TB CALCULATION

Spreadsheet Documentation

Definitions

- WHO region: designated regions provided by the World Health Organization[1]
- DALY: Disability-Adjusted Life Years (D)
  - Years of life taken by disease from population if it was in a healthy state free from disease
- Treatment Coverage (θ):
  - Ratio between number of people receiving treatment to the estimated number of people needing treatment
- Efficacy (e):
  - Percentage of population receiving treatment that were actually cured
- Data generated from WHO, UNAID database

[1]*http://www.who.int/neglected_diseases/preventive_chemotherapy/sch/en/*

Tuberculosis by Countries

Our current TB model investigates the impact of drugs on three patient groups: drug-susceptible TB **(DS-TB)**, multidrug resistant TB **(MDR-TB)**, and extensively drug-resistant TB **(XDR-TB)**. The model also makes a distinction between the drug impact of DS-TB patients with HIV and without.
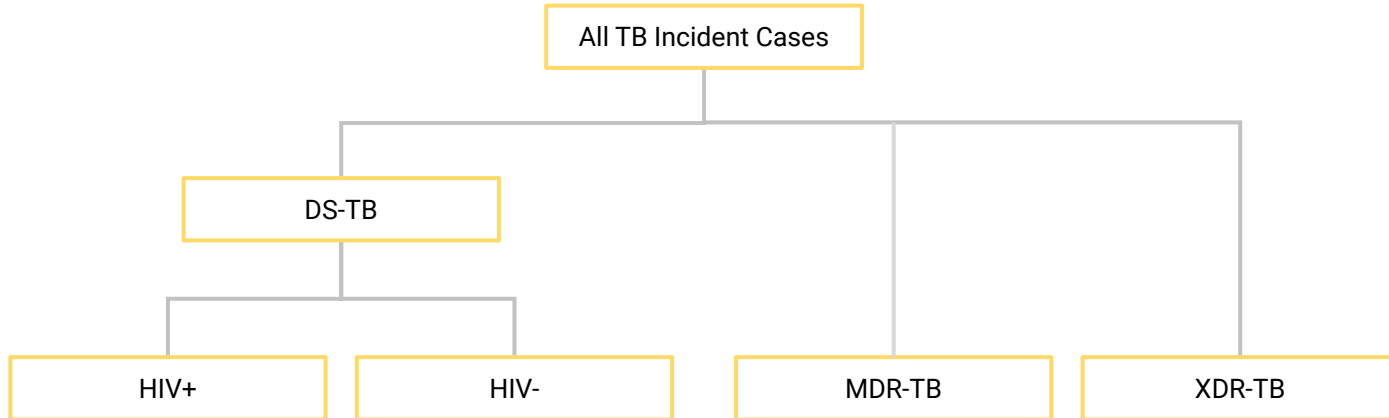
Impact Formula

$$I = \frac{D * e * \Theta}{1 - e * \Theta}$$

- Where:
  - D = DALYs
  - e = Efficacy
  - Θ = Treatment Coverage

Country Data

- **Column A:** Country
- **Column B:** Countries sorted by WHO Region
- **Column D:** DALYs

A	B	D
This model considers three variations of TB: Drug-Susceptible TB, Multi Drug-Resistant (MDR) TB and Extensively Drug-Resistant (XDR) TB. Totally Drug-Resistant (TDR) cases are currently not modeled given the very minimal number of cases reported so far in India, Iran and Italy. See cell comments for details.	WHO Region	DALY
		49,601,144.66
Afghanistan	EMR	424,662
Albania	EUR	2,211
Algeria	AFR	100,018
American Samoa	WPR	
Andorra	EUR	29
Angola	AFR	282,554
Anguilla	AMR	
Antigua and Barbuda	AMR	35
Argentina	AMR	35,133
Armenia	EUR	6,662
Aruba	AMR	
Australia	WPR	2,281
Austria	EUR	1,806
Azerbaijan	EUR	36,244

Prevalence and Incidence

- **Column M:** Total TB prevalence
- **Column N:** Total TB incidence
- **Column O:** % of cases with known HIV status
- **Column P:** # of cases with known HIV status
- **Column Q:** New and retreated cases recorded as TB/HIV+
- **Column R:** % incidence with known HIV status

