

# Global Supply & Demand of HPV Vaccines



## Market Information for Access to Vaccines (MI4A)

SAGE Meeting – Geneva, October 2019

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# Continuing our work on HPV Global Vaccine Market

- **WHO ran a HPV global market study in 2018** - conclusion: sizeable increases in supply will be required towards cervical cancer elimination. Constraints are expected until at least 2024
- Concerned by constrained HPV vaccine supply, **SAGE (October 2018) called for a comprehensive evaluation** of options for best use and allocation of the limited vaccine supply
- What we did:
  1. Update global supply and demand estimates (last update: September 2019)
  2. Analyzed supply/demand balance under different schedule/allocation scenario
  3. Provided these inputs to Laval University & LSHTM for modelling of health impact

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**GLOBAL MARKET STUDY HPV**

**Key Takeaways**

- Twelve years after the first HPV vaccine registration, less than half of WHO Member States have introduced HPV vaccine into the routine national immunization schedule. Introductions are lowest in Gavi countries and non-Gavi, non-PAHO middle-income countries (MICs).
- Supply is currently insufficient to meet demand and some countries have or will have to postpone introductions.
- WHO issued a call for action towards global cervical cancer elimination in May 2018 which, through national introductions in all countries and increased coverage, is estimated to increase total demand for HPV vaccines by at least 100M doses over the next 10 years.
- To meet the expected increase in demand due to the cervical cancer elimination initiative, sizeable increases in supply will be required. Constraints are expected until at least 2024, assuming the base case supply scenario. This timing may change depending on selected vaccination strategies and investment decisions of current manufacturers, as well as on the timing of the three programs in advanced stage of clinical development.
- Meeting the projected demand volumes required for multi-age cohort (MAC) introductions (9–14 years of age), as per WHO recommendation, will remain especially problematic in large countries, as well as meeting additional demand generated by implementing gender neutral HPV vaccination.
- Affordability of HPV vaccines in non-Gavi MICs is a barrier which needs to be addressed to encourage introduction.

**QUICK STATS**

**NUMBER OF VACCINE SUBTYPES<sup>1</sup>**  
3

**TOTAL NUMBER OF MANUFACTURERS<sup>2</sup>**  
2

**2018 ESTIMATED GLOBAL SUPPLY**  
~30 million doses (maximum)

**2019 ESTIMATED GLOBAL DEMAND**  
~30 million doses (supply constrained)

**2017 REPORTED PRICE PER DOSE (RANGE)**  
US \$4.50–\$154.28

**Purpose & Background**  
Several countries across regions and income groups have notified WHO of constraints to their access of HPV vaccines. The issue of affordability has also been raised, particularly by non-Gavi MICs. Following the announcement of a call for action towards global elimination of cervical cancer by the WHO Director General in May 2018, increasing introduction and coverage of HPV vaccine worldwide will be key. Working to understand current and future global trends and drivers of supply and demand, this study aims to address the current and expected constraints and to serve as an important resource for the development of the cervical cancer elimination strategy.

**Market Highlights**  
As of May 2018, 81 countries (42% of UN Member States, corresponding to 25% of target population) had introduced HPV into the national routine immunization schedule.<sup>3</sup> Despite carrying the greatest share of disease burden<sup>4</sup>, LICs and MICs are lagging in the introduction of HPV vaccine. To date, the majority of the countries have self-procured HPV vaccines (74% in 2017).

Currently, three HPV vaccine subtypes are available on the market: GSK's Cervarix (HPV2) using the proprietary AS04 adjuvant, and Merck's Gardasil (HPV4) and Gardasil 9 (HPV9), both using alum adjuvant. Merck's two products are also commercialized by two licensors (Instituto Butantan in Brazil and Sinergium Biotech in Argentina). Distribution agreements exist

<sup>1</sup>Vaccine subtypes differentiated by the antigen content of the various HPV vaccines. In this case there are three distinct vaccine subtypes available on the market: HPV2 (16, 18), HPV4 (16, 18, 31, 33, 35, 39, 45, 52, 58) and HPV9 (16, 18, 31, 33, 35, 39, 45, 52, 58).

