The impact of current and future vaccines on AMR

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Vaccines are an integral part of the AMR strategy

World Health Organization

People-centred approach to addressing antimicrobial resistance in human health:

WHO core package of interventions to support national action plans

Reduced and slower development of AMR
Reduced mortality and morbidity due to AMR

Pillar 1: Prevention

6. Universal access to WASH and waste management to mitigate AMR
7. Implementation of IPC components to mitigate AMR
8. Access to vaccines and expanded immunization to manage AMR

Pillar 2: Access to essential health services

9. AMR diagnosis and management health services are affordable for all
10. Uninterrupted supply of quality-assured, essential antimicrobials and health products for AMR

Pillar 3: Timely, accurate diagnosis

11. Good-quality laboratory system and diagnostic stewardship to ensure clinical bacteriology and mycology testing

Pillar 4: Appropriate, quality-assured treatment

12. Up-to-date evidence-based treatment guidelines and programmes for antimicrobial stewardship
13. Regulation to restrict sales of non-prescription antimicrobials

Foundational step: Strategic information through surveillance and research

3. National AMR surveillance network to generate good-quality data for patient care and action on AMR
4. Surveillance of antimicrobial consumption and use to guide patient care and action on AMR
5. AMR research and innovation including behavioural and implementation science

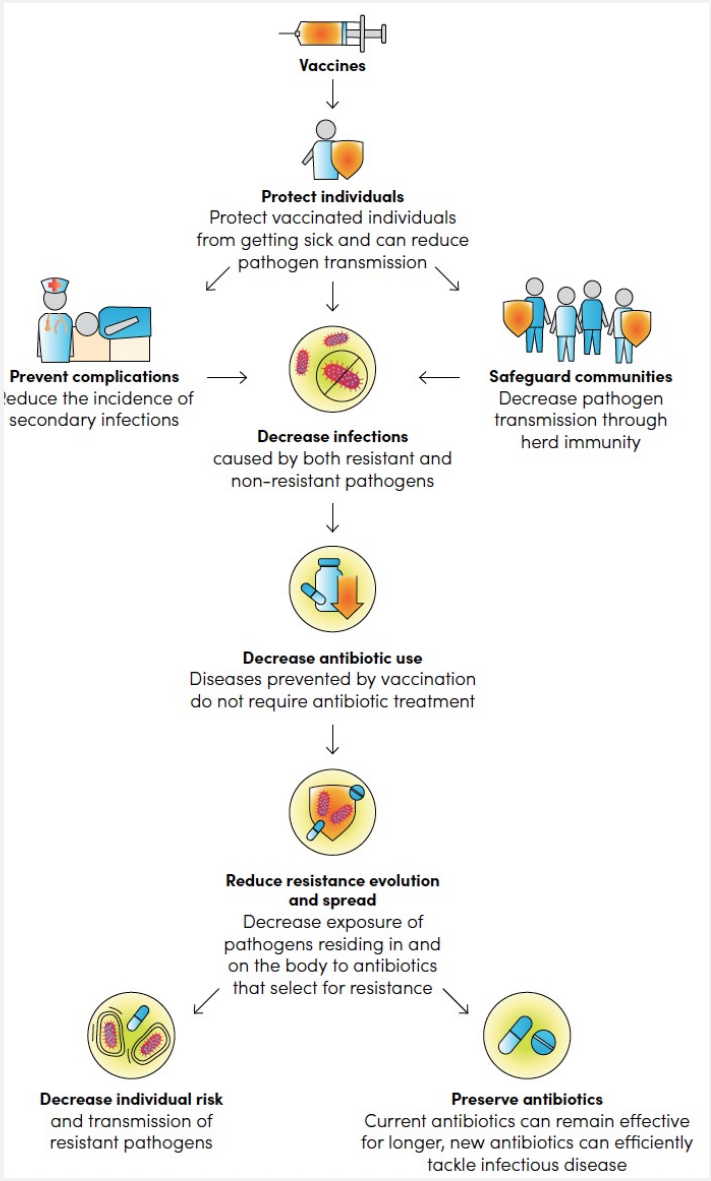
Foundational step: Effective governance, awareness and education

1. AMR advocacy, governance and accountability in the human health sector, in collaboration with other sectors
2. AMR awareness-raising, education and behaviour change of health workers and communities

https://www.who.int/publications/i/item/9789240082496

How do vaccines reduce AMR?

- Vaccines prevent infections with drug-susceptible and resistant pathogens
- Vaccines prevent individuals and communities from getting sick
- Decrease antibiotic use (causal chain)
- Suppress resistance evolution and decrease transmission of resistant pathogens (causal chain)



WHEN to evaluate the role of vaccines in reducing AMR?

OPPORTUNITIES TO CONSIDER VACCINE IMPACT ON AMR

Early Development → Advanced Clinical Development → Regulatory Approval → Policy Decision → Gavi Vaccine Investment → Vaccine Assessment in Countries → Post-licensure Evaluation

EXAMPLES WHEN THE ROLE OF VACCINES ON AMR WAS CONSIDERED

Early Development	Advanced Clinical Development	Regulatory Approval	Policy Decision	Gavi Vaccine Investment	Vaccine Assessment in Countries	Post-licensure Evaluation
N. Gonorrhea *K. pneumoniae*	RSV Influenza *S. pneumoniae*	Multiple	*S. typhi*	*Vaccines in VIS 2018 and 2024*	*S. pneumoniae*	*S. typhi* *S. pneumoniae*

Vaccines in National Action Plans Against AMR

Desk review of National Action Plans

MAJOR GAP: TO WHAT EXTENT CAN VACCINES REDUCE AMR?

