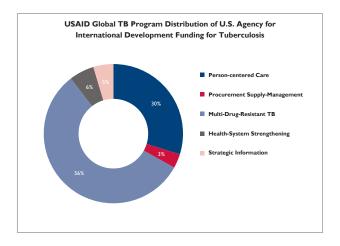




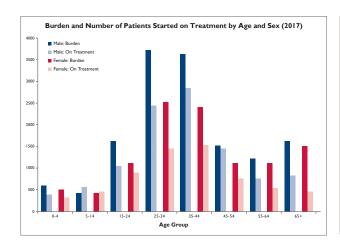
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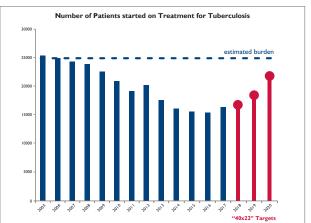


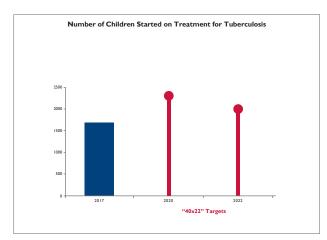


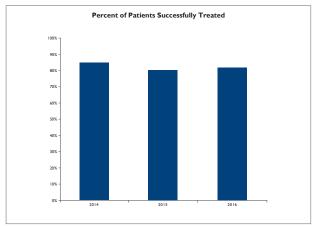


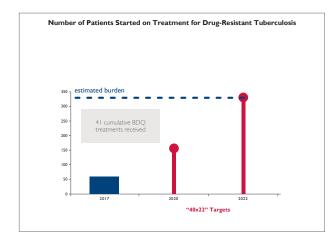
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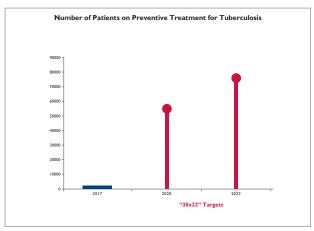




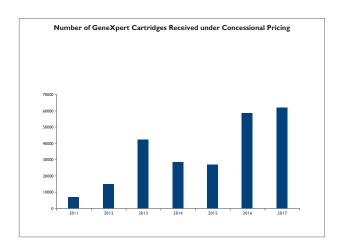


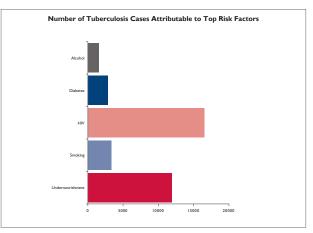


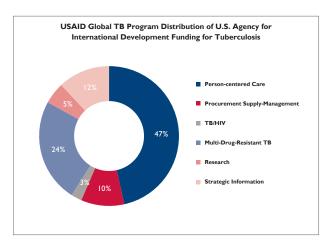




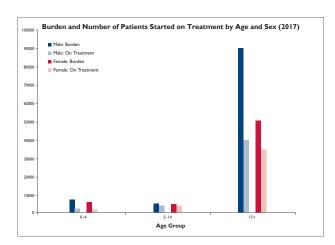
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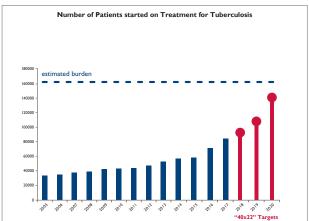


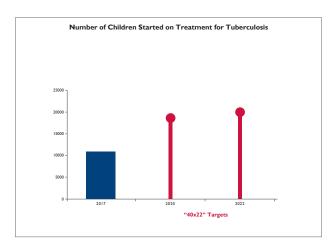


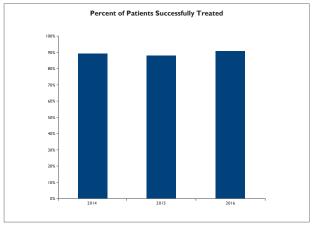


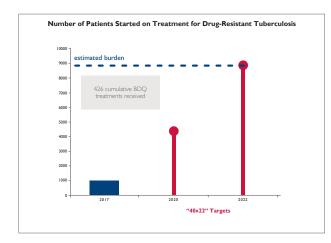
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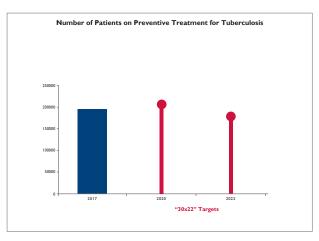