	M	N	O	P	Q	R
	TB Prevalence	TB Incidence	% TB Cases With Known HIV Status	TB Cases With Known HIV Status	TB/ HIV+	% TB Incidence With Known HIV Status
	e_prev_num	e_inc_num	TB patients with known HIV status (%)	hiv_test	hivtest_pos	= Col O, else Cell L28
	93,000.0	53,000.00	18.00%	5170	2	18.00%
	730.0	490.00	42.00%	186	0	42.00%
	50,000.0	28,000.00				34.00%
	6.0	5.00		3	0	34.00%
	12.0	8.00		0	0	34.00%
	75,000.0	82,000.00	4.90%	2434	1620	4.90%
	7.0	3.00		0	0	34.00%
	13.0	8.00	86.00%	6	5	86.00%
	15,000.0	8,400.00	14.00%	1121	672	14.00%
	2,500.0	1,900.00	70.00%	1242	17	70.00%
	14.0	7.00				34.00%
	1,900.0	1,400.00	54.00%	686	24	54.00%
	970.0	760.00				34.00%
	19,000.0	12,000.00	75.00%	6290	48	75.00%

Prevalence and Incidence

- **Column S:** # incidence with known HIV status
- **Column T:** TB/HIV+ Among Incident Cases With Known HIV Status
- **Column U:** TB/HIV- Among Incident Cases With Known HIV Status
- **Column V:** TB/HIV+ Proportion = Col T/Col S
- **Column W:** TB/HIV- Proportion = Col U/Col S

	S	T	U	V	W
				16.44%	80.34%
	# TB Incidence With Known HIV Status	TB/HIV+ Among Incident Cases With Known HIV Status	TB/HIV- Among Incident Cases With Known HIV Status	TB/HIV+ Proportion	`TB/HIV- Proportion
	= Col R * Col N	= [Col Q / Col P] * Col S	= Col S - Col T	= Col T / Col S	= Col U / Col S
	9,540	4	9,536	0.04%	99.96%
	206	0	206	0.00%	100.00%
	9,520	2,190	7,330	23.00%	77.00%
	2	0	2	0.00%	100.00%
	3		3	0.00%	100.00%
	4,018	2,674	1,344	66.56%	33.44%
	1		1	0.00%	100.00%
	7	6	1	83.33%	16.67%
	1,176	705	471	59.95%	40.05%
	1,330	18	1,312	1.37%	98.63%
	2	1	2	23.00%	77.00%
	756	26	730	3.50%	96.50%
	258	59	199	23.00%	77.00%
	9,000	69	8,931	0.76%	99.24%
	36	17	19	48.48%	51.52%

DS-TB

Incidence and DALYs

- **Column X:** Total Incident Drug Susceptible TB = Col N-Col AG-Col AW

- **Column Y**: Incident cases that are TB/HIV+ = Col X*Col V

- **Column Z:** Incident cases that are TB/HIV- = Col x*Col W

- **Column AA**: Total DALYS Lost to Drug Susceptible TB/HIV+ = (Col D - Col AR - Col BA)*Col V

- **Column AB:** Total DALYs Lost to Drug Susceptible TB/HIV- = (Col D - Col AR - Col BA)*Col W

X	Y	Z	AA	AB
				Drug-Susceptible
Total Incident Drug Susceptible TB	**Incident cases that are TB/HIV+**	**Incident cases that are TB/HIV-**	**Total DALYS Lost to Drug Susceptible TB/HIV+**	**Total DALYs Lost to Drug Susceptible TB/HIV-**
= [Col N - Col AG] - Col AW	= Col X * Col V	= Col X * Col W	(Col D - Col AR - Col BA) * Col V	(Col D - Col AR - Col BA) * Col W
49,471.67	19.14	49,452.53	153.34	396,237.92
484.32	0.00	484.32	0.00	2,185.28
22,568.13	5,190.67	17,377.46	18,541.44	62,073.53
4.03	0.00	4.03	0.00	0.00
6.45	0.00	6.45	0.00	23.04
66,092.38	43,989.18	22,103.20	151,577.06	76,162.79
2.42	0.00	2.42	0.00	0.00
6.45	5.37	1.07	23.60	4.72
6,770.44	4,058.64	2,711.80	16,975.26	11,342.10
1,636.67	22.40	1,614.27	78.55	5,660.00
5.64	1.30	4.34	0.00	0.00
1,361.87	47.65	1,314.23	77.61	2,140.87
730.75	168.07	562.68	399.47	1,337.34
9,186.87	70.11	9,116.76	211.74	27,535.58

Coverage and Impact

- **Column AC:** Treatment Coverage for TB / HIV+

- **Column AD:** Treatment Coverage for TB / HIV-

- **Column AE:** Impact of Active TB/HIV+ treatment. Efficacy of DS-TB treatment can be found in the Assumptions section

