The role of vaccines in reducing AMR

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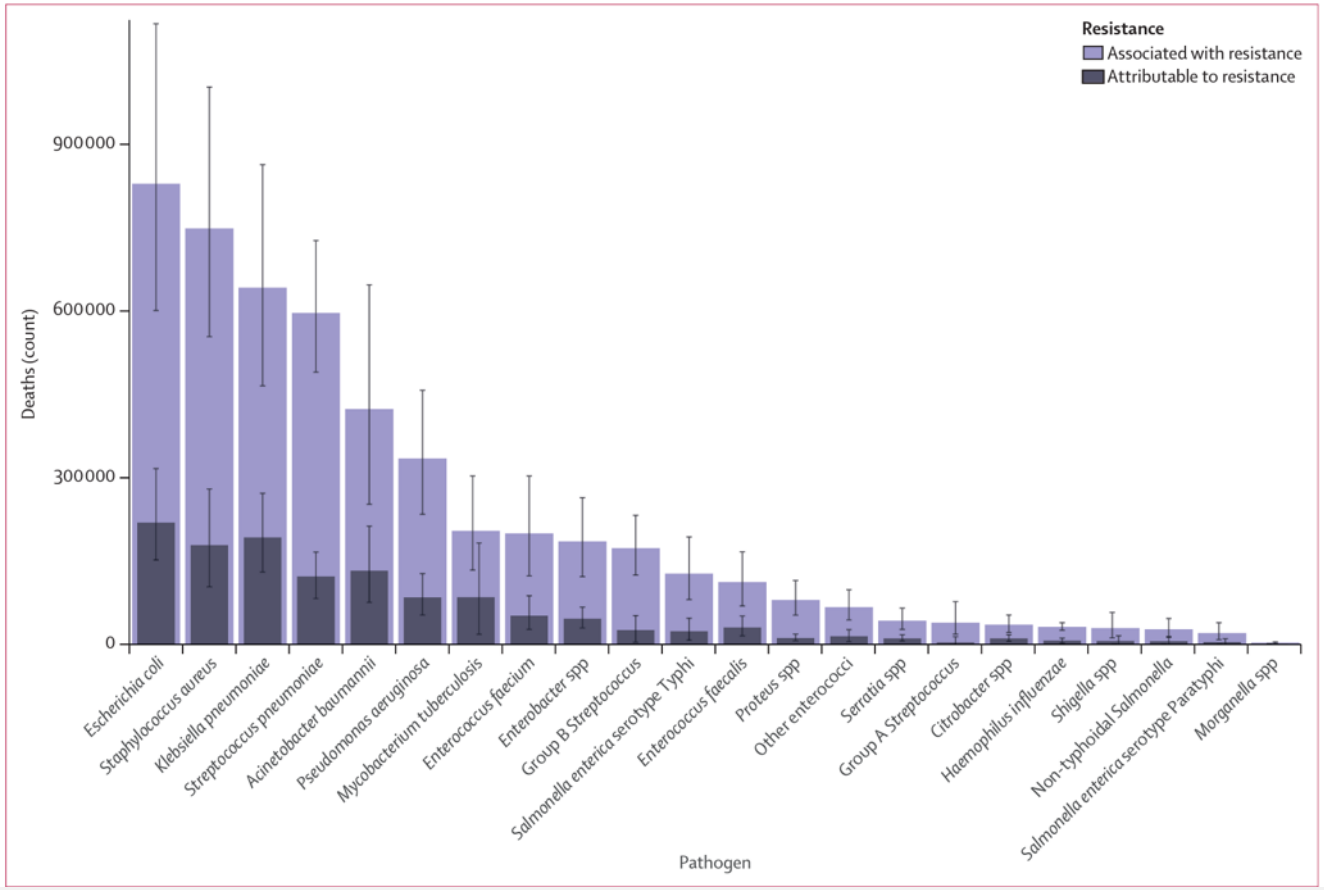
The burden of AMR

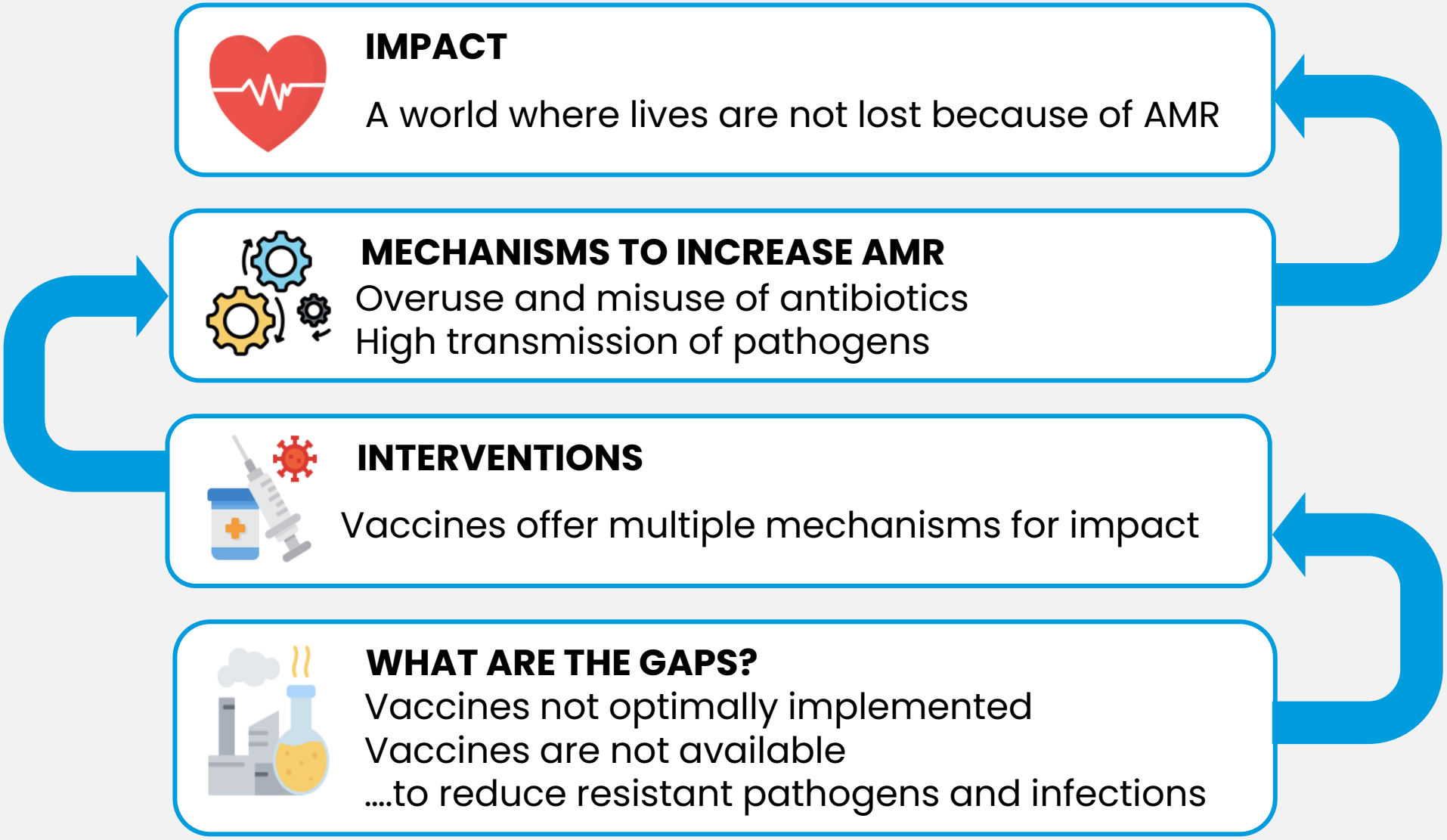
- AMR is a global health threat with **1.27 million deaths attributable** to bacterial AMR and **4.95 million deaths associated** with bacterial AMR worldwide in 2019;
- **Attributable**: deaths are the result of a progression from a drug sensitive to a drug resistant infection;
- **Associated**: deaths are the result of a progression from no infection to a drug resistant infection;
- The **six leading pathogens** for deaths associated with resistance were responsible for **929,000 (660,000–1,270,000) deaths attributable to AMR and 3.57 million (2.62–4.78) deaths associated with AMR** in 2019.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

