Typhoid Conjugate Vaccine Demand Forecasting

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The Typhoid Vaccine Acceleration Consortium (TyVAC) is led by the Center for Vaccine Development and Global Health at the University of Maryland School of Medicine, the Oxford Vaccine Group at the University of Oxford, and PATH. TyVAC is funded by the Bill & Melinda Gates Foundation.

Outline

1. Introduction
2. Model overview
3. Model inputs
4. Model outputs
5. Limitations
6. Conclusion

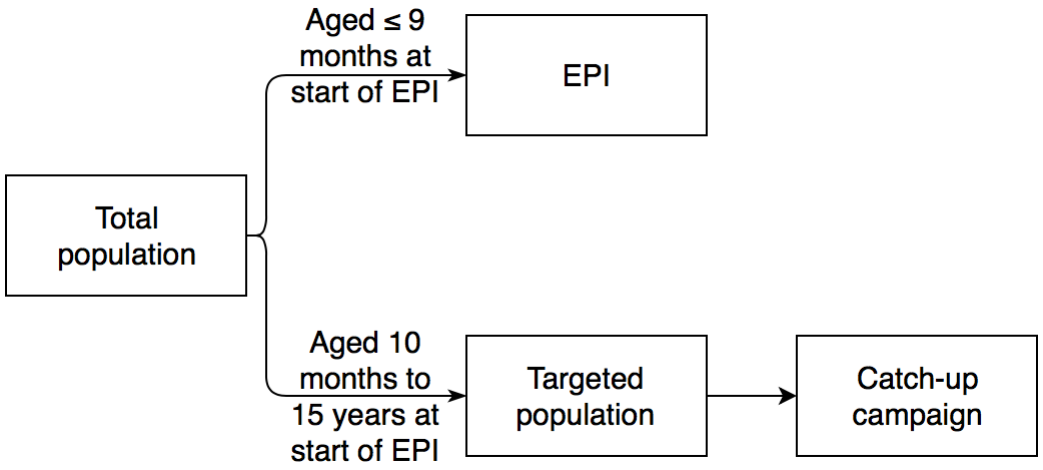
PATH/Teresa Guillien

Introduction

- Objective: Forecast demand for TCVs in 133 low- and middle-income countries per SAGE recommendations.
    - Includes routine immunization and catch up campaigns.
    - Examine a variety of scenarios to inform potential demand from 2020 to 2040.

- Three other demand forecasts exist but focus on a range of vaccine types and introduction strategies:
    - Gavi's SDF [most recent update Q1 2018]
    - CHAI [12/2016 – being updated]
    - IVI [4/2017 publication available]

Model overview



- In a given country, we assume that routine vaccination will be offered to all children at 9 months of age.
- The targeted population includes a portion (0 to 100%) of the national population that is between 10 months and 15 years at the start of routine vaccination in EPI, and who will be eligible for vaccination in the catch-up campaign.
- Forecast accounts for vaccine coverage, wastage, buffer and time to full uptake in a given country.

Base case inputs: routine + catch-up

- All low and middle income countries included (per 2017 World Bank Designation)
- UNPOP medium population projections

- Routine vaccination
  - One dose at 9 months
  - Coverage proxy: MCV1
  - Wastage rate of 15%
  - Buffer requirement: 25% of vaccine eligible population in year of introduction
- Catch-up campaign
  - Targets age 10 months to 15 years (0%, 10%, 25%, 50%, 75%, or 100% of eligible population)
  - Coverage proxy: MCV1
  - Wastage rate of 10%
  - Begins same year as routine introduction, lasts one year for most countries, two years if birth cohort > 2.5 million in year of introduction

Model inputs: year of introduction

- Base case year of introduction is based on incidence and historical speed of adoption.
- Further adjustments are made based on past engagement with typhoid research, Gavi status and expressed interest in TCVs.