- **Column AF:** Impact of Active TB/HIV- treatment

	AC	AD	AE	AF
			e TB Calculations	
	Treatment Coverage for TB / HIV+	Treatment Coverage for TB / HIV-	Impact of Active TB/HIV+ Treatment Regimen	Impact of Active TB/HIV- Treatment Regimen
	= Cell L39	= Cell L39	=(-col AD*((1-M23)-1))*(col AB/((1-col AD)+(col AD*(1-M$23))))	=(-col AE*((1-M24)-1))*(col AC/((1-col AE)+(col AE*(1-M$24))))
	65.90%	65.90%	138.45	547,006.04
	65.90%	65.90%	0.00	3,016.78
	65.90%	65.90%	16,740.65	85,692.45
	65.90%	65.90%	0.00	0.00
	65.90%	65.90%	0.00	31.80
	65.90%	65.90%	136,855.46	105,142.66
	65.90%	65.90%	0.00	0.00
	65.90%	65.90%	21.31	6.52
	65.90%	65.90%	15,326.58	15,657.76
	65.90%	65.90%	70.92	7,813.62
	65.90%	65.90%	0.00	0.00
	65.90%	65.90%	70.08	2,955.47
	65.90%	65.90%	360.67	1,846.20
	65.90%	65.90%	191.18	38,012.84

MDR-TB

MDR-TB Case Type

- **Column AG:** MDR-TB Incidence - Col AN*Col N - Col AW

- **Column AH:** New cases that have MDR-TB

- **Column AI:** % of new cases that have MDR-TB

- **Column AJ:** Retreatment cases that have MDR-TB

- **Column AK:** % of retreatment cases that have MDR-TB

- **Column AL:** Estimated new cases (any type) - Col AH/Col AI

- **Column AM:** Estimated Retreatment Cases (any type) - Col AJ/Col AK

						MDR-TB Calculations
AG	AH	AI	AJ	AK	AL	AM
MDR-TB Incidence	New cases that have MDR-TB	% of new cases that have MDR-TB	retreatment cases that have MDR-TB	% of retreatment cases that have MDR-TB	Estimated new cases (any type)	Estimated Retreatment Cases (any type)
(Col AN * Col N) - Col AW	mdr_new	e_new_mdr_pcnt	mdr_ret	e_ret_mdr_pcnt	= Col AH / Col AI	= Col AJ / Col AK
3,210.78	13	6.10%	6	8.30%	213.11	72.29
5.17	1	0.58%	1	0.00%	172.41	
4,943.00		1.40%		9.10%		
0.88	0	4.50%	0	24.00%		
1.41	0	0.00%	0	0.00%		
14,475.93		1.90%		20.00%		
0.53	0	2.20%	0	14.00%		
1.41	0	2.20%	0	14.00%		
1,482.90		2.20%		15.00%		
239.63	40	9.40%	28	43.00%	425.53	65.12
1.24		2.20%		14.00%		
34.70	21	2.30%	11	4.20%	913.04	261.90
26.61	5	2.50%	3	38.00%	200.00	7.89
2,559.95	93	13.00%	459	28.00%	715.38	1,639.29
6.36	0	3.70%	0	0.00%		

MDR-TB Case Type

- Column AN: Weighted average of proportion of new and retreatment cases that have MDR-TB
  - If the WHO reports zero new and retreatment MDR-TB cases at the country-level, the model will substitute the global average of the proportion of new and retreated MDR-TB cases out of total TB cases.
  - Countries with this fallback data will maintain a total MDR-TB impact score but will lack the further disaggregation of impact among treatment regimens. This is due to the absence of resistance rate data for new and retreated MDR-TB cases at the country-level.

AN
Weighted average of proportion of new and retreatment cases that have MDR-TB
6.66%
1.16%
19.40%
19.40%
19.40%
19.40%
19.40%
19.40%
19.40%
13.86%
19.40%
2.72%
3.85%
23.44%

Treatment Coverage

- **Column AO:** # MDR-TB Needing Treatment - Col AN*Col M
- **Column AP:** Reported # of people receiving treatment for MDR-TB
- **Column AQ:** Treatment Coverage for MDR-TB - Col AP/Col AO
- **Column AR:** DALYs Lost to MDR-TB - (Col AN*Col D) - Col BA

