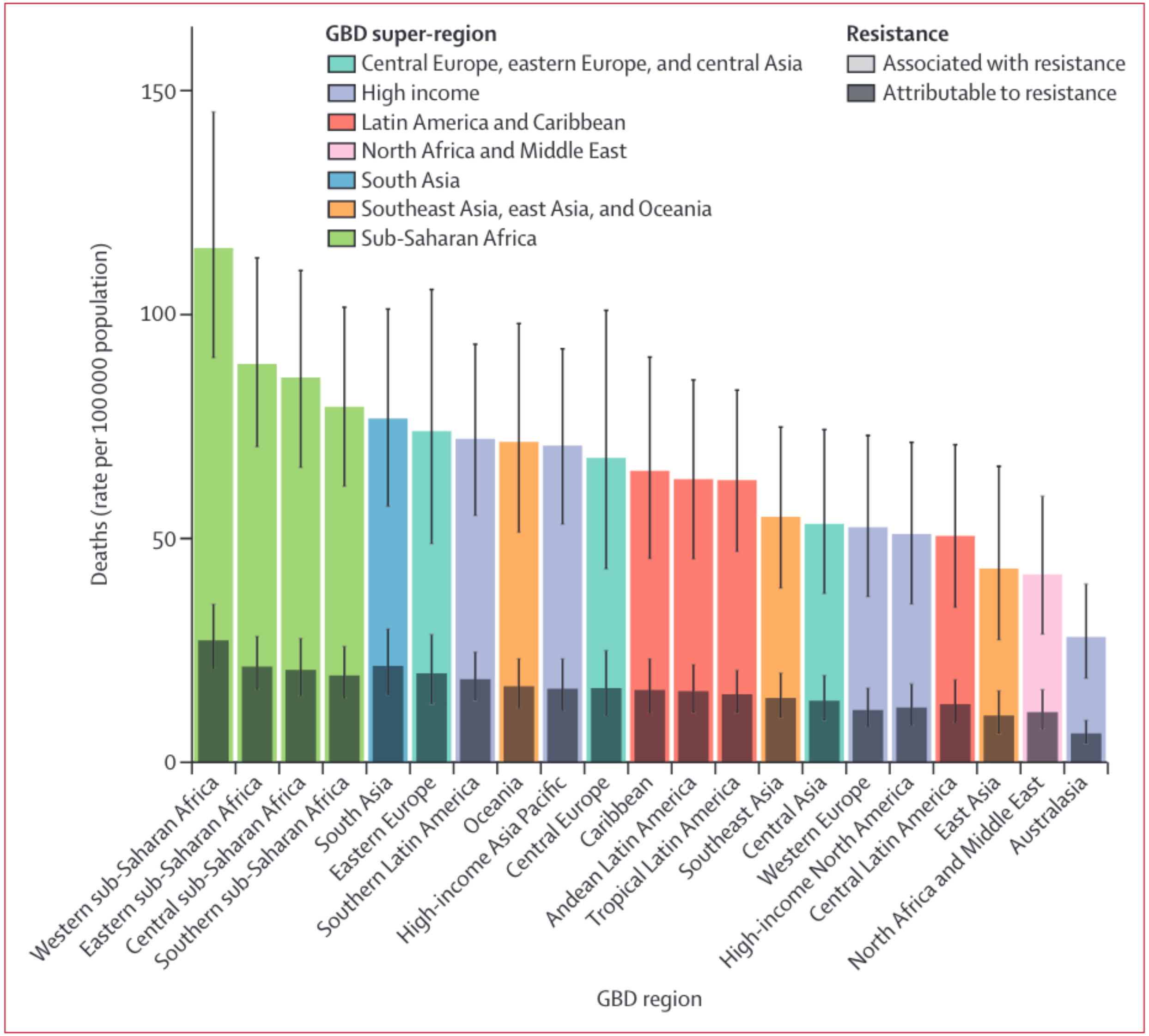
Impact épidémiologique de la vaccination sur les maladies à prévention vaccinale et antibio-résistance

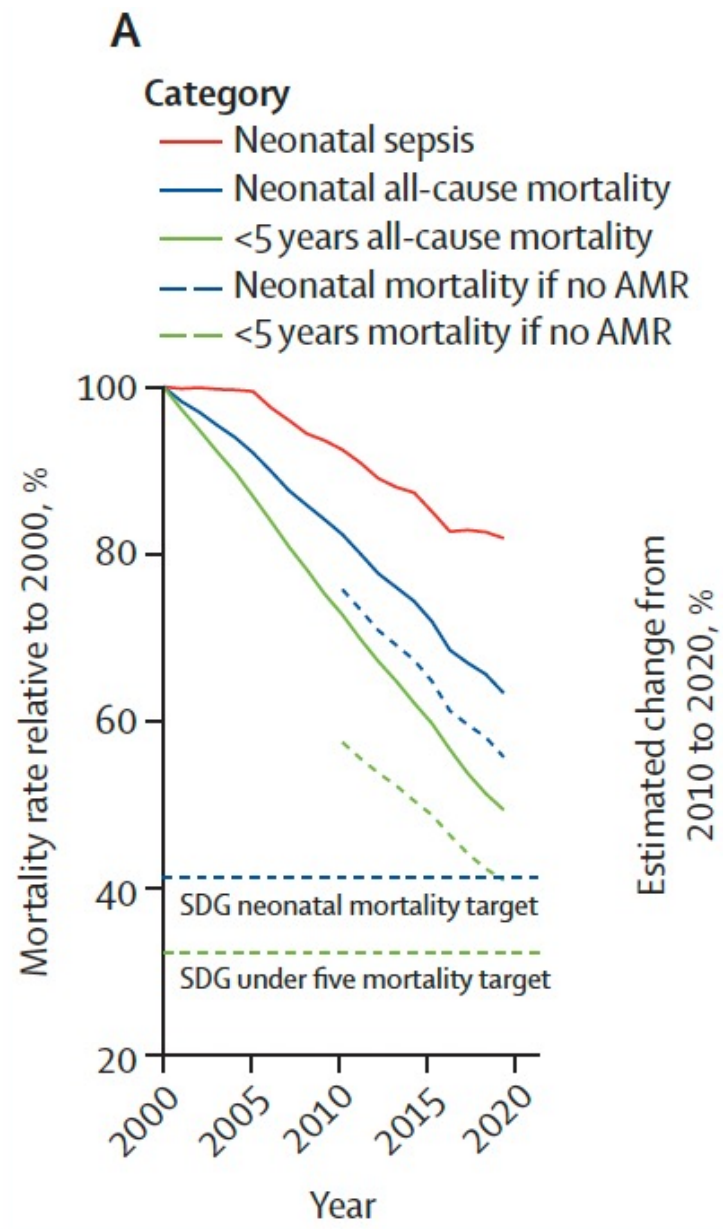
Marie-Cécile Ploy

Cours de Vaccinologie
Avril 2025

THE CHALLENGE: Antibiotic resistance imperils global health



AMR collaborators, The Lancet, January 2022



Okeke et al, 2024

Burden of resistance in animal health

of the **value of global agriculture** is constituted by **production animals**

people depend on **production animals** for their **income and livelihoods**

However, AMR burden data are scarce in animal health

AMR could increase animal mortality rates by one per cent,
an equivalent loss of US$13 billion in livestock value
(US$3 billion of which is attributed to waterborne AMR)

UNEP report 2023

Environmental complexities in transmission and spread of AMR

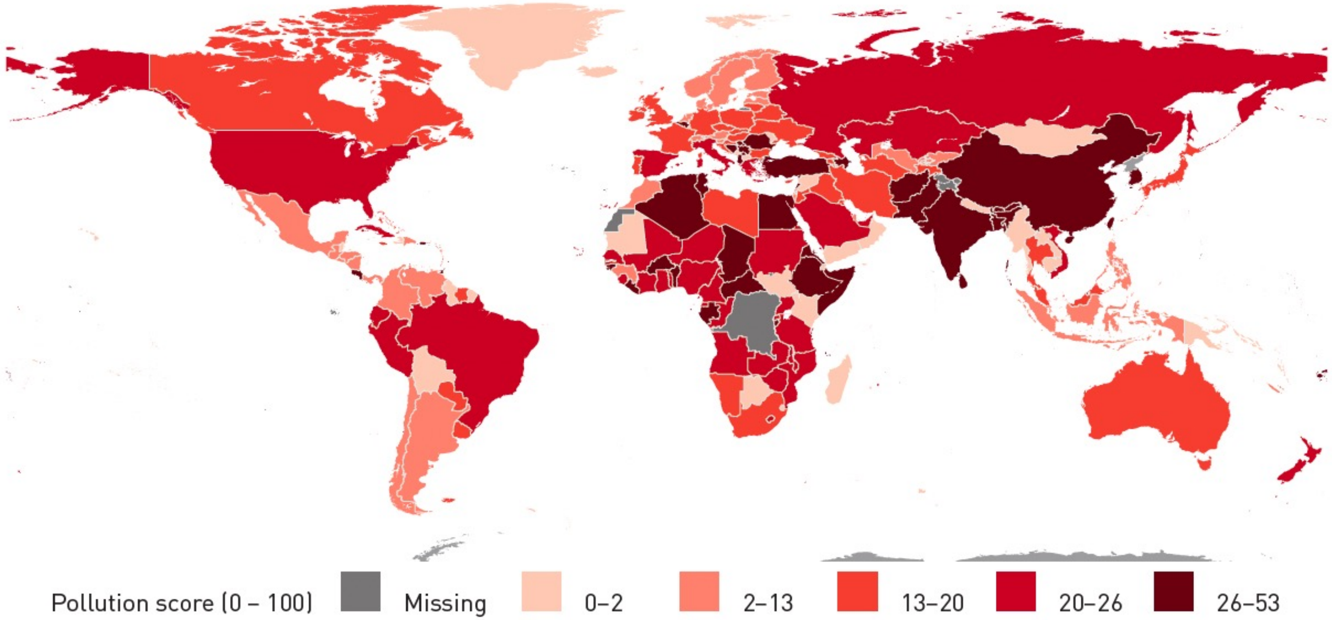


Figure 7

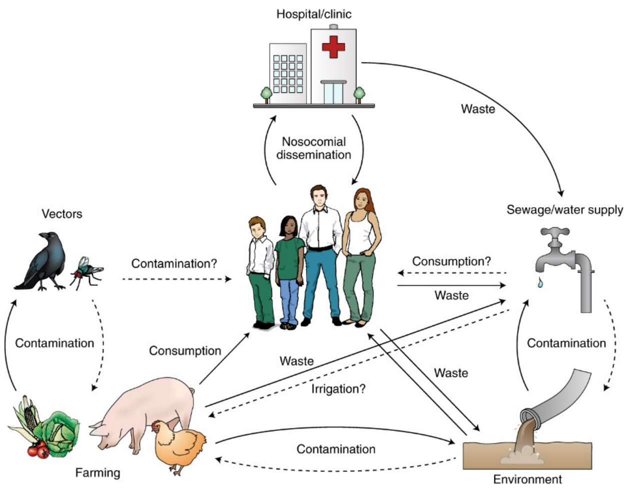
Estimated global environmental water contamination and pollution from antimicrobials
(Vivid Economics 2020)

56% of domestic and industrial wastewater globally is released into the environment with little or no treatment

Economic burden

AMR results in a gross domestic product (GDP) shortfall of US$ 3.4 trillion annually and push 24 million more people into extreme poverty (World Bank 2017).