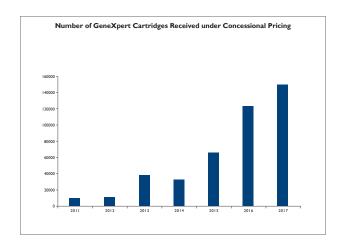


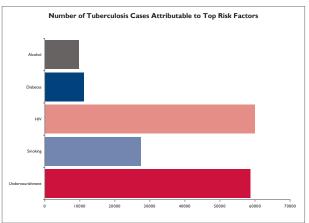


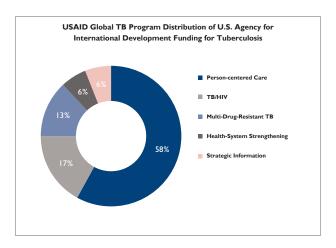




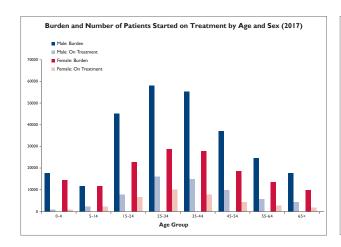
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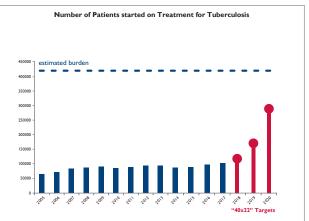


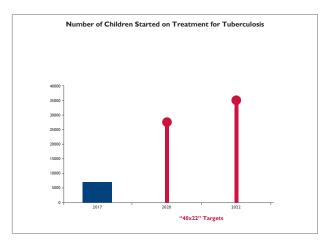


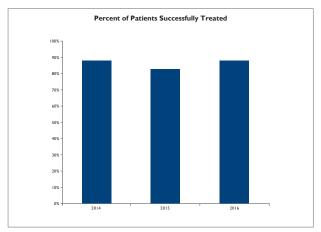


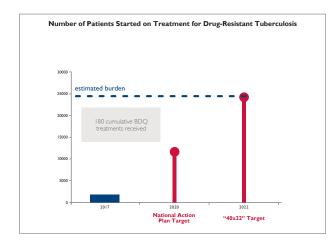
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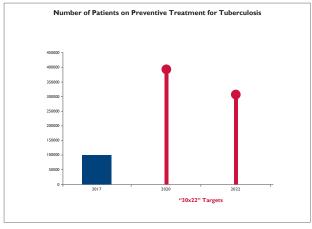




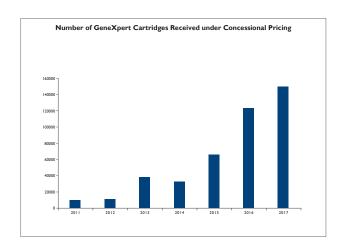


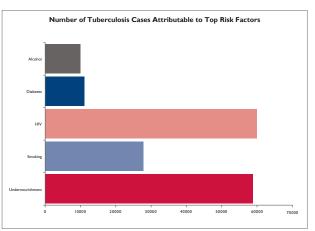


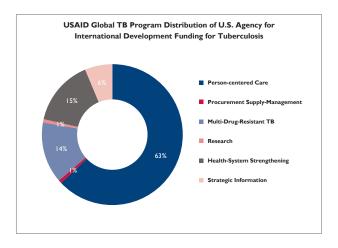




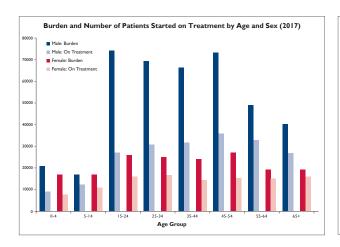
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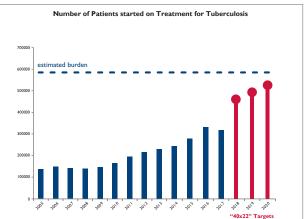