CONTEXT

National Action Plans on AMR are countries' strategies to reduce AMR

METHOD

Desk review of 77 NAPs to measure how many NAPs integrate vaccines as interventions to reduce AMR

RESULT

67 NAPs (87%) mention vaccines, but only 33 (43%) have developed indicators to capture the role of vaccines against AMR;
10 NAPS do not mention vaccines

INTERPRETATION

Some understanding of the role of vaccines in reducing AMR- but it doesn't translate to action and integration with other AMR interventions

https://globalizationandhealth.biomedcentral.com/articles/10.1186/s12992-022-00878-6

WHO report: Estimating the impact of vaccines in reducing antimicrobial resistance and use

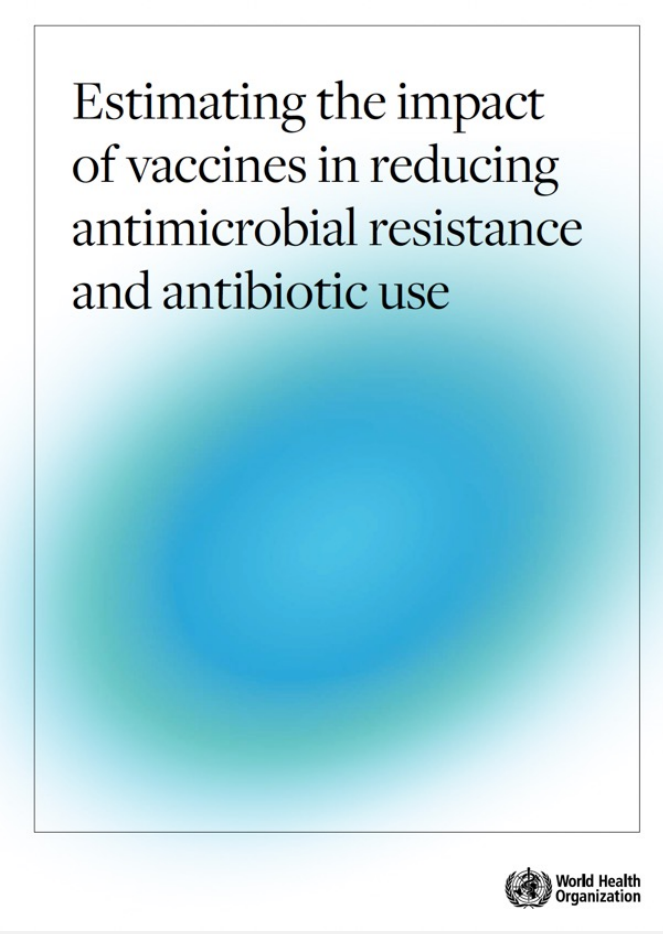
The role of vaccines in reducing AMR has been underrecognised, yet they play a vital role in protecting against pathogens and preventing infection-related complications

Vaccines in early and late-stage clinical development have the potential to annually avert up to:

- **515,000 deaths**
- **28 million DALYs**
- **US $30 billion in hospital costs**
- **US $20 billion in productivity losses**

Which are all associated with AMR

These vaccines could also help to reduce antibiotic use by **2.5 billion doses**



AMR, antimicrobial resistance; DALY, disability-adjusted life years

Methodologies to estimate the impact of vaccines on AMR

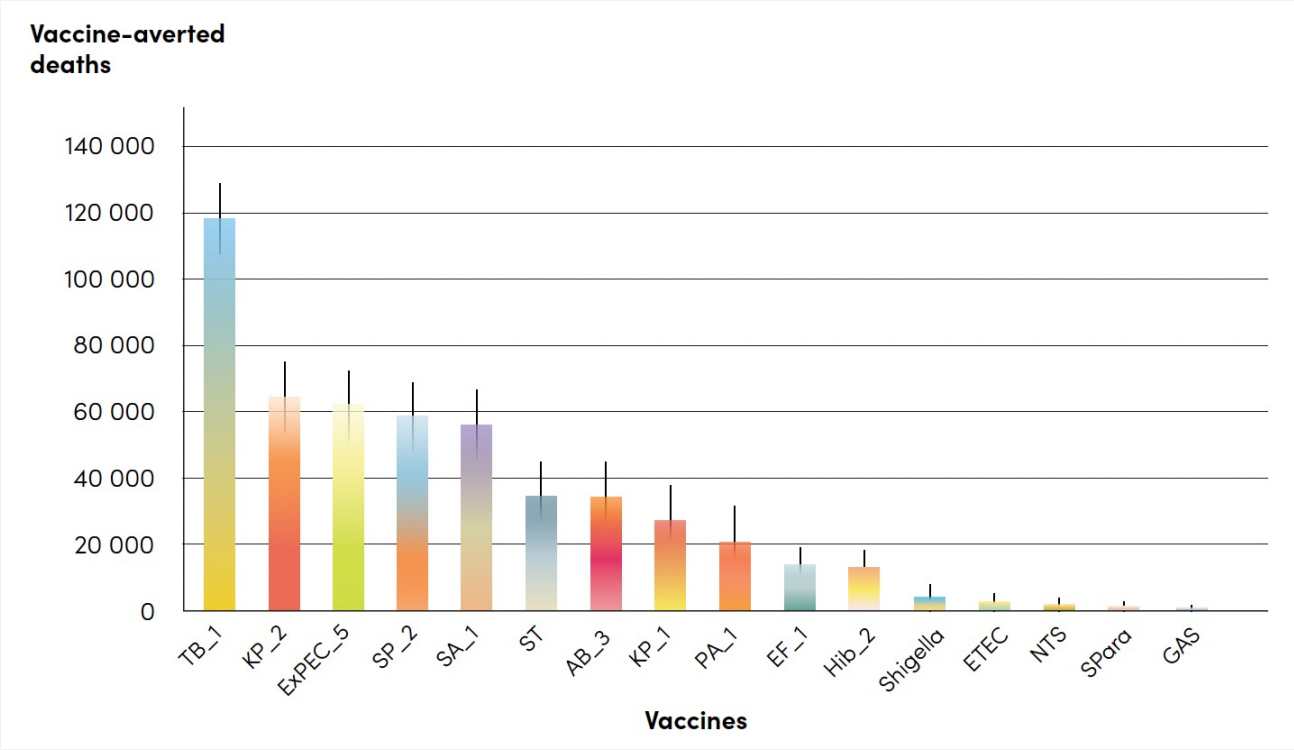
1.  Identification of 24 pathogens and 44 vaccines and their attributes.
2.  GBD data on AMR 2019 used as backbone for analyses.
3.  A static model to evaluate Vaccine averted AMR health burden
4.  Additional data on antibiotic use, consumption, syndrome and pathogen attribution.
5.  Triangulation of data on antibiotic use and consumption with vaccine averted health burden
6.  Data on length of hospital stay, cost of treatment, bed-day cost, employment and wage estimates
7.  Data conversion, meta analysis and development of AMR unit cost repository
8.  Triangulation of data on hospital costs and productivity losses with vaccine averted health burden