The number of deaths associated and attributable to resistance by pathogen, in 2019



The 'Vaccines and AMR' Paradigm



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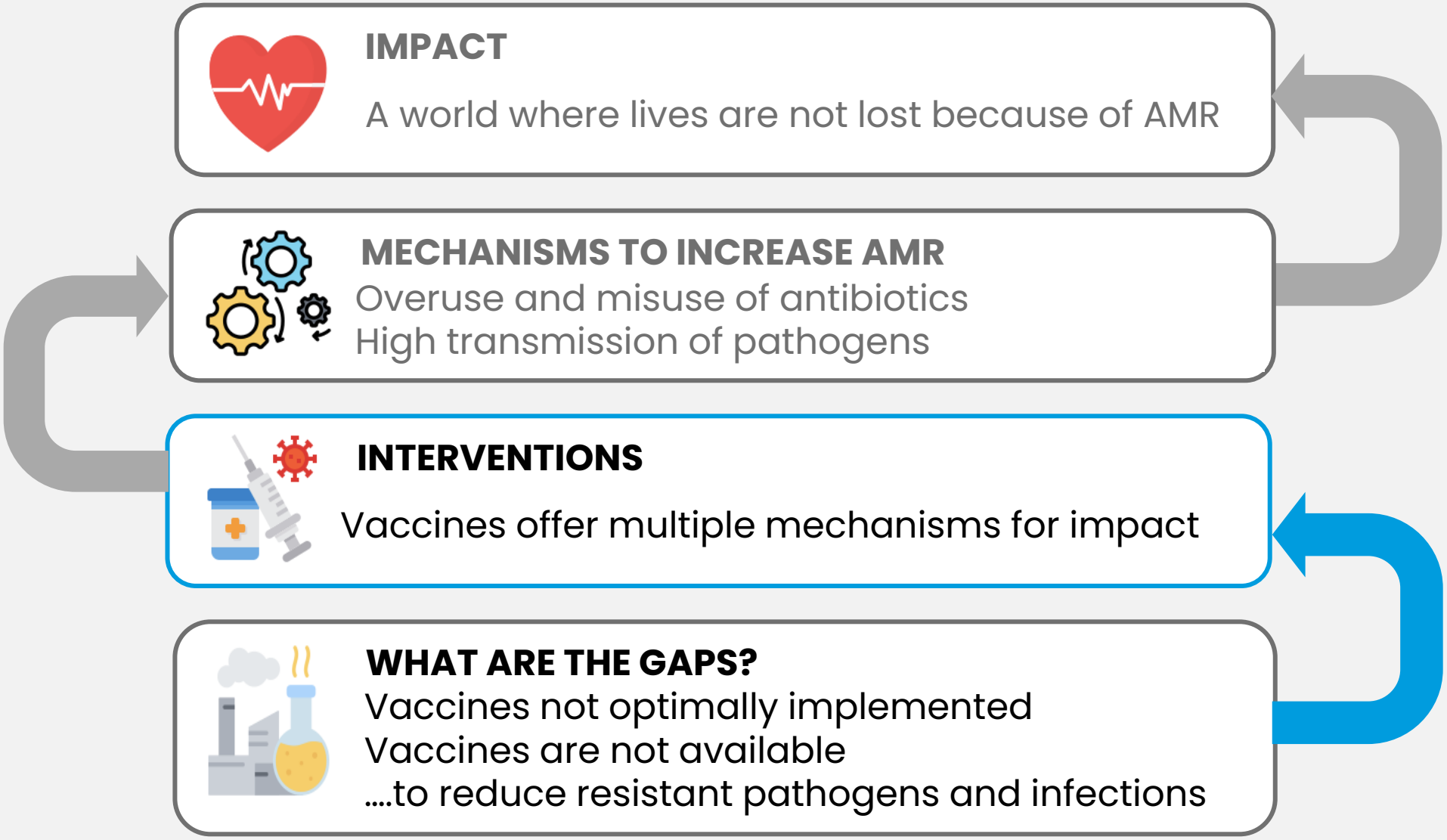
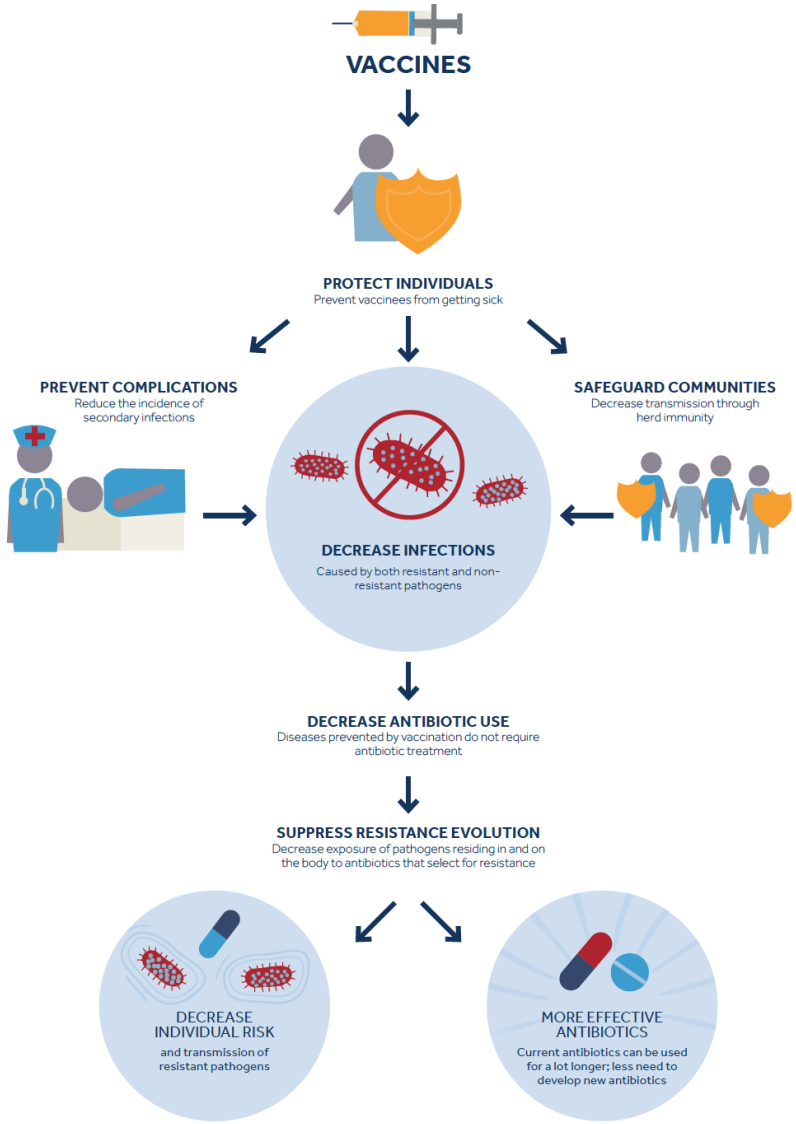