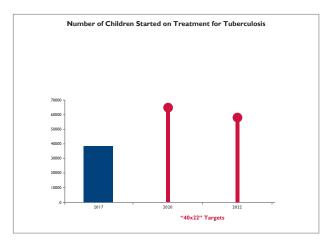


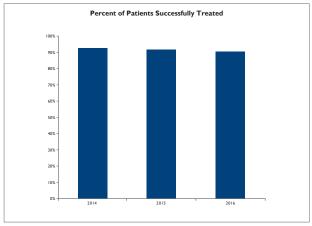


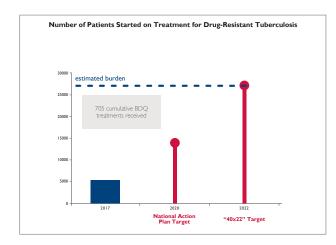
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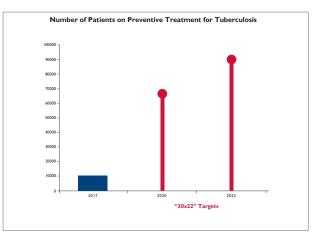




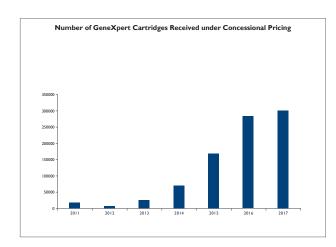


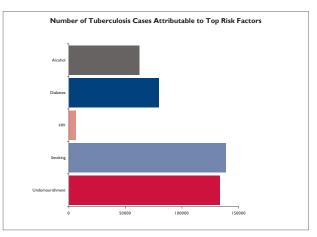


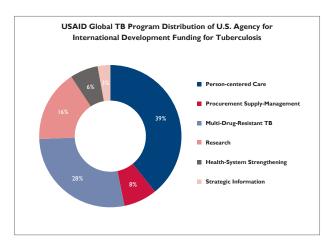




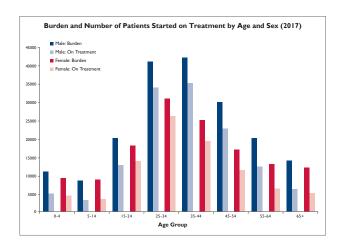
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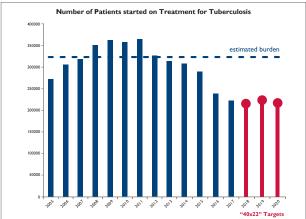


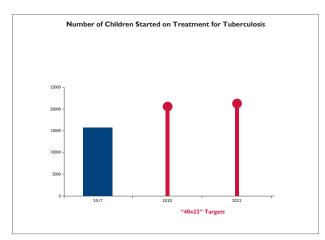


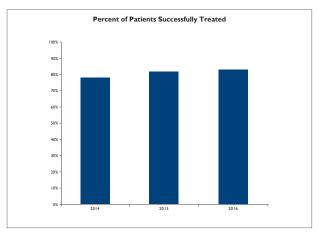


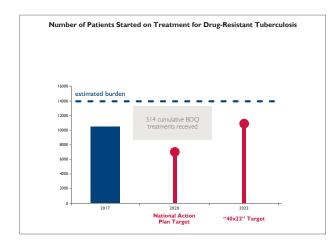
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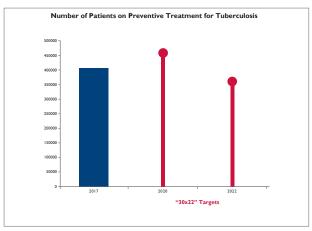