The potential impact of vaccines on averting deaths associated with AMR

Vaccines have the potential to **avert** up to

515 000 deaths

associated with AMR annually– 32% in AFRO

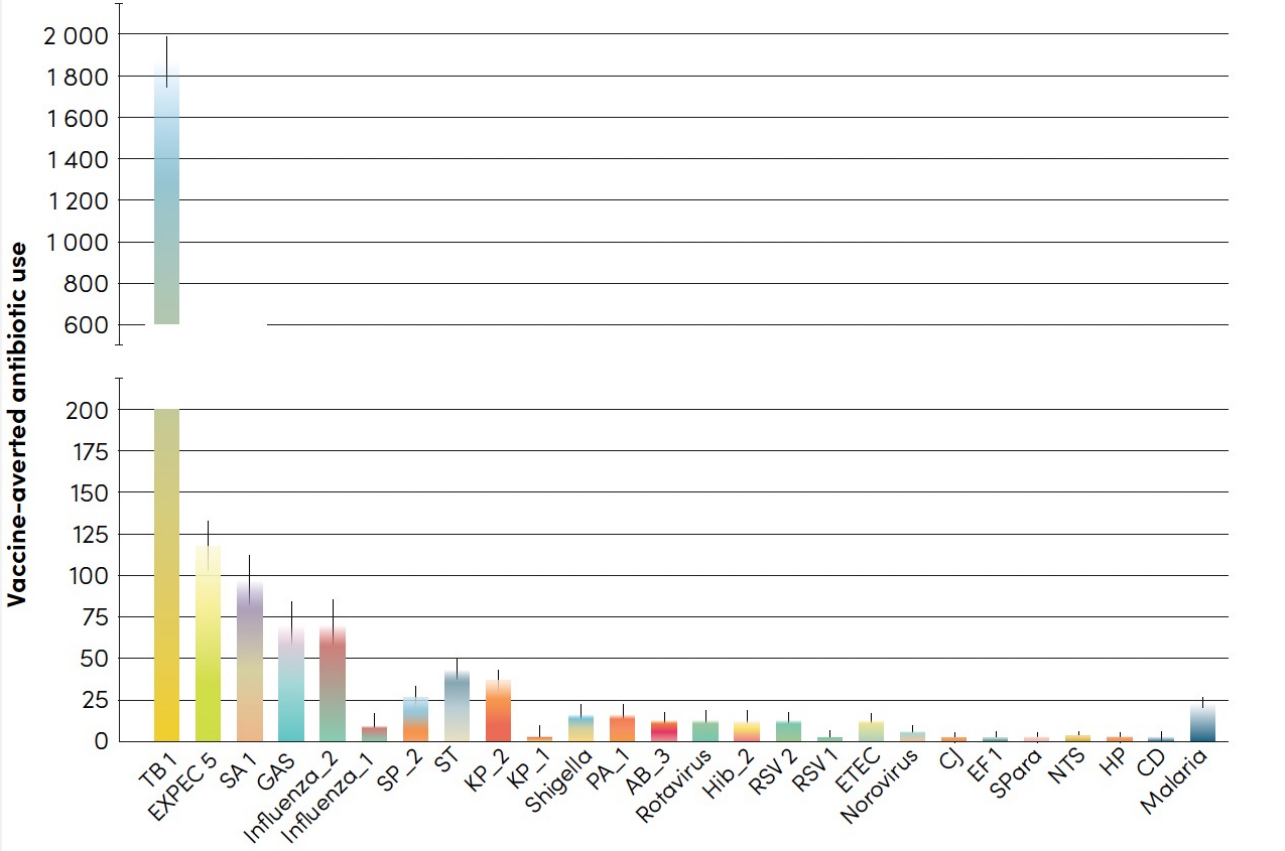


The potential impact of vaccines on averting antibiotic use

Vaccines have the potential to **avert** up to

2.5 billion

of defined daily **doses of antibotics** annually – 22% of the evaluated burden – 40% in SEARO