<u>Incidence (per year)</u>

Low: <10 cases per 100,000

Medium: 10 to 100 cases per 100,000

High: 100 to 500 cases per 100,000

Very high: >500 cases per 100,000

<u>Historical speed of vaccine adoption</u>

Based on number of new vaccines (PCV, Rotavirus, HPV) introduced as of mid-2017 and average length between each vaccine PQ and actual introduction

Model inputs: year of introduction

- We used a matrix to classify countries into groups based on incidence and adopter levels
- Then we adjusted the base introduction year for the following factors:
    - Countries will apply for funding in the last year of Gavi support
    - Countries engaged in typhoid surveillance and research

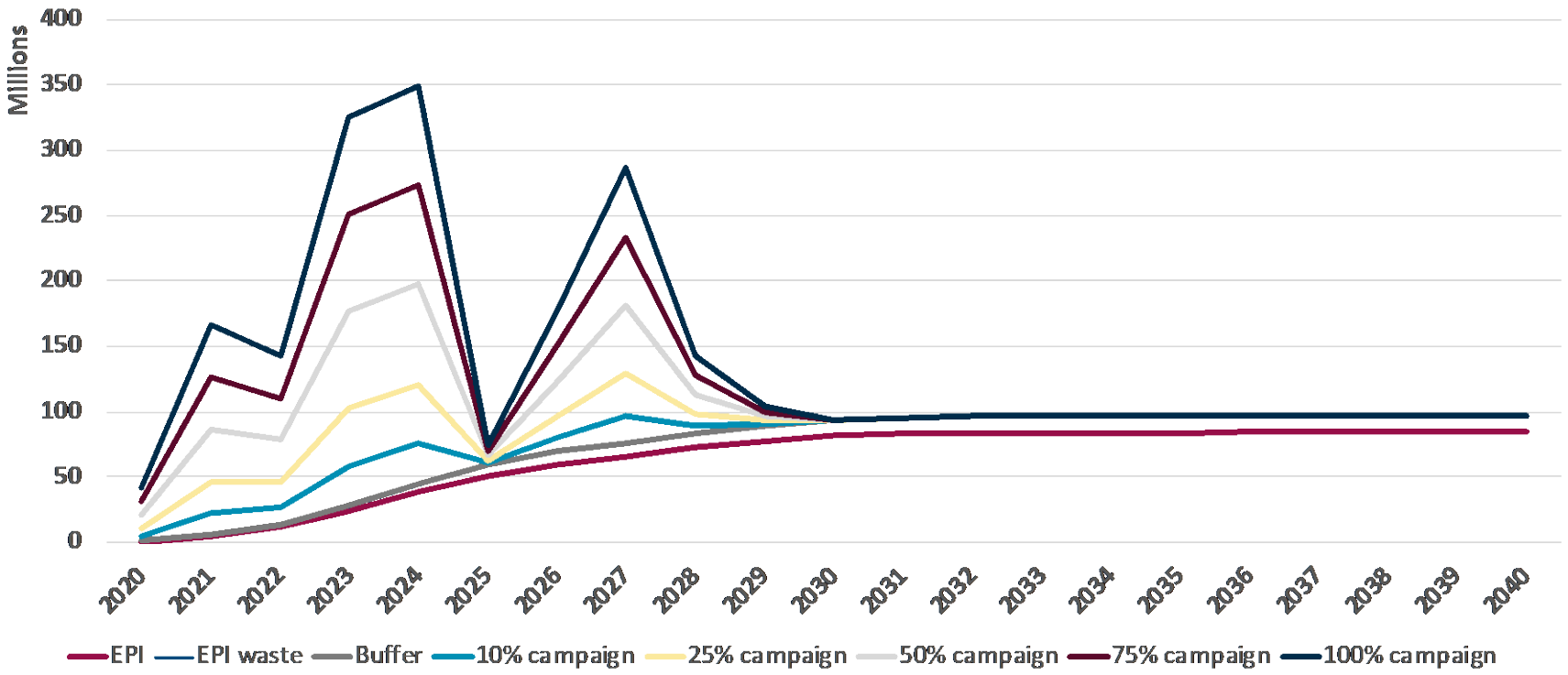
	Very high incidence	High incidence	Medium incidence	Low incidence
Early adopter	2021	2022	2027	Not before 2040
Medium adopter	2023	2024	2028	Not before 2040
Late adopter	2025	2026	2029	Not before 2040
Not adopting	Not before 2040	Not before 2040	Not before 2040	Not before 2040