The complex network of antibiotic resistance



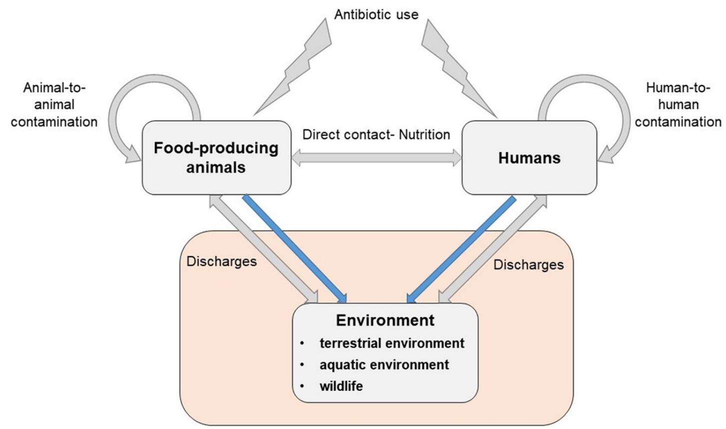


Fig. 1. The flow of antimicrobial resistance and antibiotics across the One Health continuum of food-producing animals, humans, and the environment. Grey arrows indicate flow of resistance genes and resistant bacteria; blue arrows indicate flow of antibiotic residues.

T. Walsh, 2018

Haenni et al, Environment international, 2022

Transform political declarations into operational actions

2015

Global Action Plan on AMR

Food and Agriculture Organization of the United Nations | OIE World Organisation for Animal Health | World Health Organization

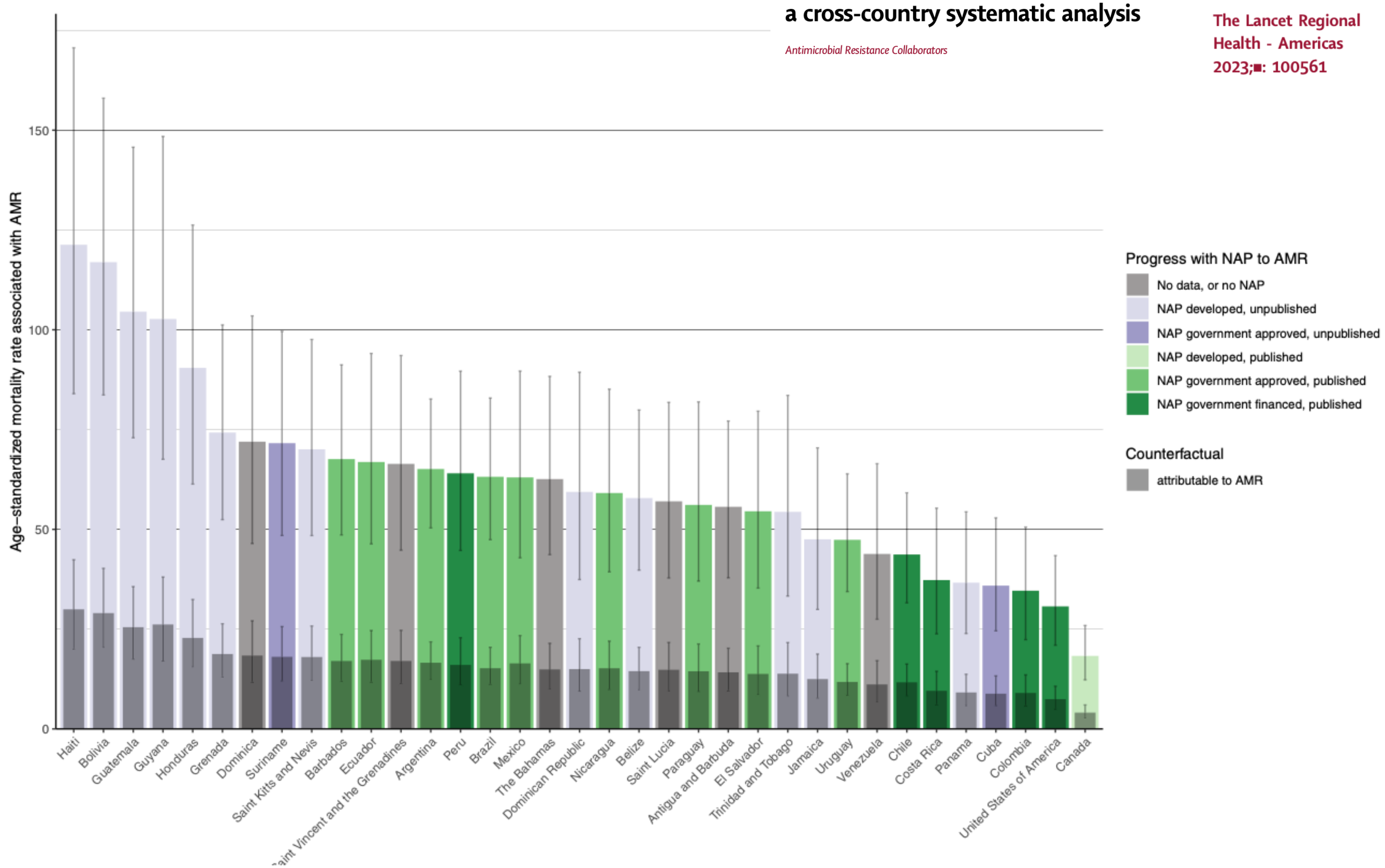
- ➢ Design and implement national Action Plans with a One health approach
- ➢ The national actions plans should include a research agenda

National action plans on AMR in Latin America (WHO data)

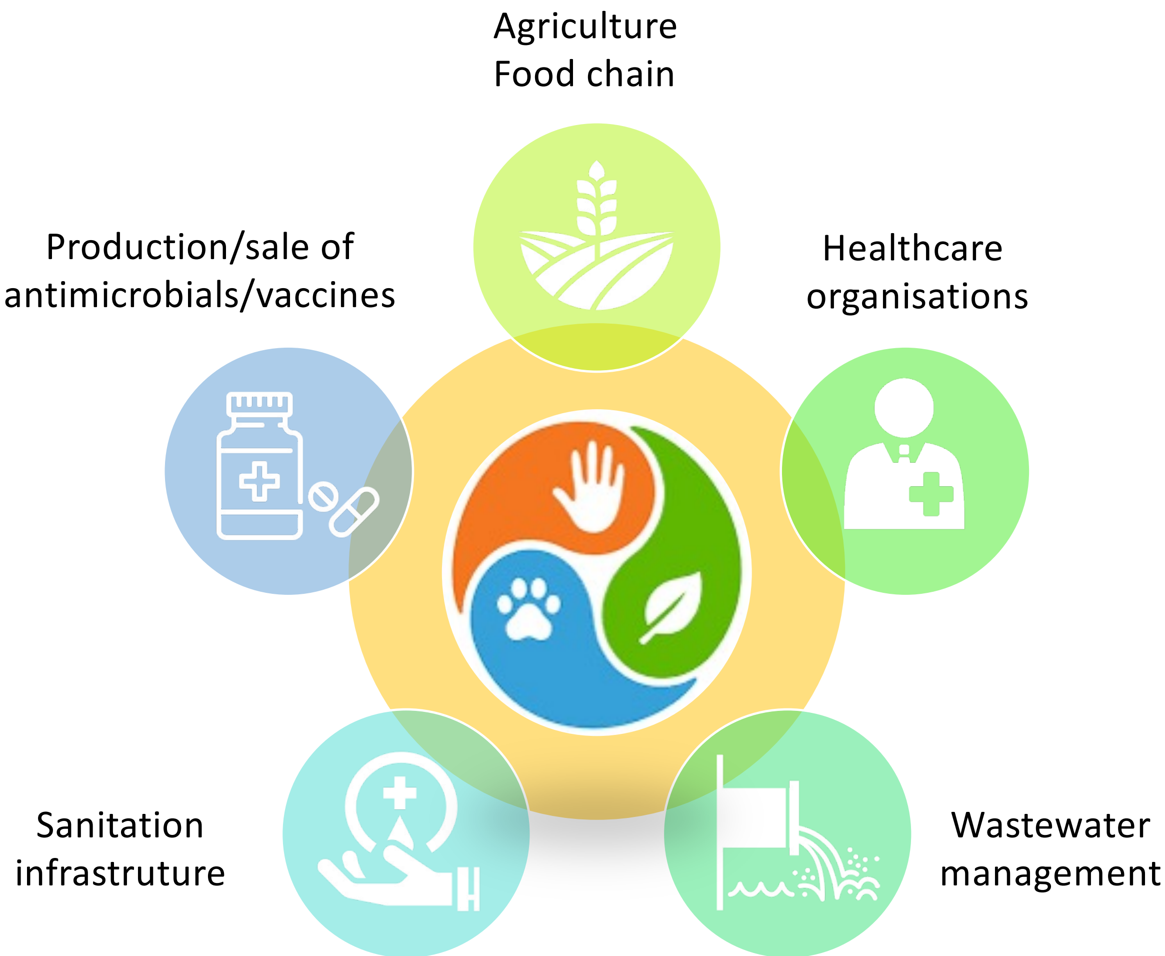
The burden of antimicrobial resistance in the Americas in 2019: a cross-country systematic analysis

