Target generic prices for novel treatments for drug-resistant tuberculosis

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Rationale

New drugs are being developed for shorter course tuberculosis treatment, and for multi-drug resistant TB (MDR-TB).

Currently, treatment for MDR-TB can cost over $1000 US per patient-course in low income countries; far higher prices elsewhere.

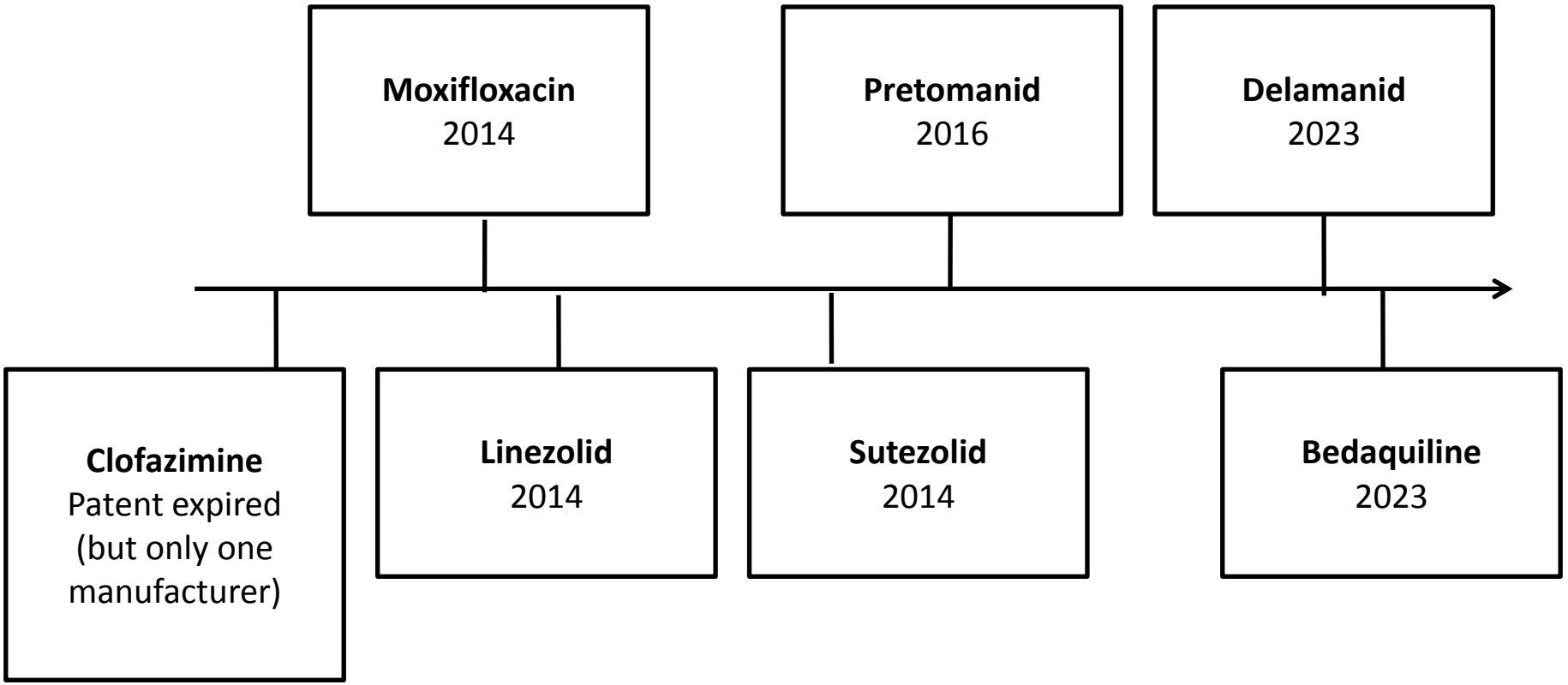
Prices of treatments for MDR-TB and XDR-TB are straining health budgets.

However some of these drugs are close to patent expiry.

This study calculated target generic prices for novel TB treatments.

Patent Expiry Dates of key TB drugs

Group 1-3 drugs – already generic
Group 4 drugs – basic use patents expiring from 2014
Group 5 drugs – patent expiry 2016-2023



Methods

Online database: www.infodriveindia.com shows costs per kg of exported API (active pharmaceutical ingredient). API costs obtained for all Group 1-4 drugs, linezolid and clofazimine.

