Context-specific modelling in low-resource settings:

Additional impact and resource to expand to universal HPV vaccination

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Topics of this talk

- IARC/WHO's context-specific modelling framework to inform cervical cancer prevention policies in LMICs

- Expansion to universal HPV vaccination: expected impact, resource needed

Context-specific modelling framework

Objective of context-specific modelling framework

*According to **IARC/WHO's position and mandate**, we aim to support LMICs in decisions on **cervical cancer prevention policies**, by providing estimates of relevant **epidemiological and economical indicators** using **advanced predictive models** informed by **high-quality empirical data***

***Validated models** with vignettes and working examples publicly available on:*
https://iarc-miarc.gitlab.io/methis/methis.website/

***Living databases** with data from literature and our data collection efforts*
CHRONOS: HPV prevalence surveys
COEUS: societal cost of CC surveys

METHIS - modelling platform, databases, and workflow

The framework provides estimates of the expected impact of vaccination & screening.

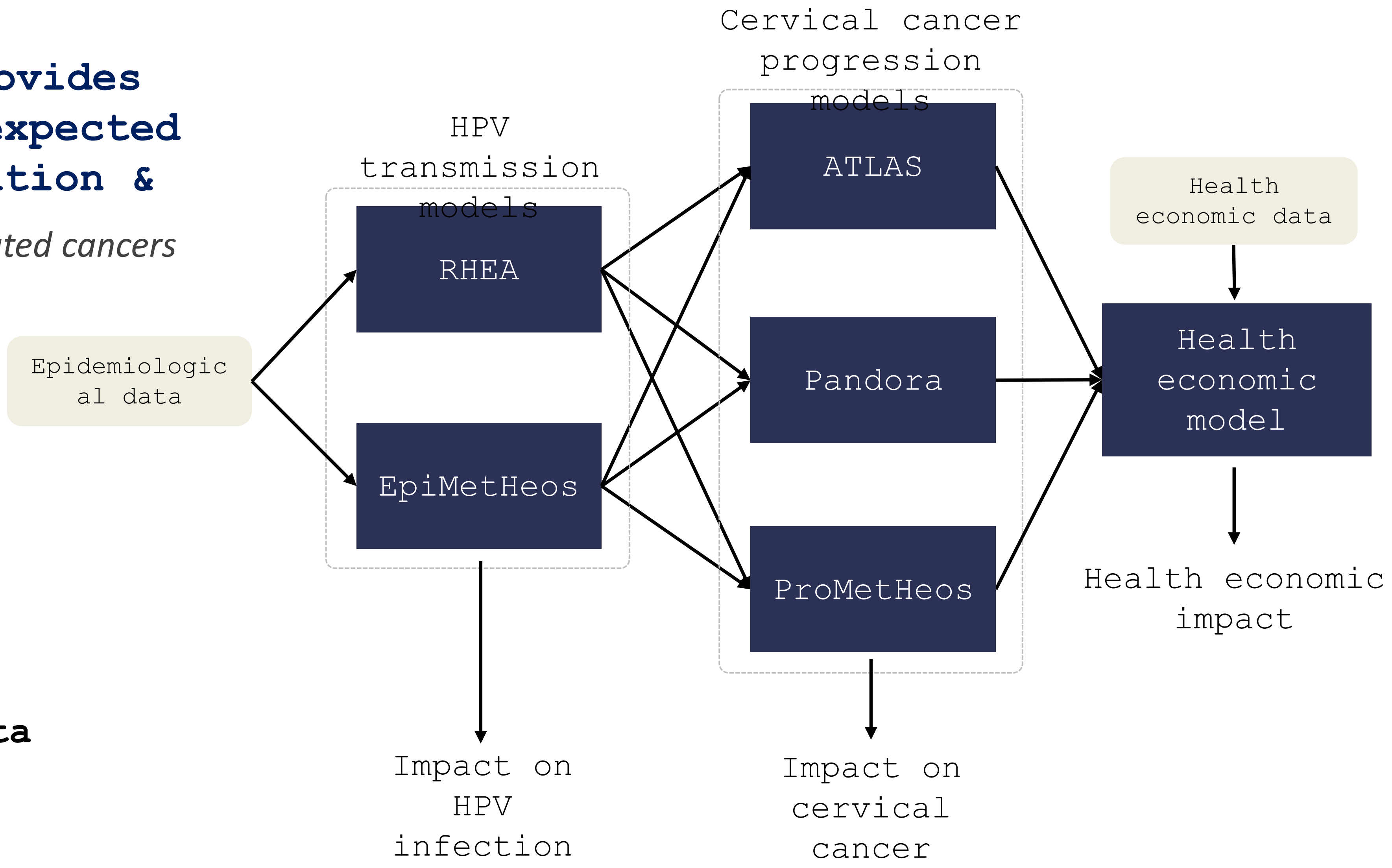
** Adaptable to other HPV-related cancers*

Adaptable to

- Data availability - *input*
- Complexity of decision - *output*

Solutions to lack of data

- Collect the data
- Approximate the data



Epidemiological data

HPV transmission models

RHEA

EpiMetHeos

Cervical cancer progression models

ATLAS

Pandora

ProMetHeos

Health economic data

Health economic model

Impact on HPV infection

Impact on cervical cancer

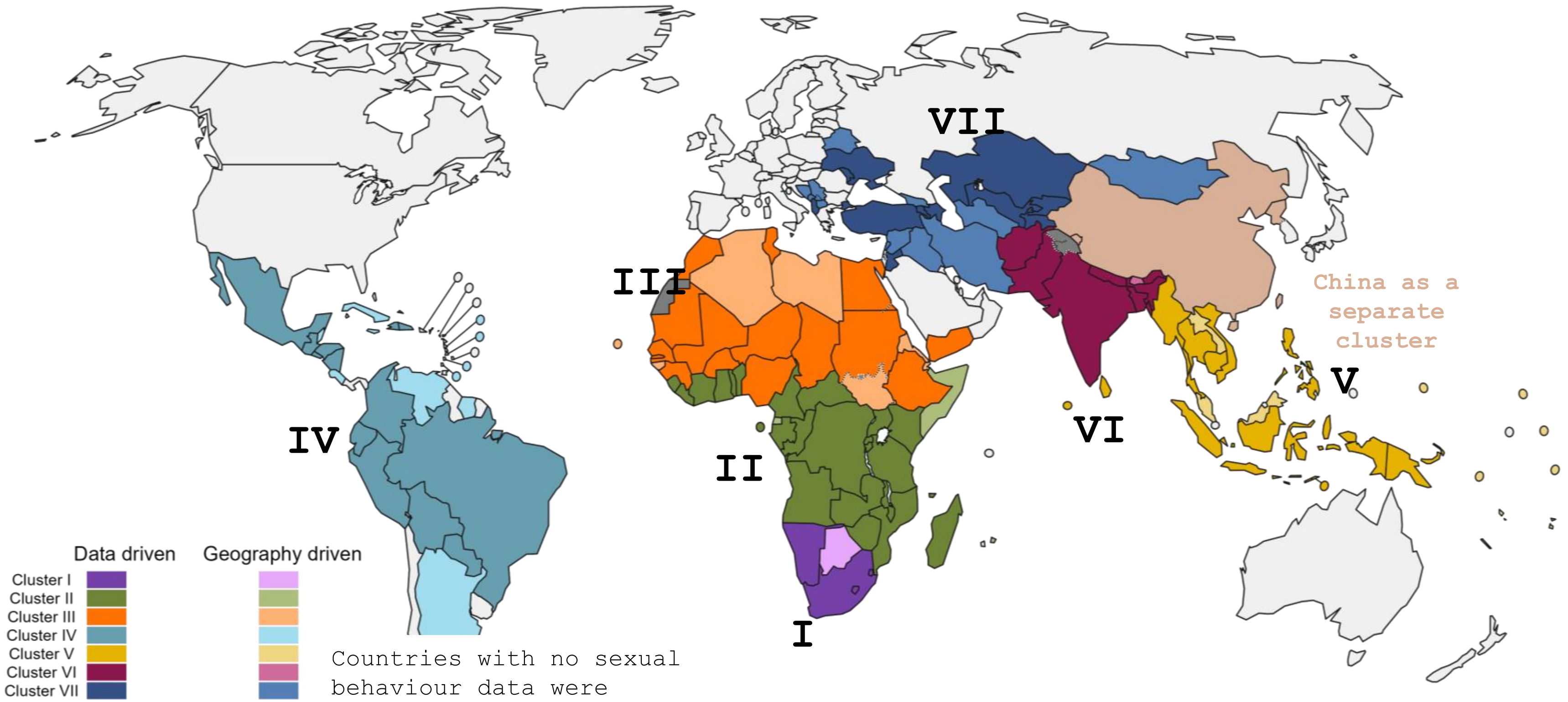
Health economic impact

Modelling platform website: https://iarc-miarc.gitlab.io/methis/methis.website/

Modelling 132 LMICs while coping with scarce data

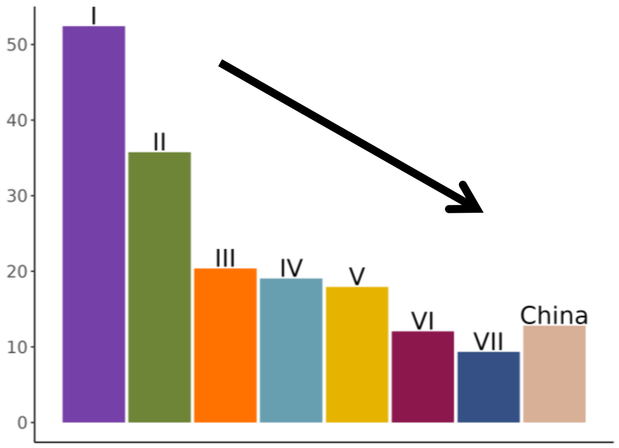
- **Footprinting: 7 archetypes/clusters identified with sexual behaviour data [1,2]**
- **Country-specific models can be calibrated:**
  - Rely upon maximum amount of available data from each country
  - Complemented by data for missing variables imputed from the cluster

Data sources:
1. DHS
2. UNAIDS
3. GLOBOCAN



Countries with no sexual behaviour data were assigned based on geographical proximity

Decreasing incidence of cervical cancer [3]



Figures made by Macacu
Man et al. eLife (2023) – footprinting
Man et al. (manuscript in preparation)

Framework ready for a range of decision questions of cervical cancer prevention policies ✓

- **Expansion to "universal" vaccination** *
  - **Female catch-up / MAC**
  - **Routine boys vaccination**
  - Special populations
    - Out-of-school girls
    - Displaced populations
    - People living with HIV

**** Modelling work on target prioritization:***

- *Drolet et al. Lancet Infect Dis (2021)*
- *Man et al. JNCI Monograph (2024)*
- *Bernard et al. SD consortium slides (2025)*

- **Fair price for 9-valent vaccines**
- **Integration of vaccination & screening**

Context-specific modelling results for expansion to “universal” vaccination:

- Expected health impact
- Resource needed
- Global vaccine supply

Methods

Structuring decision process to define female catch-up age range

Epidemiological indicators

Step 1. Determine health need with dose efficiency*

* *Dose efficiency = Number of doses needed to prevent 1 cervical cancer*

- **Local perspective - *"Equitable in a jurisdiction"***
  MIN. age range with dose efficiency still comparable to primary target age (9-14 yrs)

- **Global perspective - *"Equitable in the world"***
  MAX. age range with still acceptable dose efficiency. Now based on max. 250 doses needed to prevent 1 cervical cancer. It can be based on back-calculation from global vaccine supply and cross-antigen comparison.