<sup>2</sup>This number indicates only the companies that have full manufacturing capacity, and does not include licensed companies providing a portion of the manufacturing process or distributors that simply commercialize the product in some locations.

<sup>3</sup>Reported database as of 15 May 2018.

<sup>4</sup>HPV cases (all cancers), women. Source: IARC, Globocan data, 2012.

WORLD HEALTH ORGANIZATION / GLOBAL MARKET STUDY 1 Working Document – September 2018



# Global Supply scenarios for HPV Vaccines



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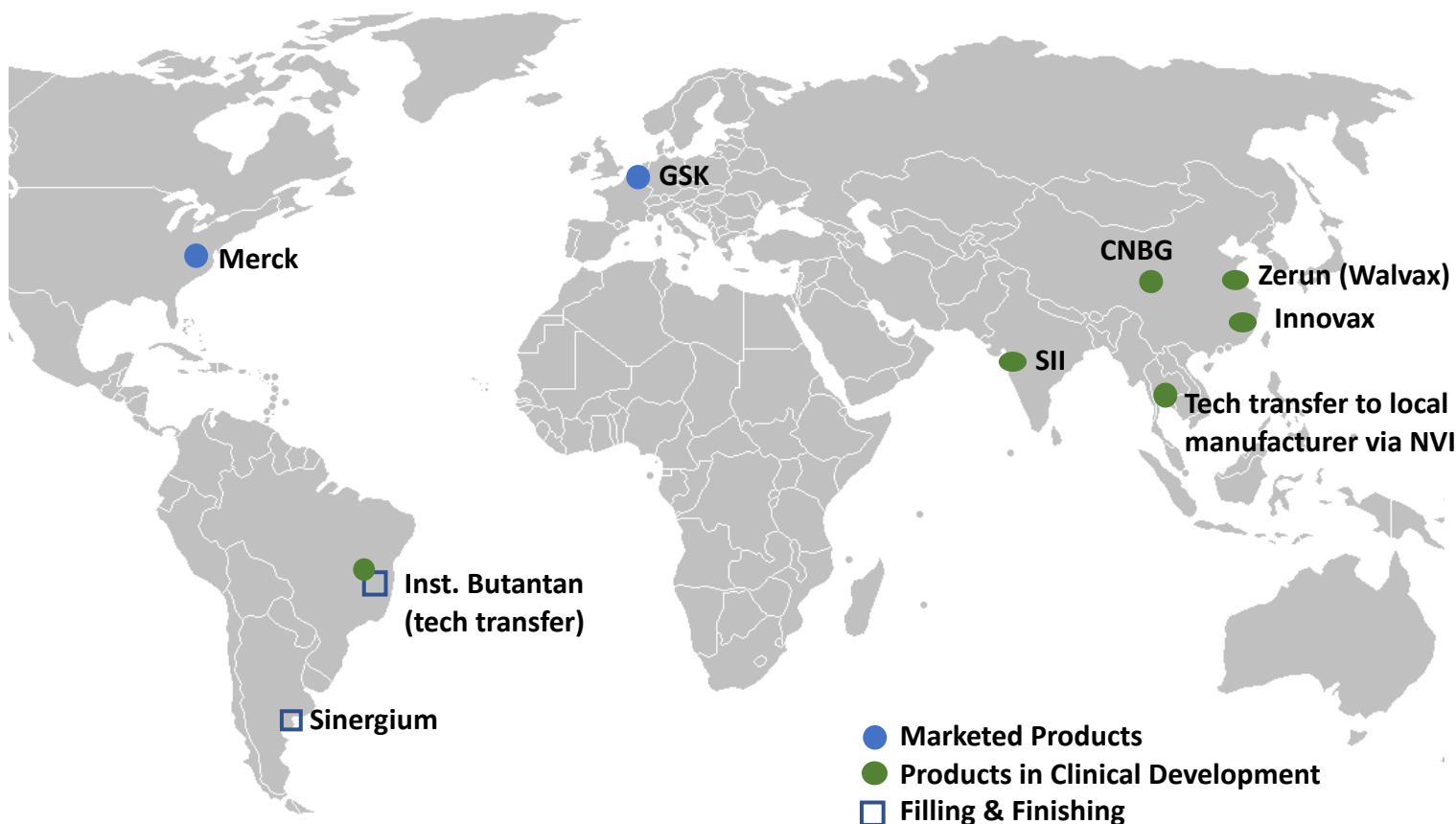
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# HPV's suppliers overview