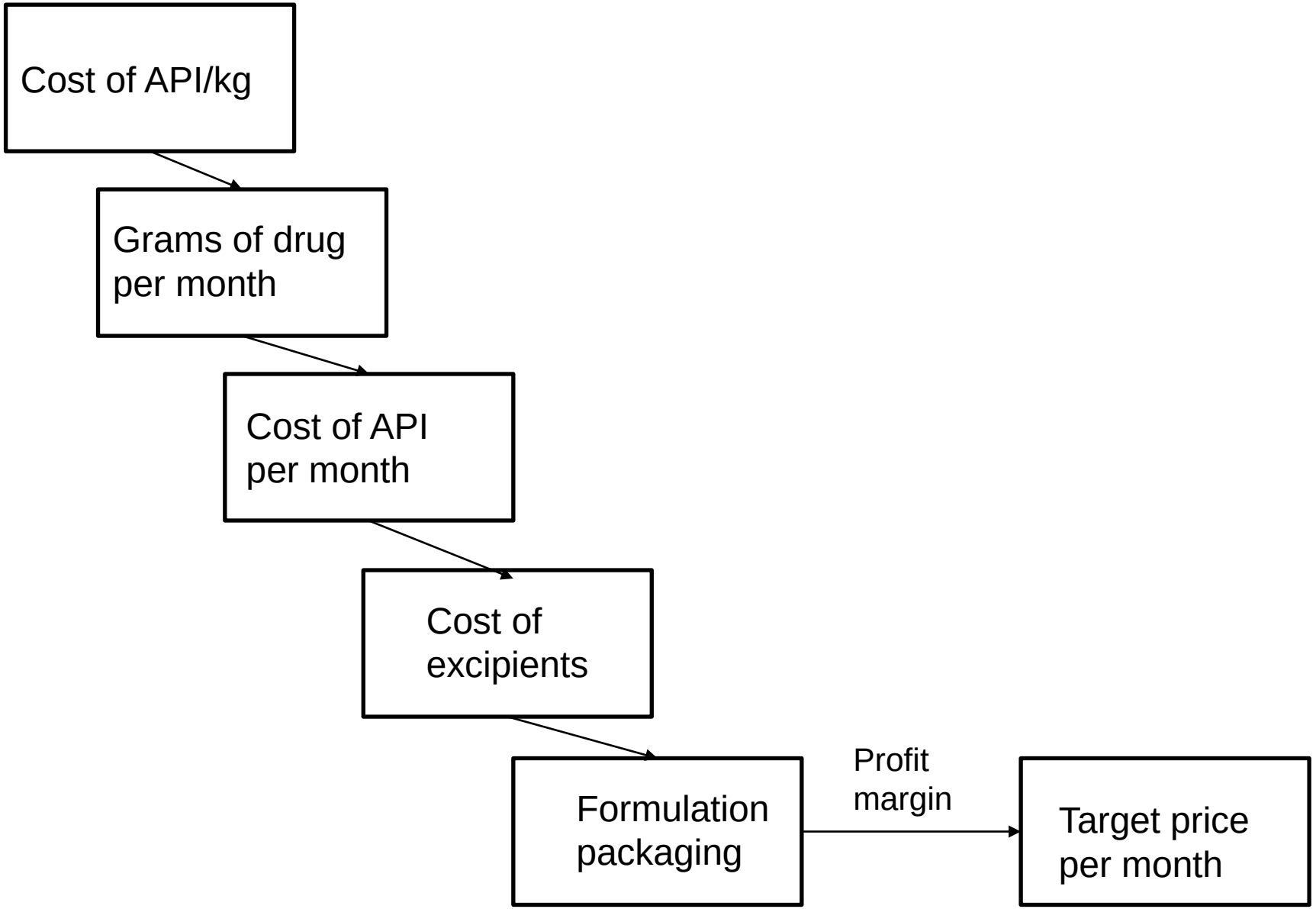
We also collected prices by country, and from the Global Drug Facility (GDF)

Sutezolid – structurally similar to linezolid (single atom difference) similar costs of production assumed. **Posizolid** – structurally similar to linezolid, but 3X higher costs of production

Delamanid and Bedaquiline – analysis of routes of chemical synthesis, cost of raw materials and predicted yield

- **Pretomanid** – production cost assumed to be 4X higher than delamanid, based on chemical structure.