Economical indicators

Step 2. Verify economical constraints

- **Local perspective**
  - ➢ Total vaccine budget in % EPI budget and % total health expenditure
  - ➢ ICER below cost-effectiveness threshold

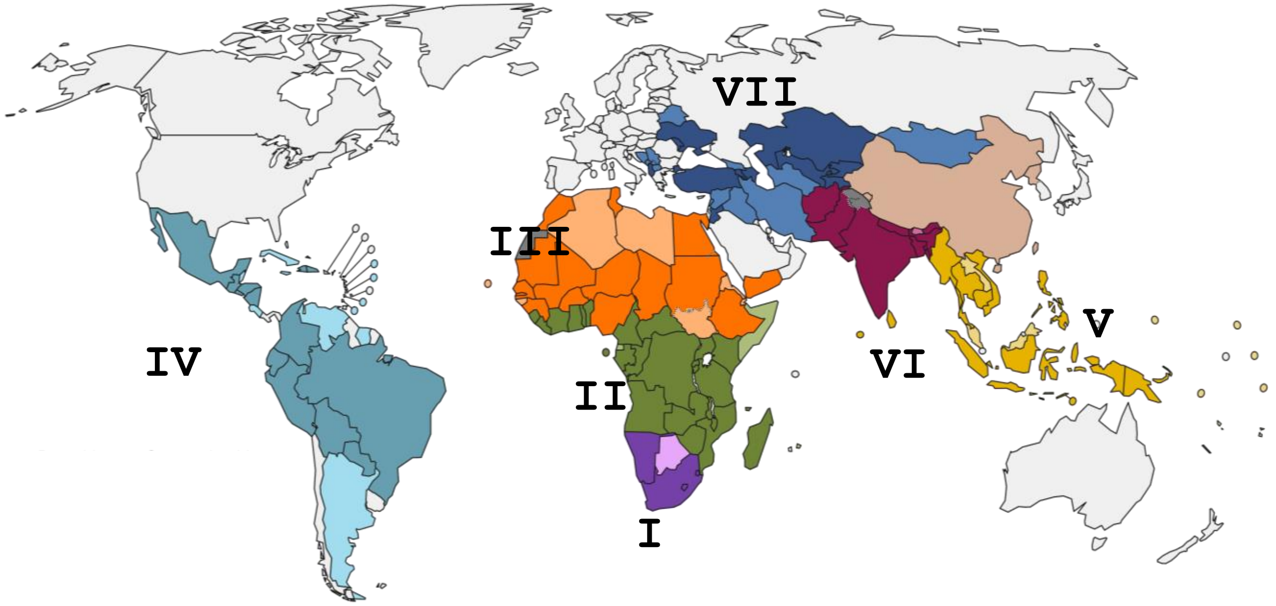
Results

Female catch-up age range based on dose efficiency

	Catch-up age range	
Cluster/ archetypes	MIN - LOCAL perspective	MAX - GLOBAL perspective
I	10-16	10-30
II	10-16	10-30
III	10-18	10-23
IV	10-18	10-25
V	10-20	10-27
China	10-20	10-24
VI	10-20	10-24
VII	10-19	10-20

Increasing age of sexual debut ↓

Increasing cervical cancer lifetime risk ↑

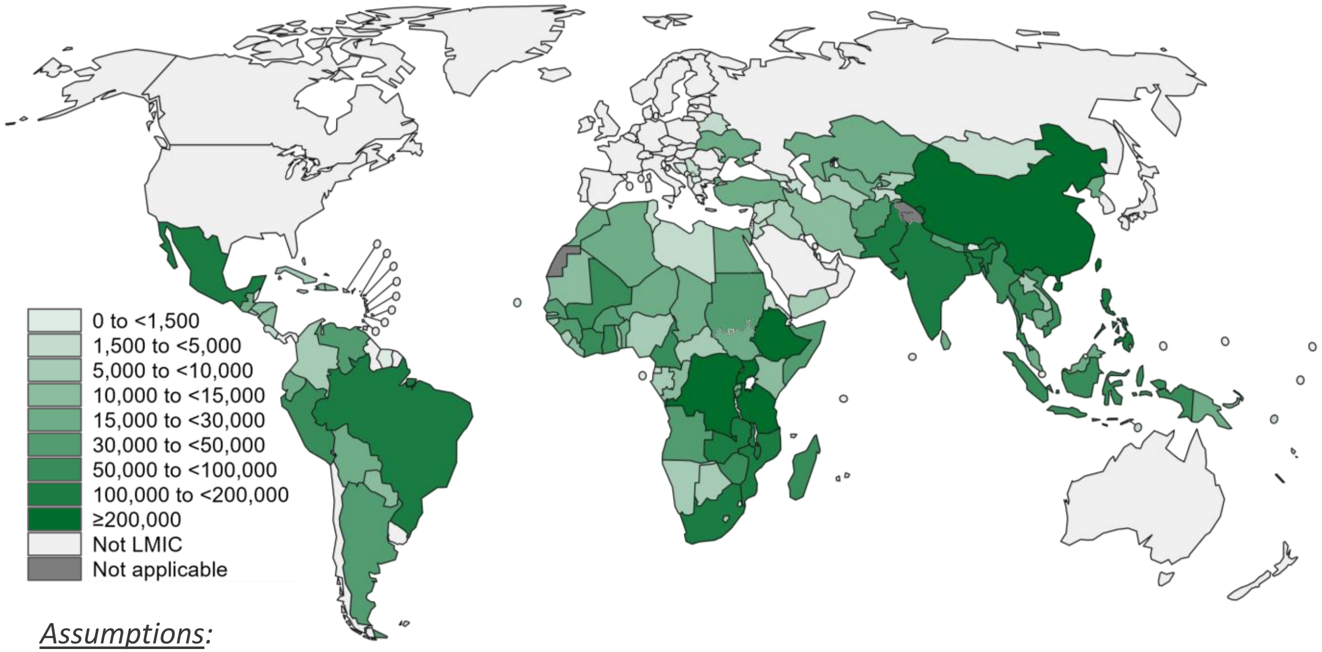


Macacu et al. (manuscript in preparation)

Results

Health impact of female catch-up

	Estimated numbers of cervical cancer cases prevented	
	MIN - LOCAL perspective	**MAX - GLOBAL perspective**
Total LMICs	3,640,075	5,188,804
WHO Regions		
Americas	374,581	555,994
Eastern Mediterranean	248,104	310,713
European	106,612	114,555
Western Pacific	1,004,844	1,234,302
South-East Asia	471,581	603,367
Africa	1,434,353	2,369,873



<u>Assumptions</u>:

- *Catch-up age range = MIN – LOCAL perspective*
- *90% ideal vaccination coverage*

** Similar maps can be generated for other catch-up age ranges, coverages, including boys, and for other HPV-related cancers*

Macacu et al. (manuscript in preparation)

Results

Doses needed to expand to "universal" vaccination

	5-year routine girls (baseline)	**One-off female catch-up/MAC**		**5-year routine boys**
		MIN - LOCAL perspective	**MAX - GLOBAL perspective**	
Total LMICs	297 M	403 M	644 M	315 M
Four populous LMICs				
India	57 M	108 M	153 M	62 M
China	40 M	71 M	98 M	45 M
Nigeria	15 M	19 M	29.5 M	16 M
Indonesia	11 M	18 M	31.5 M	12 M

M = millions

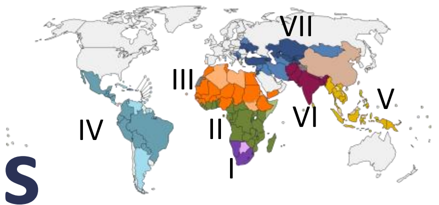
Assumptions:
- *Based on population in 2025*
- *Single dose schedule*
- *Doses needed to vaccinate previously unvaccinated women, girls and boys based on WHO HPV Dashboard coverage data*