How do vaccines reduce AMR?

- 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)

Leveraging Vaccines to Reudce Antibiotic Use and Prevent AMR: An Action Framework



https://www.who.int/publications/m/item/leveraging-vaccines-to-reduce-antibiotic-use-and-prevent-antimicrobial-resistance

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
N. Gonorrhea *K. pneumoniae*	RSV Influenza *S. pneumoniae*	Multiple	*S. typhi*	*Vaccines in VIS 2018 and 2024*	*S. pneumoniae*	*S. typhi* *S. pneumoniae*

EXAMPLES WHEN THE ROLE OF VACCINES ON AMR WAS CONSIDERED

HOW to evaluate the role of vaccines in reducing AMR?
Multiple mechanisms for impact

1.  Vaccine averted AMR *health burden*

2.  Changes in AMR *prevalence* after vaccine introduction

3.  Vaccine averted *antimicrobial use*

4.  …resulting in AMR economic burden
…other mechanisms

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Stories from the field: the impact of vaccines on AMR *health burden*, in Zimbabwe

CHALLENGE
Outbreaks of highly resistant typhoid and cholera between 2017-2019 in Harare, Zimbabwe

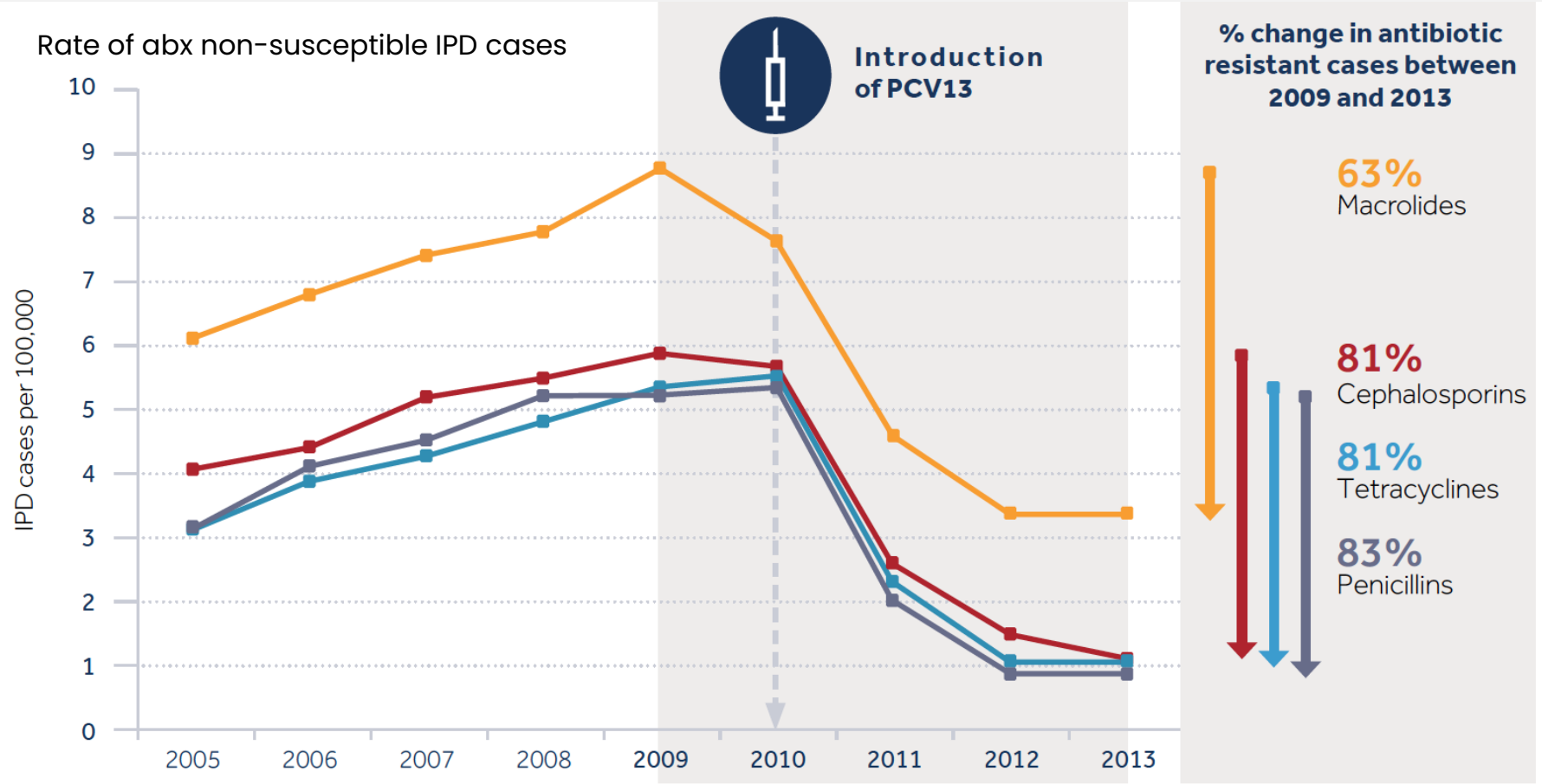
ACTION
Administration of 318,000 doses of typhoid and 1.5 million doses of cholera vaccines through campaigns

IMPACT
Successful control of outbreaks
Introduction of TCV in routine immunization

FUTURE DIRECTIONS
Strengthening routine immunization and WASH interventions to prevent future outbreaks

Photos credit: WHO/Kudzai Tinago

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).