A constrained supply ecosystem in evolution



<b>Merck Gardasil 4v &amp; 9v</b>	Adjuvant: Alum Sched.: 2 doses (9-15) or 3 doses (15+) Pres.: 1 dose vial (PQ) / PFS (non PQ)
<b>GSK Cervarix 2v</b>	Adjuvant: AS04 Sched.: 2 doses (9-15) or 3 doses (15+) Pres.: 1,2 dose vial (PQ)/ PFS (non PQ)
<b>Innovax 2v</b>	<u>Phase III - BLA submitted, plant inspections completed, clinical file under revision</u> Adjuvant: Alum Schedule: 3 doses Presentation: 1 dose vial
<b>Walvax 2v</b>	<u>Phase III - Preparation for BLA</u> Adjuvant: Alum Schedule: 3 doses Presentation: 1 dose vial
<b>SII 4v</b>	<u>Phase III - in recruitment</u> Adjuvant: Alum Schedule: 2 or 3 doses Presentation: 1,2,5 doses vial
<b>CNBG 4v</b>	<u>Phase III - in recruitment</u> Adjuvant: Alum Schedule: 3 doses Presentation: 1, 3, 5 doses vial

# Supply analysis based on various sources

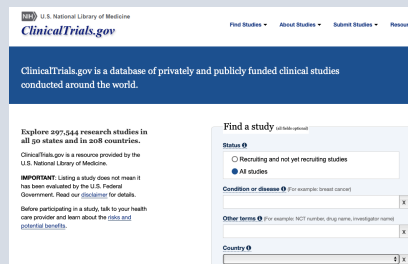
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## Step One Information Gathering