** Figures also available for other stratifications (e.g., introduction status, GAVI, region)*

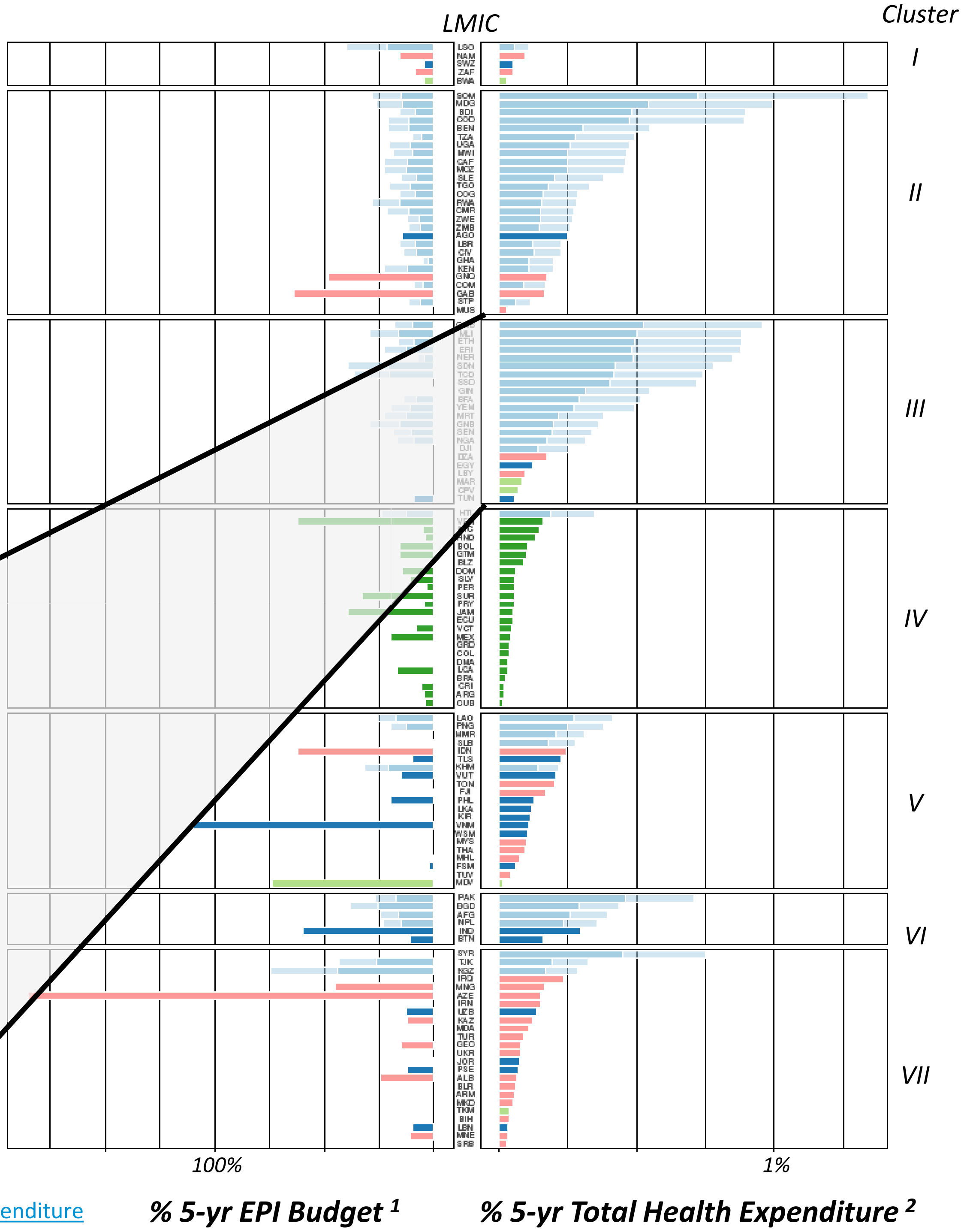
Macacu et al. (manuscript in preparation)

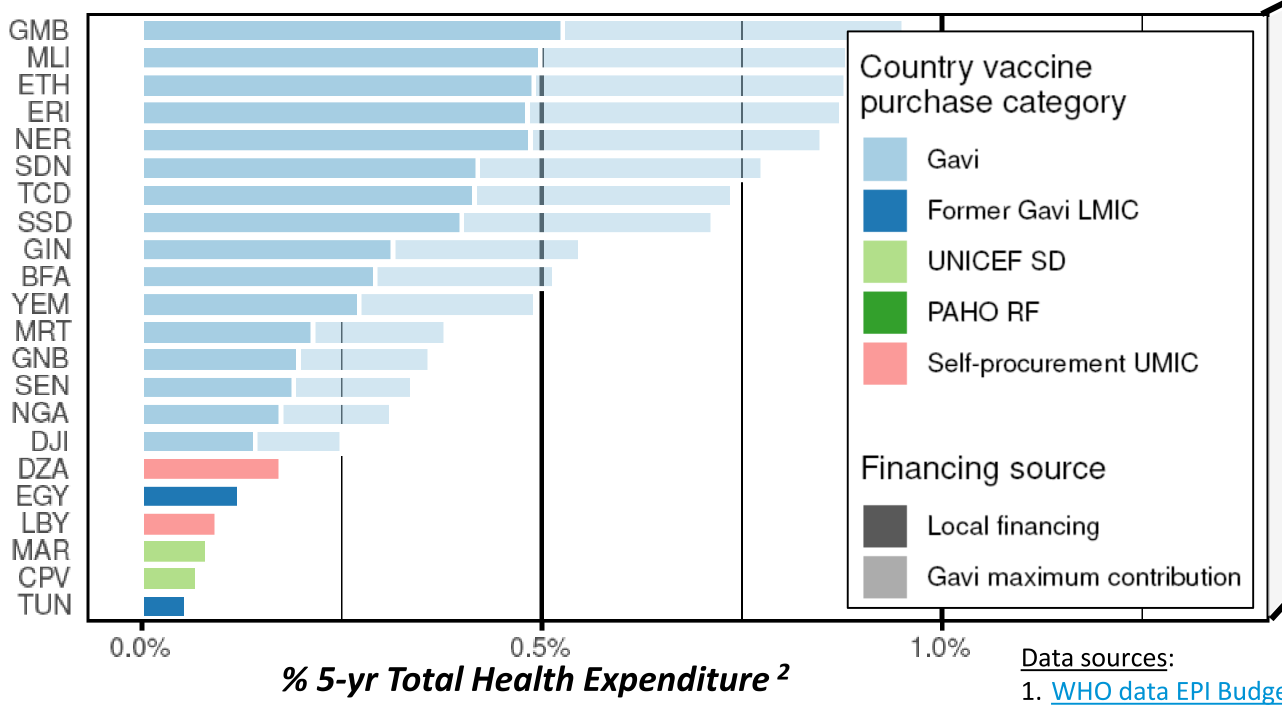
Results

Budget impact analysis



- For ~130 LMICs and MIN catch-up age range
- GAVI support is substantial





Data sources:
1. WHO data EPI Budget
2. WHO data Total Health Expenditure

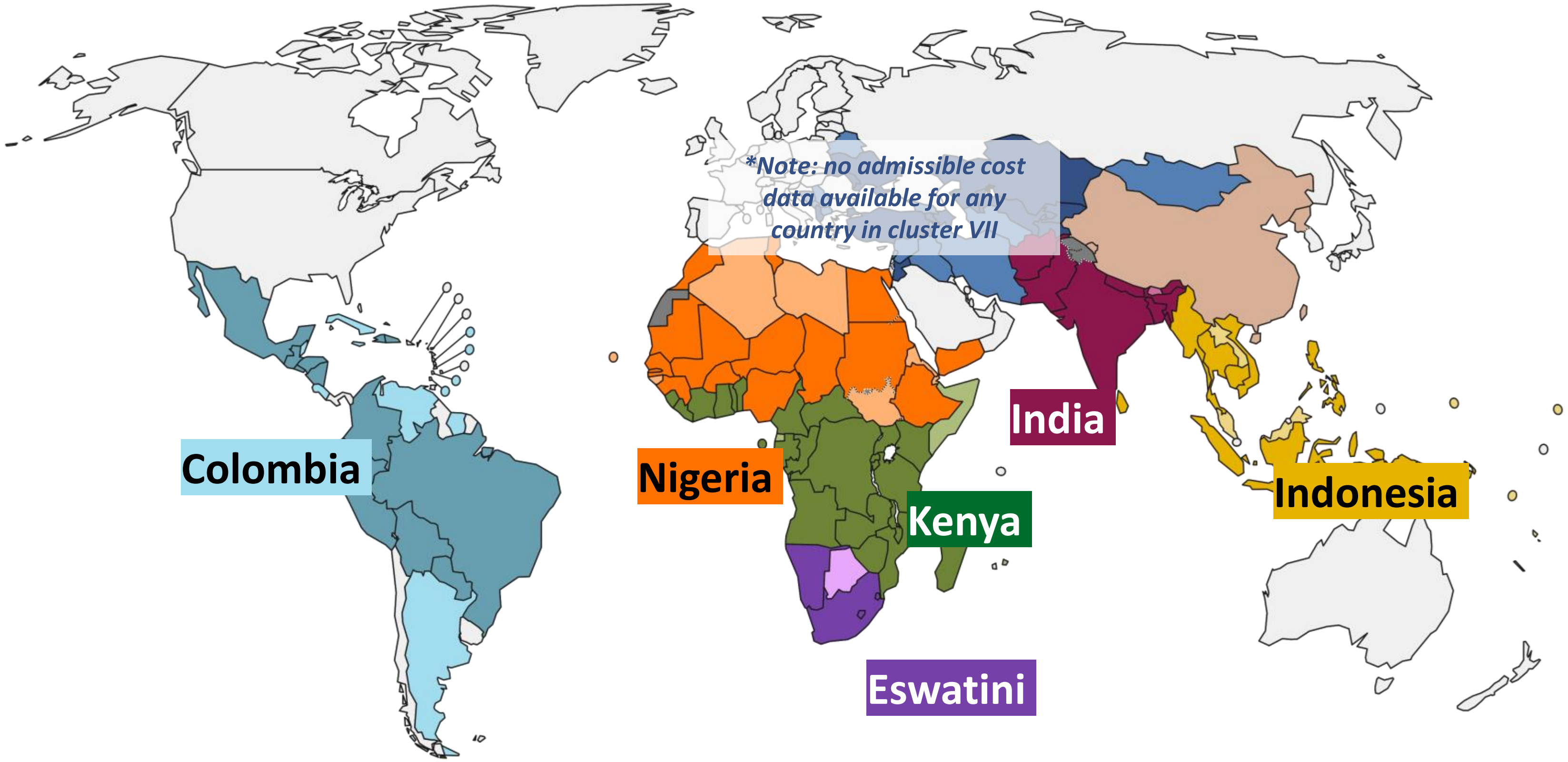
Dagne et al. (manuscript in preparation)

Methods

Countries selected for cost-effectiveness analysis

- Bottleneck: high-quality cervical cancer treatment cost data available for only ~20 LMICs

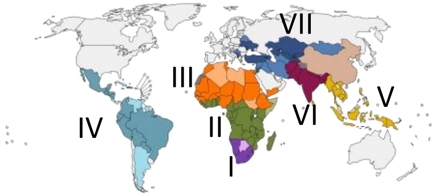
- One country per cluster with available data selected for CE analysis



Fuady et al. JCO Glob Oncol (2024)