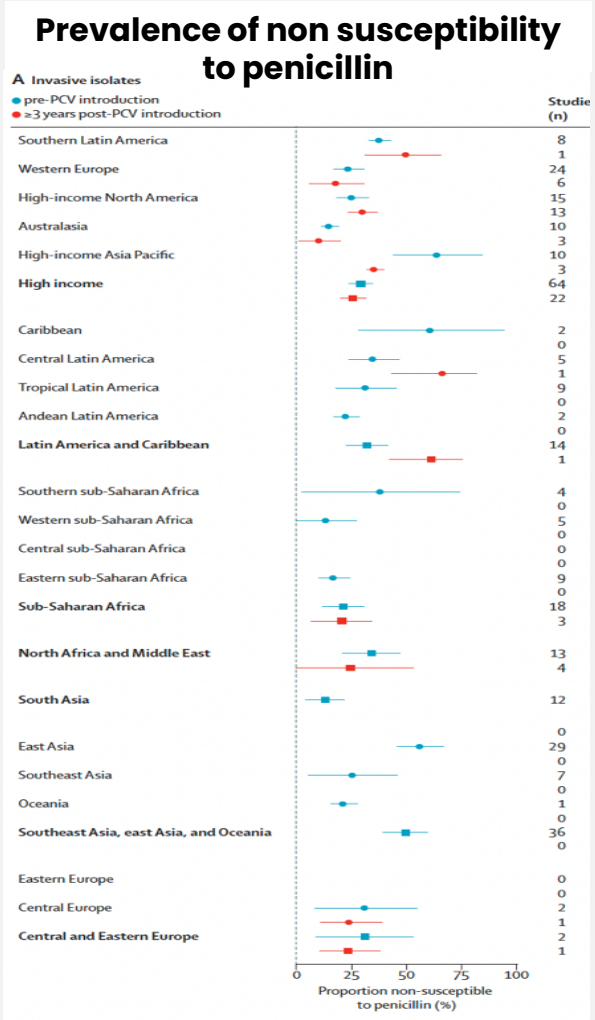
Impact of PCV on *S. pneumo non-susceptibility*

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/

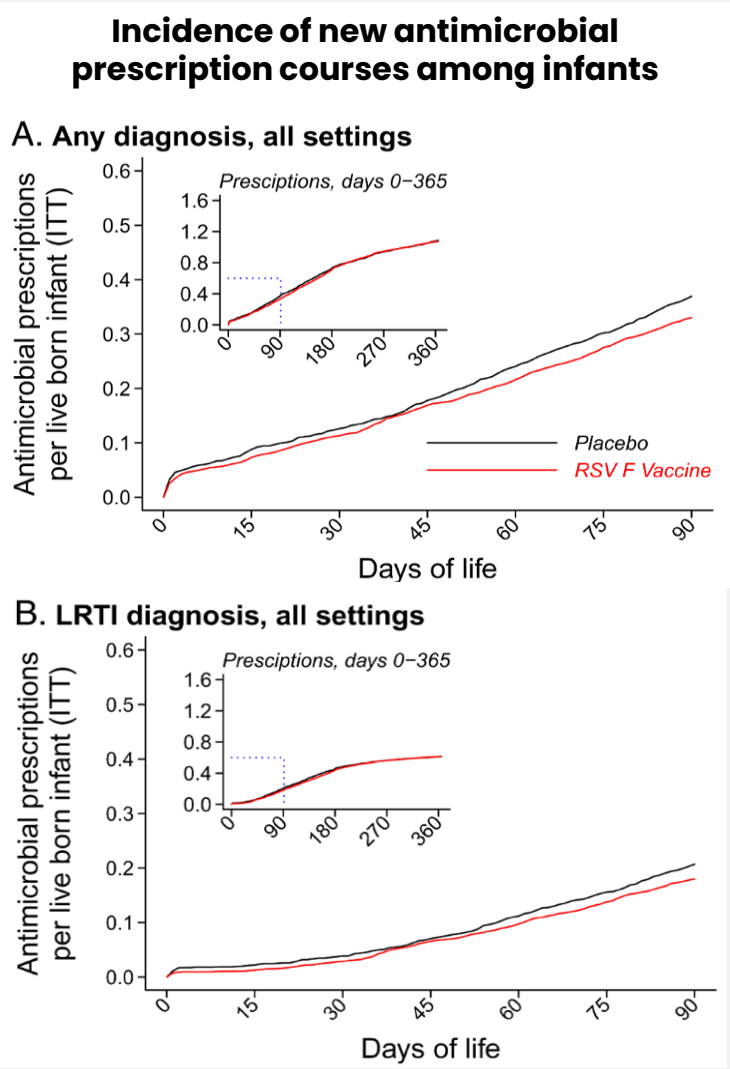
Maternal RSV vaccine impact on *antimicrobial prescribing*

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

Seasonal influenza vaccine impact on *antimicrobial prescribing*

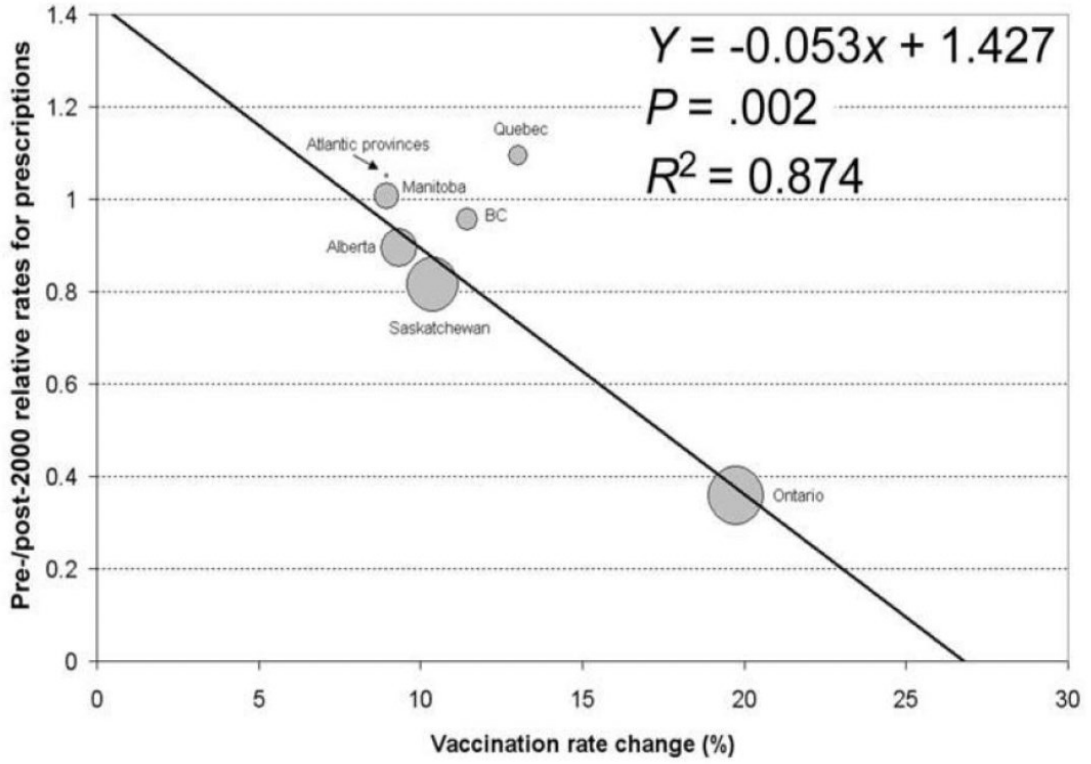
Ecologic observational study, Canada (1997-2007)