Antimicrobial Resistance Collaborators

The Lancet Regional Health - Americas 2023;■: 100561



Transforming value chains & moving toward a One Health approach



For a sustainable impact on AMR, we need to adopt a One Health approach

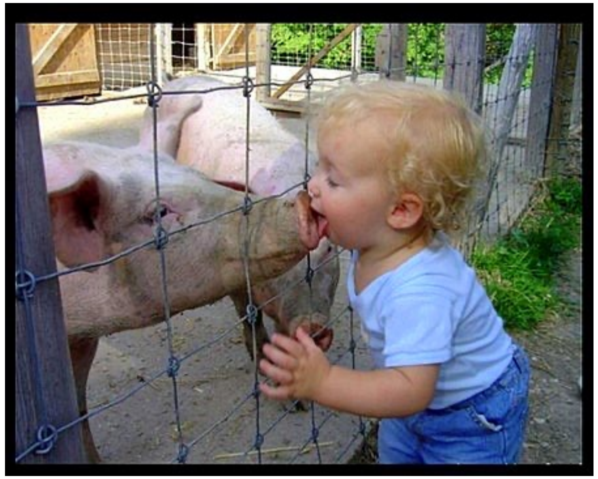
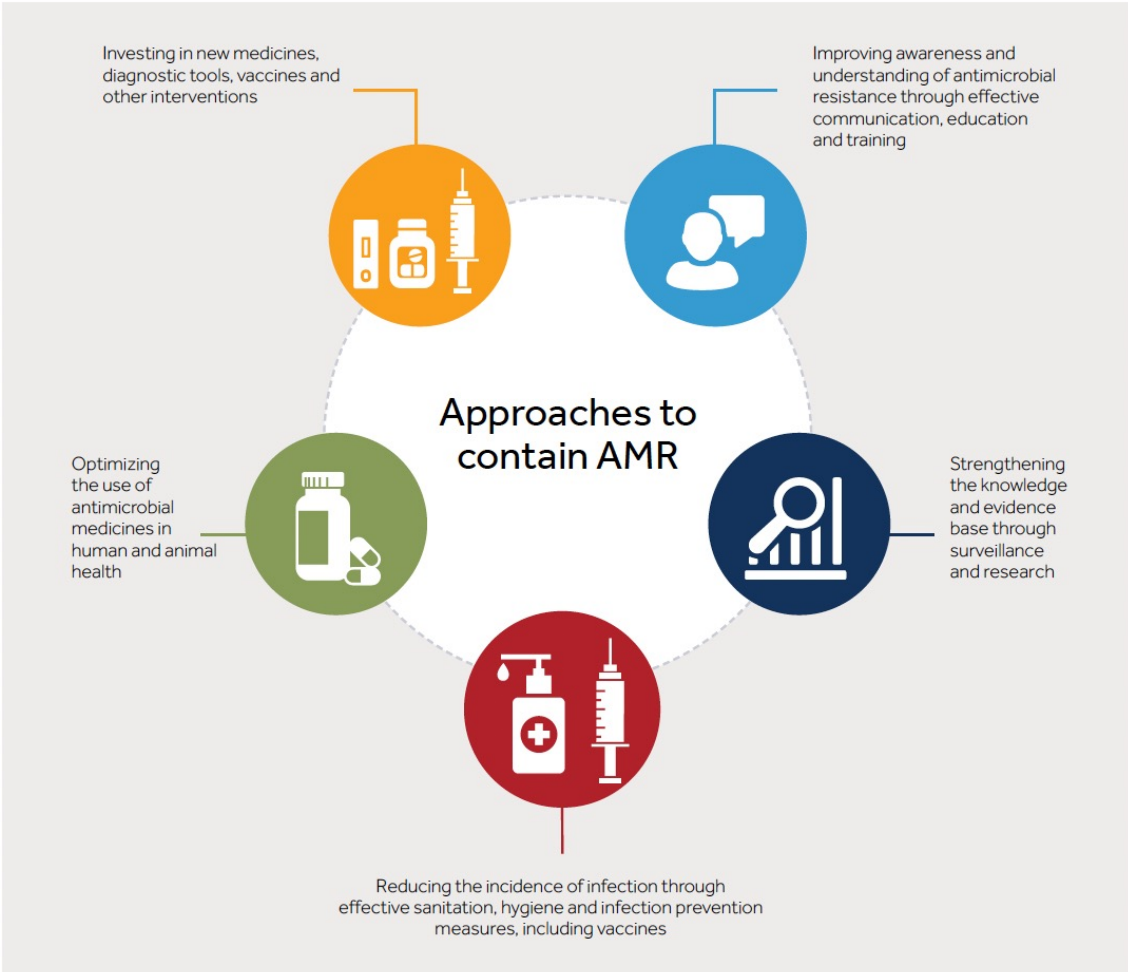
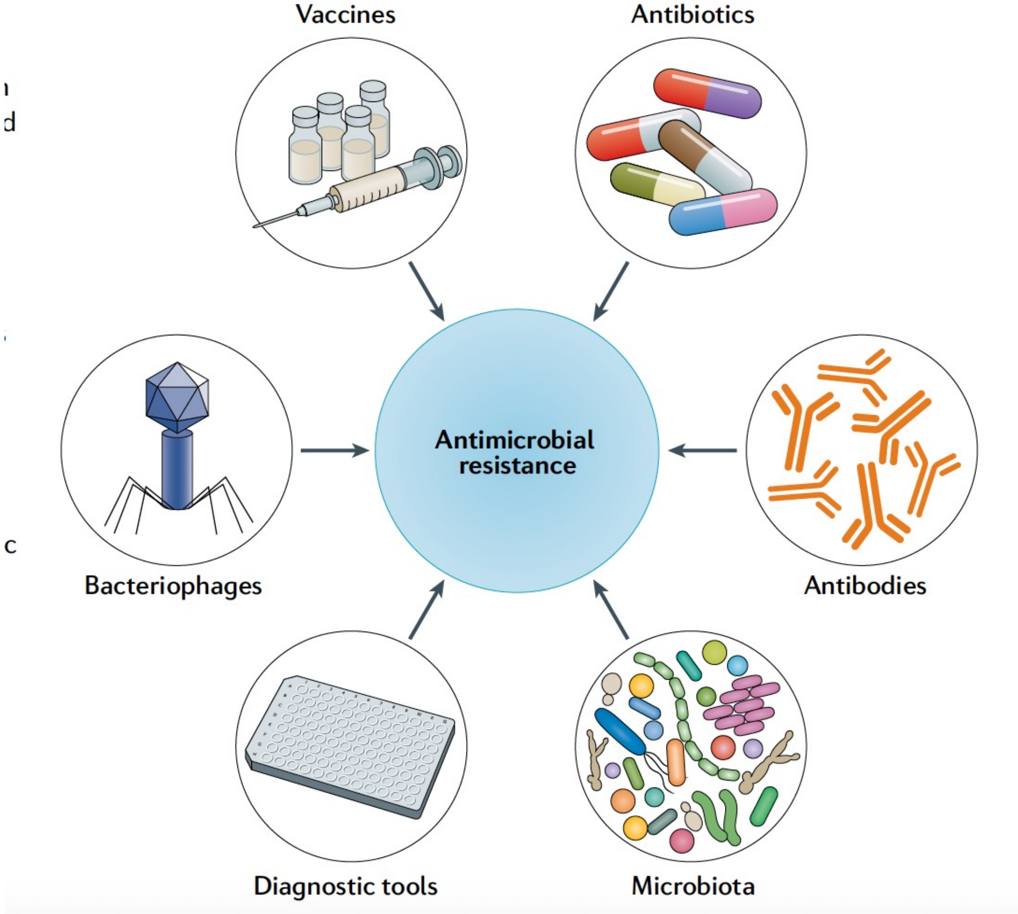


Fig. 1. Strategic objectives of the Global Action Plan on Antimicrobial Resistance