Results

Cost effectiveness analysis

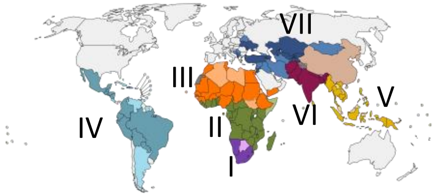


Cluster/ archetypes	Country	Cost-effective catch-up age range
I	Eswatini	10-30
II	Kenya	10-29
III	Nigeria	10-18
IV	Colombia	10-30
V	Indonesia	10-30
VI	India	10-28

Dagne et al. (manuscript in preparation)

Results

Cost effectiveness analysis



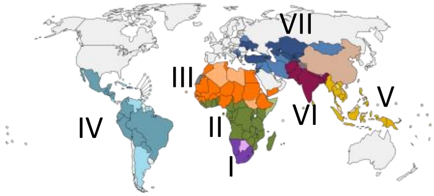
Cluster/ archetypes	Country	Cost-effective catch-up age range	MIN - LOCAL perspective
I	Eswatini	10-30	10-16
II	Kenya	10-29	10-16
III	Nigeria	10-18	10-18
IV	Colombia	10-30	10-18
V	Indonesia	10-30	10-20
VI	India	10-28	10-20

- MIN – LOCAL perspective cost-effective in all 6 LMICs
- Even cost-saving for Eswatini and India (high CC treatment costs and GPD per capita)

Dagne et al. (manuscript in preparation)

Results

Cost effectiveness analysis



Cluster/ archetypes	Country	Cost-effective catch-up age range	MAX - GLOBAL perspective
I	Eswatini	10-30	10-30
II	Kenya	10-29	~~10-30~~
III	Nigeria	10-18	~~10-23~~
IV	Colombia	10-30	10-25
V	Indonesia	10-30	10-27
VI	India	10-28	10-24

NOT cost-effective

- MAX – GLOBAL perspective cost-effective in 4/6 LMICs
- NOT cost-effective in 2/6 LMICs (low GDP per capita)

Dagne et al. (manuscript in preparation)

Key take-aways

- **IARC/WHO's modelling platform, databases, and workflow ready** for a range of decision questions on cervical cancer prevention policies in LMICs
- **Scope of female catch-up/MAC in LMICs**
  - MIN catch-up age range (up to 16-20)
    should be cost-effective and <1% total health expenditure
  - MAX catch-up age range (up to 24-30)
    can be often cost-effective
    but may be constrained by local budget or global vaccine supply
- **Projections on global vaccine supply and resource available needed** to guide local and global decisions on "universal" vaccination

Acknowledgement

IARC - Public Health Decision Science Team	Iacopo Baussano Alina Macacu Damien Georges Abrham Dagne Indira Adhikari Rachel Wittenauer Ahmad Fuady Andrea Gini Mattis Eynard
Funding	Gates Foundation (INV-039876)

Thank you for your attention!

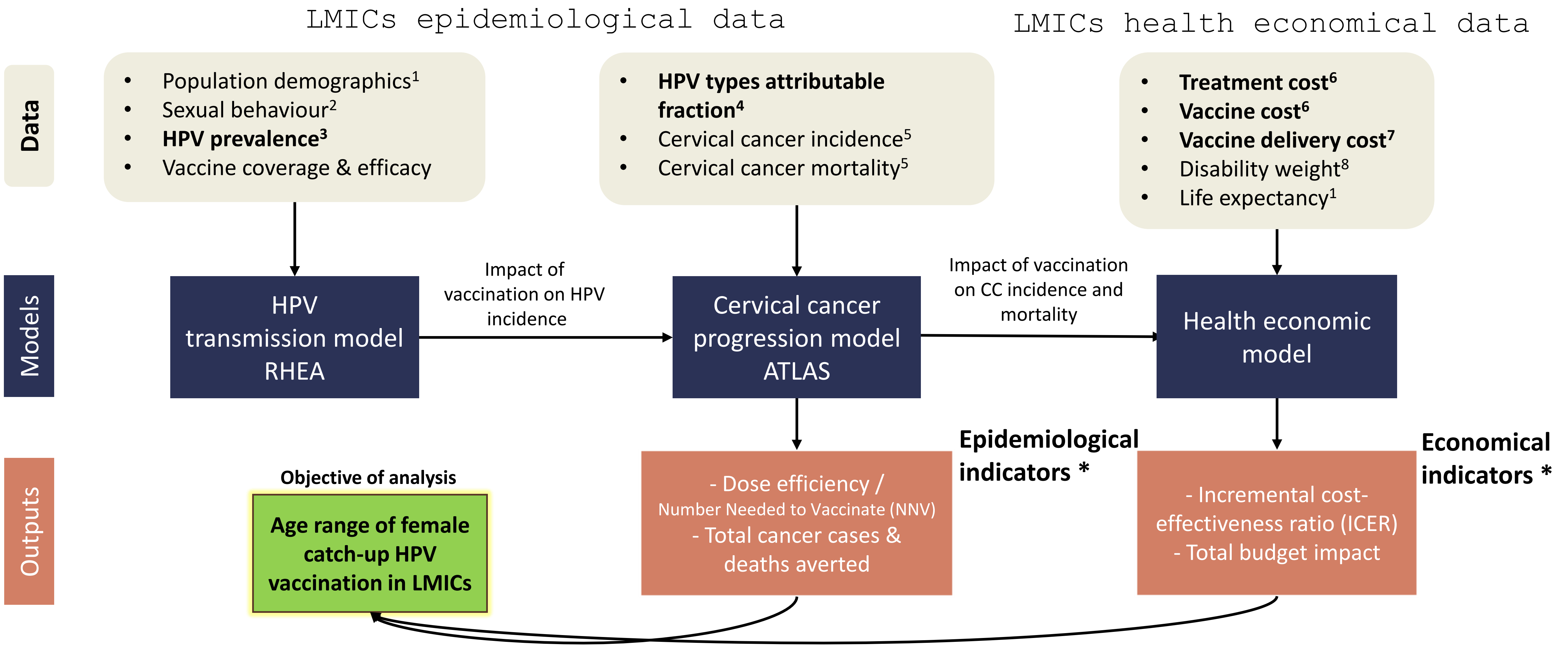
Appendix Slides

Methods

Data sources:

1. UNDP WPP
2. Demographic and Health Surveys
3. Country specific from lit.
4. Wei *et al.*, 2024
5. GLOBOCAN
6. Country specific from lit.
7. Pooled estimate from lit.
8. IHME/GBD

Overview of data, models, and workflow



LMICs epidemiological data

LMICs health economical data

Data

- Population demographics[1]
- Sexual behaviour[2]
- **HPV prevalence[3]**
- Vaccine coverage & efficacy

- **HPV types attributable fraction[4]**
- Cervical cancer incidence[5]
- Cervical cancer mortality[5]

- **Treatment cost[6]**
- **Vaccine cost[6]**
- **Vaccine delivery cost[7]**
- Disability weight[8]
- Life expectancy[1]

Models

HPV transmission model RHEA

Impact of vaccination on HPV incidence

Cervical cancer progression model ATLAS

Impact of vaccination on CC incidence and mortality

Health economic model

Outputs

Objective of analysis

Age range of female catch-up HPV vaccination in LMICs

- Dose efficiency / Number Needed to Vaccinate (NNV)
- Total cancer cases & deaths averted

Epidemiological indicators *

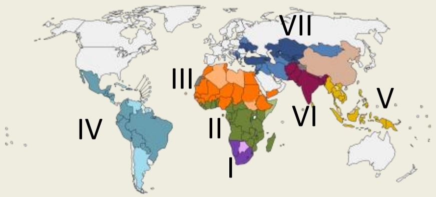
- Incremental cost-effectiveness ratio (ICER)
- Total budget impact