Model inputs: year of introduction

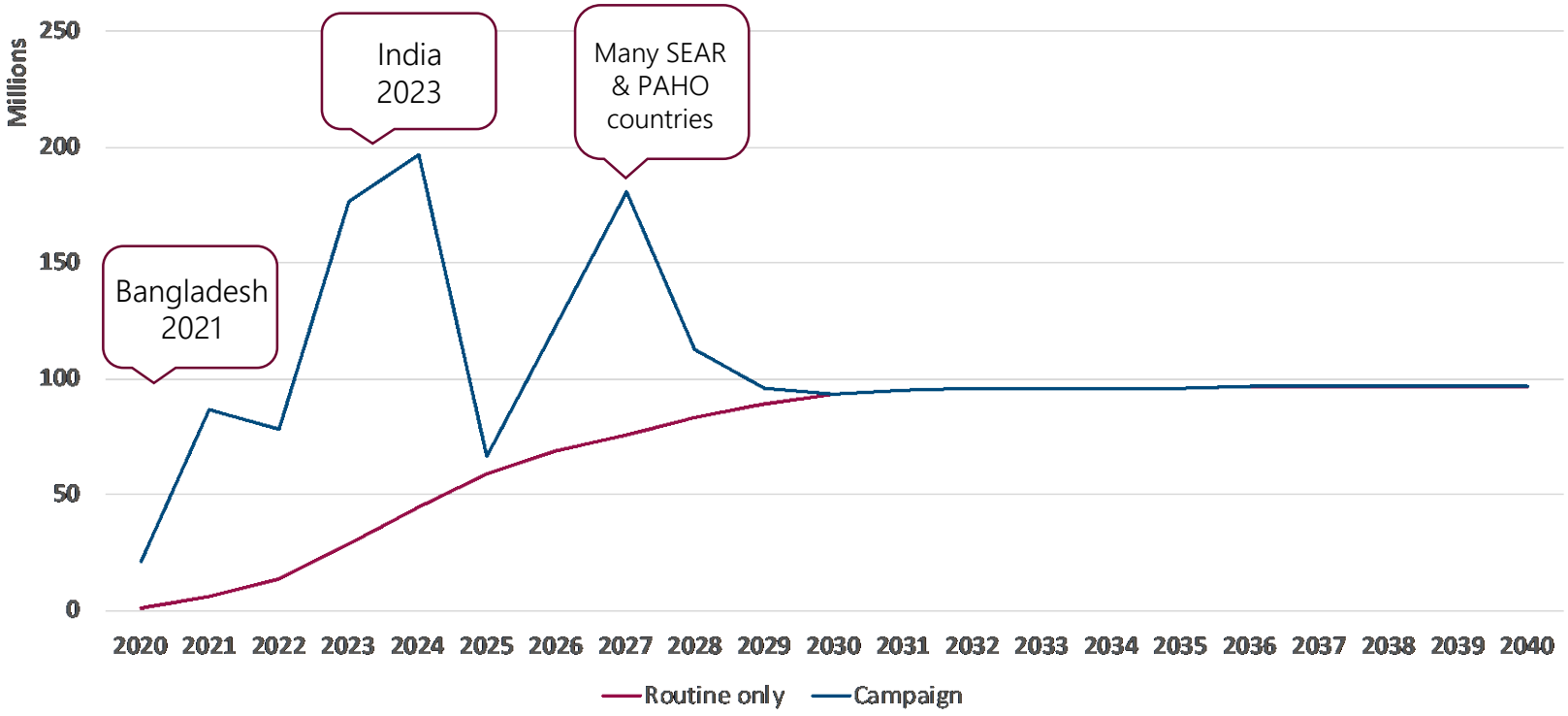
2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
Liberia	**Bangladesh**	**Angola**	**DR Congo**	**Benin**	**Afghanistan**	**Cambodia**	Argentina	Albania	**Azerbaijan**
Pakistan	**Ethiopia**	Botswana	**Ghana**	**Bhutan**	**Guinea-Bissau**	Cape Verde	**Armenia**	Costa Rica	Belize
Zimbabwe	**Kenya**	**Burkina Faso**	**India**	**Burundi**		**Côte d'Ivoire**	**Bolivia**	**Georgia**	Grenada
	Malawi	**Cameroon**	**Lao PDR**	**Chad**		**Indonesia**	Brazil	Iraq	**Haiti**
	Nepal	**Central African Republic**	**Madagascar**	Congo		**Myanmar**	Colombia	Jamaica	Jordan
	Senegal	**Gambia**	**Niger**	**Djibouti**		Samoa	Dominican Republic	Kazakhstan	Lebanon
	Tanzania	**Mauritania**	**Nigeria**	**Eritrea**		South Africa	Ecuador	Mauritius	**Mongolia**
		Micronesia	**Sierra Leone**	**Kiribati**		**Sri Lanka**	El Salvador	Turkey	St. Lucia
		Papua New Guinea	**Solomon Islands**	Malaysia		**Sudan**	Fiji	**Uzbekistan**	St. Vincent and the Grenadines
		Philippines	**Uganda**	**Mali**		Vanuatu	Guatemala		Suriname
		Rwanda		**Mozambique**			**Guyana**		Turkmenistan
		Sao Tome and Principe		Namibia			**Honduras**		
		Zambia		Swaziland			Libya		
				Thailand			Mexico		
				Togo			Panama		
							Paraguay		
							Peru		
							Venezuela		
							Yemen		