### Data collection from manufacturers



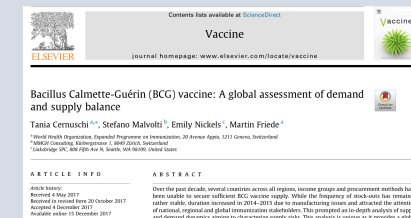
### Review of clinical trials data



### Review of product documentation



### Literature review



## Step Two Validation

### Bilateral in-depth validation with manufacturers



### Validation with available analyses from partners



### Triangulation with demand

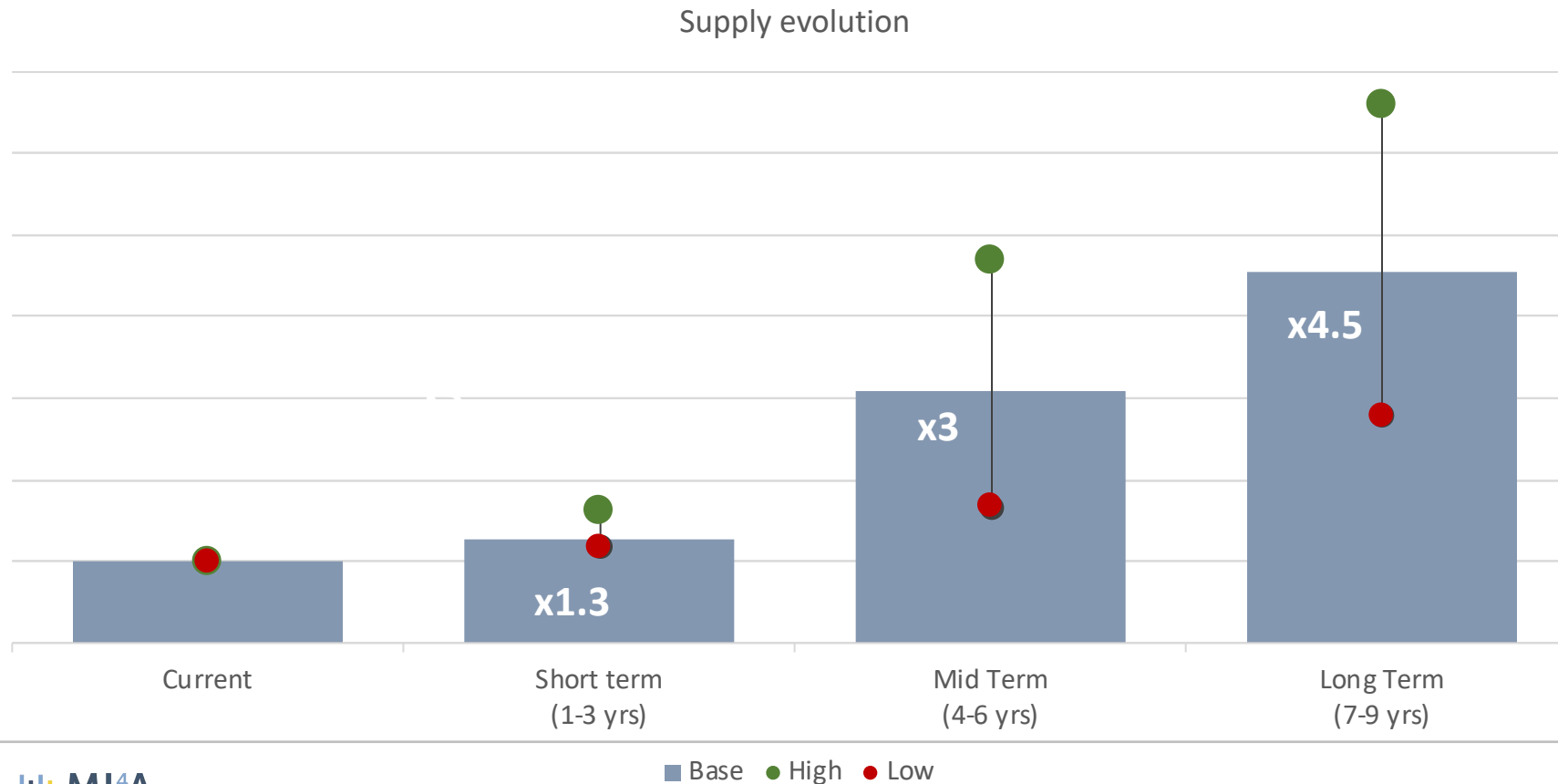


100% input received



# Supply to slowly grow in the short term, followed by steep ramp up from year 4-5

Available supply for commercialization may vary by +/-50% driven by manufacturers decisions and success in development/scale-up



# Global Vaccine Demand

Current programmatic  
dose requirement and  
implications of different  
schedules



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*Health agents are pictured during the first day of the yellow fever  
vaccination campaign in Kinshasa, on August 17, 2016.*