Methods – calculation of treatment cost



Methods – low and high target prices

Lower target price

1c per pill for formulation

10c per month for packaging

10% profit margin

Volume demand assumption:
>1 million treatment courses / year
Validated from GDF price comparisons

Higher target price

4c per pill for formulation

35c per month for packaging

50% profit margin

Volume demand assumption:
>100,000 treatment courses / year
Validated from HCV cost analysis

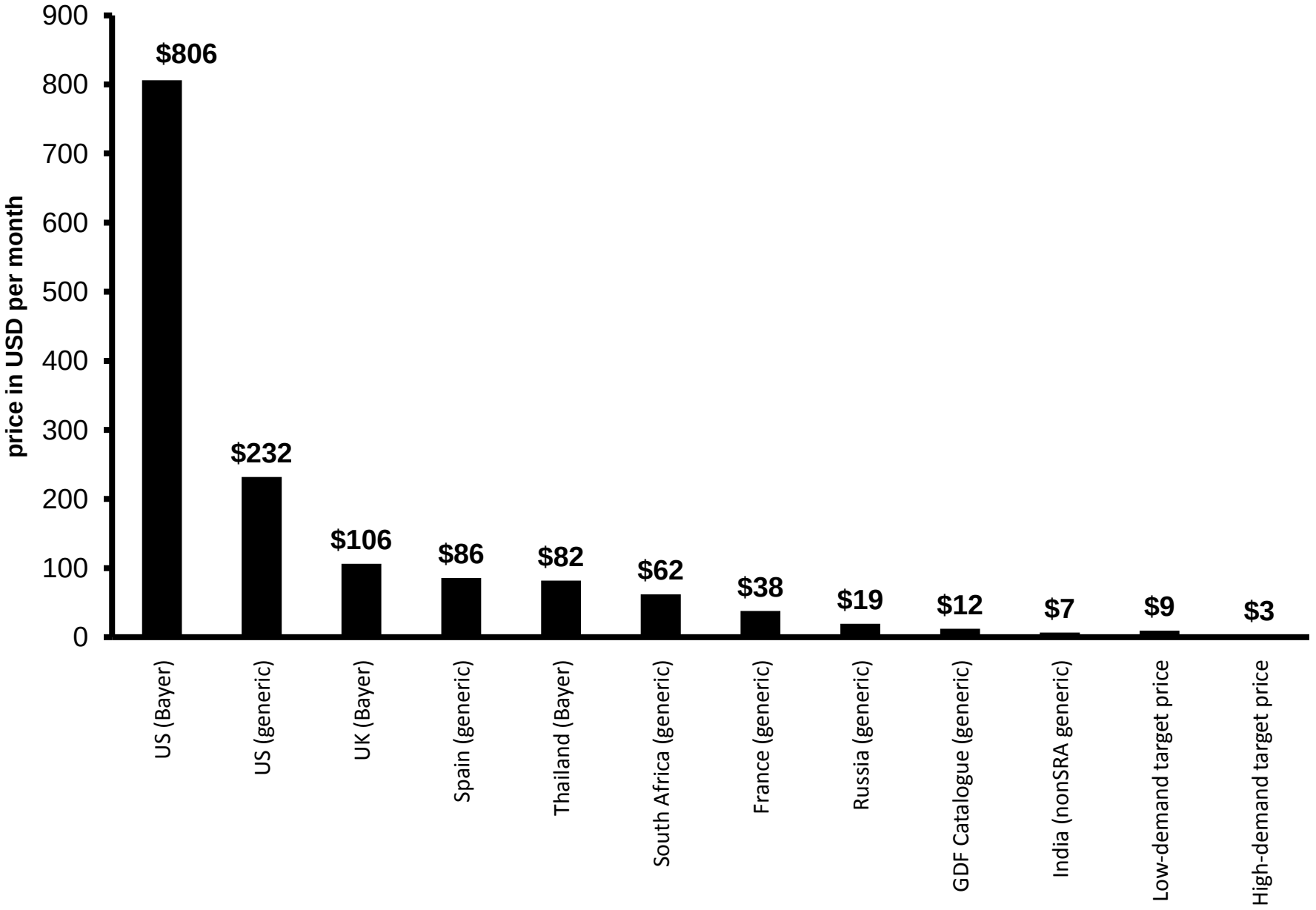
Group 1 and 2 drugs – current production costs

Drug	Patent	Daily dose	Exports 2014	API cost/kg	Target price	Current GDF price
Group 1						
Isoniazid	Expired	300mg	86,000 kg	$13-$38/kg	**$0.8-$3.1**	**$0.6/month**
Pyrizinamide	Expired	1600mg	137,000 kg	$20-$28/kg	**$3.9-$11**	**$2.3/month**
Ethambutol	Expired	1200mg	305,000 kg	$40-$49/kg	**$5.1-$11.5**	**$2.8/month**
Group 2						
Amikacin	Expired	1000mg	6.9m vials	n/a	**$7.3-$47.2**	**$38.6/month**
Kanamycin	Expired	1000mg	2m vials	n/a	**$13.2-$52.8**	**$25.2/month**
Capreomycin	Expired	1000mg	0.9m vials	n/a	**$108-$173**	**$138/month**