Introduction of free seasonal influenza vaccine for those >6 mo, in 2000 (Ontario, Canada)

64% greater reduction in respiratory antibiotic prescriptions after universal vaccine introduction than status quo use

Reductions of secondary bacterial infections like pneumonia and otitis media

Association between influenza vaccination rate and rates of antibiotic prescription, Ontario, Canada



https://academic.oup.com/cid/article/49/5/750/308812

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

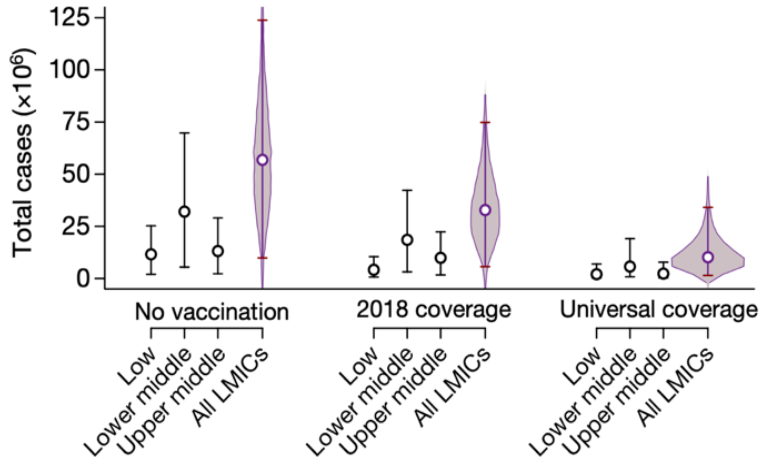
VACCINE IMPACT WITH 90% COVERAGE

PCV could avert additional 21.7 million antibiotic treated episodes

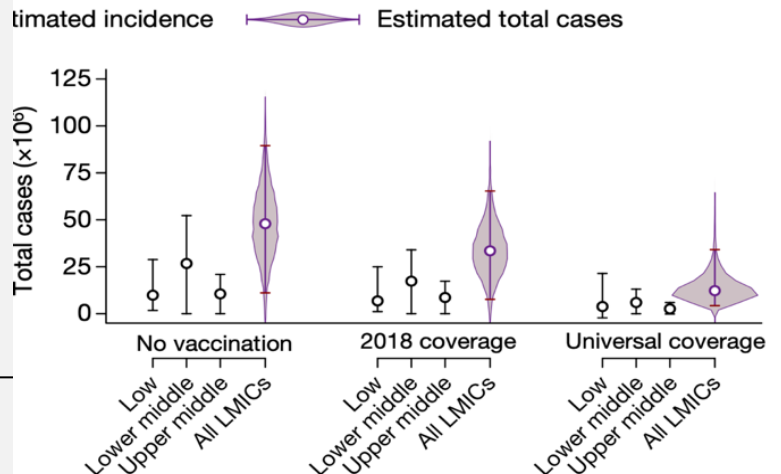
Rotavirus vaccines could avert additional 18.3 million antibiotic treated episodes

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



Impact of influenza and pneumococcal vaccines on *antimicrobial use*

Systematic review and meta-analysis

What is the evidence on the effect of vaccines on antibiotic consumption?

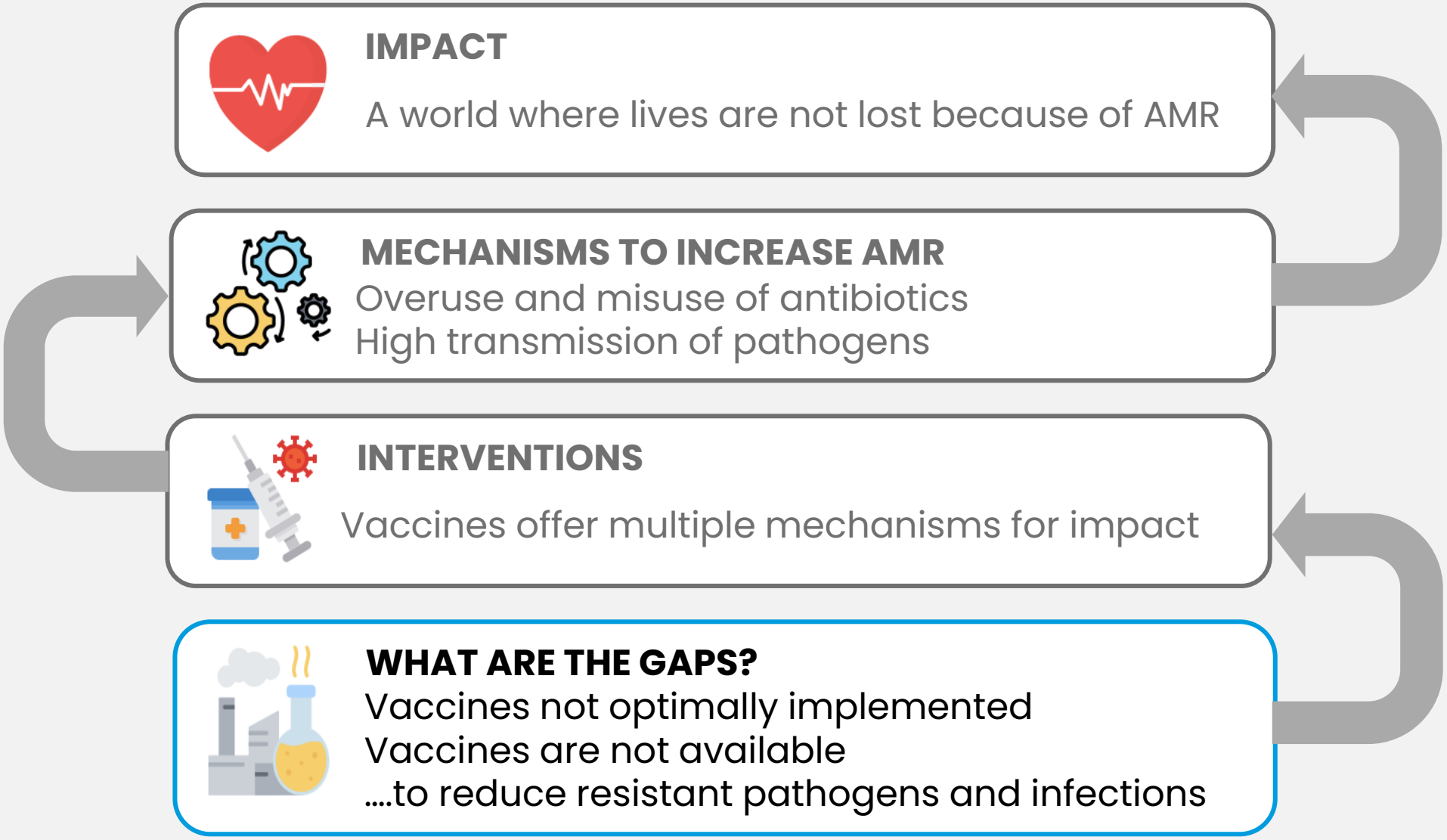
High-certainty evidence that influenza vaccine reduces antibiotic use in healthy adults by 28.1%

Moderate-certainty evidence that pneumococcal vaccines reduce antibiotic use in children up to 6 years.