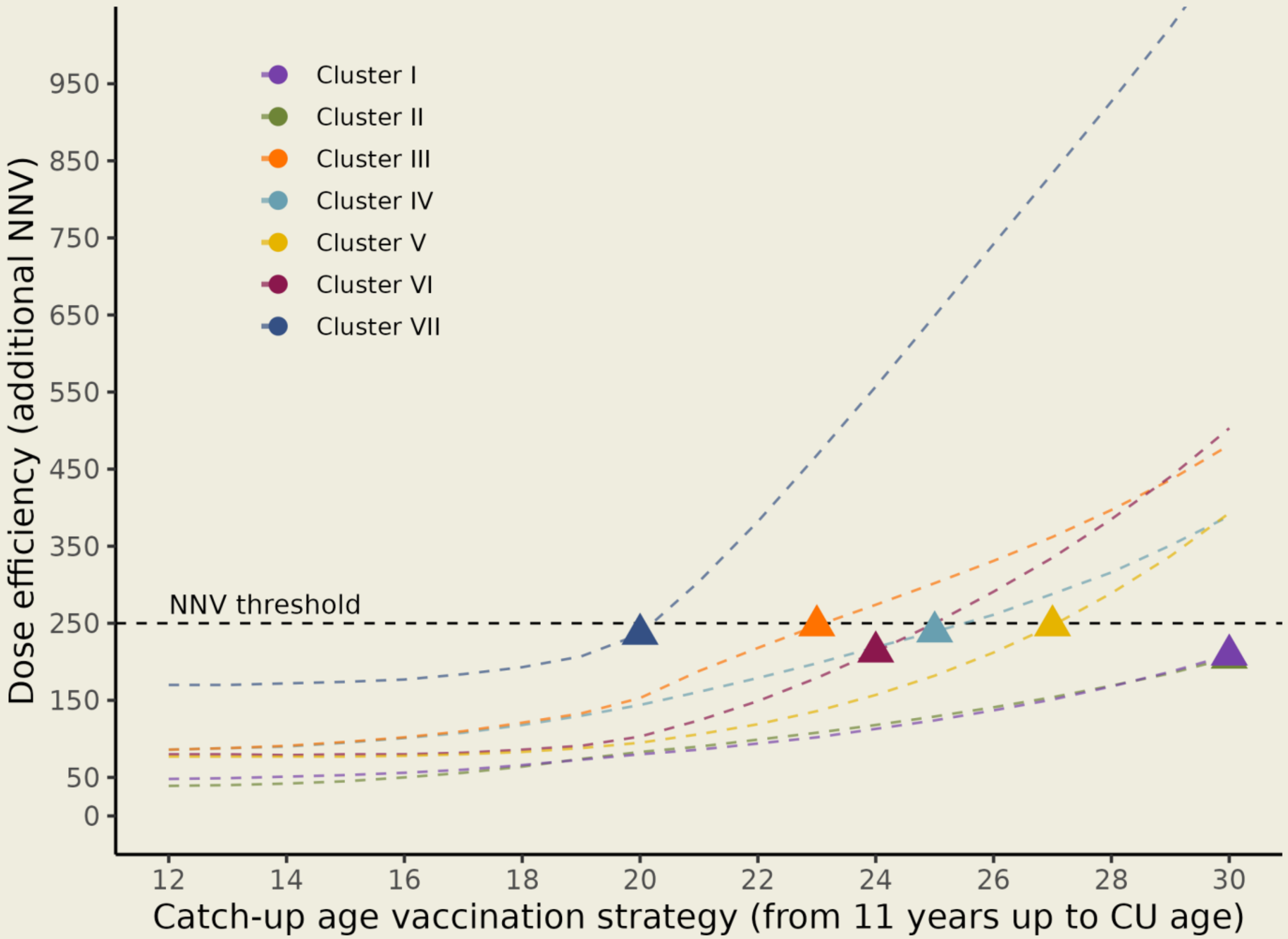
Economical indicators *

** These **data, models, indicators and workflow** are also applicable for many other decision questions in LMICs.*

Results

GLOBAL “optimum” catch-up vaccination age



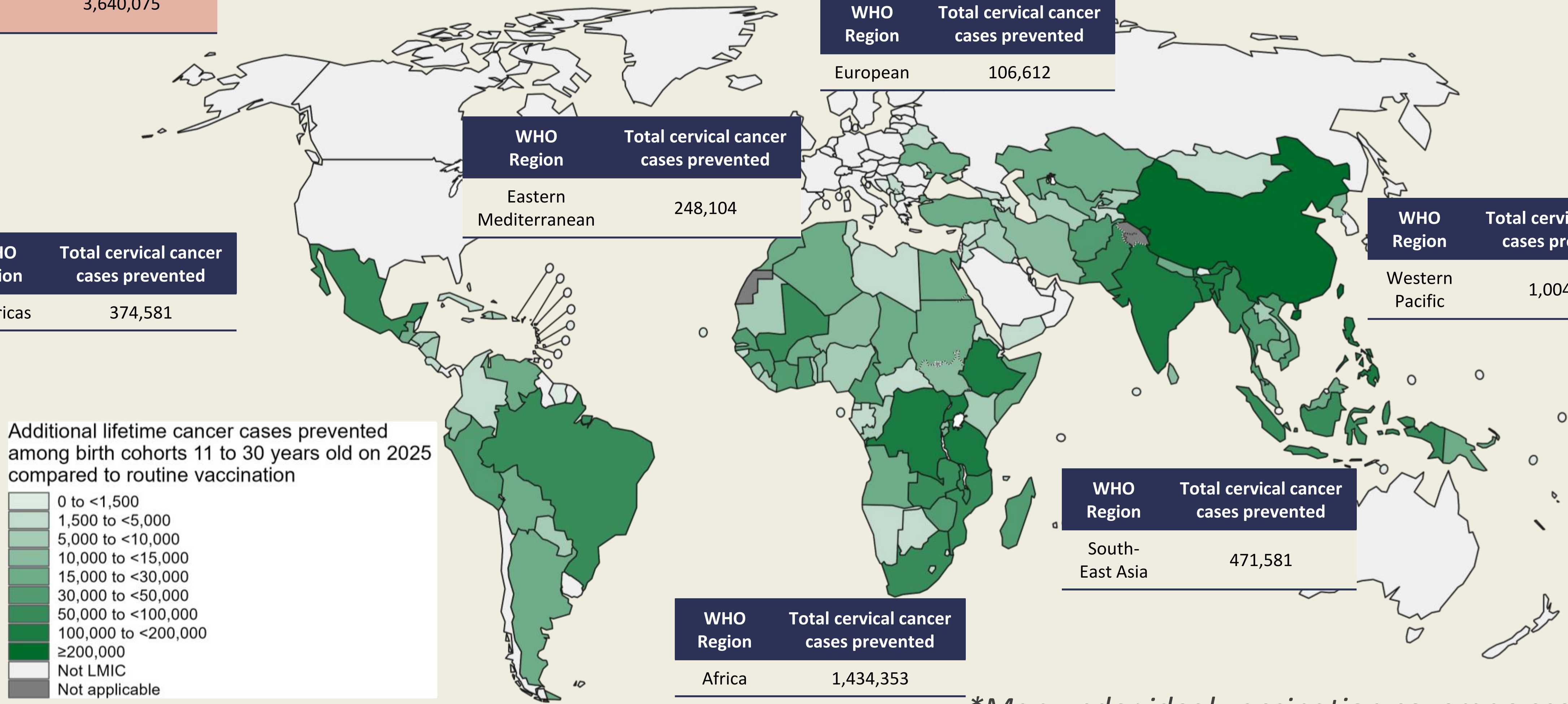


“Optimum” CU vaccination strategy:

GLOBAL: Setting the same dose efficiency threshold globally for all clusters; each cluster achieves that efficiency at a different CU age. All clusters will be vaccinated up to an equally efficient CU age (“globally”).

Impact of CU vaccination: ***LOCAL “optimum” CU age***

WHO Region	Total cervical cancer cases prevented
TOTAL LMICs	3,640,075



WHO Region	Total cervical cancer cases prevented
Americas	374,581

WHO Region	Total cervical cancer cases prevented
Eastern Mediterranean	248,104

WHO Region	Total cervical cancer cases prevented
European	106,612

WHO Region	Total cervical cancer cases prevented
Western Pacific	1,004,844

WHO Region	Total cervical cancer cases prevented
South-East Asia	471,581

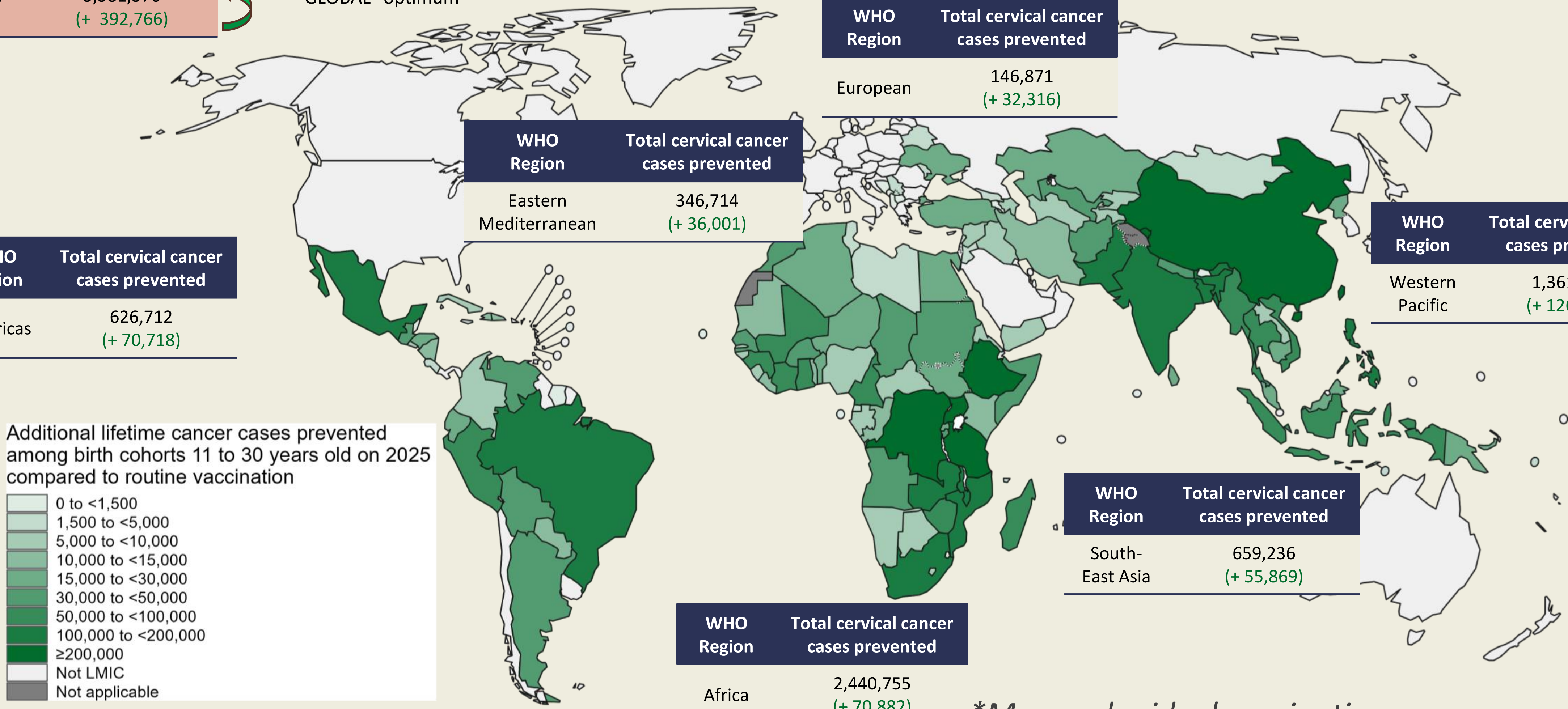
WHO Region	Total cervical cancer cases prevented
Africa	1,434,353

**Map under ideal vaccination coverage scenario : 90%*

Impact of CU vaccination: ***highest CU age analysed (30 years)***

WHO Region	Total cervical cancer cases prevented
TOTAL LMICs	5,581,570 (+ 392,766)

Additional compared to using GLOBAL “optimum”



WHO Region	Total cervical cancer cases prevented
European	146,871 (+ 32,316)

WHO Region	Total cervical cancer cases prevented
Eastern Mediterranean	346,714 (+ 36,001)

WHO Region	Total cervical cancer cases prevented
Western Pacific	1,361,282 (+ 126,980)

WHO Region	Total cervical cancer cases prevented
Americas	626,712 (+ 70,718)