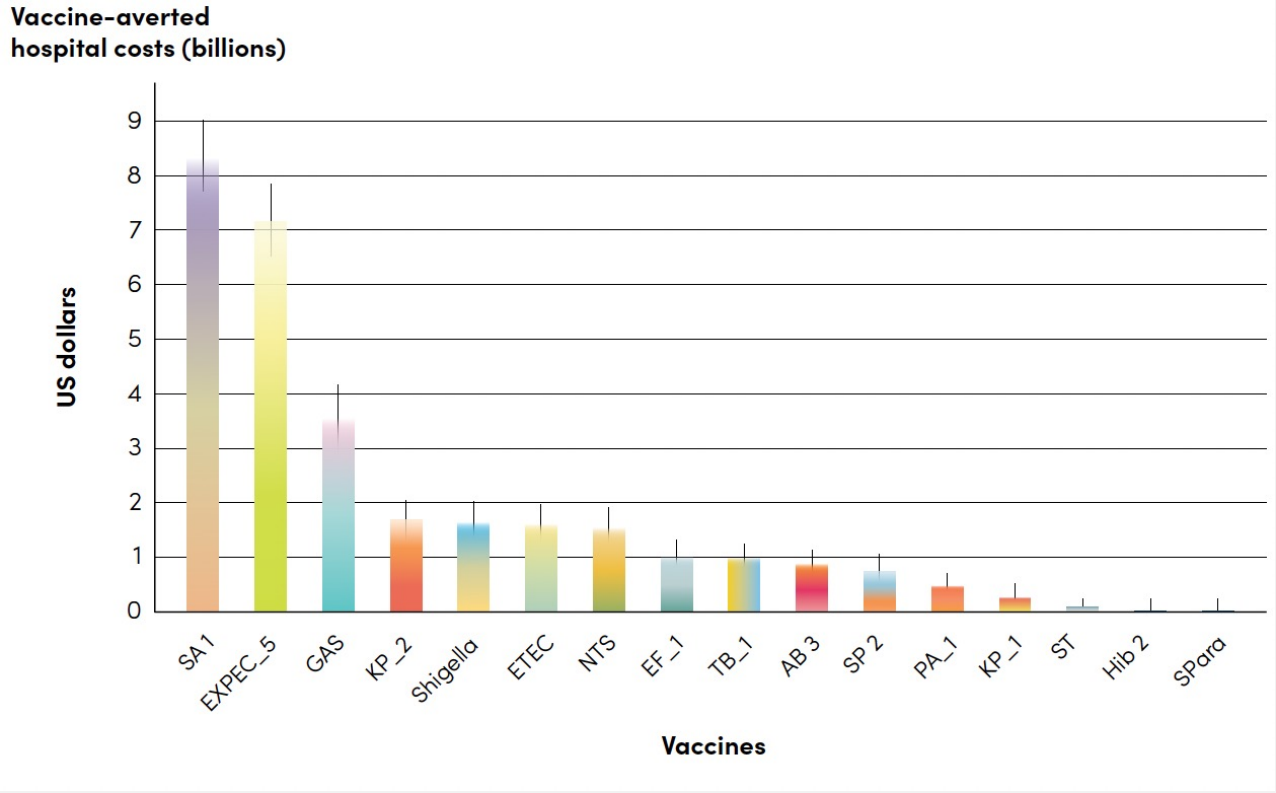


The potential impact of vaccines on averting hospital costs associated with AMR

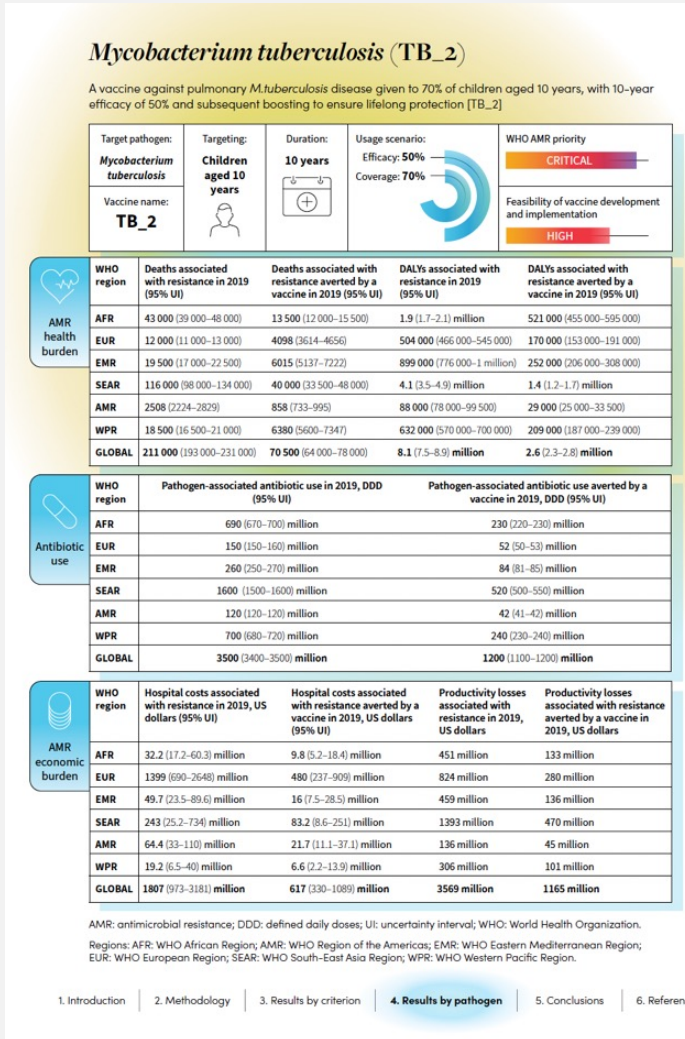
Vaccines have the potential to **avert** up to

US $ 30 billion

in hospital costs associated with treating resistant infections annually – 30% in AMRO



Additional Resources



Mycobacterium tuberculosis (TB_2)

A vaccine against pulmonary *M.tuberculosis* disease given to 70% of children aged 10 years, with 10-year efficacy of 50% and subsequent boosting to ensure lifelong protection [TB_2]

Target pathogen:	Targeting:	Duration:	Usage scenario:	WHO AMR priority
Mycobacterium tuberculosis	Children aged 10 years	10 years	Efficacy: 50% Coverage: 70%	CRITICAL
Vaccine name: TB_2				Feasibility of vaccine development and implementation: HIGH