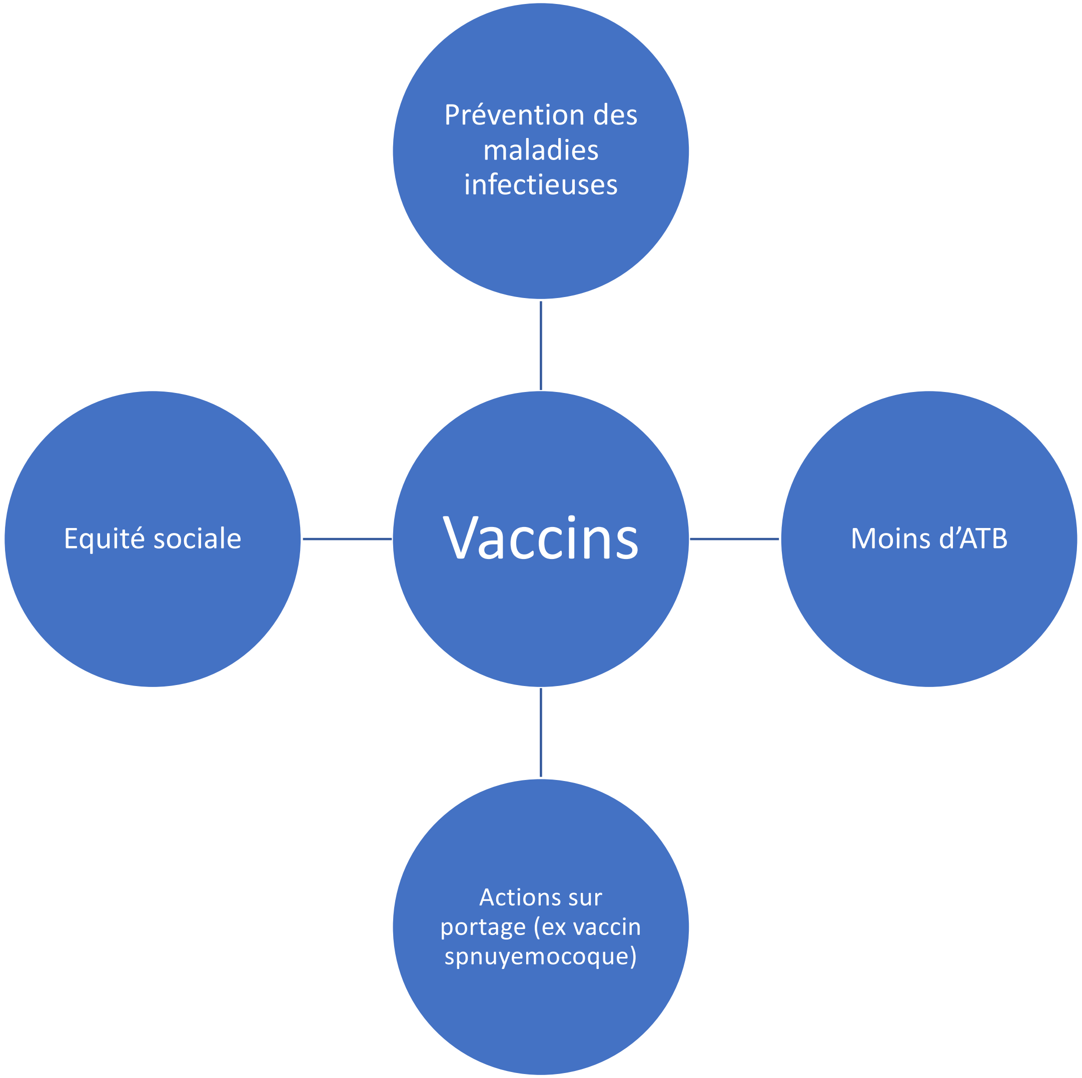


WHO report 2020

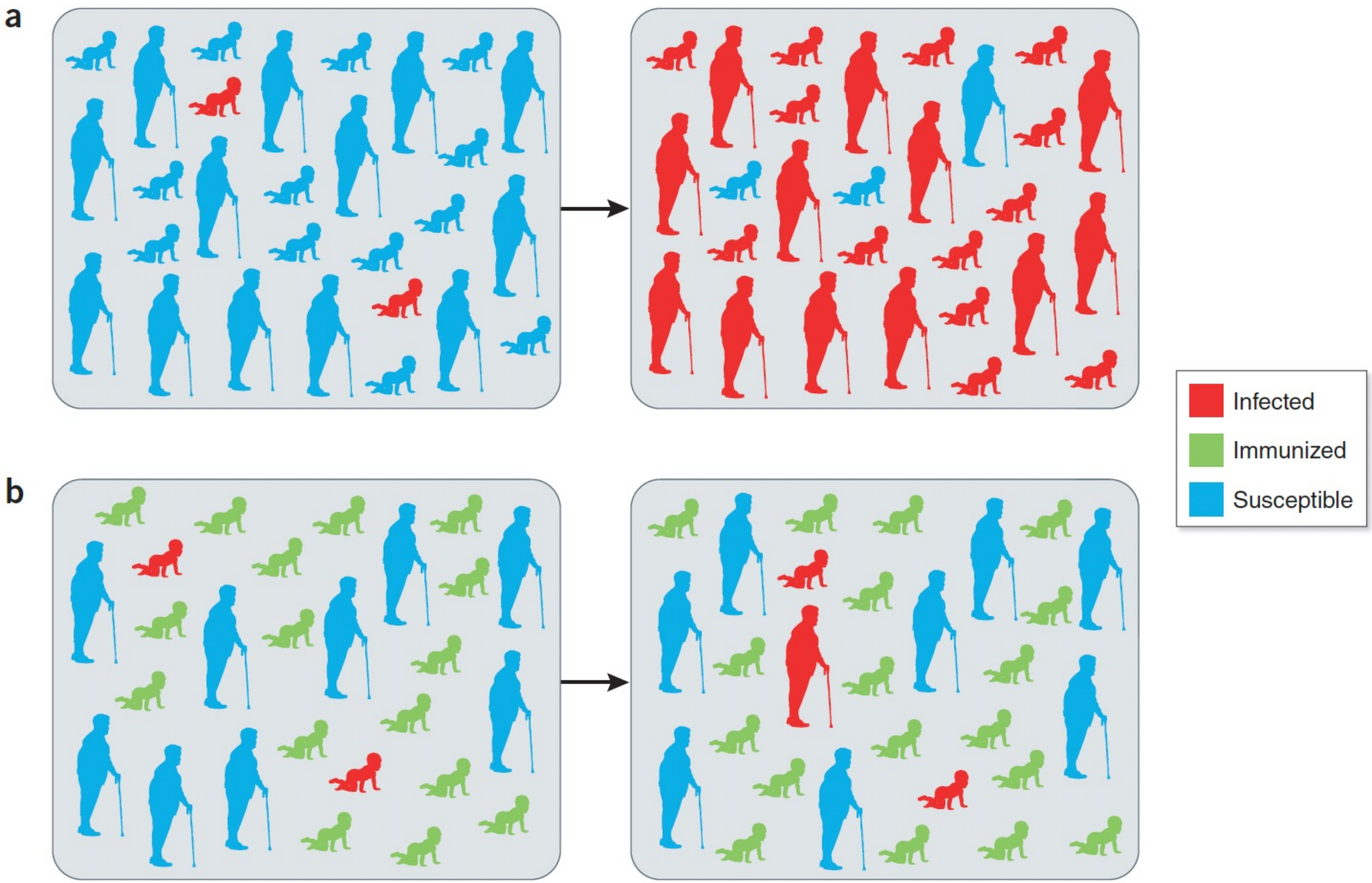
Therapeutic and preventive approaches



Micoli et al, Nature Reviews Microbiology, 2021


Prévention des maladies infectieuses
Equité sociale
Vaccins
Moins d'ATB
Actions sur portage (ex vaccin spnuyemocoque)

Herd immunity



Jansen et al, Nature medicine, 2018

?

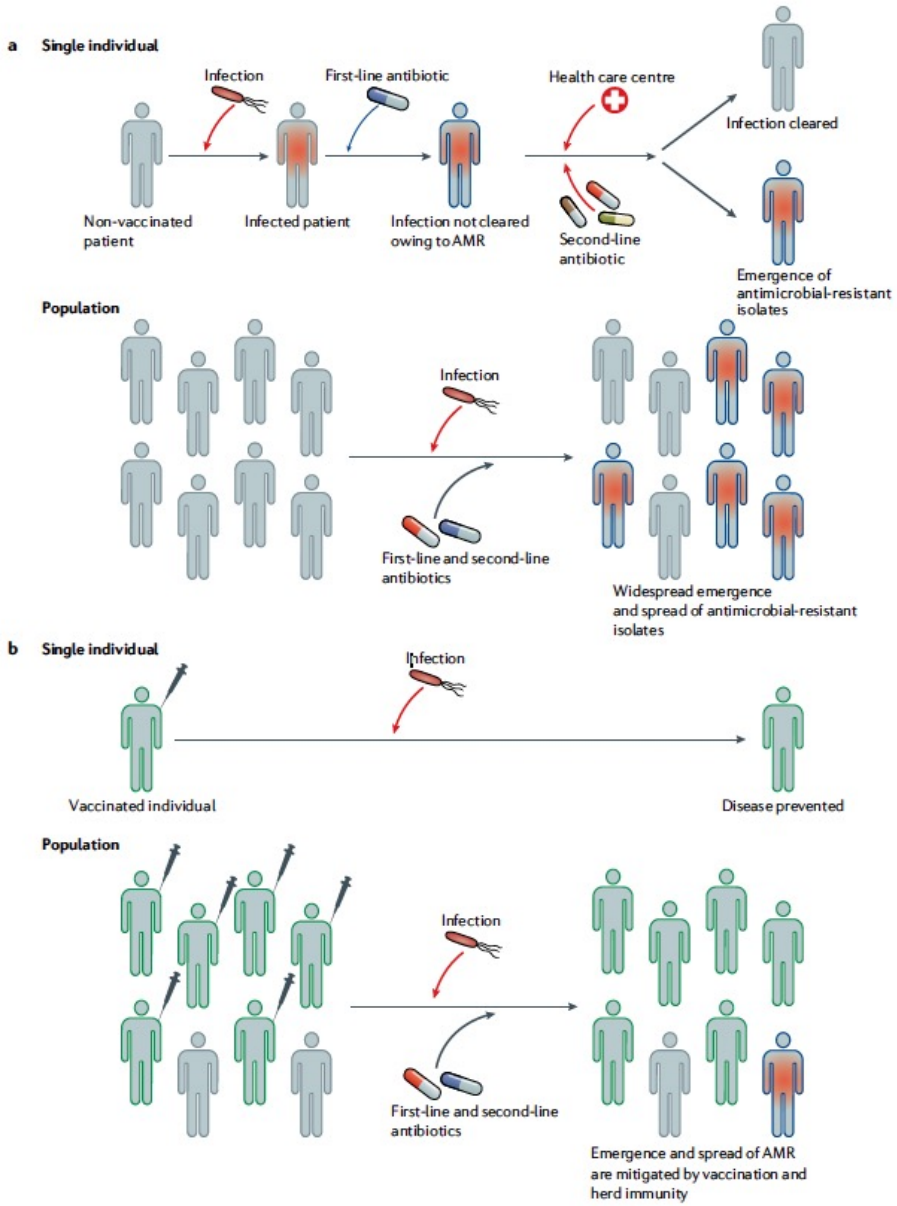
- Rapport OMS 2024

Les vaccins

→ Outil essentiel dans le cadre d'une réponse globale visant à réduire la résistance aux antimicrobiens