AO	AP	AQ	AR
# MDR-TB Needing Treatment	# MDR-TB Receiving Treatment	Treatment Coverage for MDR-TB	DALYs Lost to MDR-TB
= Col AN * Col M	conf_mdr_tx	= Col AP / Col AO	(Col AN * Col D) - Col BA
6,191	0	0.00%	25,726.37
8	0	0.00%	23.34
9,700	56	0.58%	17,656.75
1	0	0.00%	0.00
2	0	0.00%	5.05
14,550	3	0.02%	49,880.88
1	0	0.00%	0.00
3	0	0.00%	6.20
2,910		0.00%	6,202.23
346	128	36.94%	840.18
3		0.00%	0.00
52	31	59.91%	56.52
37	15	40.19%	63.25
4,454	286	6.42%	7,731.88

MDR-TB Impact

- **Column AS:** Impact of MDR-TB Treatment Regimen - Divides by two because the average length of MDR-TB treatment is two years

- **Column AT:** Impact of Z+S+Lfx+Eto+Cs+PAS
  Impact * Col BR

- **Column AU:** Impact of S+Lfx+Eto+Cs+PAS
  Impact * Col BS

- **Column AV:** Impact of Km+Lfx+Eto+Cs+PAS
  Impact * Col BT

AS	AT	AU	AV
Impact of MDR-TB Treatment Regimen		**Impact of MDR-TB Treatment Regimen**	X
$((-col\ AR*((1-M\$25)-1))$ $*(col\ AS/((1-col\ AR)+(col$ $AR*(1-M\$25)))))/2$	Z+S+Lfx+Eto+Cs+PAS	S+Lfx+Eto+Cs+PAS	Km+Lfx+Eto+Cs+PAS	C
0.00	0.00	0.00	0.00
0.00	0.00	0.00	0.00
24.53	7.28	1.13	16.12
0.00	0.00	0.00	0.00
0.00	0.00	0.00	0.00
2.47	0.72	0.11	1.64
0.00	0.00	0.00	0.00
0.00	0.00	0.00	0.00
0.00	0.00	0.00	0.00
90.55	24.05	3.72	62.78
0.00	0.00	0.00	0.00
11.41	4.14	0.64	6.62
7.56	2.49	0.39	4.68
122.94	26.47	4.10	92.37

XDR-TB

Calculation

- **Column AW:** XDR-TB Incidence
  Col AN*Col N*L31

- **Column AX:** # XDR-TB Needing Treatment
  L31*Col AO

- **Column AY:** # XDR-TB Receiving Treatment
  Col AX*Col AZ

- **Column AZ:** Treatment Coverage for XDR-TB

- **Column BA:** DALYs lost to XDR-TB
  Col AN*Col D*L31

- **Column BB:** Impact of XDR-TB Treatment Regimen, divides by two because the average length of XDR-TB is two

- **Column BC:** Sums impact of all types of TB

AW	AX	AY	AZ	BA	BB	BC
			XDR-TB Calculations			
XDR-TB Incidence	# XDR-TB Needing Treatment	# XDR-TB Receiving Treatment	Treatment Coverage for XDR-TB	DALYs lost to XDR-TB	Impact of XDR-TB Treatment Regimen	Total TB Treatment Impact
Col AN * Col N * Cell L31	Cell L31 * Col AO	= Col AX * Col AZ	= Cell M38	Col AN * Col D * Cell L31	Col AW * Col AZ * Cell L26 * Cell L73	
317.55	557	212	38.00%	2,544.37	104.64	547,249.13
0.51	1	0	38.00%	2.31	0.09	3,016.88
488.87	873	332	38.00%	1,746.27	71.82	102,529.44
0.09	0	0	38.00%	0.00	0.00	0.00
0.14	0	0	38.00%	0.50	0.02	31.82
1,431.69	1,309	498	38.00%	4,933.27	202.88	242,203.47
0.05	0	0	38.00%	0.00	0.00	0.00
0.14	0	0	38.00%	0.61	0.03	27.85
146.66	262	100	38.00%	613.41	25.23	31,009.56
23.70	31	12	38.00%	83.09	3.42	7,978.51
0.12	0	0	38.00%	0.00	0.00	0.00
3.43	5	2	38.00%	5.59	0.23	3,037.19
2.63	3	1	38.00%	6.26	0.26	2,214.69
253.18	401	152	38.00%	764.69	31.45	38,358.41