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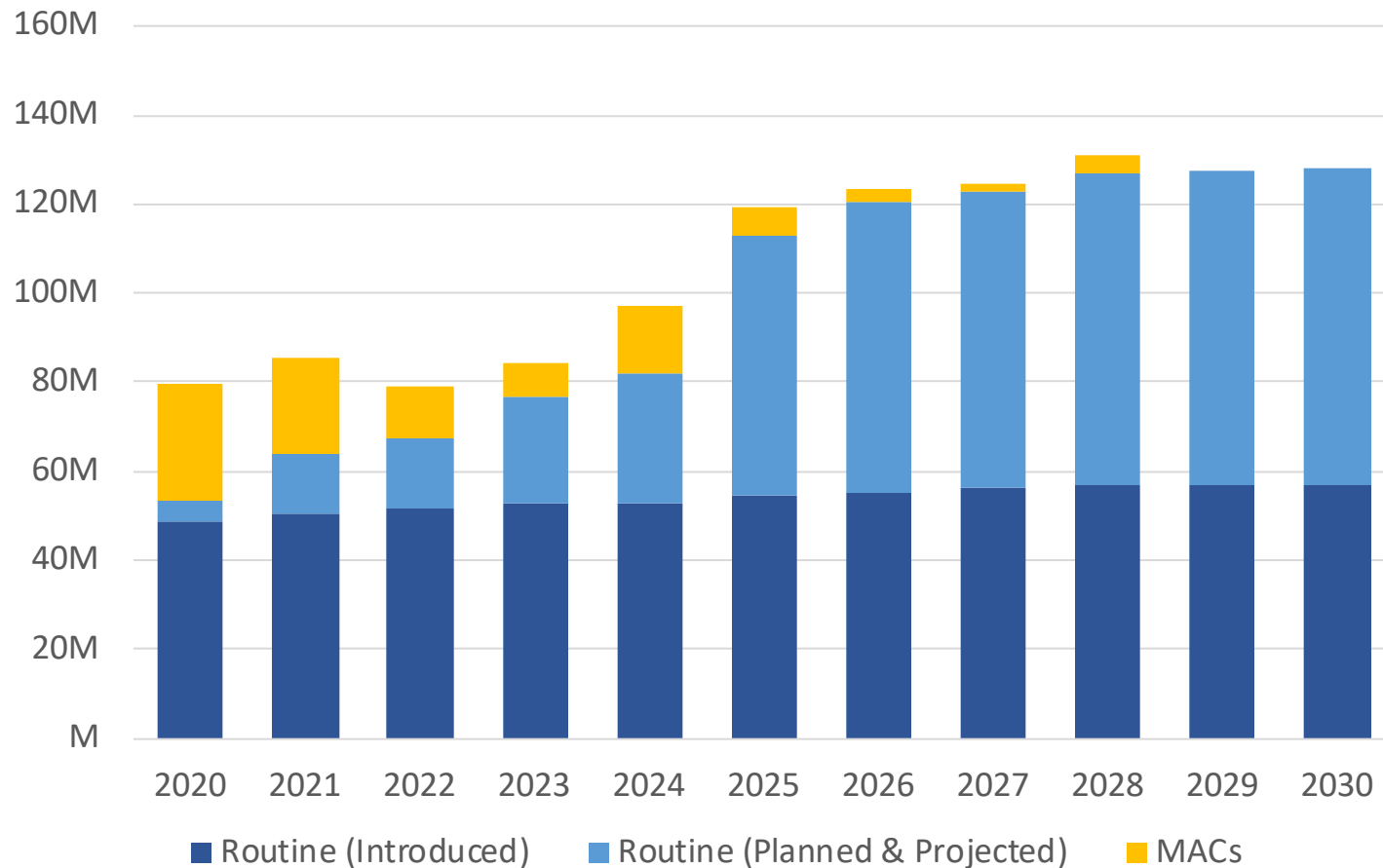
# Global demand Scenarios



Strategy	Doses	Age routine (years)	Interval (months)	MACs (9-14 yo)	Catch-up (@14 yo)
1	2	9	0, 6 (max 12-15)	YES	NO
2	2	9	0, 6 (max 12-15)	NO	NO
3	1	9		YES	NO
4	1	9		NO	NO
5	1+1	9	0, 36 - 60	NO	NO
6	1+1	9	0, 36 - 60	NO	YES
7	2	13 or 14 Switch to 9 or 10 yo when possible	0, 6 (max 12-15)	NO	SWITCH to 9 or 10 yo when possible