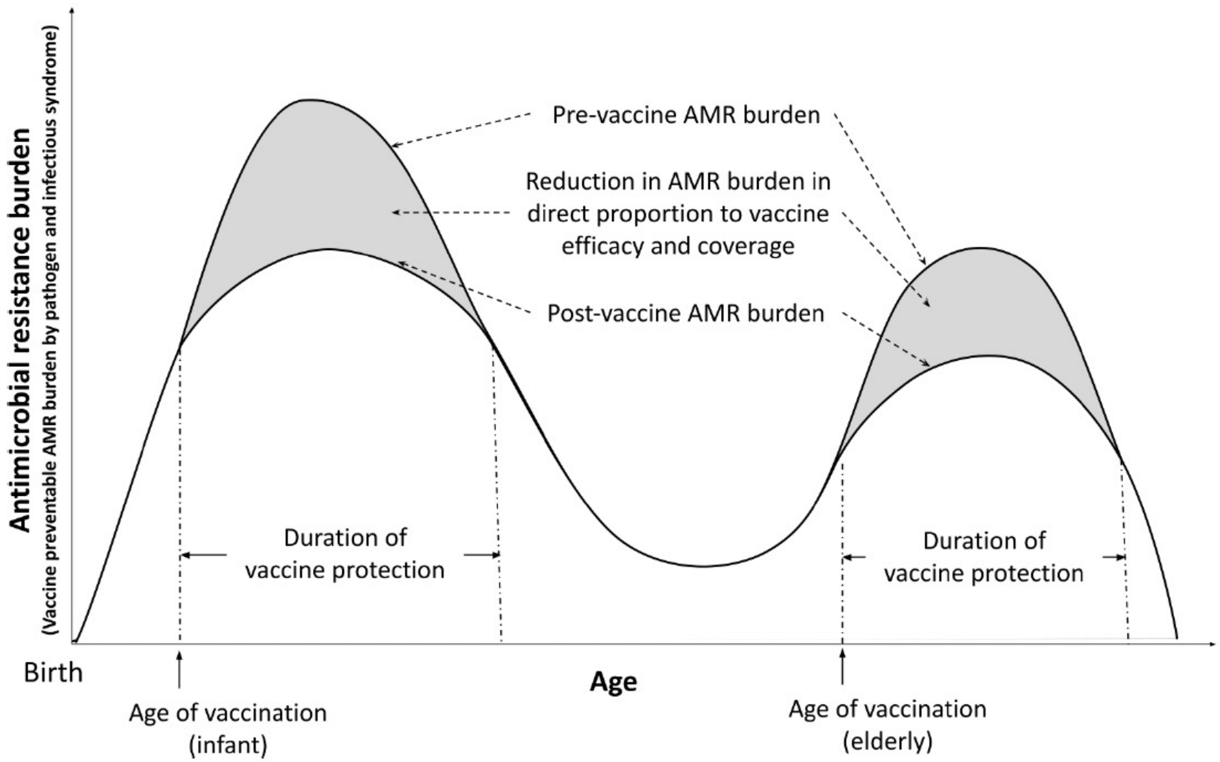
→**Une meilleure utilisation des vaccins vis-à-vis de 23 pathogènes pourrait réduire l'utilisation d'antibiotiques de 2,5 milliards de doses par an (22% de l'utilisation actuelle des antibiotiques)**

→ À l'échelle mondiale, les coûts hospitaliers associés au traitement de ces agents pathogènes résistants seraient de 730 milliards USD par an (1/3 des coûts associés à AMR)



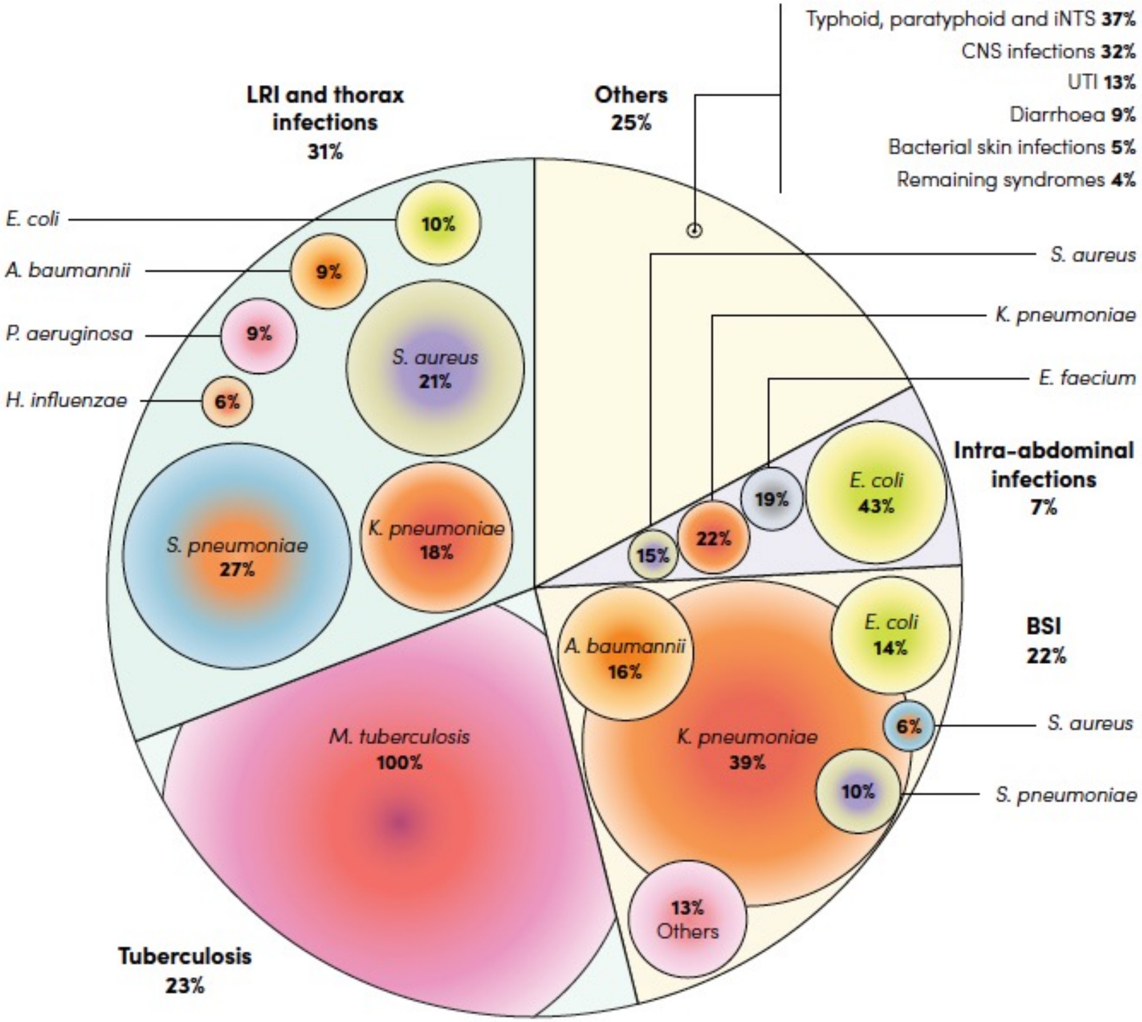
Micoli et al, Nature Reviews Microbiology, 2021