Resistance Rates

BD	BE	BF	BG	BH	BI	BJ	BK	BL	BM	BN	BO	BP	BQ	BR	BS	BT
				Original	Fallback											
previously treated cases resistance rates		new MDR-TB cases resistance rates		previously treated cases resistance rates estimate		new MDR-TB cases resistance rates estimate		previously treated cases portion of drug combination estimate			new MDR-TB cases drug combination portion of total percent of MDR-TB cases of those with DST estimate			weighted average drug combination drug combination estimate		
H+R+E+S	Multidrug	H+R+E+S	Multidrug	H+R+E+S	Multidrug	H+R+E+S	Multidrug	Z+S+Lfx+Eto+Cs+PAS	S+Lfx+Eto+Cs+PAS	Km+Lfx+Eto+Cs+PAS	Z+S+Lfx+Eto+Cs+PAS	S+Lfx+Eto+Cs+PAS	Km+Lfx+Eto+Cs+PAS	Z+S+Lfx+Eto+Cs+PAS	S+Lfx+Eto+Cs+PAS	Km+Lfx+Eto+Cs+PAS
				use region average if the region has data; OW, use global average	use region average if the region has data; OW, use global average	use region average if the region has data; OW, use global average	use region average if the region has data; OW, use global average	1	2	3	1	2	3	1	2	3
				10.53%	10.45%	1.50%	2.12%	28%	4.37%	67.43%	39%	6.09%	54.59%	30.06%	4.65%	65.29%
				5.08%	13.36%	0.84%	2.79%	34%	5.26%	60.73%	40%	6.27%	53.24%	34.74%	5.38%	59.88%
				10.53%	10.45%	1.50%	2.12%	28%	4.37%	67.43%	39%	6.09%	54.59%	30.06%	4.65%	65.29%
0.90%	1.9%,	0.20%	0.80%	0.90%	1.9%,	0.20%	0.80%	40%	6.25%	53.36%	42%	6.45%	51.85%	40.73%	6.31%	52.97%
				10.53%	10.45%	1.50%	2.12%	28%	4.37%	67.43%	39%	6.09%	54.59%			
				5.44%	11.74%	0.83%	2.16%	34%	5.19%	61.26%	41%	6.27%	53.22%			
				10.53%	10.45%	1.50%	2.12%	28%	4.37%	67.43%	39%	6.09%	54.59%	28.44%	4.40%	67.15%
				10.53%	10.45%	1.50%	2.12%	28%	4.37%	67.43%	39%	6.09%	54.59%	29.17%	4.52%	66.32%

Resistance to certain drugs is what determines the recommended treatment regimen, and can therefore be used to estimate the proportions of people that receive each regimen. These calculations are initially split into either new TB cases or retreatment cases, since there is unique resistance rate data for both. Once each category of MDR-TB drug resistance has a proportion calculated, the retreated and new cases are combined into the final section that determines the proportion of all MDR-TB cases that are receiving each treatment regimen.

- **Range BD:BG:** Hand-inputted new and retreatment data

- **Range BH:BK:** Applies regional and global averages

- **Range BL:BN:** Previously treated MDR-TB cases with resistance to Z+S+Lfx+Eto+Cs+PAS, S+Lfx+Eto+Cs+PAS, and Km+Lfx+Eto+Cs+PAS

- **Range BO:BQ:** Newly treated MDR-TB cases with resistance to Z+S+Lfx+Eto+Cs+PAS, S+Lfx+Eto+Cs+PAS, and Km+Lfx+Eto+Cs+PAS

- **Range BR:BT:** Percentage of MDR-TB cases that are either resistant to Z+S+Lfx+Eto+Cs+PAS, S+Lfx+Eto+Cs+PAS, and Km+Lfx+Eto+Cs+PAS

Patent Holder Rankings

- **Column J:** Company producing TB drugs
- **Column K:** Drugs that respective company produces
- **Column L:** Final impact of respective company

	J	K	L
	Company	**Drug(s)**	**Final Impact**
	Pfizer Inc	E, Cs, PAS, Eto	13,422,958.30
	Merck	S, Z	13,401,348.02
	F. Hoffmann-La Roche Ltd	H	13,398,454.29
	Sanofi	R	13,398,454.29
	Daichii Sankyo	Ofx, Lfx	9,793.28
	Eli Lilly	Cm	3,250.56
	Bristol-Myers Squibb	Amk	3,250.56
	Kyorin Pharmaceutical Co., Ltd	Gfx	2,437.92
	Bayer Healthcare	Mfx	2,437.92
	Overall Impact for TB Drugs		53,642,385.16

Manufacturer Rankings

Our impact scores can be used to assess the performance of companies involved in the manufacturing sector of the pharmaceutical industry. Manufacturing and distribution data provided by the WHO provides important information such as cost, drug strength, and the total number of units (TNU) of each drug that are involved in shipments of a variety of medicines.