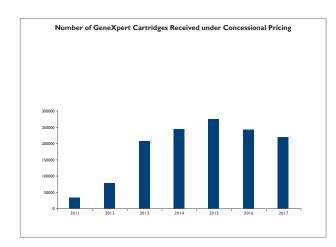


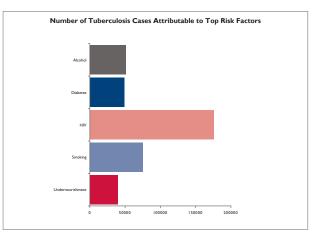


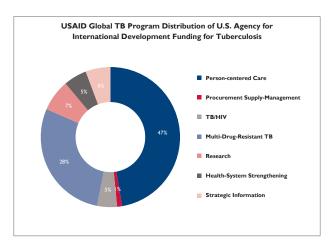




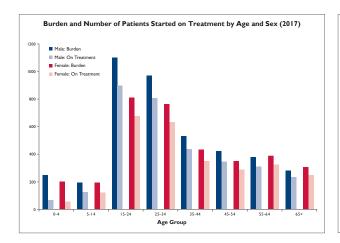
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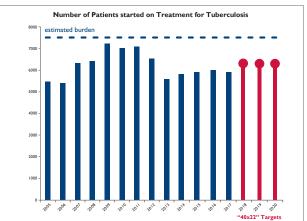


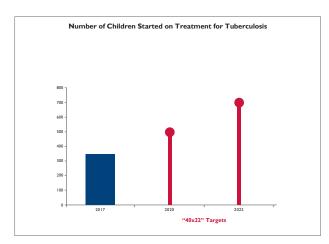


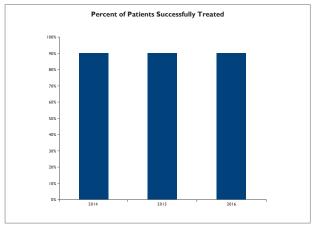


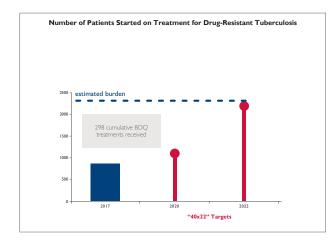
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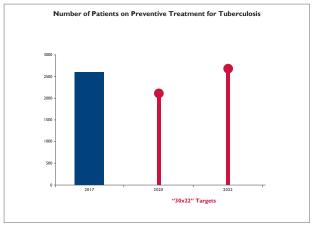




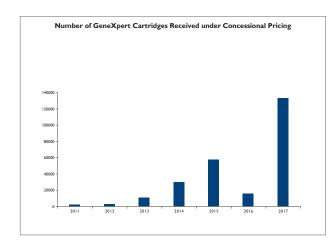


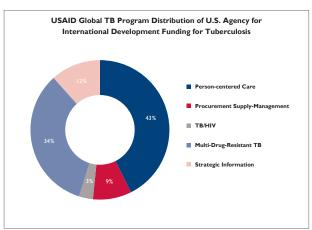




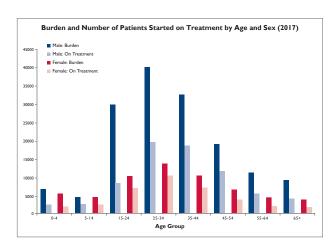


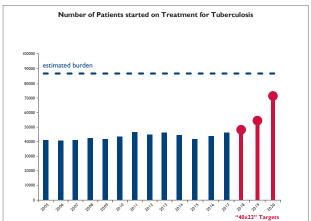
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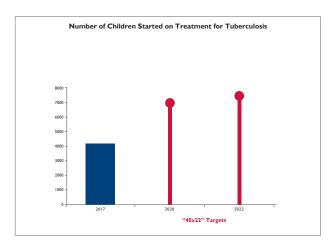


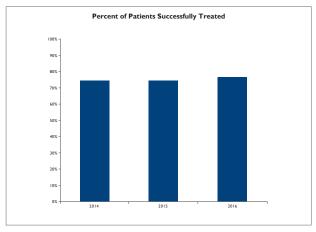


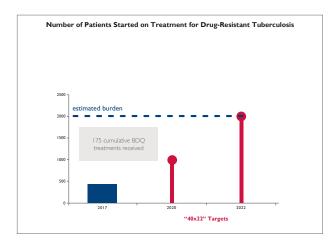
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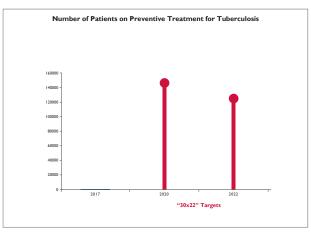