Modélisation de l’impact de la vaccination sur la résistance aux antimicrobiens



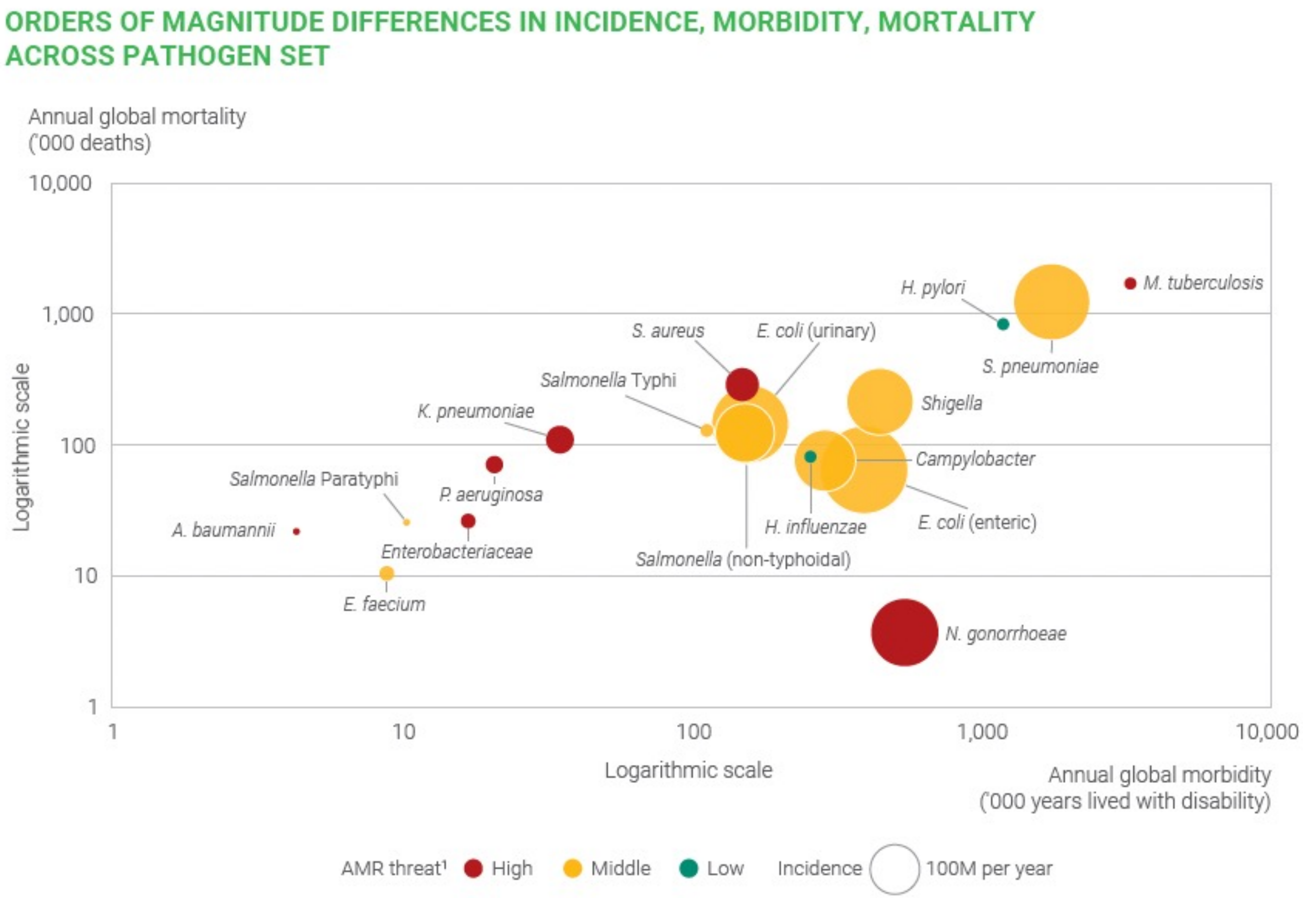
Kim C, et al. BMJ Glob Health 2023

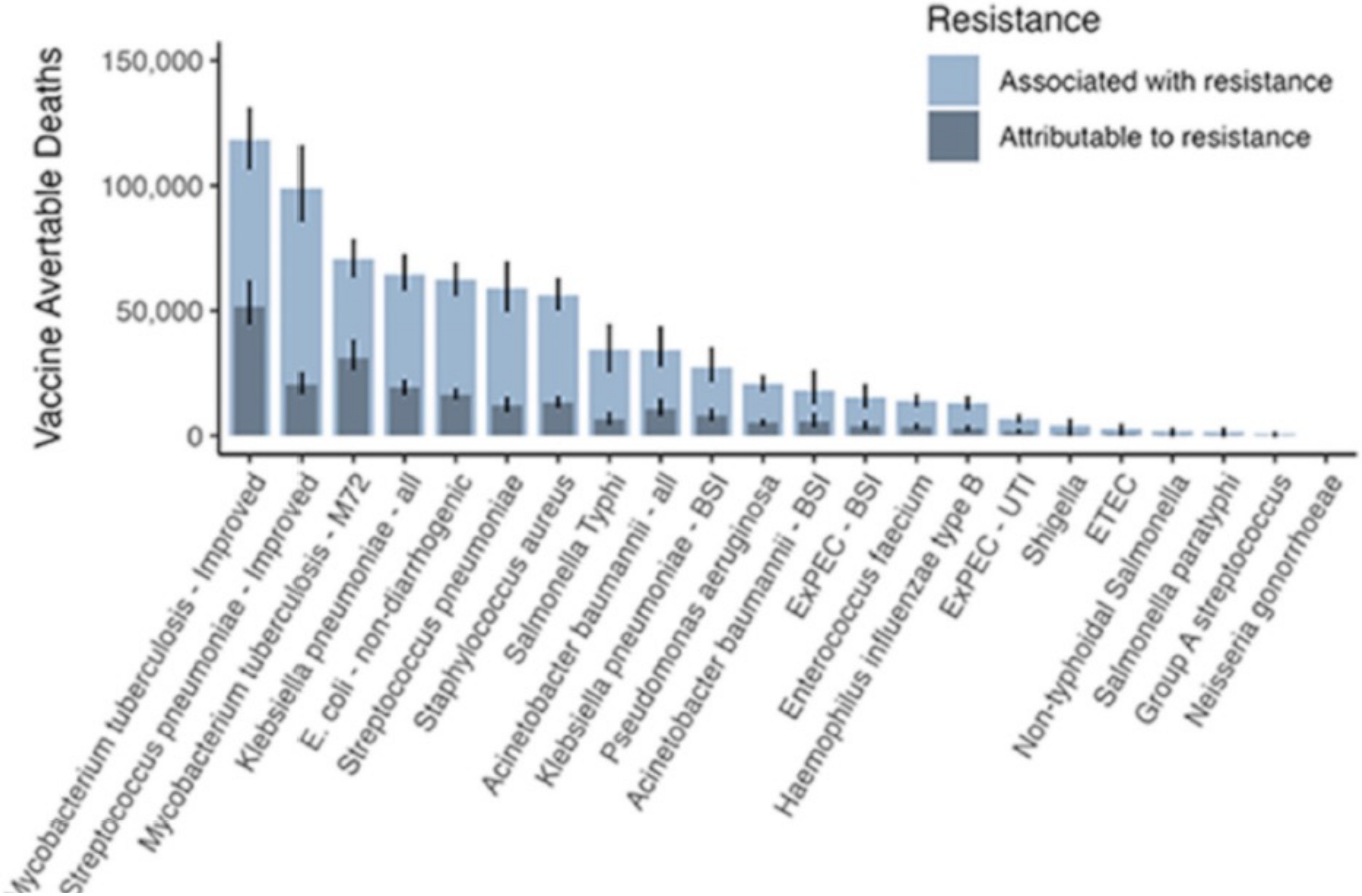
Fig. 3.4. Estimated potential vaccine-preventable deaths associated with AMR by infectious syndrome and pathogen in 2019[a]



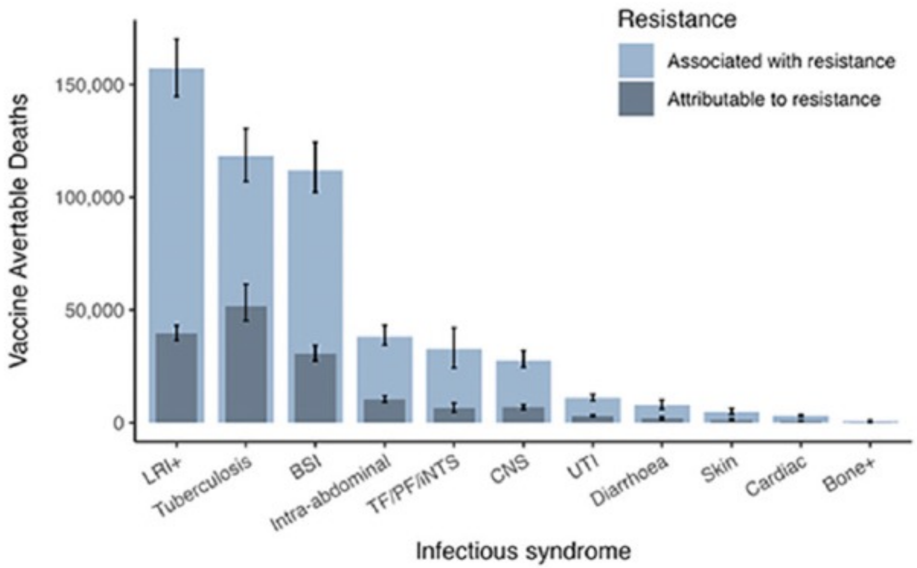
WHO report 2024

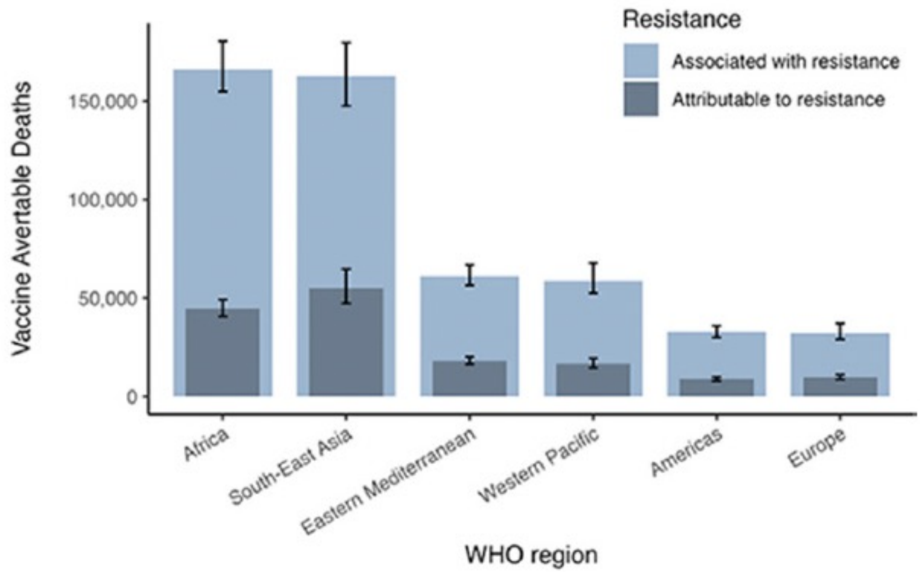
Pour quels agents pathogènes?





Kim C, et al. BMJ Glob Health





Kim C, et al. BMJ Glob Health 2023

Projections

- Chaque année :
  - Les vaccins contre le pneumocoque→ économise de 33 millions de doses d'ATB si 90 % des enfants du monde et des adultes concernés vaccinés;
  - Les vaccins contre la fièvre typhoïde → économise de 45 millions de doses d'ATB, si on accélérait leur introduction dans les pays à forte charge de morbidité ;
  - Les vaccins contre *Plasmodium falciparum* → économise jusqu'à 25 millions de doses d'ATB (ceux-ci étant souvent utilisés à mauvais escient contre cette maladie) ;
  - Les vaccins contre la tuberculose → économise entre 1,2 et 1,9 milliard de doses d'ATB

Infections invasives à pneumocoque

(bactériémies, méningites)