This data can be used to determine the proportion of certain classes of drugs that each manufacturer in the database is responsible for shipping.

Manufacturer Rankings

We are able to calculate the lives saved from individual shipments of drugs so that the total number of lives saved by manufacturer can be determined. The calculation that is used is:

$$TNU / (365 * DD)$$

- Where:
  - TNU = total number of units, or, number of pills sent in a specific order
  - DD = the daily dose, or the assumed average maintenance dose per day for a drug

This allows us to calculate the total lives saved due to a single drug or the total lives saved for that drug due to an individual manufacturer. We can use the proportion of total lives saved by a manufacturer to estimate the proportion of the total impact that will be attributed to that company in terms of DALYs.

Manufacturer Rankings

The WHO's Global Price Reporting Mechanism allows us to track 21 manufacturers of drugs that target TB. Lupin Limited is a company that manufactures four TB drugs: Ethambutol (E), Isoniazid (H), and Rifampicin, (R), and Rifampicin+Isoniazid (R+H). Let's calculate the DALYs saved by Ethambutol:

Using our formula we find that, in 2010, E alone saved a total of 53,949.89 lives. We can also see that E produced by Lupin Ltd. was calculated to have saved 7,054.26 lives. This means that Lupin Ltd.'s E contributed to 13.08% of all lives saved by E.

We also know from our previous calculations that E alleviates 13,398,454.29 DALYs globally. Therefore, we can state that **E produced by Lupin Ltd. alleviates 1,751,924.28 DALYs.**

Manufacturer Rankings

The same process can be repeated for the drugs H, R, and R+H:

H: 6,073,703.35 DALYs alleviated

R: 14,518,052.88 DALYs alleviated

R+H: 14,670,697.41 DALYs alleviated

Summing the DALYs alleviated by all three drugs yields **35,262,453.64, which can be considered Lupin Ltd.'s global impact on TB in 2010.**

Assumptions for 2013

Efficacy of treatment for HIV+ TB	73%
Efficacy of treatment for HIV- TB	88%
Efficacy of MDR-TB treatment	52%
Efficacy of XDR-TB treatment	28%
(Estimated) % known HIV status	46%
% of TB cases tested for HIV (with known HIV status)	48%
% of TB cases tested for HIV that are HIV+	13%
% of MDR-TB that is XDR-TB	9.60%
% global antiretroviral treatment coverage (TB/HIV+)	70%
Proportion of new TB cases that are MDR-TB	3.50%
Proportion of retreatment TB cases that are MDR-TB	20.50%
XDR-TB Treatment Coverage	57%
Drug-Susceptible-TB Treatment Coverage	58%

Credit Proportions for DS-TB, MDR-TB, and XDR-TB

DS-TB treatment regimens	Drug proportion of regimen	Proportional impact per drug
R (Months 1 to 6)	0.25	10,842,565.11
H (Months 1 to 6)	0.25	10,842,565.11
E (Months 1 to 2)	0.25	10,842,565.11
Z (Months 1 to 2)	0.25	10,842,565.11

XDR-TB treatment regimens	Drug proportion of regimen	Proportional impact per drug
Cs	0.33	18,576.25
Km, Amk, or Cm	0.11	6,192.08
Lfx, Mfx, Gfx, or Ofx	0.08	4,644.06

MDR-TB treatment regimens	Drug proportion of regimen	Proportional impact per drug
Z + S + Lfx + Eto + Cs + PAS		
Z	0.17	7,289.01
S	0.17	7,289.01
Lfx	0.17	7,289.01
Eto	0.17	7,289.01
Cs	0.17	7,289.01
PAS	0.17	7,289.01
S + Lfx + Eto + Cs + PAS		
S	0.20	343.56
Lfx	0.20	343.56
Eto	0.20	343.56
Cs	0.20	343.56
PAS	0.20	343.56
Km + Lfx + Eto + Cs + PAS		
Km	0.20	4,007.12
Lfx	0.20	4,007.12
Eto	0.20	4,007.12
Cs	0.20	4,007.12
PAS	0.20	4,007.12

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Let's calculate the impact of the drug Z in the Dominican Republic (DR) in 2013. We will first retrieve DR's treatment coverage and efficacy data.