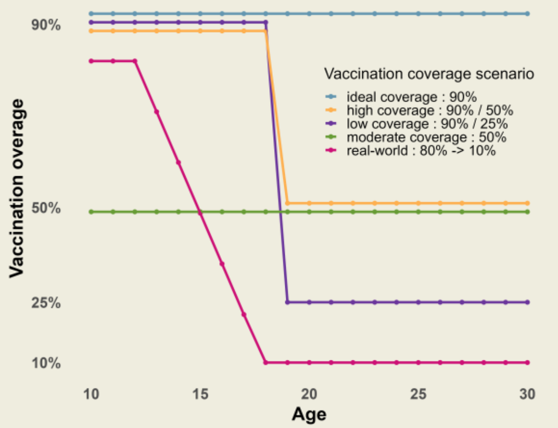
WHO Region	Total cervical cancer cases prevented
South-East Asia	659,236 (+ 55,869)

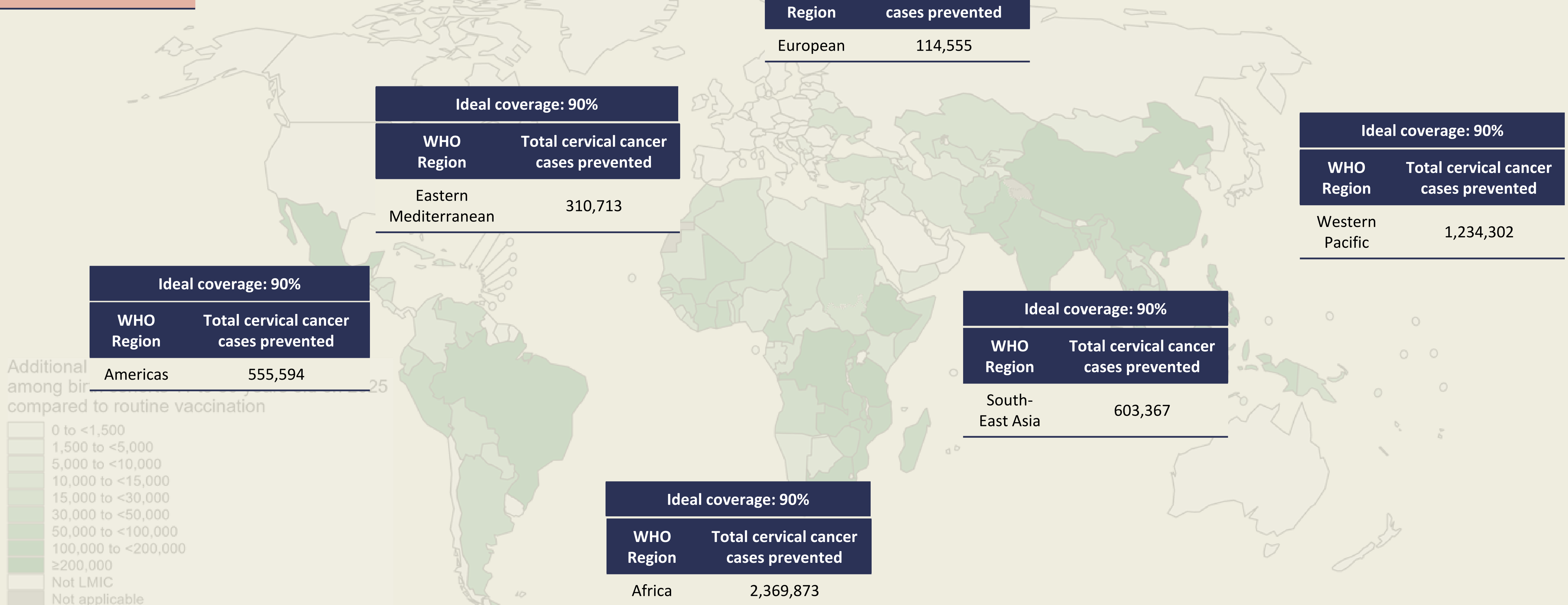
WHO Region	Total cervical cancer cases prevented
Africa	2,440,755 (+ 70,882)

**Map under ideal vaccination coverage scenario : 90%*

Impact of vaccination coverage scenarios

WHO Region	Total cervical cancer cases prevented
TOTAL LMICs	5,188,804





Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
European	114,555

Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
Eastern Mediterranean	310,713

Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
Western Pacific	1,234,302

Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
Americas	555,594

Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
South-East Asia	603,367

Ideal coverage: 90%

WHO Region	Total cervical cancer cases prevented
Africa	2,369,873

GLOBAL "optimum" CU age

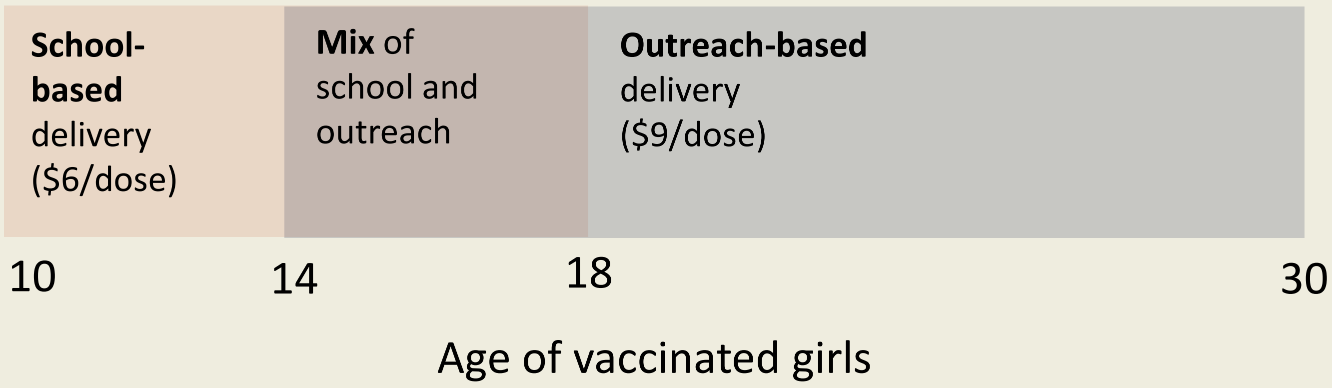
**Map under ideal vaccination coverage scenario : 90%*

Methods

Cost estimates

- ✓ Treatment costs
- ✓ Vaccine delivery costs
- ✓ Vaccine purchase costs

Vaccine delivery costs detail

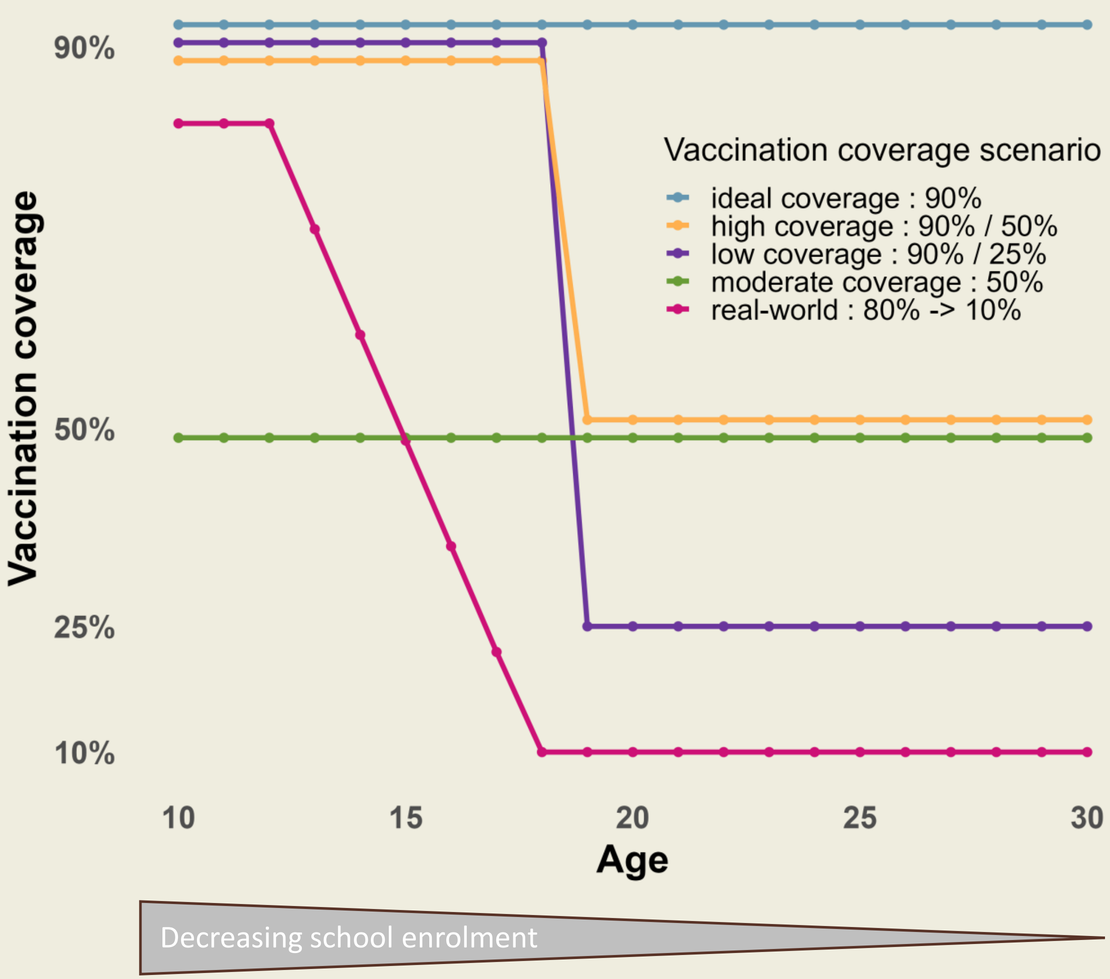


School-based delivery ($6/dose)

Mix of school and outreach

Outreach-based delivery ($9/dose)

Sensitivity Analysis: Impact of vaccination coverage



"Ideal" vaccination coverage (*main analysis*)

Sensitivity analyses of other coverage scenarios:

Moderate drop-off for girls older than 18

Moderately successful implementation

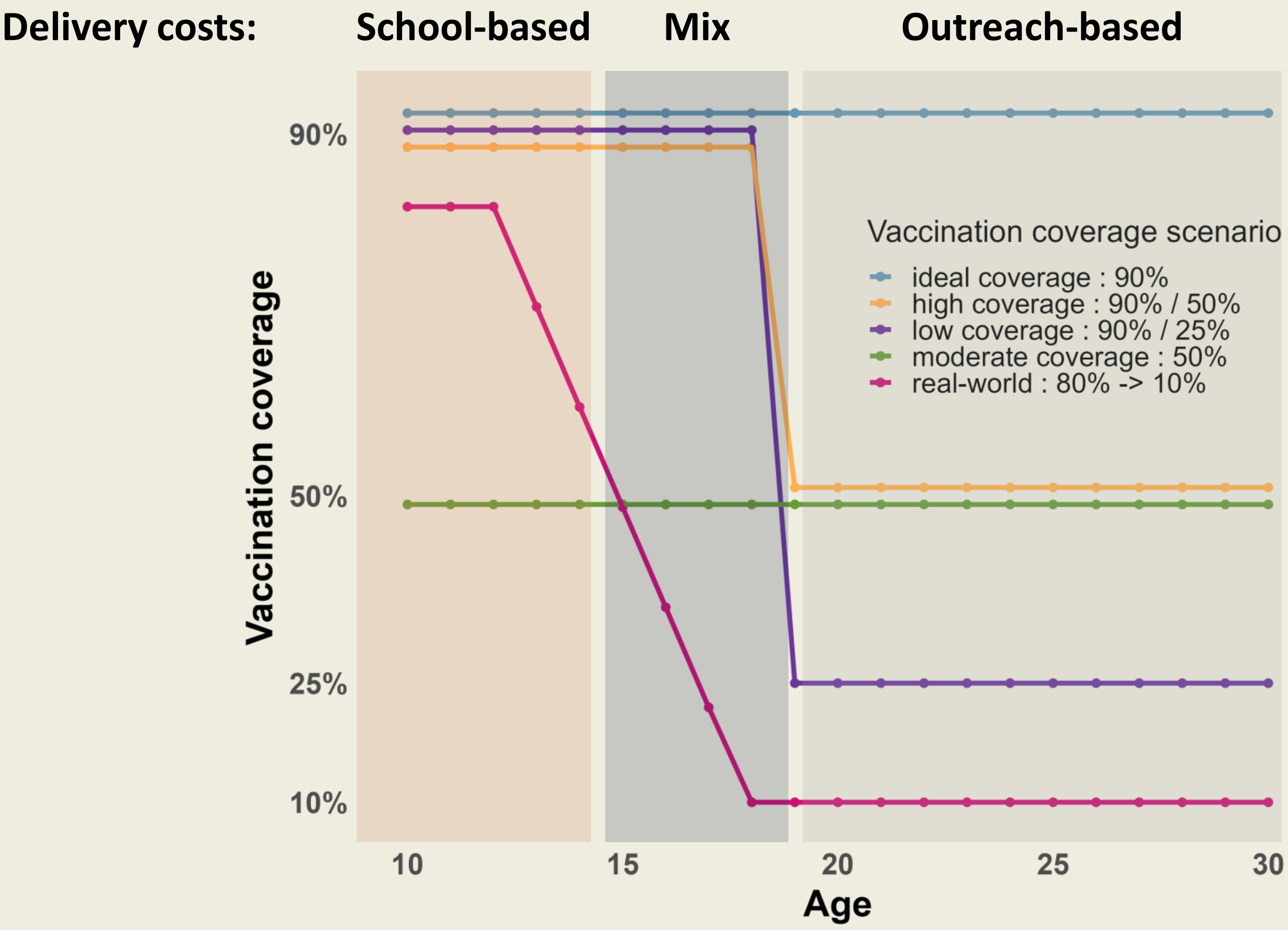
Large drop-off for girls older than 18

Based on Rwanda CU program to 18yo, with minimal coverage for women >18

Methods: Vaccine delivery costs by coverage scenario

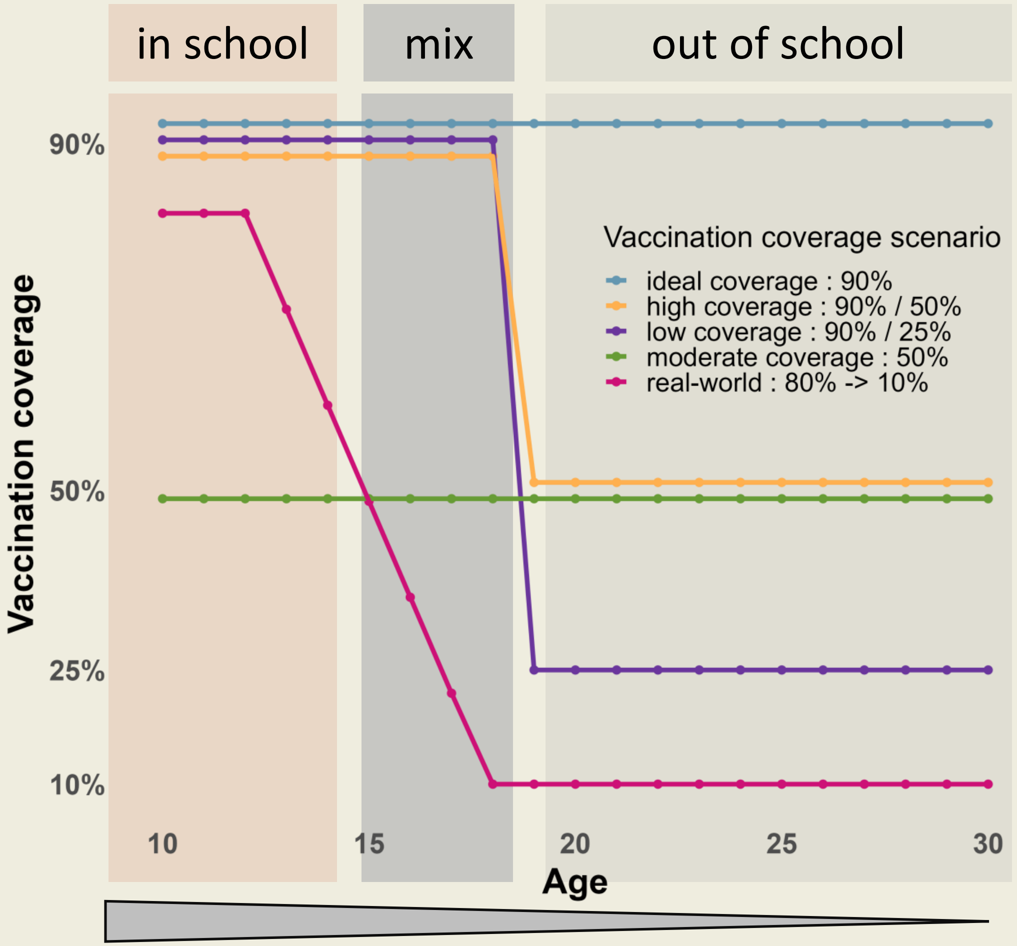
We also applied these delivery strategy-specific costs to each coverage scenario (*results not presented today*)

Between these 5 coverage scenarios and calculating each with costs associated with the 3 main delivery strategies, <u>our analysis encompasses results across a wide range of possible real-world catch-up program designs</u>



Sensitivity analysis

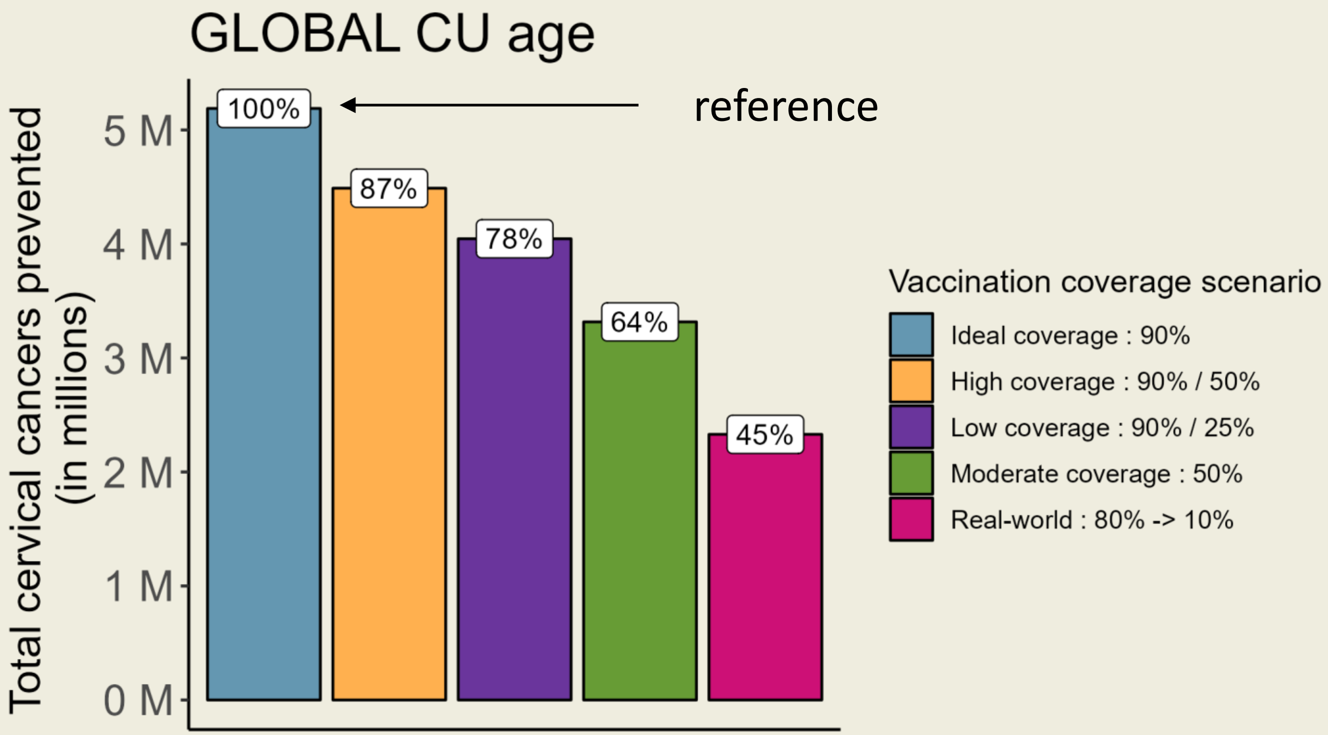
Impact of vaccination coverage scenarios



Decreasing coverage with increasing age. *Out of school individuals are harder to reach by vaccination programs (depending on the local context and the delivery approach).*

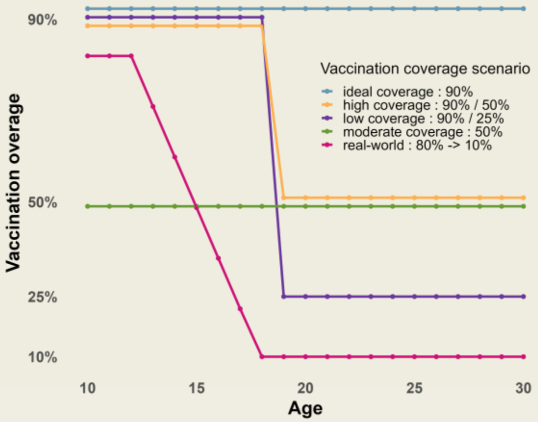
"Ideal" vaccination coverage 90% (*main analysis*)

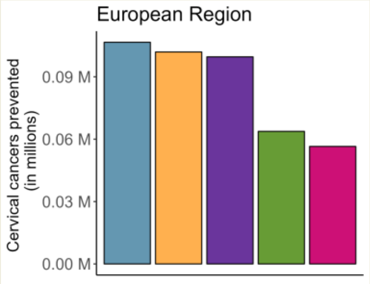
The selected values for LOCAL and GLOBAL "optimum" CU ages were **robust to variations in vaccination coverage**.