Group 3 and 4 drugs – current production costs

Drug	patent	Daily dose	Exports 2014	API cost/kg	Target price	Current GDF price
Group 3						
Levofloxacin	Expired	1000mg	91,000 kg	$110-$268/kg	**$7.4-$19.7**	**$3.9/month**
Moxifloxacin	2014	400mg	37,000 kg	$180-$360/kg	**$3.5-$9.4**	**$18.1/month**
Group 4						
Prothionamide	Expired	750mg	600kg	$118	**$4.7-$10.5**	**$10.9/month**
Cycloserine	Expired	750mg	900kg	$835-$1030	**$21.3-$39.3**	**$27.7/month**

Price of Moxifloxacin by country

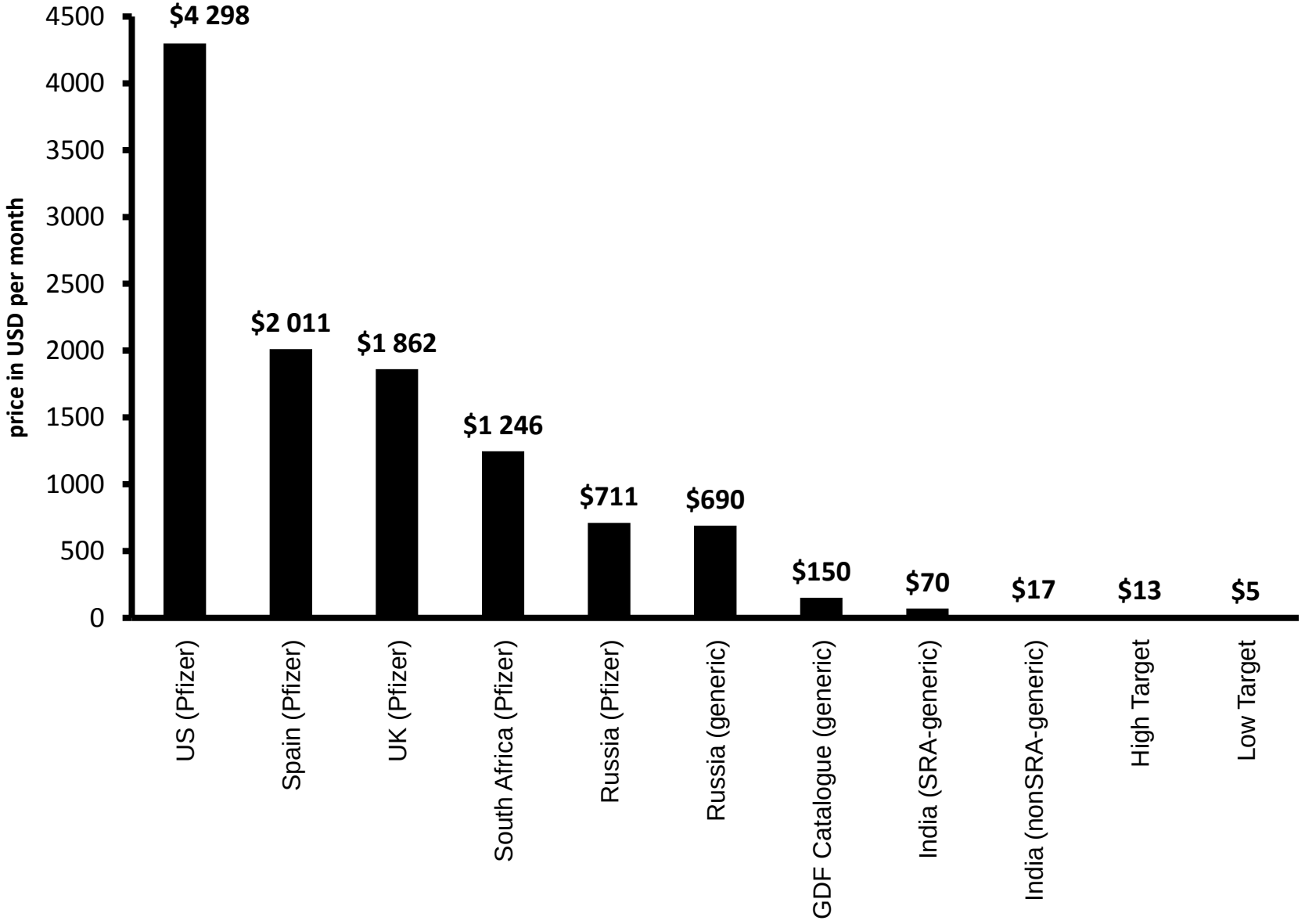


Group 5 drugs predicted production costs