- MDR-TB Treatment Coverage
  - **11.48%**

- MDR-TB Efficacy

  - **52%**

DR's MDR-TB DALYs will be slightly harder to find. We need to first calculate the proportion of new and retreatment cases that have MDR-TB:

$$x = \frac{a + b}{c + d}$$

a = # of new cases that have MDR-TB

b = # of retreatment cases that have MDR-TB

c = Estimated new cases (any type)

d = Estimated retreatment cases (any type)

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

The completed formula and result can be found below:

$$x = \frac{30 + 62}{454.44 + 310}$$

$$x = \quad 12.03\%$$

Now we can multiply this number by DR's DALYs, 18,000, and then subtract the DALYs lost to XDR-TB, 207.94. This gives us **1,958.06 DALYs lost to MDR-TB**.

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Now we can calculate the **impact of all MDR-TB treatment regimens**. Note that we divide the impact by two because the length of MDR-TB treatment is two years.

$$I = \frac{1,958.06 * 11.48\% * 52\%}{1 - 11.48\% * 52\%} \; / \; 2$$

$$I = 62.16$$

The next step will be to **attribute credit amongst the three MDR-TB regimens**. We can do this by multiplying the impact of all MDR-TB treatment regimens by the proportion of all MDR-TB cases that are receiving the regimen that includes Z: **Z+S+Lfx+Eto+Cs+PAS (Regimen 1)**. To derive this proportion we need to first obtain the percentage of previously treated MDR-TB cases that use Regimen 1.

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Drug	Previously treated	Newly treated
H+R	33.7%	50%
H+R+E	3.3%	3.3%
H+R+S	11%	11%
H+R+E+S	3.81%	0.5%

According to the WHO, the estimated H+R resistance in previously treated cases in Dominican Republic is **33.70%** while for newly treated cases it is **50%**. The list of known drug resistance rates can be found in the table to the left.

Example: Drug Score
Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Given the values above, we can calculate the estimated MDR-TB treatment resistances to treatments that include pyrazinamide. According to studies conducted in South Africa, the resistance to pyrazinamide (Z) is 42.25% . We use this value as a global estimate for the resistance of Z due to the absence of data for the resistance of Z as a part of a treatment regimen. Both H+R+E and H+R+E+S can be taken with or without Z. We calculate their estimated resistance rates as follows:

Drug	Previously treated	Newly treated
H+R	33.7%	50%
H+R+E without Z	3.3% * (1-42.25%) = 1.9%	3.3% * (1-42.25%) = 1.9%
H+R+E+Z	3.3% * 42.25% = 1.39%	3.3% * 42.25% = 1.39%
H+R+S	11%	11%
H+R+S without Z	11% * (1-42.25%) = 6.35%	11% * (1-42.25%) = 6.35%
H+R+E+S+Z	3.81% * 42.25% = 1.61%	0.5% * 42.25% = .21%

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

We use these values to calculate the proportion of each resistance rate out of the total resistance rates of all drugs.

Drug	Previously treated	Newly treated
H+R	33.7% / 51.81% = 65%	50% / 64.8% = 77.16%
H+R+E without Z	1.9% / 51.81% = 3.66%	1.9% / 64.8% = 2.93%
H+R+E+Z	1.39% / 51.81% = 2.68%	1.39% / 64.8% = 2.14%
H+R+S	11% / 51.81% = 21.23%	11% / 64.8% = 16.97%
H+R+S without Z	6.35% / 51.81% = 12.25%	6.35% / 64.8% = 9.79%
H+R+E+S+Z	1.61% / 51.81% = 3.1%	.21% / 64.8% = 0.32%

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Given the estimated resistance rates for these MDR-TB treatments, we can calculate the portion of each MDR-TB treatment used. Referring back to Table IIB, we can see that:

  1. Those with resistance to H+R and H+R+E without Z are treated by the Z+S+Lfx+Eto+Cs+PAS MDR-TB treatment regimen.

  2. Those with resistance H+R+E+Z are treated by the S+Lfx+Eto+Cs+PAS MDR-TB treatment regimen.

  3. Those with resistance H+R+S, H+R+E+S without Z, and H+R+E+S+Z are treated by the Km+Lfx+Eto+Cs+PAS MDR-TB treatment regimen.

Therefore, the weights for treatment regimens for the previously and newly treated can be calculated in the following way on the next page.