Need for future research to strengthen the evidence base, and collection of data on antibiotic use in upcoming vaccine trials.

https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(19)30381-7/fulltext

The 'Vaccines and AMR' Paradigm



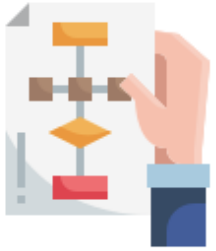
Vaccines are underecognised as tools in preventing AMR

- Important **opinion-building articles** do not mention vaccines at all;
- Immunization and AMR scientists/advocates need to ensure that **vaccines are recognized and used** as interventions to reduce AMR.

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

Vaccines in National Action Plans Against AMR

Desk review of National Action Plans



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

Vaccines against *Klebsiella pneumoniae* need to be developed to reduce AMR

Modelling analysis of CHAMPs, BARNARDS, and NeoObs studies

BURDEN

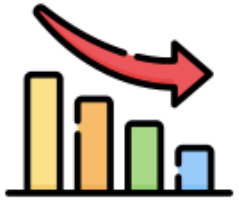
1 million newborns yearly die with neonatal sepsis, with *Klebsiella pneumoniae* as the leading cause of such infections.

RESISTANCE

50-80% resistance to standard treatments (e.g., ampicillin and gentamicin) and significant resistance to second-line therapies.

METHOD

Modelling to estimate the potential impact of a maternal vaccine with 70% efficacy against neonatal sepsis cases and deaths caused by *K. pneumoniae*, with coverage comparable to the maternal tetanus vaccine



RESULT

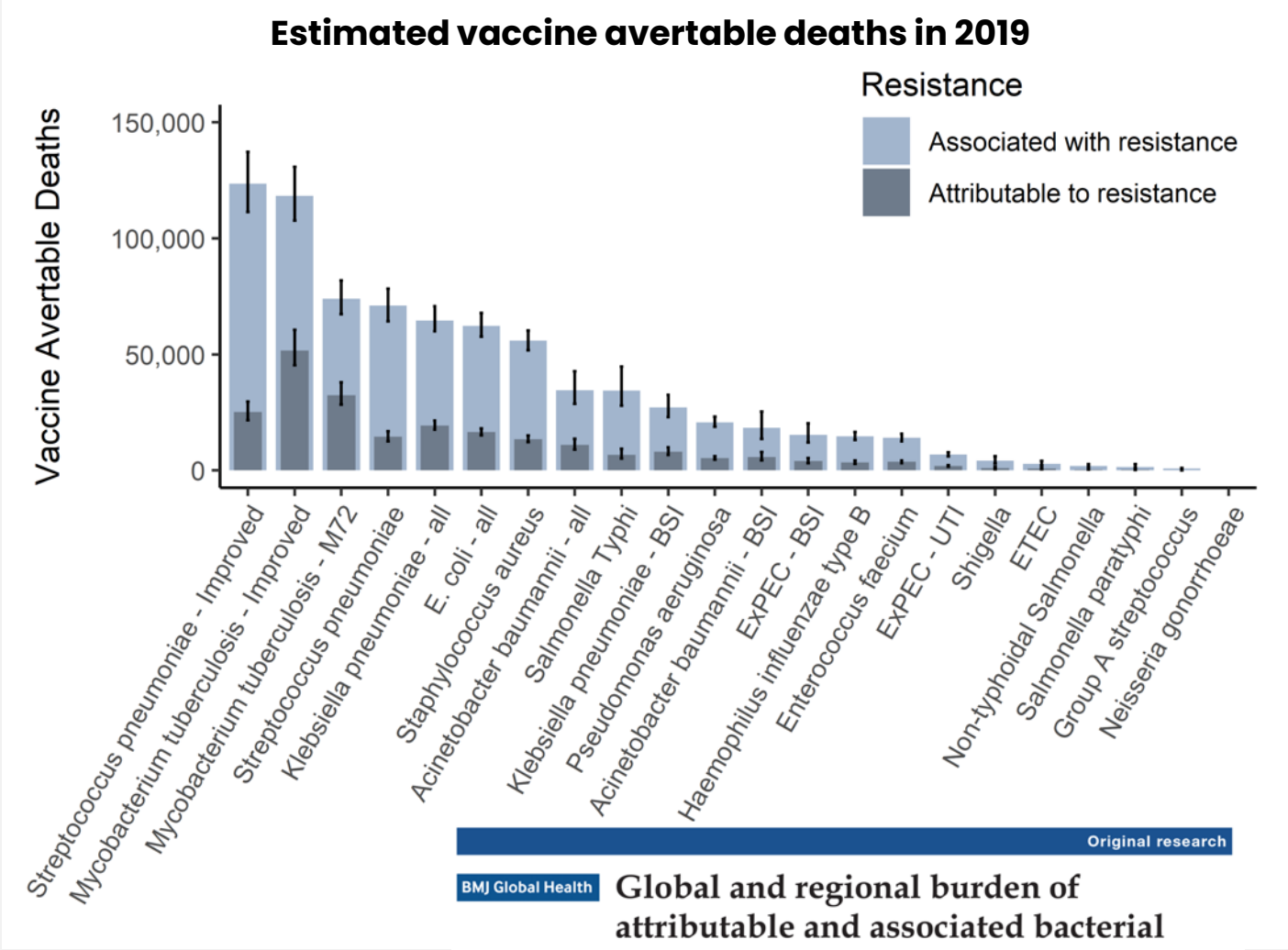
K. Pneumoniae vaccine could prevent approximately 399,015 cases of neonatal sepsis and around 80,258 neonatal deaths annually worldwide, 50-80% are associated with AMR

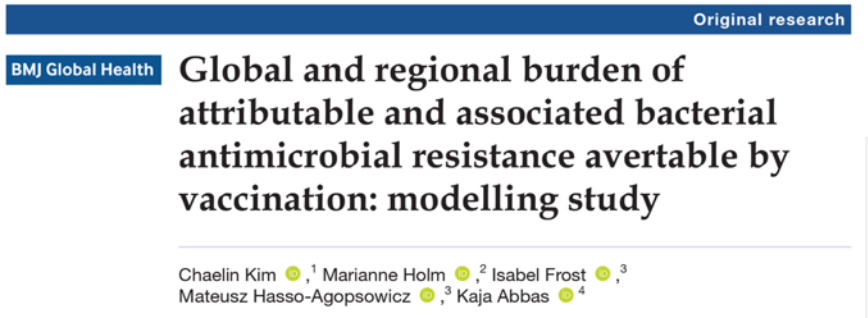
https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1004239#sec015