Bold font indicates Gavi eligibility as of 2018.

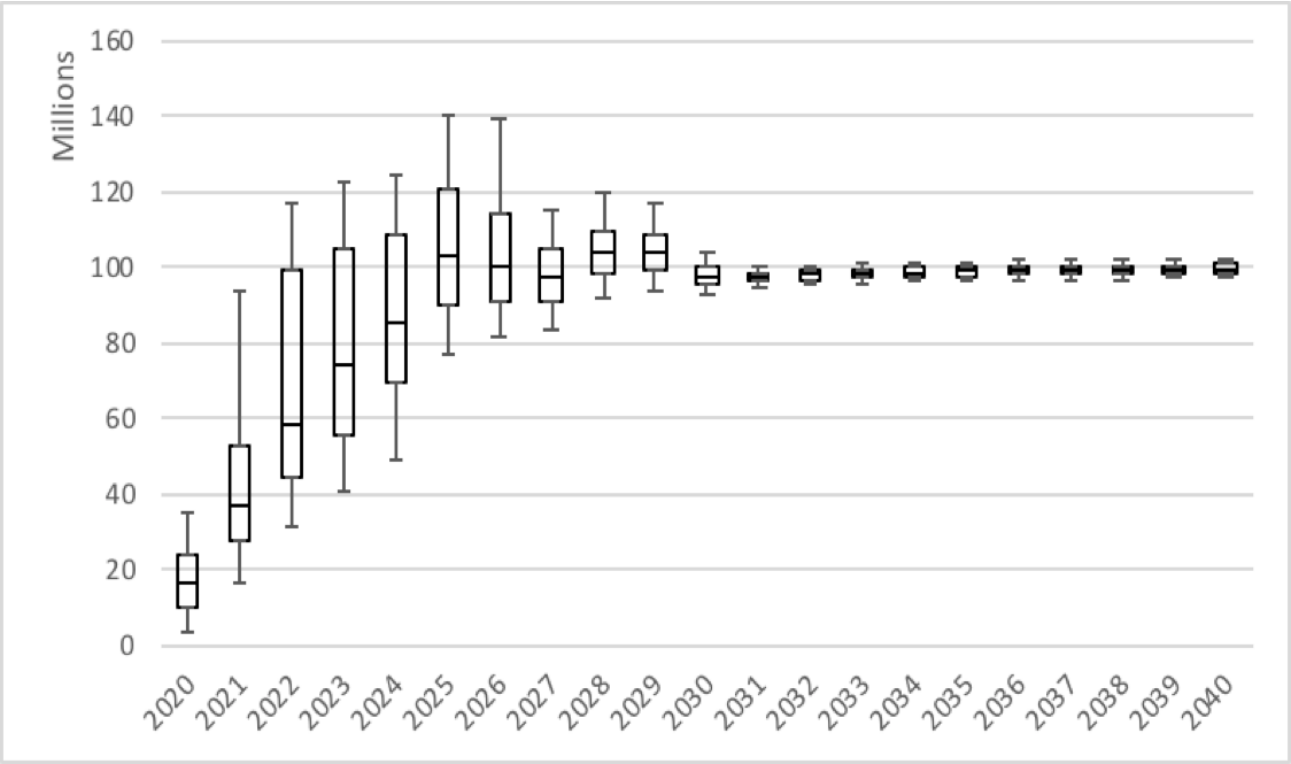
Model outputs: routine + catch-up



Landmarks in the roll-out process (with 50% campaign example)



Probabilistic sensitivity analysis



- Estimated by systematically varying target population, coverage rate, and introduction year.
- This is mainly driven by changes in the target population.