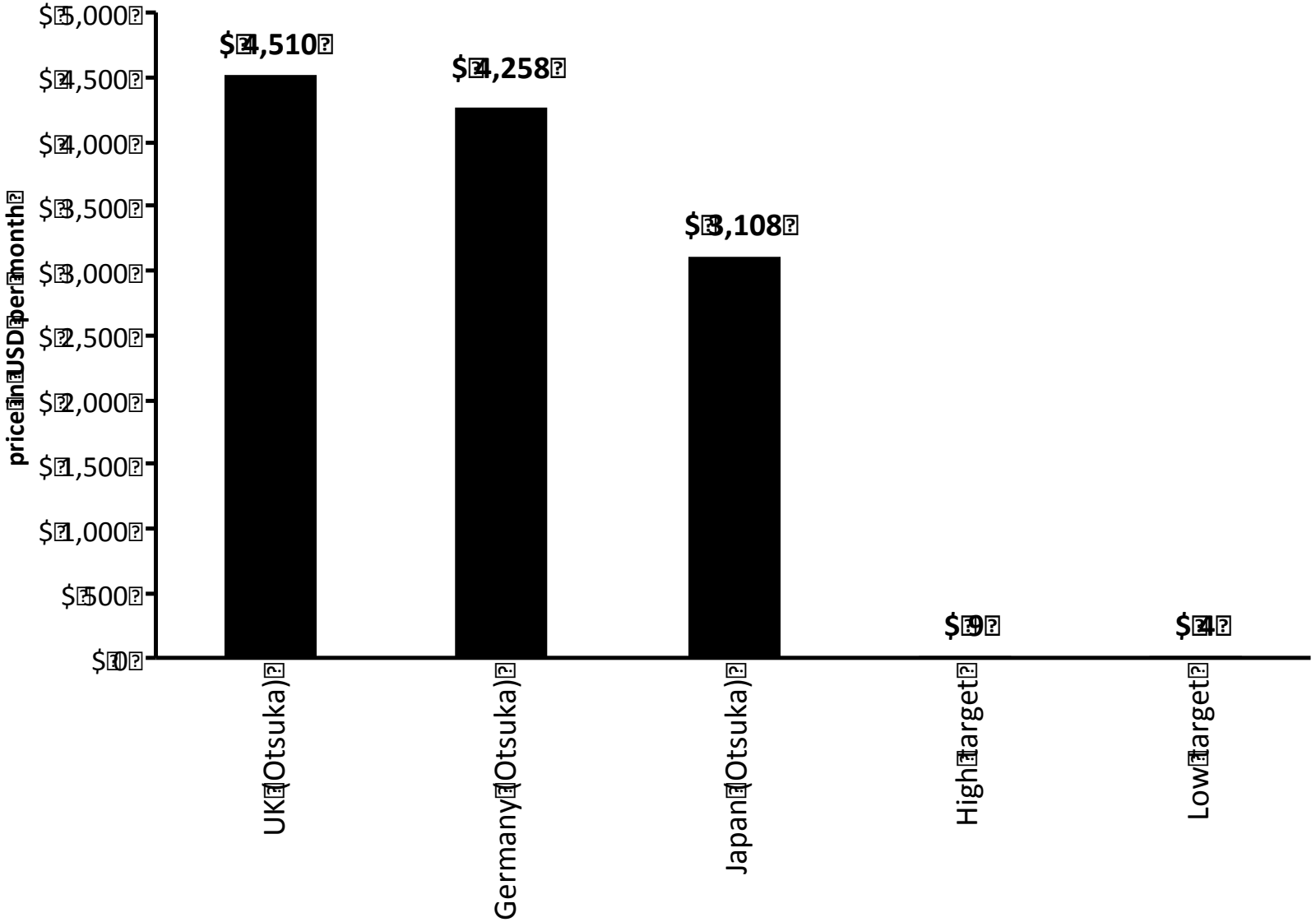
Drug	Patent	Daily dose	Exports 2014	API cost/kg	Target price	Current GDF price
Group 5						
Clofazimine	Expired	300mg	8,300 kg	$256/kg	**$6.2-$16.4**	**$99/month**
Linezolid	2014	600mg	11,000 kg	$175-$350/kg	**$4.9-$12.8**	**$193/month**
Sutezolid	2014	1200mg	None	$175-$350/kg	**$4.9-$12.8**	No prices
Posizolid	2019	600mg	None	$525-$1050	**$11.4-$13.4**	No prices
Delaminid	2023	200mg	None	$250-$500	**$3.5-$8.6**	**$3,108*/month**
Pretomanid	2016	200mg	None	$1000-$2000	**$8.2-$21.2**	No prices
Bedaquiline	2023	400mg	None	$2600-$3250	**$8.8-$16.4**	**$136/month**