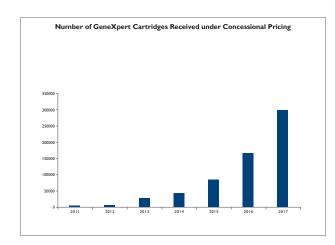


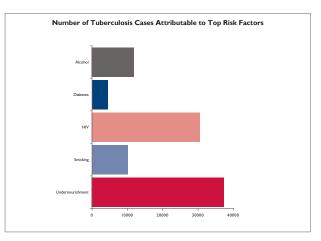


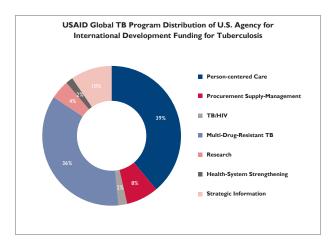




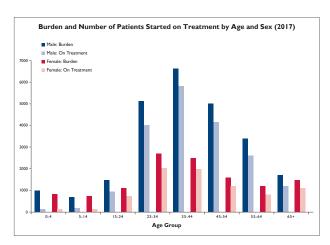
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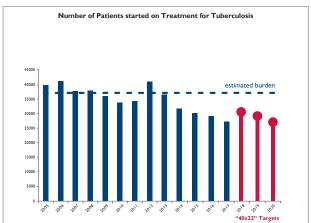


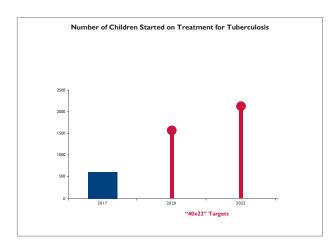


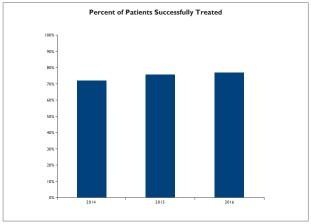


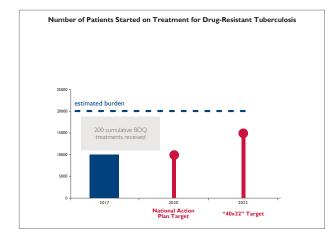
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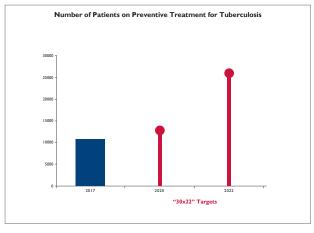




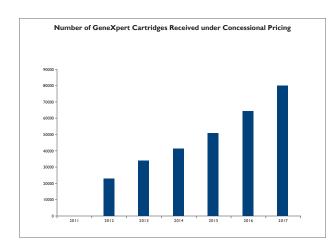


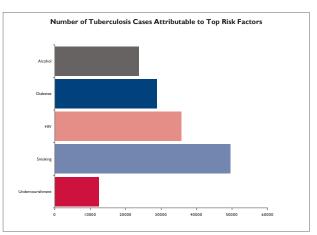


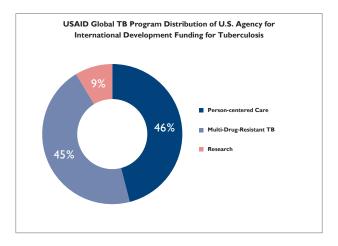




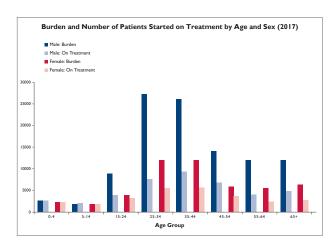
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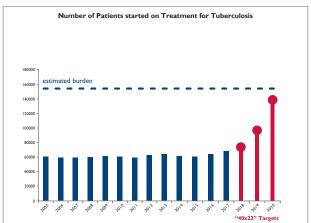