# Routine 2-dose scenarios (current recommendation)



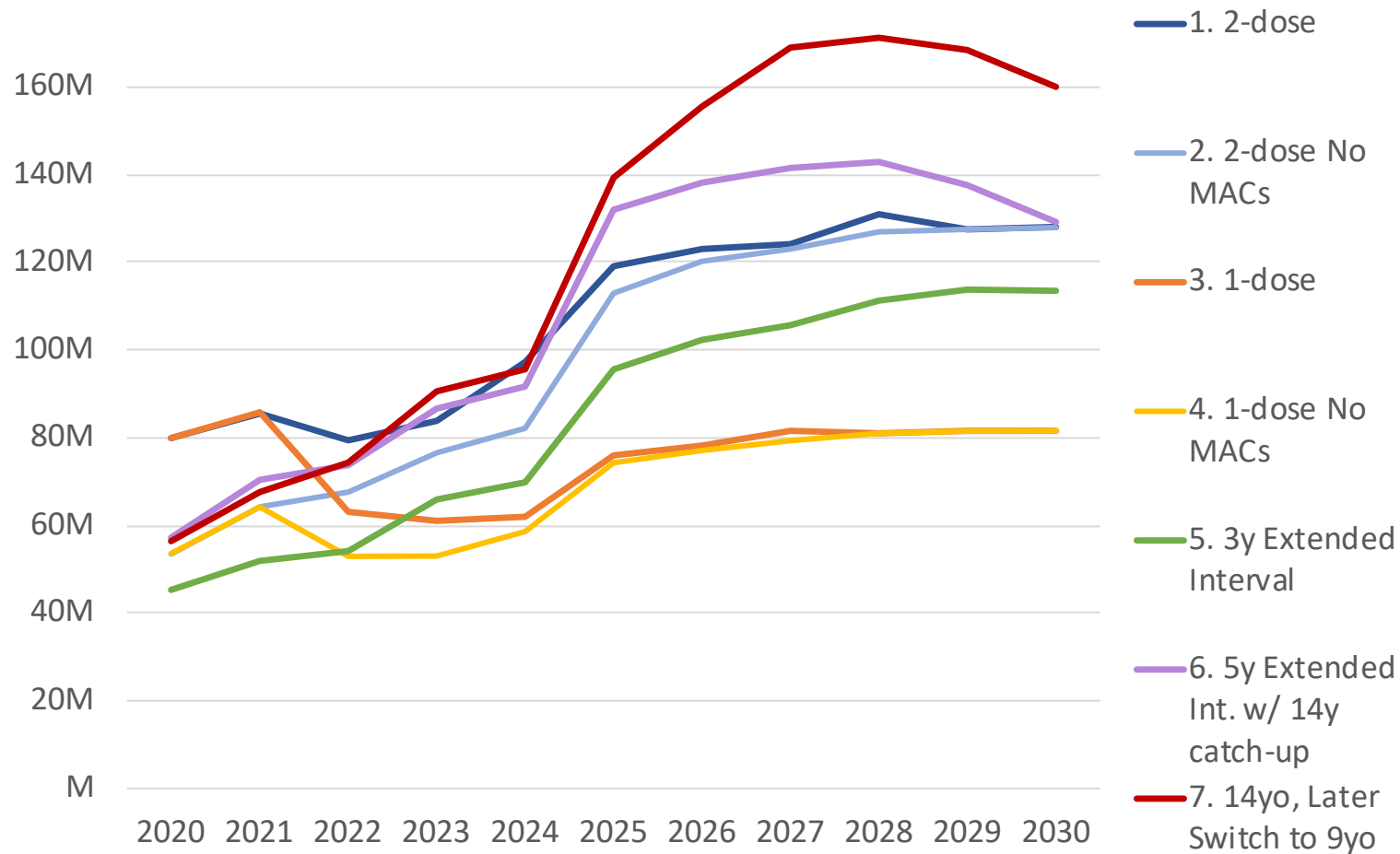
## Assumptions:

- All countries introduce by 2029
- Gender neutral only in countries with existing recommendations
- *These apply to all scenarios, 1-7*

## Results:

- Programmatic dose requirement reaches and stabilizes at ~120M doses in 2025
- MACs have been distributed across years, but remain an important contributor to dose requirement in the next 5 years