Model limitations

- Uncertainty in adoption scenarios
  - Incidence data show significant uncertainty
  - Difficult to capture all relevant predictors of vaccine introduction date
- Uncertainty about countries' interest in performing catch-up campaigns with or without Gavi incentives
- Difficult to assess risk factors so it is unclear how to define a high-risk population in each country.
  - Therefore, model uses set percentages of the eligible population
- Projected Gavi status subject to change
- Country population estimates may differ from UN estimates
  - This is already the case with Pakistan's application for support

Conclusions

- By **2040**, annual demand for TCV in routine setting could reach ~**100 million doses.**
- Use of **initial catch-up campaigns introduces high variability** into annual demand estimates, especially before 2030.
- Campaigns **targeting large percentages of the eligible population** may cause **demand to exceed 200 million doses per year.**
- Current **production capacity has been stated as 50 million doses per year**, with the ability to **expand to 200 million dose capacity.**
- The potential to exceed production capacity means that it will be **important to coordinate introductions, especially between high population countries.**
- Demand forecast updates **will be undertaken** as additional information is available.

Learn more at:

http://takeontyphoid.org

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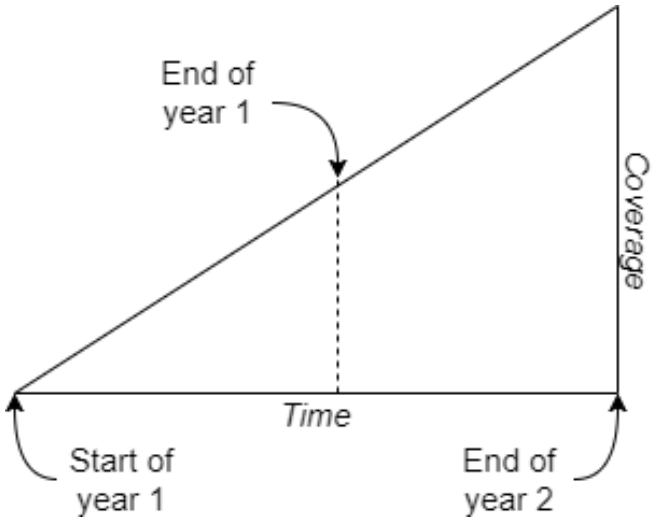
Additional information

Model inputs: vaccine coverage

- "Vaccine coverage" refers to the maximum percentage of the country's eligible population that will be immunized once the country reaches full uptake of the vaccine.
- Our base case scenario assumes that TCV coverage will be equal to coverage for the first dose of measles-containing vaccine (MCV1) as of June 2018.
- The most recent estimate of MCV1 was carried forward unchanged to the end of the model's time horizon (2040).

Model inputs: vaccine uptake

- "Vaccine uptake" refers to how quickly a vaccine spreads through a country's medical system once introduced.
- We assume linear spread during 1 to 4 years, based on size of birth cohort
    - Larger birth cohort=longer uptake time
- Example of 2 year time to uptake:

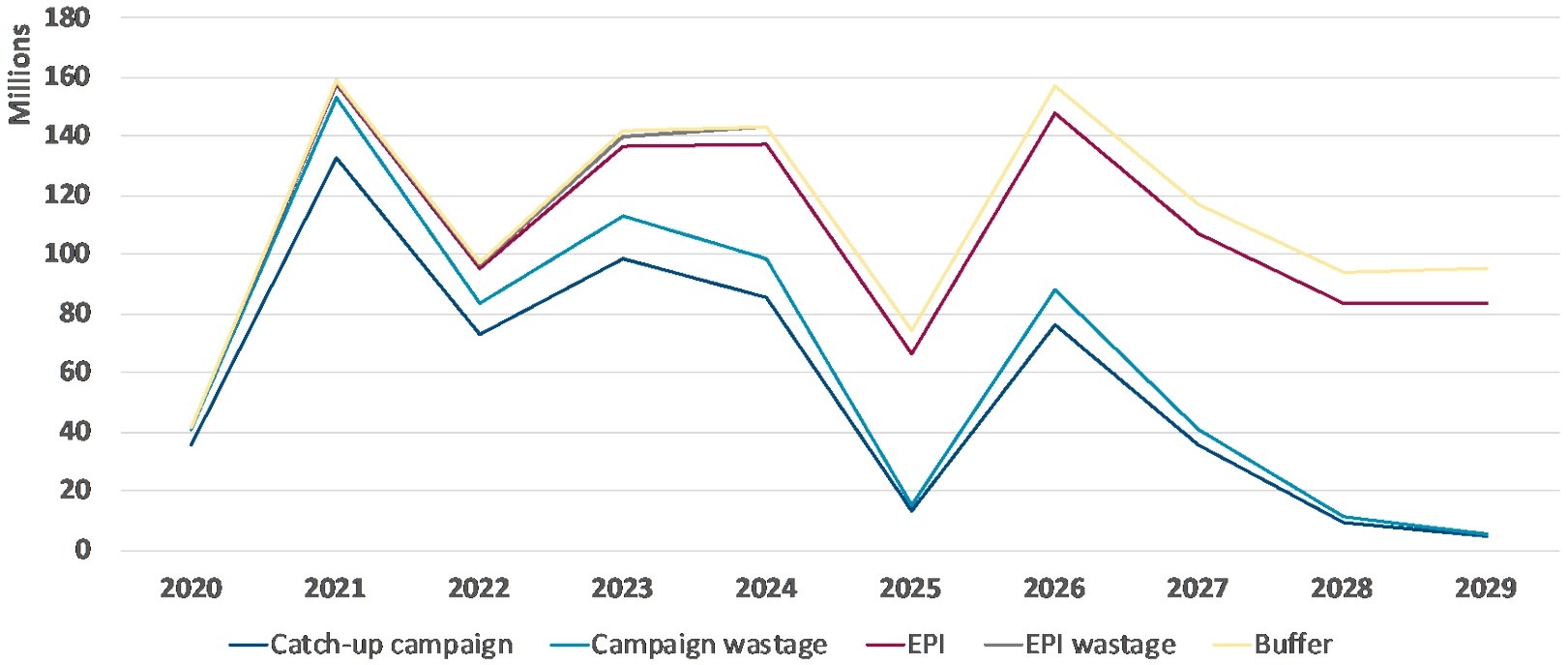


Model inputs: disease incidence

- Country specific disease incidence for all ages helps estimate each country's year of introduction
- There are significant discrepancies in estimates from our three sources:
    - IHME global burden of disease study
    - Unpublished data from Vittal Mogasale of IVI
    - Marina Antillón, et al., *PLoS Neglected Tropical Diseases* (2017)
- We use median estimate in our base case