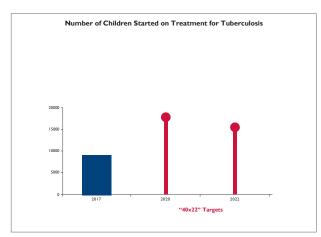


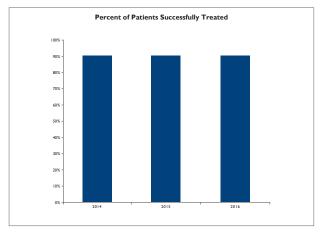


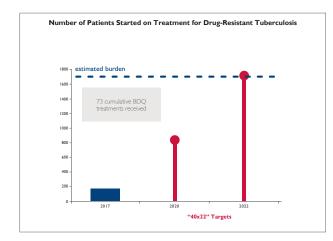
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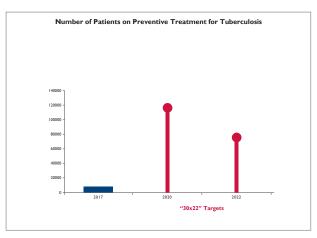




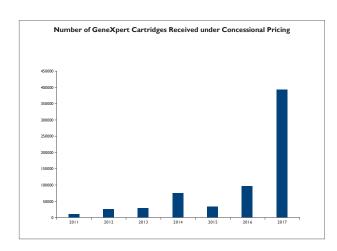


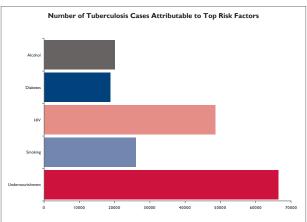


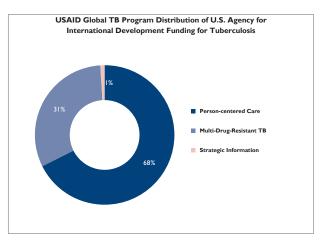




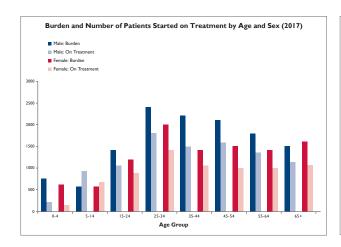
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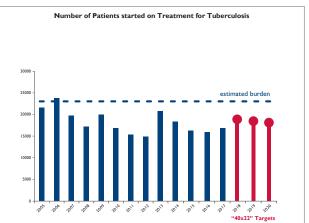


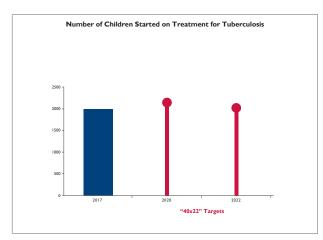


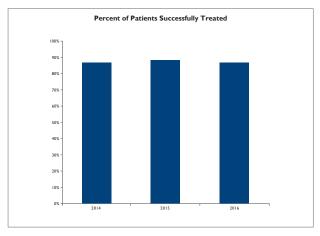


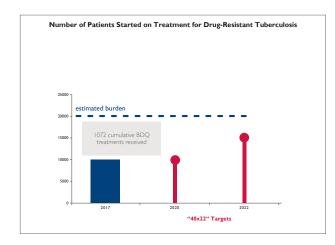
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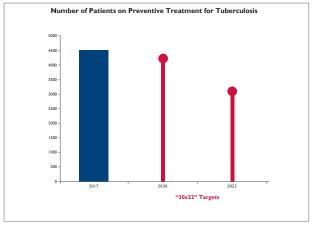




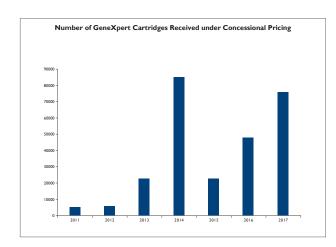


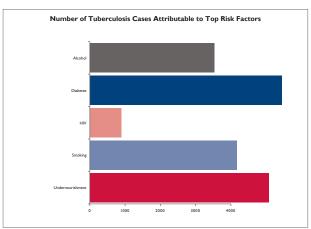


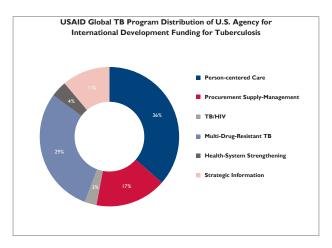




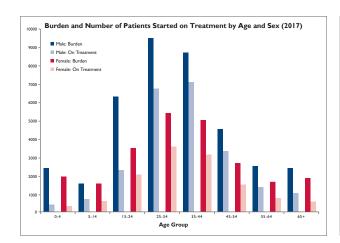
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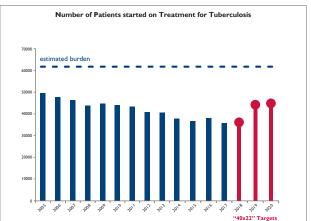