New vaccines to avert AMR health burden

GAP

- Static model to estimate impact of vaccines for 15 pathogens on AMR using IHME data, vaccine direct effect
- ***Mycobacterium tuberculosis***: 118,250 (107,668 - 130,801) deaths associated with resistance averted by a WHO vaccine with an 80% efficacy given to neonates, with life long protection or boosting.
- **Other vaccines** with over 50K averted deaths: Mtb (M72), *Streptococcus pneumoniae (improved)*, *Klebsiella pneumoniae*, *E. Coli*, *S. aureus*





https://gh.bmj.com/content/8/7/e011341.info

Estimated vaccine averted health burden by syndrome and WHO region

Vaccines could avert up to 166K deaths associated with AMR in the WHO African Region

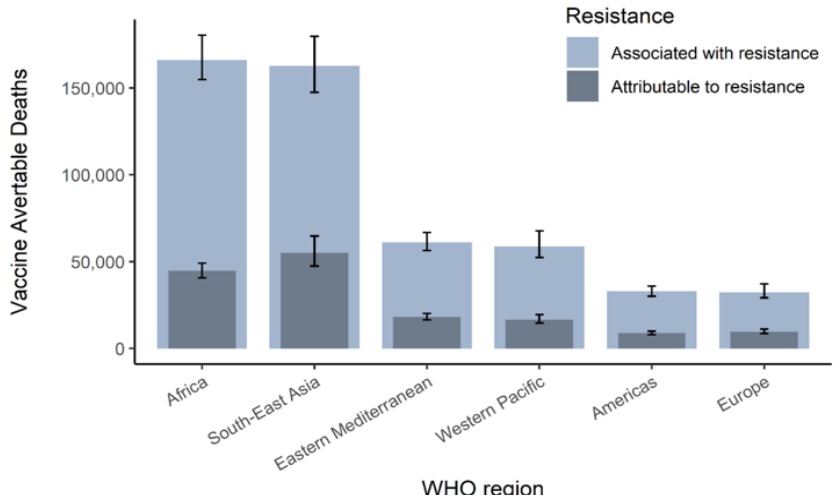
Vaccines could avert up to 163K deaths associated with AMR in the WHO SEARO Region

Vaccines could avert up to 157K deaths associated with AMR due to lower respiratory infections

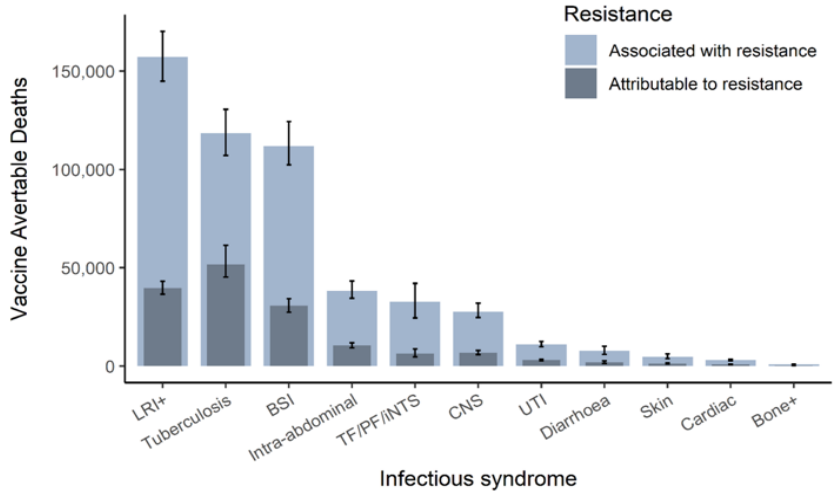
Vaccines could avert up to 112K deaths associated with AMR due to bloodstream infections

https://gh.bmj.com/content/8/7/e011341.info

Estimated vaccine impact in WHO regions



Estimated vaccine impact by syndrome



New vaccine impact: Estimates of averted antimicrobial use

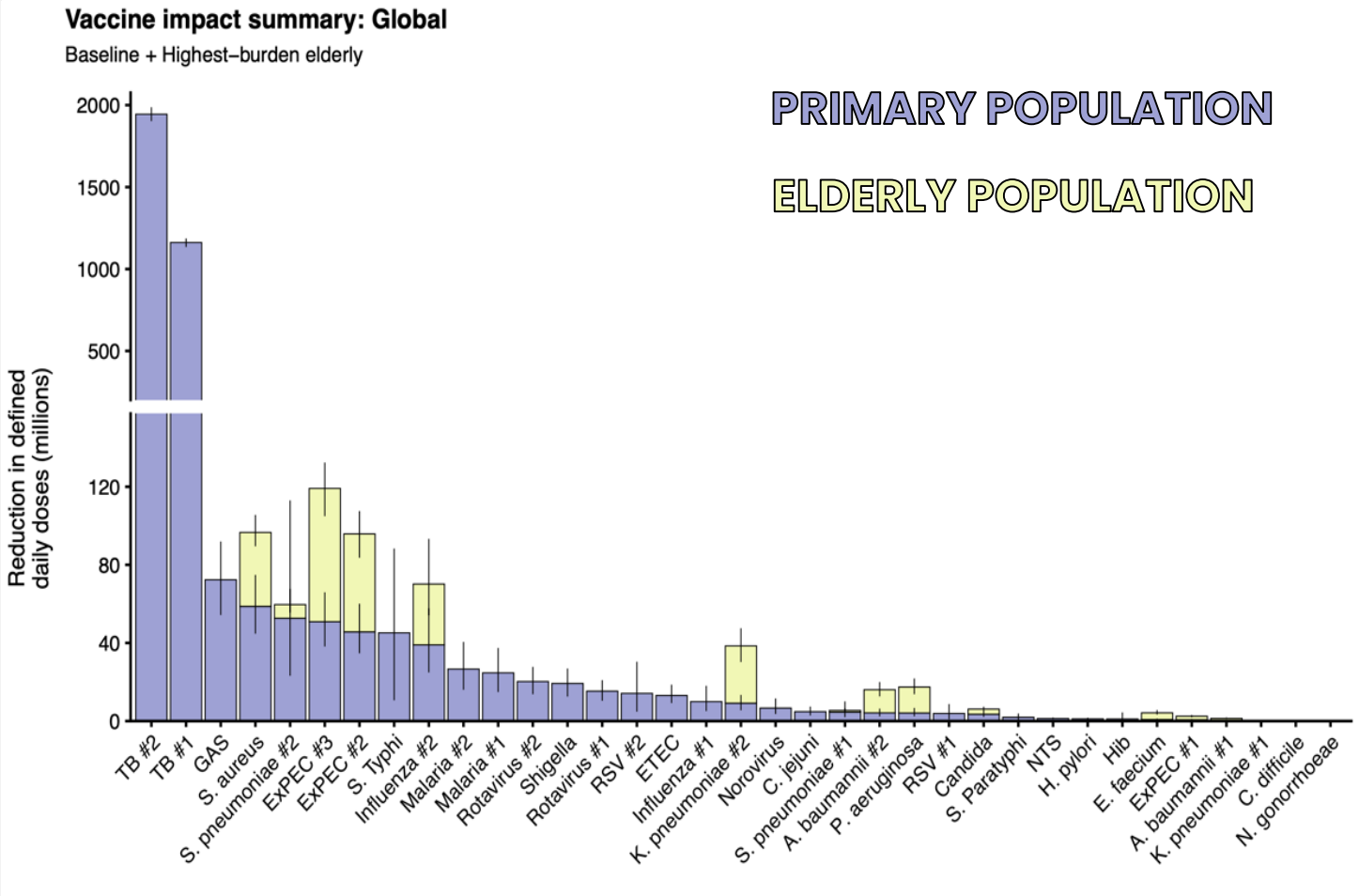
LSHTM and WHO modelling analyses- unpublished