AMR health burden

WHO region	Deaths associated with resistance in 2019 (95% UI)	Deaths associated with resistance averted by a vaccine in 2019 (95% UI)	DALYs associated with resistance in 2019 (95% UI)	DALYs associated with resistance averted by a vaccine in 2019 (95% UI)
AFR	43 000 (39 000–48 000)	13 500 (12 000–15 500)	1.9 (1.7–2.1) million	521 000 (455 000–595 000)
EUR	12 000 (11 000–13 000)	4098 (3614–4656)	504 000 (466 000–545 000)	170 000 (153 000–191 000)
EMR	19 500 (17 000–22 500)	6015 (5137–7222)	899 000 (776 000–1 million)	252 000 (206 000–308 000)
SEAR	116 000 (98 000–134 000)	40 000 (33 500–48 000)	4.1 (3.5–4.9) million	1.4 (1.2–1.7) million
AMR	2508 (2224–2829)	858 (733–995)	88 000 (78 000–99 500)	29 000 (25 000–33 500)
WPR	18 500 (16 500–21 000)	6380 (5600–7347)	632 000 (570 000–700 000)	209 000 (187 000–239 000)
GLOBAL	211 000 (193 000–231 000)	70 500 (64 000–78 000)	8.1 (7.5–8.9) million	2.6 (2.3–2.8) million

Antibiotic use

WHO region	Pathogen-associated antibiotic use in 2019, DDD (95% UI)	Pathogen-associated antibiotic use averted by a vaccine in 2019, DDD (95% UI)
AFR	690 (670–700) million	230 (220–230) million
EUR	150 (150–160) million	52 (50–53) million
EMR	260 (250–270) million	84 (81–85) million
SEAR	1600 (1500–1600) million	520 (500–550) million
AMR	120 (120–120) million	42 (41–42) million
WPR	700 (680–720) million	240 (230–240) million
GLOBAL	3500 (3400–3500) million	1200 (1100–1200) million