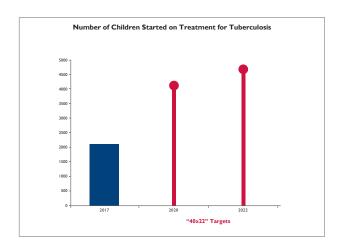


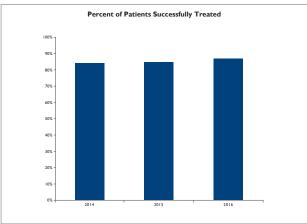


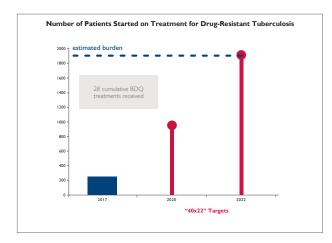
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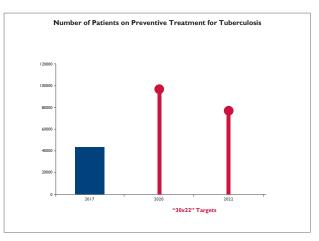




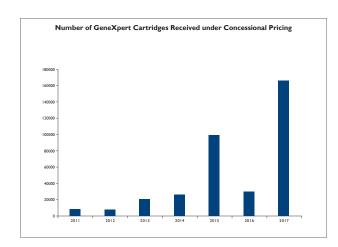


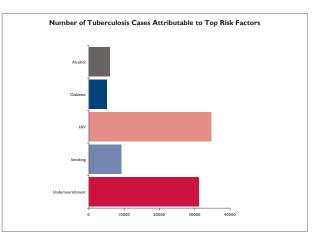


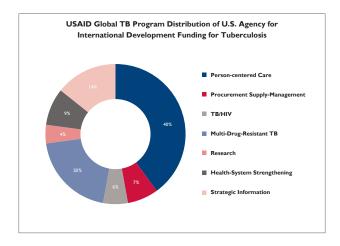




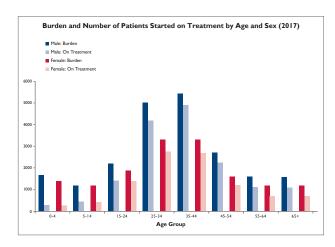
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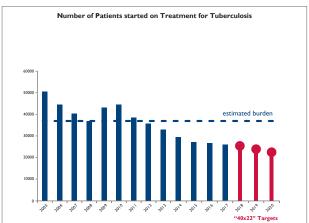


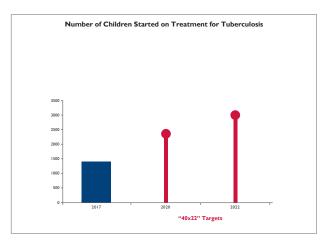


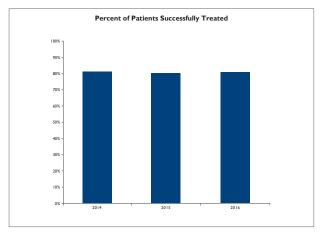


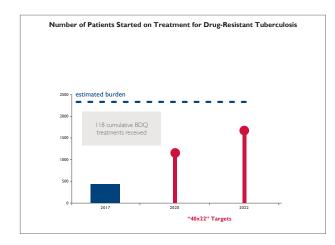
REPUBLIC OF ZIMBABWE

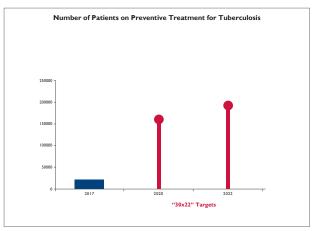












REPUBLIC OF ZIMBABWE