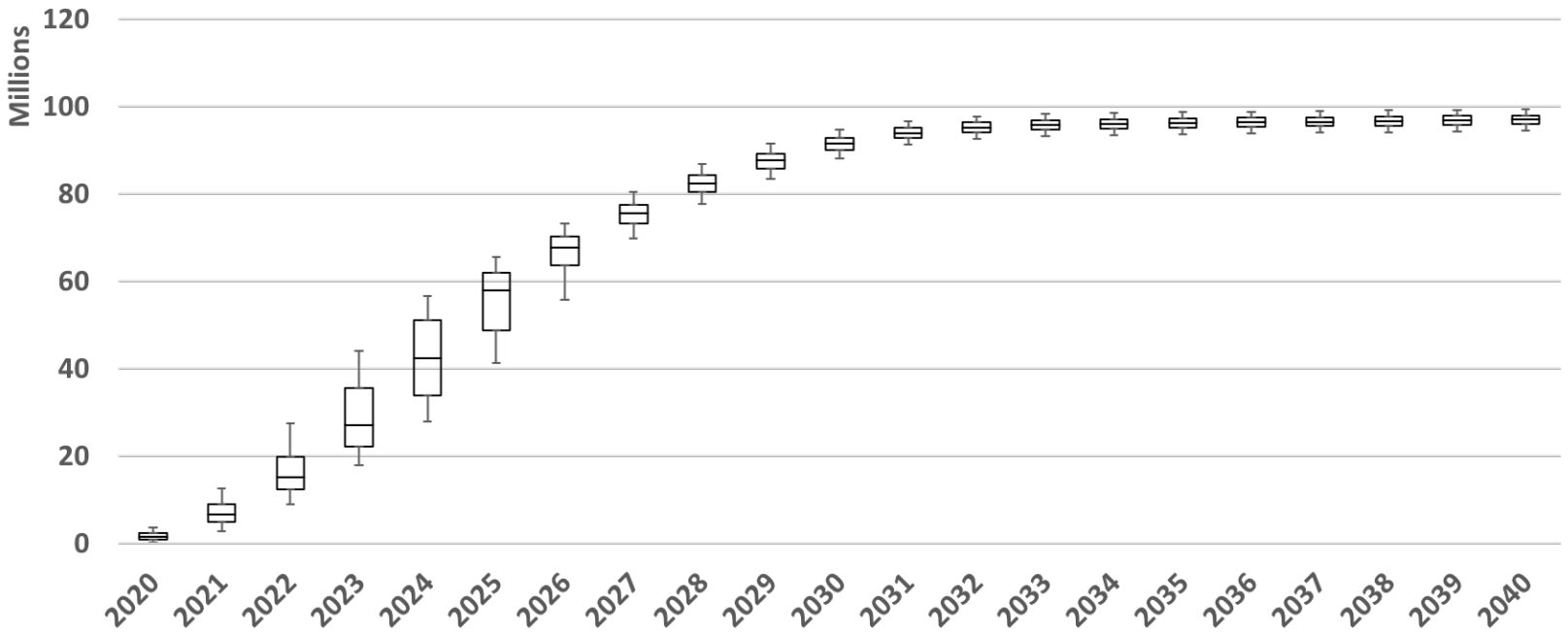
Country	Typhoid fever incidence rate per 100,000, all age IHME (GBD 2016)	Typhoid fever incidence rate per 100,000, all age Antillon (2017)	Typhoid fever incidence rate per 100,000, all age, Mogasale (risk factor adjusted) 2017	Median incidence rate per 100,000
Afghanistan	73.96	1,233.49	744.26	744.26
Albania	0.2	63.37		34.78
Algeria	36.65	27.83	13.4	27.83
Angola	98.5	287.06	586.17	287.06
Argentina	0.29	52.23	27.43	27.43
Armenia	0.3	14.32	10.45	10.45
Azerbaijan	0.4	35.81	14.3	14.3
Bangladesh	545.09	1,100.71	315.51	545.09
Belarus	0.11	8.65		4.38
Belize	1.81	132.71	33.55	33.55
Benin	172.21	1,925.84	410.89	410.89

Scenario analysis: no campaigns in non-Gavi countries



Gavi countries use campaigns targeting 100% of eligible population; non-Gavi countries do not run campaigns. Results are identical to base case after 2030.

Scenario analysis: probabilistic sensitivity analysis without campaign



This was performed to assess the impact of target population percentage on our probabilistic sensitivity analysis. Percent of population targeted for campaigns was shown to account for 69% of the variation.

Summary of country groups

	Early adopters	Medium adopters	Late adopters	Non-adopters	Total nb of countries
Very high incidence	0	3	2	1	6
High incidence	16	22	14	6	58
Medium incidence	23	11	12	12	58
Low incidence	1	2	4	4	11
Total nb of countries	40	38	32	23	133

Detailed adjustments

Based on TyVAC knowledge	Knowledge of TCV
Gavi application + 18 months	Intro is 1 year earlier
Bangladesh 2021	Burkina Faso
Liberia 2020	China
Madagascar 2020	Ethiopia
Malawi 2020	Ghana
Nepal 2021	Guinea-Bissau
Pakistan 2020	India
Tanzania 2021	Indonesia
Zimbabwe 2020	Kenya
	Senegal
	South Africa
	Sudan
	Thailand
	Uganda
	Vietnam

Model inputs: year of introduction

Countries not introducing TCV before 2040
Algeria, Belarus, **Bosnia and Herzegovina**, Bulgaria, China, Comoros, Croatia, **Cuba**, Egypt, Equatorial Guinea, Gabon, **Guinea**, Iran, **Korea DPR**, **Kyrgyzstan**, **Lesotho**, Macedonia, Maldives, **Moldova**, Montenegro, **Nicaragua**, Romania, Russia, Serbia, **Somalia**, **South Sudan**, Syria, **Tajikistan**, **Timor-Leste**, Tonga, Tunisia, **Ukraine**, **Vietnam**