Analysis of vaccine impact on antimicrobial use for 27 pathogens

TB vaccines could reduce antimicrobial use by 1200-1800 million Defined Daily Doses annually

GAS vaccine could reduce antimicrobial use by 70 million DDDs annually

Estimated vaccine avertable antibiotic use in 2019



Gavi VIS 2024: Evaluation framework for routine use vaccines

Ranking Criteria

Criteria	Indicators
Health impact	Total future deaths averted 2026-2040, and per 100,000 vaccinated
	Total future DALYs averted 2026-2040, and per 100,000 vaccinated
Value for money	Vaccine Procurement cost per death averted
	Vaccine Procurement cost per DALY averted
Equity and social protection impact	Disproportionate impact of disease on vulnerable groups
	Vaccination contributes to addressing underlying gender-related barriers faced by caregivers, adolescents and health workers and/or gender associated differences in immunisation coverage
Gavi comparative advantage	Degree of vaccine market challenges
	Gavi role in addressing challenges
Economic impact	Direct medical cost averted
	Indirect cost averted

Modulating Criteria

Criteria	Indicators
Modulate up	
Global health security impact	Epidemic potential of disease
	Impact on AMR
	Climate change risks and mitigation
Other impact	Total U5 deaths averted 2026-2040, and per 100,000 vaccinated
Contribution to global agenda	Fit with global development (SDGs), immunization (IA2030) agendas and other relevant global targets
Broader health system benefits	No specific indicator – evaluated case-by-case
Contextual	
Implementation feasibility	Ease of supply chain integration
	Need for healthcare worker training/ behaviour change
	Requirements of vaccination timepoint
	Need for demand promotion (e.g., acceptability, understanding of disease burden)
	Availability of epidemiological data to inform programmes
	Diagnostics availability/ needs
Alternate interventions	Optimal use of current and future alternative interventions (prevention and treatment)

How are vaccines integrated into global AMR strategies?

https://www.who.int/publications/i/item/9789241509763

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

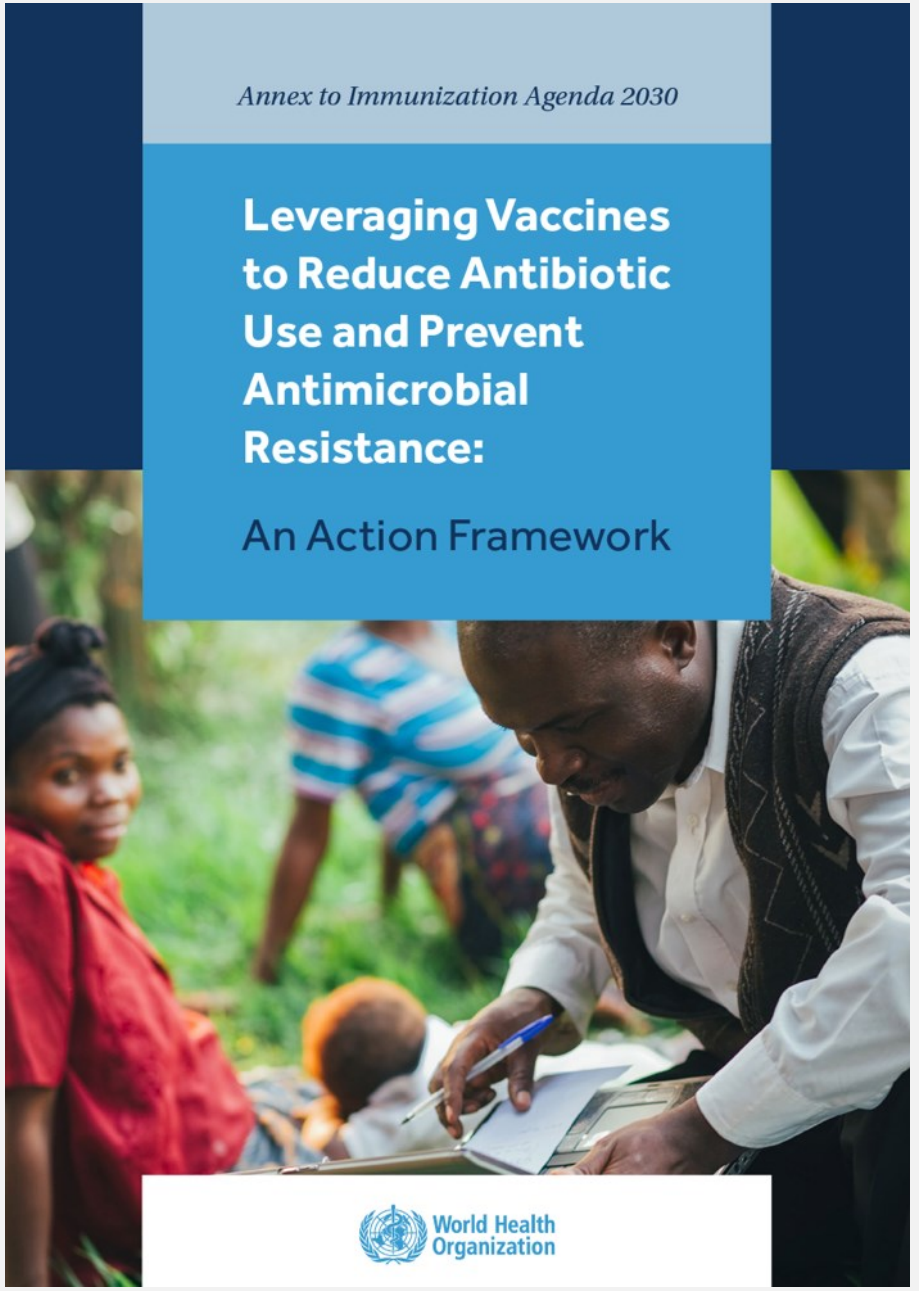
https://www.who.int/publications/m/item/global-research-agenda-for-antimicrobial-resistance-in-human-health

The Action Framework to leverage vaccines against AMR and AMU

Expanding use of licensed vaccines to maximize impact on AMR

Develop new vaccines that contribute to prevention and control of AMR

Expanding and sharing knowledge of vaccine impact on AMR



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Leadership and Advocacy to Drive Action

5 MILLION ANNUAL DEATHS ASSOCIATED WITH AMR

Vaccines can reduce:

- Incidence of infections
- Antibiotic use
- Evolution of resistance

We need better:

- Vaccine use
- Implementation
- Vaccines
- Trials
- Data

Opportunity for change:

UN HIGH LEVEL MEETING ON AMR, 26 September, NYC

Thank you