# Comparing dose requirement across 7 scenarios



## Results:

- Scenarios w/ MACs have the highest short-term programmatic dose requirement
- 3y extended interval results in lowest doses in the short-term
- One dose greatly reduces dose required in mid and long run
- 14yo with later switch to 9yo increases requirements considerably in the long run



# Global supply demand balance

Implications for  
supply allocation



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# Dynamic supply-demand balance

	Base Supply			Low Supply		
Demand Scenarios	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)
#1 2-dose + MACs						
#2 2-dose <u>No</u> MACs						
#3 1-dose + MACs						
#4 1-dose <u>No</u> MACs						
#5 3y Extended Interval						
#6 5y Ext. Int. + 14yo						
#7 14yo, Later 9yo						



As a result of persistent shortages in past years, demand has been influenced (e.g. MACs postponement, program delayed)



More extensive implementation of commercially attractive gender neutral and adult catch-up policies will influence balance



Refusal of specific products (based on valency or country of origin) constituting relevant share of supply would influence balance



# Base Supply Detailed Results: no MACs/catch up scenarios

Scenarios with no MACs/catch up contribute most to relieving supply constraints, allowing more countries to introduce sooner

	Lives <u>Not</u> Saved due to supply constraints in specific countries not served		
	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)
#2: 2-dose <u>No</u> MACs	20K (9 countries)		
#4: 1-dose <u>No</u> MACs	20K (9 countries)		
#5: 3y Extended Interval			

Adoption of a 3-years interval between 1st and 2nd doses from 2020 by all Gavi and PAHO RF countries further contributes to the improvement of the supply-demand balance freeing supply in the 2020-2021 critical period.

# Base Supply Detailed Results: Scenarios w/ MACs/catch-up

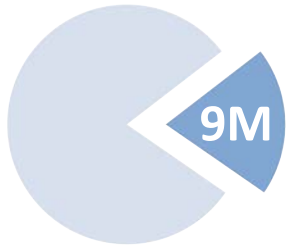
MACs and catch-up scenarios intensify supply constraints in the short term, with more introductions postponed

	Lives <u>Not</u> Saved due to supply constraints in specific countries not served		
	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)
#1: 2-dose w/ MACs	143K (27 countries)		
#3: 1-dose w/ MACs	103K (23 countries)		
#6: 5y Ext. Int. + 14y catch-up	45K (10 countries)		
#7 14yo, Later Switch to 9yo	56K (21 countries)		

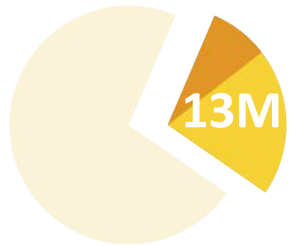
Of all alternative strategies, adoption of (#6) a 5 years extended interval between 1<sup>st</sup> and 2<sup>nd</sup> dose and (#7) intro in 14 yo with later switch to 9yo have the best outlook.



# Impact of vaccinating boys for girls in low income/high burden settings



2019 demand for use in boys is **~9M** doses (18% of global demand)



**Other HICs adding boys** would require **additional ~4M** doses (1/3 Gavi demand)

**Alternative use of doses: 9** low- and middle-income countries forecasted to have a delayed routine introductions in short term would be able to introduce

**Implications:** In short run, planned introductions would be delayed in **12** low- and middle-income countries.

# Conclusion



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# Key takeaways

- **In the short-term, supply remains constrained** especially for LICs and LMICs across all scenarios (9 to 27 country intros possibly postponed):
  - **No MACs/catch-up scenarios** minimises impact of supply constraints (further improved with an extended interval schedule)
- **Supply/demand balance expected to improve in the mid-term** subject to certain conditions:
  - Current suppliers success in **expanding capacity** as communicated (time and size)
  - Pipeline producers success in **reaching market** (albeit with small volumes) and PQ
  - **Country acceptance** for all products irrespective of valency or country of origin





# Thank you!



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