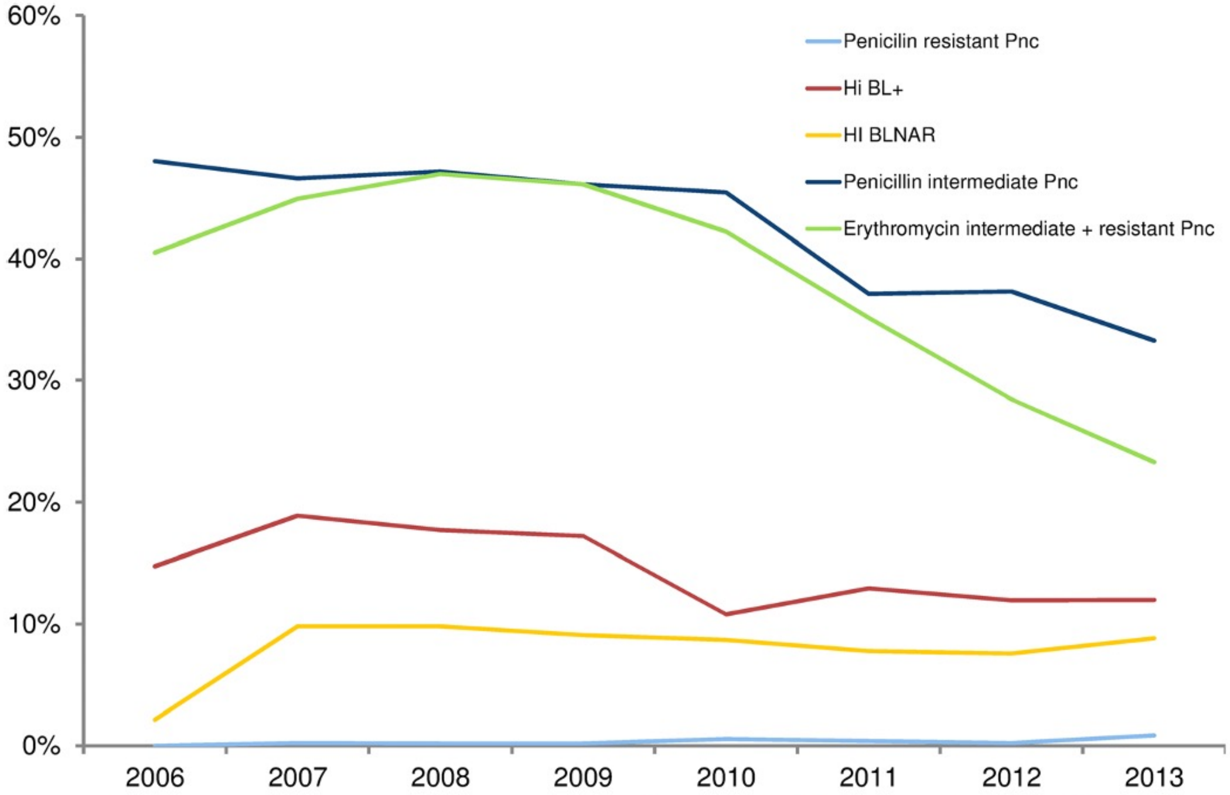


Fig. 1 Antibiotic resistance of *Streptococcus pneumoniae* and *Haemophilus influenzae* isolated from nasopharyngeal flora in 7200 infants with acute otitis media between 2006 and 2013. Pnc: *pneumococcus*; Hi: *H. influenzae*; BL+: ß-lactamase–producing strains; BLNAR: ß-lactamase–nonproducing ampicillin-resistant strains

Angoulvant et al, 2015

Fig. 3. Impact of pneumococcal vaccine on rates of drug-resistant invasive pneumococcal disease (IPD) in the United States of America[a,b]

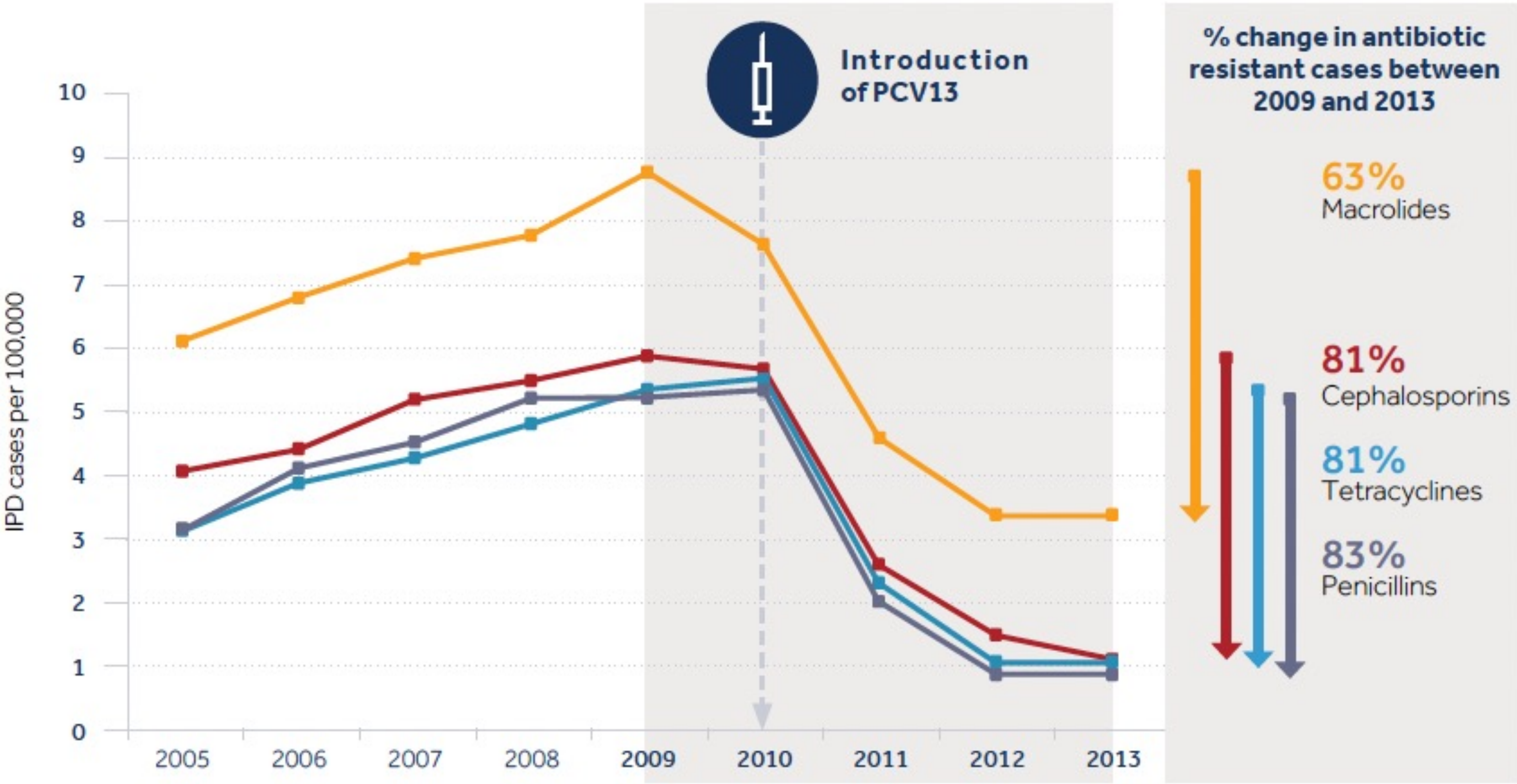
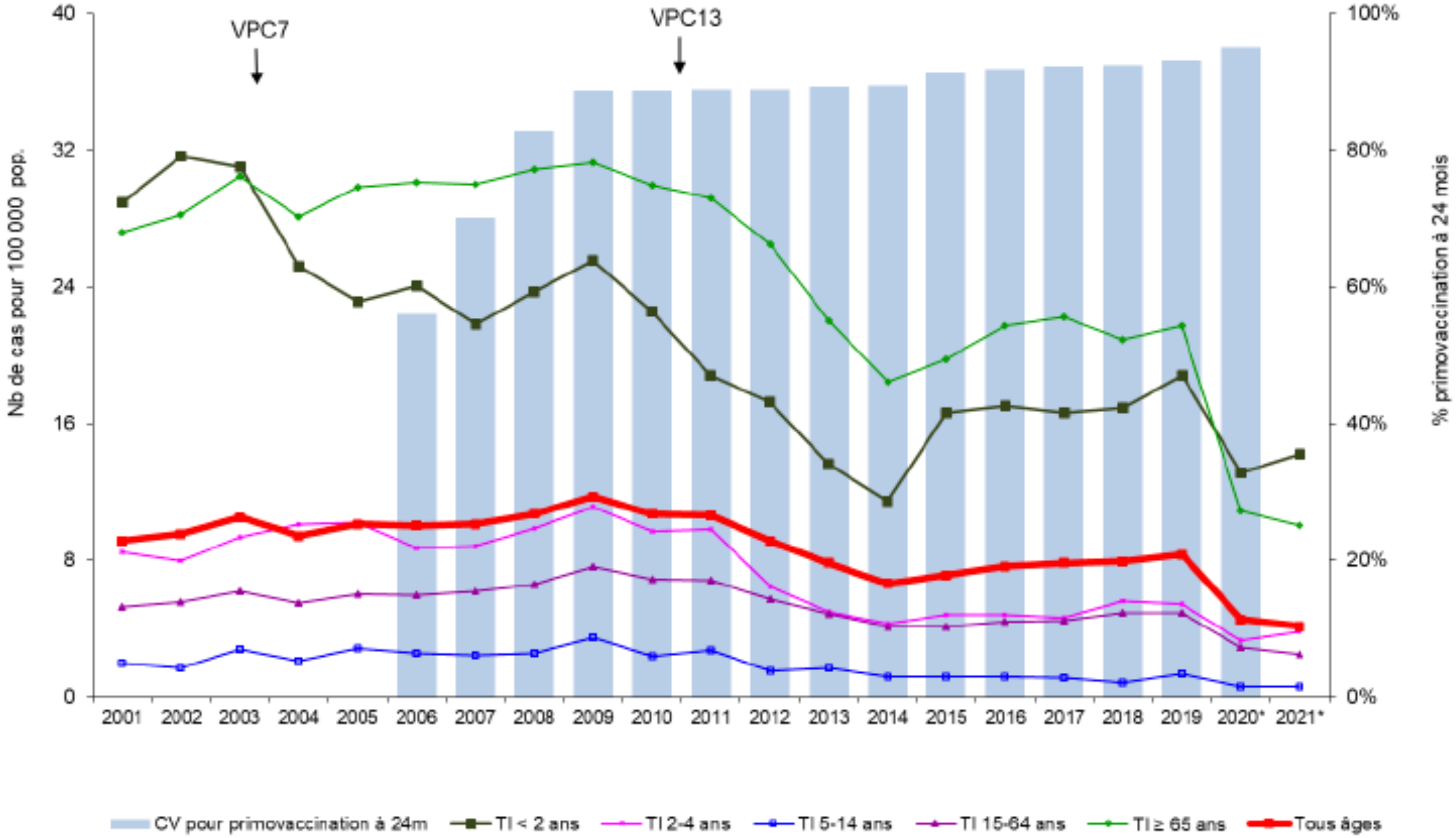
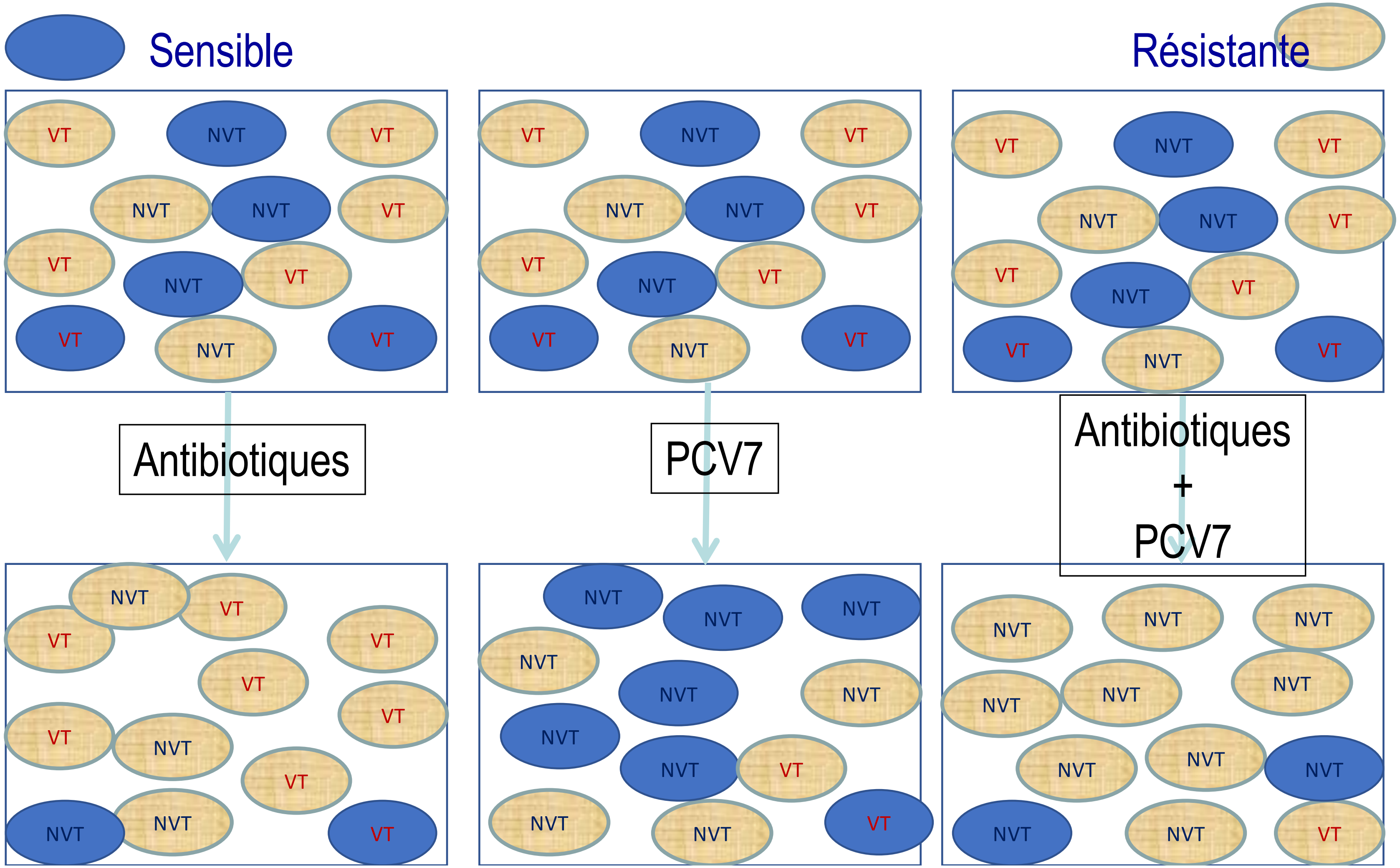