Vaccination coverage results

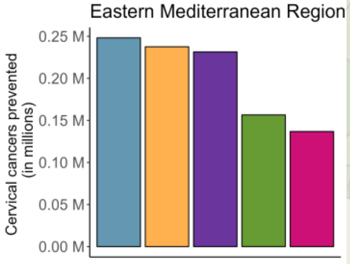
“local optimum” CU age



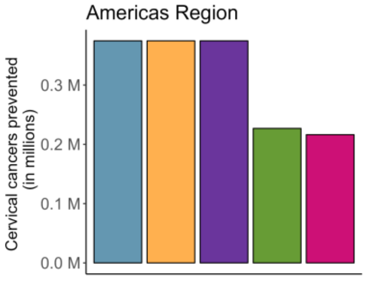


Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
European	106,612

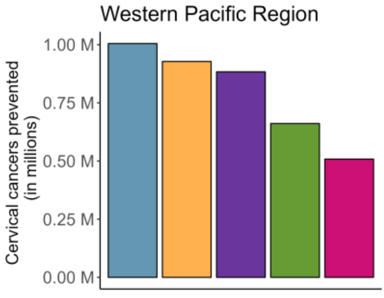
Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
Eastern Mediterranean	248,104



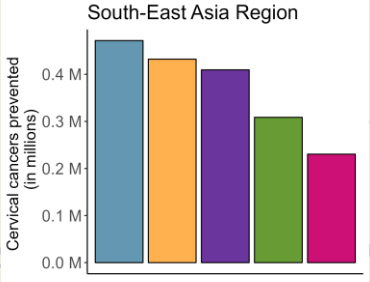
Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
Americas	374,581

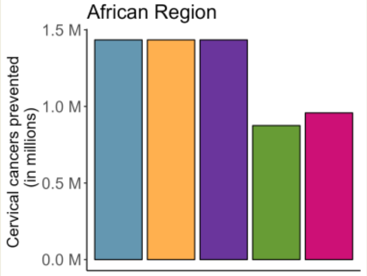


Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
Western Pacific	1,004,844



Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
South-East Asia	471,581





Ideal coverage: 90%	
WHO Region	Total cervical cancer cases prevented
Africa	1,434,353

er cases prevented
to 30 years old on 2025
ccination

10,000 to <15,000
15,000 to <30,000
30,000 to <50,000
50,000 to <100,000
100,000 to <200,000
≥200,000
Not LMIC
Not applicable

**Map under i*

verage scenario : 90%

Key take-aways

Cluster	LOCAL CU age	GLOBAL CU age
I	11-16	11-30
II	11-16	11-30
III	11-18	11-23
IV	11-18	11-25
V	11-20	11-27
VI & China	11-20	11-24
VII	11-19	11-20

- Based on epidemiological dose efficiency, two “optimum” CU age vaccination strategies were identified for LMIC countries:
  - ❑ **<u>GLOBAL CU age</u>: same dose efficiency threshold globally** for all clusters (from 20 for cluster VII to 30 for clusters I & II).
    All clusters will be vaccinated up to an **equally efficient CU age (“globally”).**
  - ❑ **<u>LOCAL CU age</u>:** for each cluster, up to this CU age (from 16 for clusters I & II to 20 for clusters V & VI), **the dose efficiency remains similar compared to the recommended primary vaccination target (9-14).**
    Each cluster will be vaccinated **optimizing dose efficiency per cluster (“locally”).**
- The dose efficiency is robust to changes in vaccination coverage.
  High vaccination coverage is important to achieve to maximize the number of cancer cases prevented.
- Constraints and considerations other than epidemiological indicators will impact CU vaccination decisions.
  What is the health economics perspective on the optimum CU vaccination age?

Methods

Analysis approach and assumptions

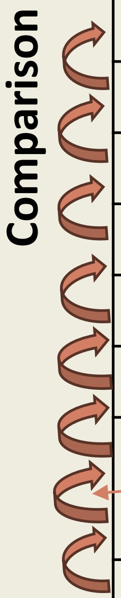
Approach

1. **Cost-effectiveness**: Assess cost effectiveness of CU age vaccination strategies

ICER "optimum" CU age = Highest CU age that is cost-effective, under the 30% GDP per capita threshold.

2. **Affordability**: Budget impact of different "optimum" CU ages

Total financial cost of vaccination program



Maximum CU vaccination age	# additional cohorts targeted
10 (Routine)	NA
11	1
12	2
13	3
14	4
15	5
⋮	⋮
30	20

$$ICER_{i,i+1} = \frac{\Delta Cost}{\Delta DALY} = \frac{(V_{i+1}+T_{i+1}) - (V_i+T_i)}{DALY_{i+1} - DALY_i}$$

V=vaccine cost (procurement + delivery)
T=treatment cost
i = CU age
DALY = Disability-adjusted life years

Assumptions

- Single dose vaccination
- Vaccination coverage 90% ("ideal")*
- 3 % discount rate applied to both costs and health outcomes
- Healthcare payer perspective
- All costs reported in 2023 $USD

*Additional vaccine coverage scenarios were analysed as a sensitivity analysis

LMICs already doing some CU

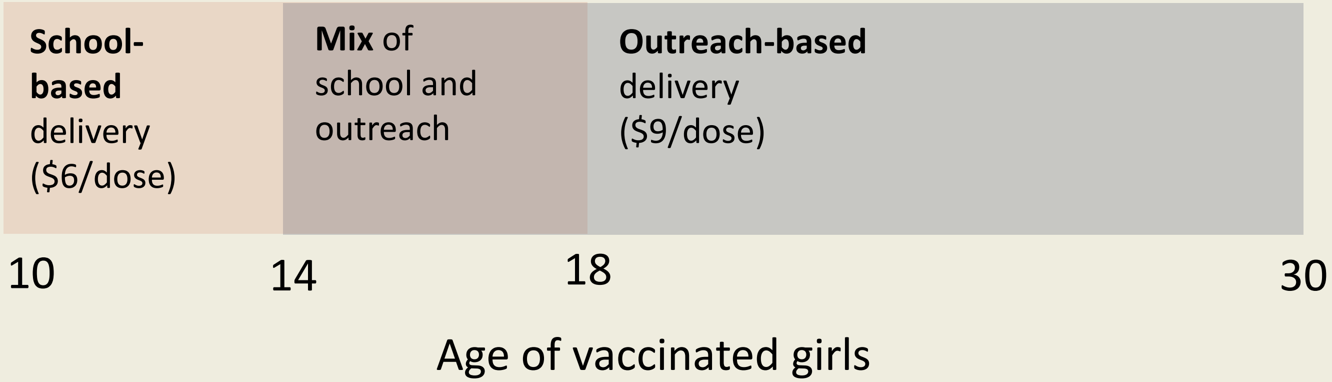
Country	Year CU programme	Ages targeted	Gender	Doses	Main delivery approach	Notes
Belize	2022	10-14	Both	2	School	
Botswana	2019-2020	10-13	Girls only	2	School + facility	CU and primary target ages are the same! In 2020 no second doses because of Covid
Cabo Verde	2022	11-14	Girls only	1	Facility	
Cote d'Ivoire	2021	10-14	Girls only	2		
Dominican Republic	2020	10-14	Girls only	2	School	
Ecuador	2015-2016	9-11	Girls only	2	School + facility	CU and primary target ages are the same!
Georgia	2022	13-18	Girls only	2	Facility	
Grenada	2019	11-14	Both	2	School	
Honduras	2020	12-12	Girls only	2	Facility	
Kenya	2021	11-14	Girls only	2	Facility	
Mauritius	2017-2018	11-11	Girls only	3	School	
Moldova	2019	11-14	Girls only	2	Facility	
Montenegro	2023	10-14	Girls only	1		
North Macedonia	2021	14-14	Girls only	2	School	
Rwanda	2014	13-14	Girls only	3	School	
Tonga	2022	11-17	Girls only	1		
Uzbekistan	2021	12-14	Girls only	2	School	
Zimbabwe	2018	11-14	Girls only	2	School + facility	

Methods

Cost estimates

- ✓ **Treatment costs**
- ✓ **Vaccine delivery costs**
- ✓ **Vaccine purchase costs**

Vaccine delivery costs details (in 2023 USD)



School-based delivery ($6/dose)

Mix of school and outreach

Outreach-based delivery ($9/dose)

Table: Treatment, vaccine, and vaccine delivery cost by country (in 2023 USD)

Country	GDP per capita	Treatment Cost	Vaccine cost per dose	Vaccine delivery cost		
				Mode of delivery (age in years)		
				School-based (10-14)	Mixed (14-18)	Outreach (19-30)
Nigeria	1,596.6	1668	4.50	6.21	7.27	9.31
Kenya	1,952.3	883	4.50		6.56	
India	2,480.8	3882	4.50		7.01	
Eswatini	3,610.6	40717	4.50		6.95	
Indonesia	4,876.3	2766	11.53		6.80	
Colombia	6,947.4	3063	10.65		6.69	