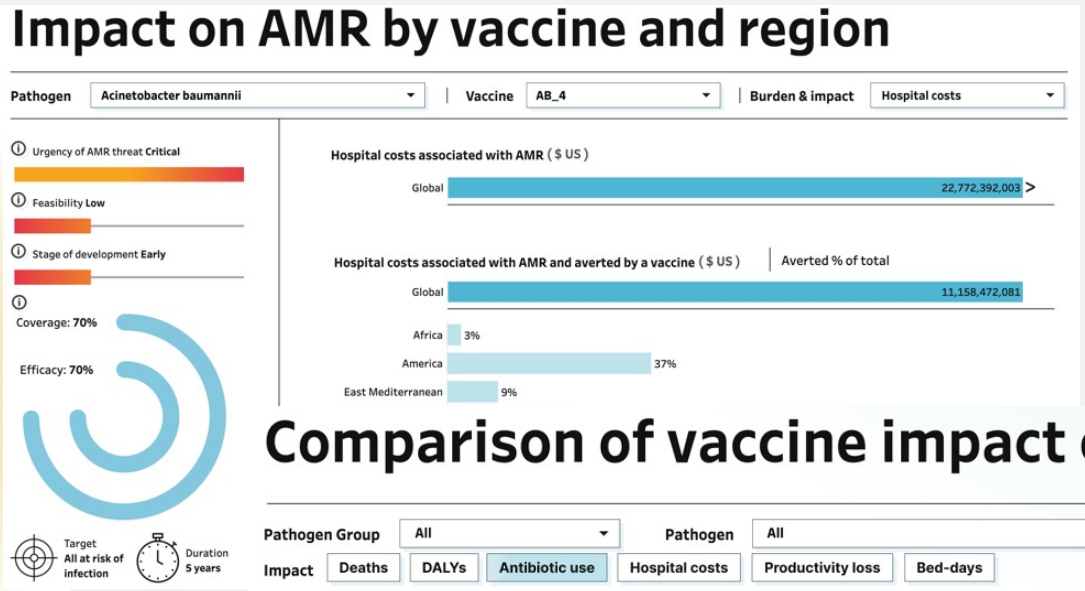
AMR economic burden

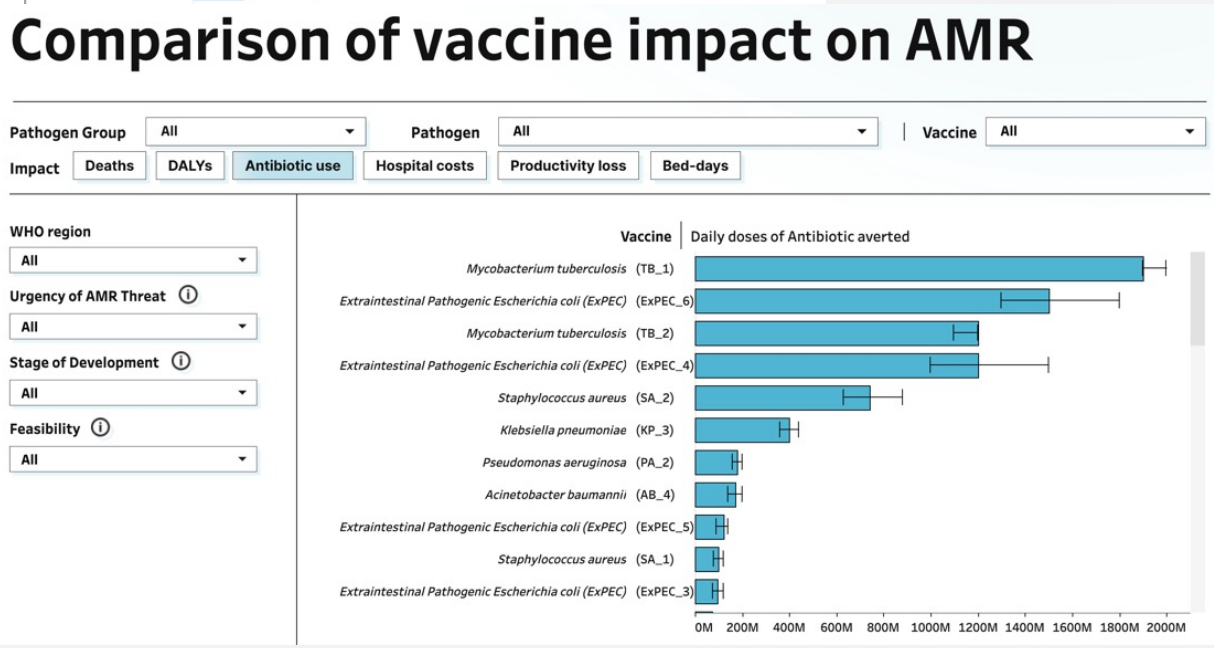
WHO region	Hospital costs associated with resistance in 2019, US dollars (95% UI)	Hospital costs associated with resistance averted by a vaccine in 2019, US dollars (95% UI)	Productivity losses associated with resistance in 2019, US dollars	Productivity losses associated with resistance averted by a vaccine in 2019, US dollars
AFR	32.2 (17.2–60.3) million	9.8 (5.2–18.4) million	451 million	133 million
EUR	1399 (690–2648) million	480 (237–909) million	824 million	280 million
EMR	49.7 (23.5–89.6) million	16 (7.5–28.5) million	459 million	136 million
SEAR	243 (25.2–734) million	83.2 (8.6–251) million	1393 million	470 million
AMR	64.4 (33–110) million	21.7 (11.1–37.1) million	136 million	45 million
WPR	19.2 (6.5–40) million	6.6 (2.2–13.9) million	306 million	101 million
GLOBAL	1807 (973–3181) million	617 (330–1089) million	3569 million	1165 million

AMR: antimicrobial resistance; DDD: defined daily doses; UI: uncertainty interval; WHO: World Health Organization.

Regions: AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; EUR: WHO European Region; SEAR: WHO South-East Asia Region; WPR: WHO Western Pacific Region.

1. Introduction | 2. Methodology | 3. Results by criterion | **4. Results by pathogen** | 5. Conclusions | 6. References





Limitations

Methodology Limitations:

- Findings based on modeling analyses, not direct observations.
- Reliance on GRAM Project estimates, which have limitations, especially in LMICs.
- GRAM lacks data on key areas (e.g., TB associated with HIV, full morbidity outcomes).

Data Gaps in AMR Impact:

- DALYs underreported for conditions like enteric pathogens, malaria-linked infections, and GAS.
- Full morbidity outcomes could significantly increase vaccine impact on AMR estimates.

Static Model Approach:

- Focuses on direct vaccine effects; indirect benefits (e.g., herd immunity) excluded.
- Standardized approach limits pathogen-specific dynamics analysis.

Coverage Assumptions:

- For vaccines in early development model assumes moderate/high coverage --Likely overestimating

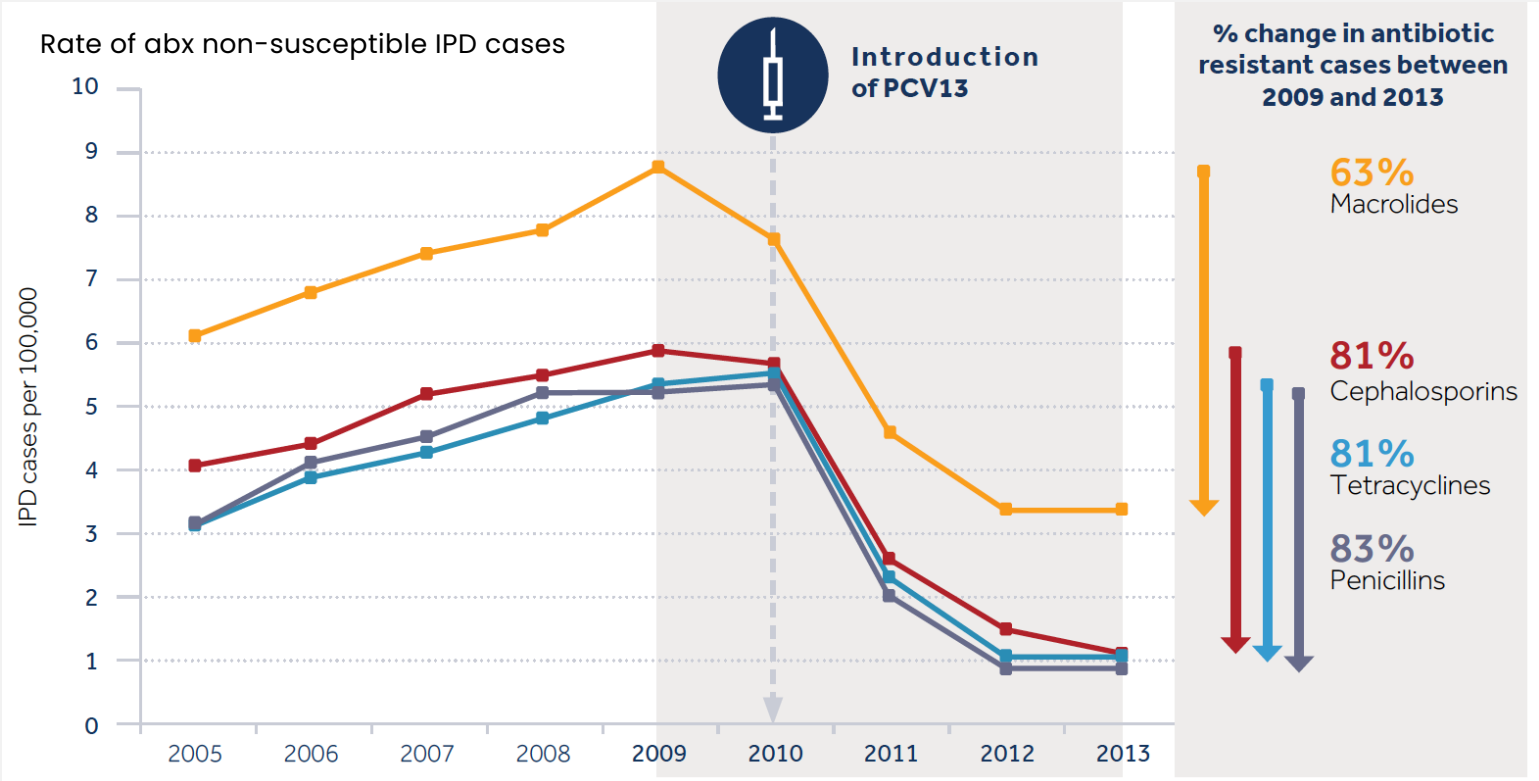
Unexplored Factors:

- Excludes analysis of vaccine-averted reduction in antibiotic use on future AMR prevalence.
- Omits vaccine effects on non-target pathogens (e.g., influenza vaccine reducing S. pneumoniae infections).

Scope of Analysis:

- Focused on routine vaccination impact; missed potential impact of vaccination campaigns.
- Evaluated vaccine effects on antibiotic use but not on antimicrobials or secondary infections.
- Did not address vaccines' impact on drug-susceptible pathogens, focusing on AMR-specific effects.

Impact of pneumococcal vaccine on *prevalence* of non-susceptible invasive pneumococcal disease, USA



IPD: invasive pneumococcal disease; PCV: pneumococcal conjugate vaccine.

[a] Jansen KU, Knirsch C, Anderson AS. The role of vaccines in preventing bacterial antimicrobial resistance. Nat Med. 2018;24(1):10-9.

[b] Tomczyk S, Lynfield R, Schaffner W, Reingold A, Miller L, Petit S, et al. Prevention of Antibiotic-Nonsusceptible Invasive Pneumococcal Disease with the 13-Valent Pneumococcal Conjugate Vaccine. Clin Infect Dis. 2016; 62(9).

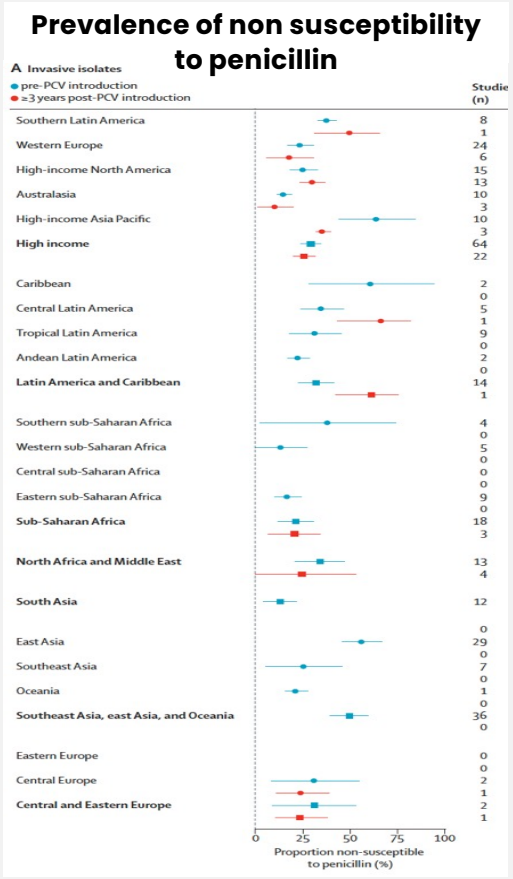
Impact of PCV on *S. pneumo non-susceptibility*

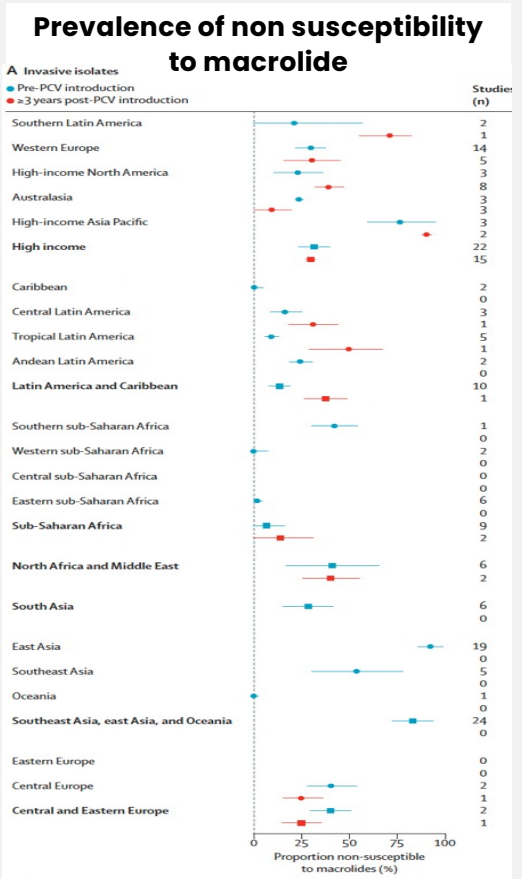
559 global studies on over 310,000 pediatric isolates

11.5% decrease in isolates that are non-susceptible to penicillin

7.5-9.7% decrease of isolates non-susceptible to other antibiotics

Over 10-year period after PCV introduction





https://pubmed.ncbi.nlm.nih.gov/34485957/

PCV and rotavirus vaccines reduce *antibiotic use* in children in LMICs

Analysis of Demographic Health Surveys (DHS) and Multiple Indicator Cluster Surveys (MICS)