*Little info available on pricing of delamanid – price in Japan quoted

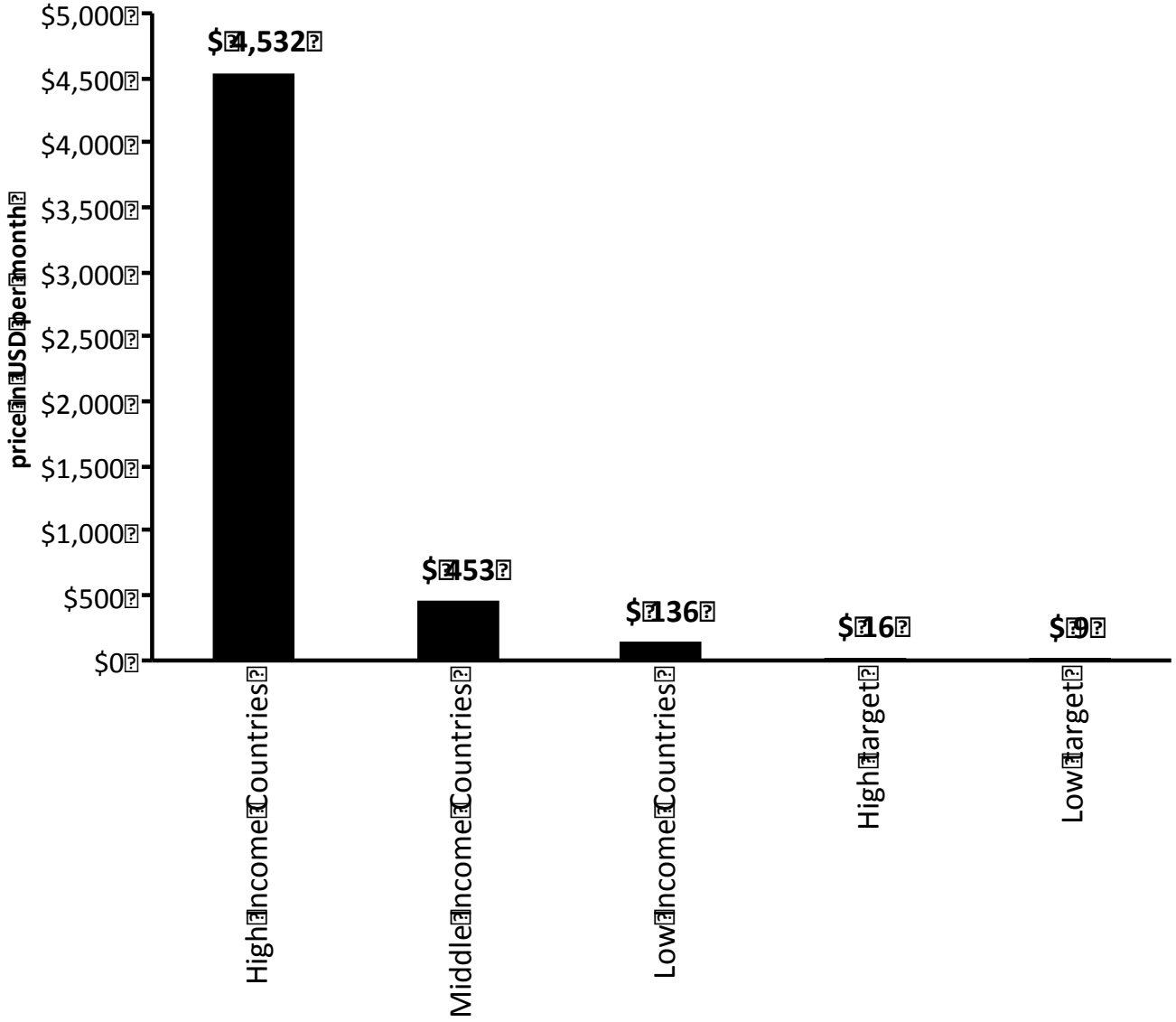
Price of Linezolid by country



Price of Delamanid by country

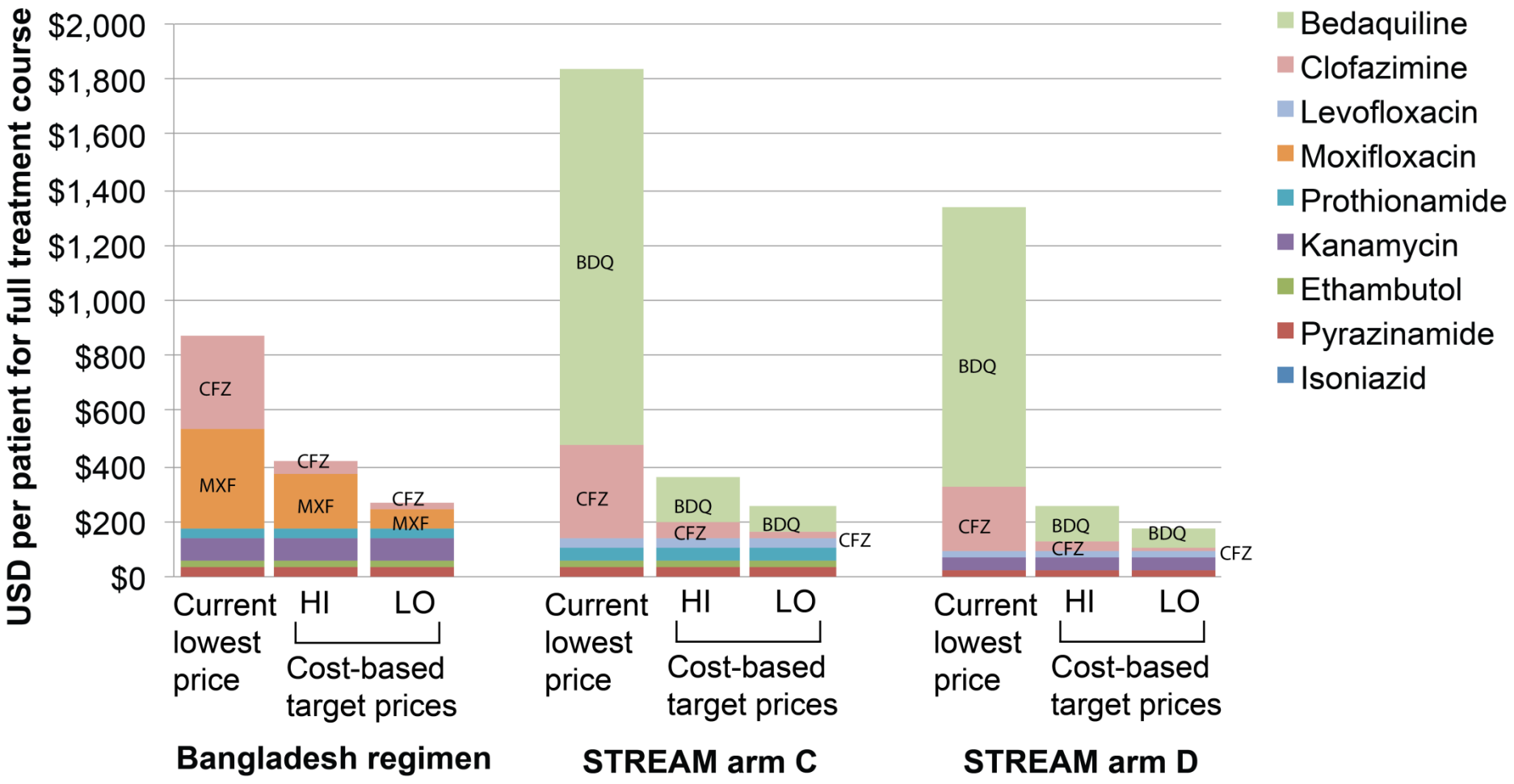


Price of Bedaquiline by region

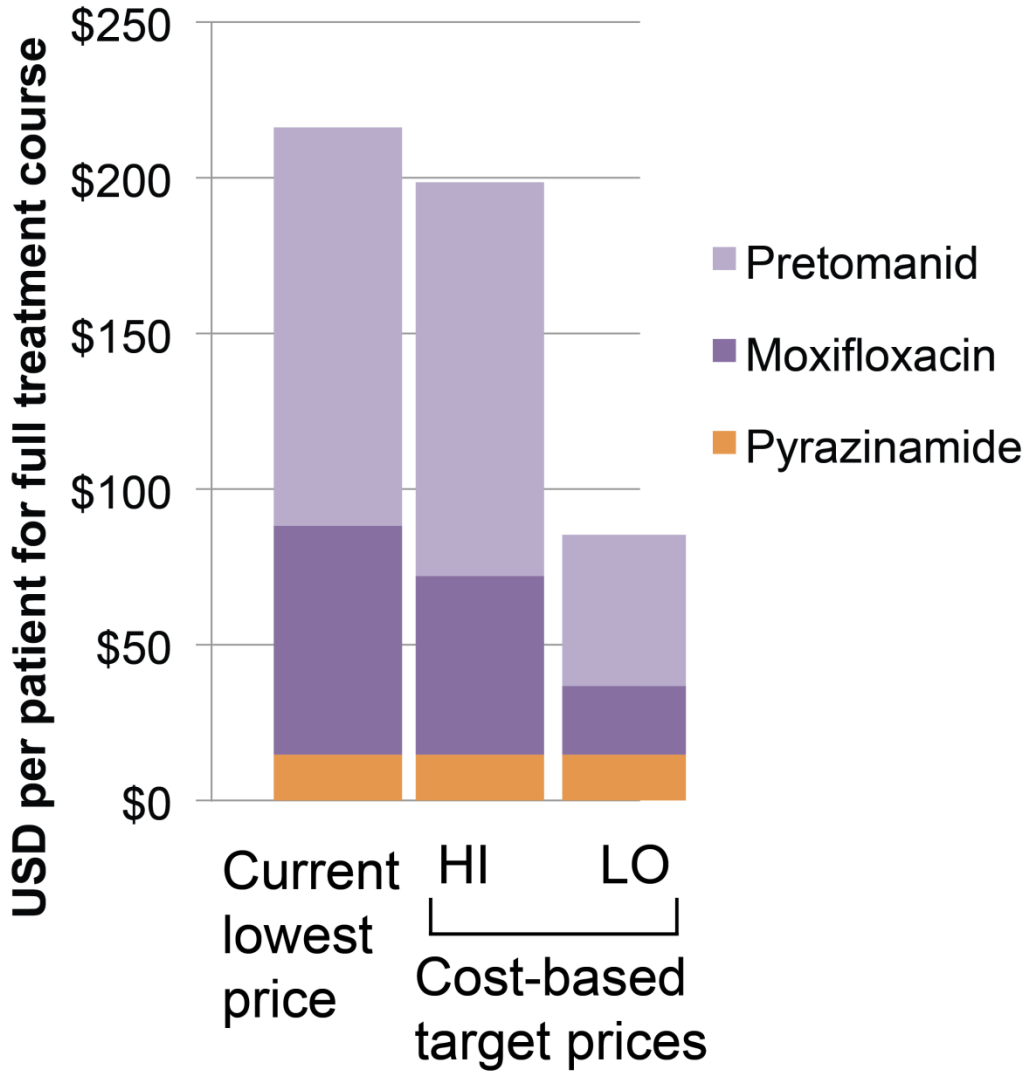


Assumed monthly dose is 28.4 x 100mg pills – average number per 28 days in STREAM arm C.

Potential prices for treatment courses



Potential prices for treatment courses



Limitations of the analysis

1. Volume demand assumes that drugs for MDR-TB can be ordered centrally at low prices. Currently there are multiple drugs with different buyers, which limits the potential for savings. Low prices will depend on simplified market, with fewer drugs purchased, or standardised treatment courses.

2. There could be secondary patents enforced on some TB drugs, even after the basic patents have expired.

3. Target production prices for delamanid, pretomanid and bedaquiline were predicted based on routes of chemical synthesis and predicted yields – these estimates need to be validated by generic producers.

4. Upscaling production of some combination treatments could require pivotal clinical trial efficacy results: this may take another 2-4 years

Conclusions

1. There is the potential to produce combination treatments for MDR-TB for $100-$400 per patient-course.

2. There are currently large differences in TB drug prices between countries, even for drugs which should already be generic. Some drugs are available in India at prices well below GDF levels (e.g. moxifloxacin, linezolid).

3. Competitive large-scale generic manufacture could allow treatment of at least 10 times more MDR-TB cases while still operating within the procurement costs of current budgets. This would require overcoming patent barriers, competitive pricing and scaling-up surveillance and case detection to increase demand.