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Drug resistance	Treatment regimen	Proportion of treatment (previously treated cases)	Proportion of treatment (newly treated cases)
H+R only	Z+S+Lfx+Eto+Cs+PAS	65% + 3.66% = 68.72%	77.16% + 2.93% = 80.1%
H+R+E without Z			
H+R+E+Z	S+Lfx+Eto+Cs+PAS	2.68%	2.14%
H+R+S	Km+Lfx+Eto+Cs+PAS	21.23% + 12.25% + 3.1% = 28.59%	16.97% + 9.79% + 0.32% = 17.75%
H+R+E+S without Z			
H+R+E+Z+S			

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

With the proportion of MDR-TB treatment for each regimen calculated for both newly and previously treated cases we can calculate the weight of each MDR-TB regimen. For the Dominican Republic, we have 30 new cases and 62 retreatment cases of MDR-TB (55). There are a total of 92 MDR-TB cases in the Dominican Republic: 32.6% are new cases and 67.4% are retreatment cases. We calculate the weight of each treatment as follows:

Regimen	Weight of MDR-TB treatment
Z+S+Lfx+Eto+Cs+PAS	(67.4%*68.72%) + (32.6%*80.1%) = 72.43%
S+Lfx+Eto+Cs+PAS	(67.4%*2.68%) + (32.6%*2.14%) = 2.52%
Km+Lfx+Eto+Cs+PAS	(67.4%*28.59%) + (32.6%*17.75%) = 25.05%

Example: Drug Score

Impact of pyrazinamide in an MDR-TB regimen in the Dominican Republic in 2013

Now we must multiply the total MDR-TB impact score by the weight of each treatment. In the case of the Dominican Republic, we see that:

$I_{Z+S+Lfx+Eto+Cs+PAS}$ = 62.16 * 72.43% = 45.03

$I_{S+Lfx+Eto+Cs+PAS}$ = 62.16 * 2.52% = 1.56

$I_{Km+Lfx+Eto+Cs+PAS}$ = 62.16 * 25.05% = 15.57

Recall that our goal is to calculate the impact of Z. Additionally, recall that every component drug in the MDR-TB regimen Z+S+Lfx+Eto+Cs+PAS gets 17% credit. We simply need to multiply the impact of the regimen Z+S+Lfx+Eto+Cs+PAS by 17% to derive the impact of Z:

I_Z = 45.03 * 17% = **7.65**

Example: Country Score
Impact of TB drugs in the Dominican Republic in 2013

The impact of all XDR-TB drugs can be easily found because we have already calculated the proportion of new and retreatment cases that have MDR-TB. We can multiply this number by DR's DALYs, 18,000, and the percentage of MDR-TB cases that are XDR-TB, 9.6%, to arrive at DR's **XDR-TB DALYs: 207.94**. From here we can plug DR's treatment coverage and efficacy data into the general impact formula to arrive at 39.48. We divide this number by two because the average length of XDR-TB treatment is two. Now we know that **the impact of XDR-TB drugs in DR in 2013 is 19.74**. Recall the impact of all MDR-TB regimens in DR in 2013: **62.16**. DS-TB is calculated in a very similar way. The impacts of DS-TB HIV+ drugs and DS-TB HIV- drugs are 2,874.05 and 12,426.44, respectively.

The sum of the four types of TB is **15,382.40, the impact of TB drugs in the Dominican Republic in 2013.**

Example: Disease Score
Impact of TB drugs in 2013

To calculate the global impact of all TB drugs in 2013 we simply apply the steps used to find the impact of TB drugs in the Dominican Republic to all remaining countries. We sum the resulting outputs to obtain **43,542,034.23, the global impact of TB drugs in 2013.**

Example: Company Score
Impact of Merck on TB in 2013

Merck produces the drugs **S** and **Z**. The drug Z appears in one DS-TB and one MDR-TB regimen. Recall the process of calculating Z's impact in an MDR-TB regimen on the Dominican Republic. These steps should be repeated for every other country to derive **Z's global MDR-TB impact: 7,289.33.**

All four drugs in a DS-TB regimen are given equal credit. Divide the global impact of DS-TB HIV+ and DS-TB HIV- by four to derive **Z's global DS-TB impact: 10,842,565.11.**

The drug S appears in two MDR-TB regimens. Multiply the impact of MDR-TB drugs in the regimen Z + S + Lfx + Eto + Cs + PAS by 17%. Then multiply the global impact of MDR-TB drugs in the regimen S + Lfx + Eto + Cs + PAS by 20%. Sum the two resulting numbers to obtain **7,632.56: S's global MDR-TB impact**.

The sum of all three numbers yields **10,857,486.68, the global impact of Merck on TB in 2013**.