VACCINE IMPACT WITH RECENT COVERAGE

PCV prevents 23.8 million antibiotic treated episodes annually

Rotavirus vaccine prevents 13.7 million antibiotic treated episodes annually

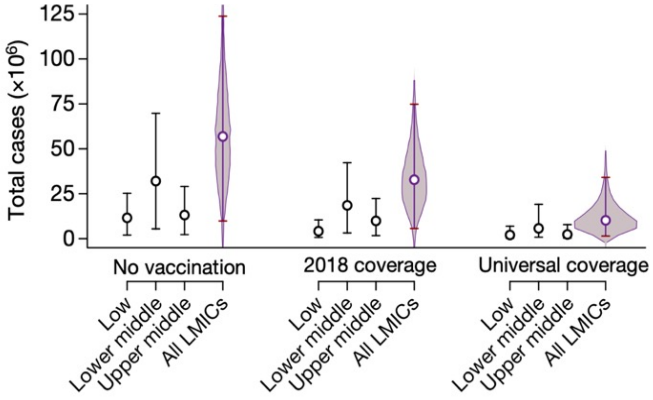
VACCINE IMPACT WITH 90% COVERAGE

PCV could avert additional 21.7 million antibiotic treated episodes

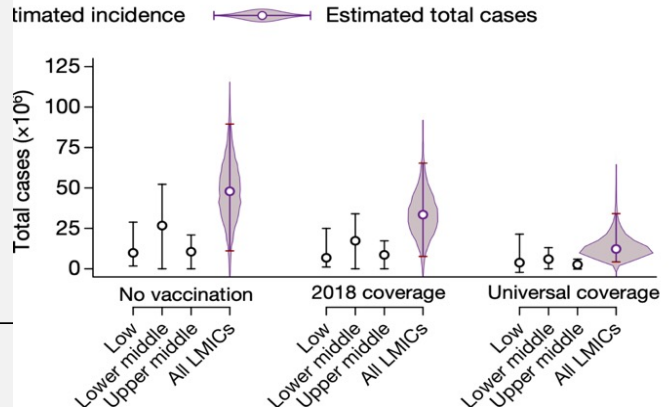
Rotavirus vaccines could avert additional 18.3 million antibiotic treated episodes

https://www.nature.com/articles/s41586-020-2238-4

Total PCV10/13 vaccine-preventable antibiotic consumption and incidence, children 24-59 months



Total rotavirus vaccine-preventable antibiotic consumption and incidence, children 0-23 months



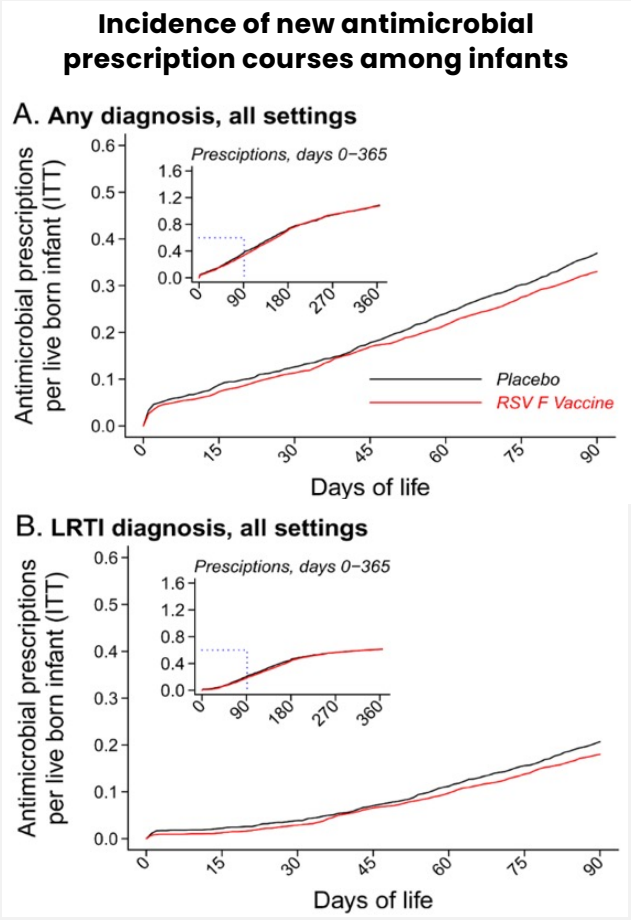
Maternal RSV vaccine impact on *antimicrobial prescribing*

Novavax vaccine trial conducted in 11 countries

Reduced antimicrobial prescriptions for ‘any diagnosis’ in infants born to mothers who received the RSV vaccine
Vaccine efficacy = 12.9%

Reduced antimicrobial prescriptions for ‘acute lower respiratory tract infections’
Vaccine efficacy= 16.9%

Over the first three months of infant’s life



https://www.pnas.org/doi/10.1073/pnas.2112410119

Conclusions

Vaccines have the potential to annually avert up to **515 000 deaths** and **US$ 30 billion in hospital costs** associated with AMR, and **2.5 billion antibiotic doses**.

The **impact of vaccines** in reducing AMR **needs to be recognized** by stakeholders in AMR and immunization. Global, regional and national AMR and immunization strategies and implementation frameworks **should include vaccines as interventions to reduce AMR**.

The **introduction of existing vaccines should be accelerated** and their **coverage increased**. All existing paediatric vaccines should reach the immunization targets of IA2030, and the use of vaccines in older age groups should be considered.

To prepare for the introduction of newly developed vaccines, the **impact of vaccines on AMR should be systematically evaluated** and embedded into existing decision frameworks.

To enable vaccine development, delivery and implementation to combat AMR, **include AMR endpoints in clinical trials**, develop **PPCs** for impactful vaccines, create **research roadmaps** for challenging vaccines.

Thank you