Figure 1. Évolution du taux d'incidence des infections invasives à pneumocoques par année selon l'âge, et évolution de la couverture vaccinale (CV) à l'âge de 24 mois, France métropolitaine, 2001-2021



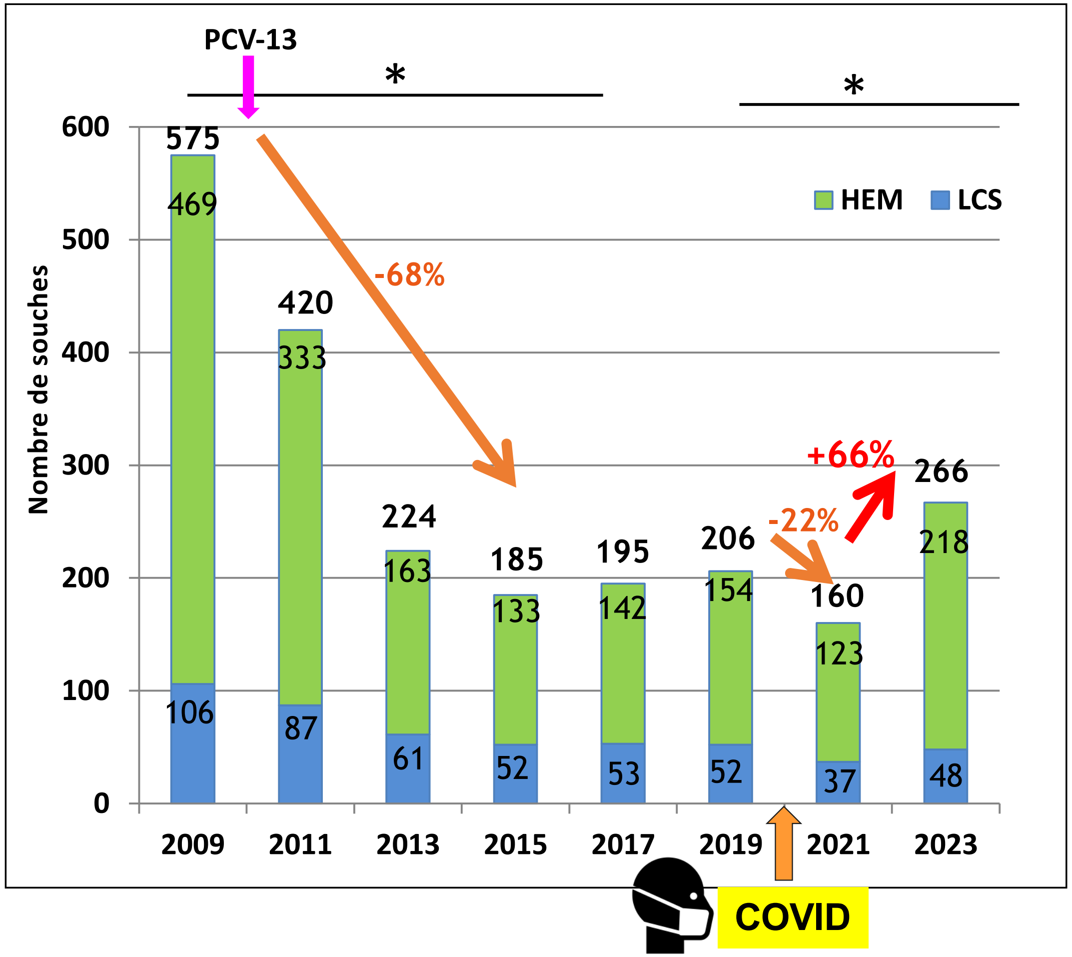
* 2020 et 2021 : contexte pandémique Covid-19 Source : Epibac, (estimations Santé publique France), certificats de santé du 24e mois (données Drees, traitement SpF)

D'après R. Cohen ACTIV

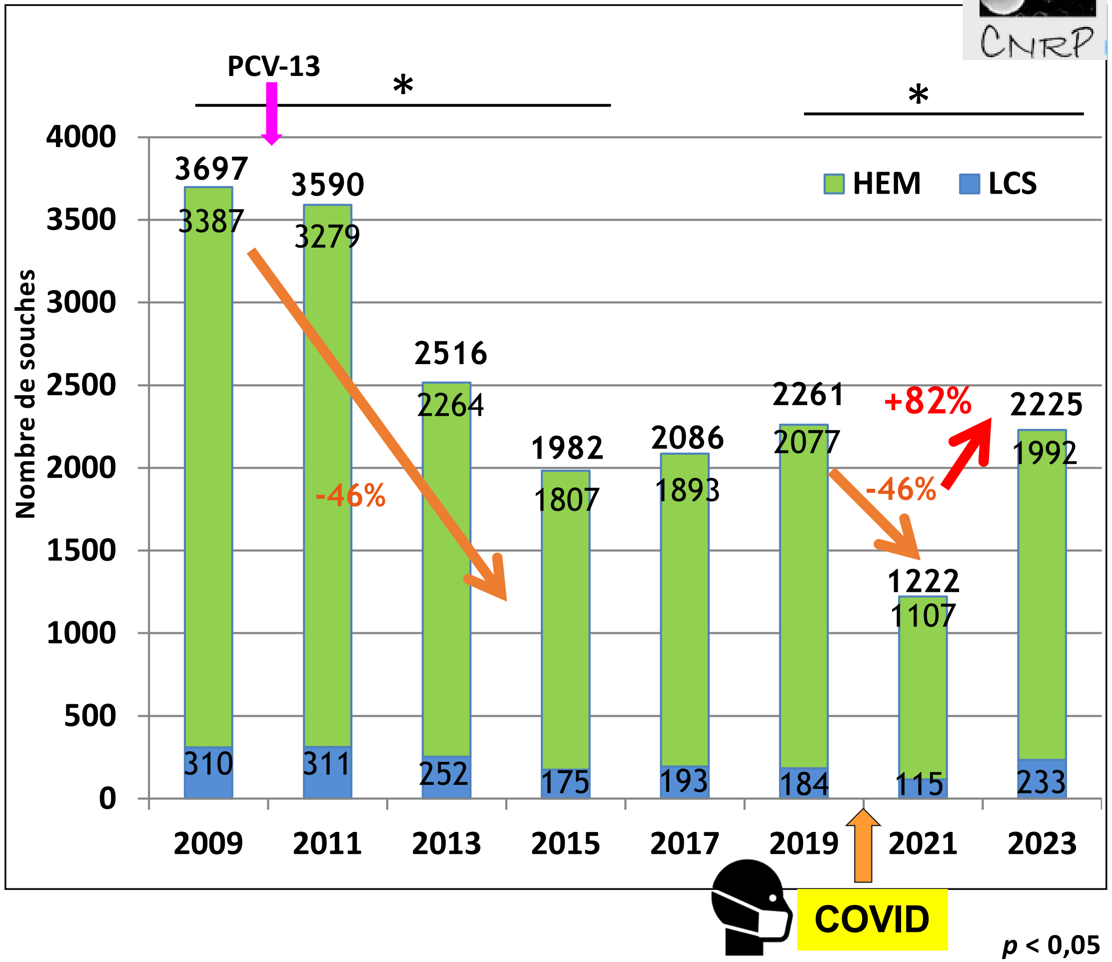


Répartition des souches de pneumocoque isolées d’infections invasives, selon l’âge

Enfants (N = 2231)



Adultes (N = 19579)

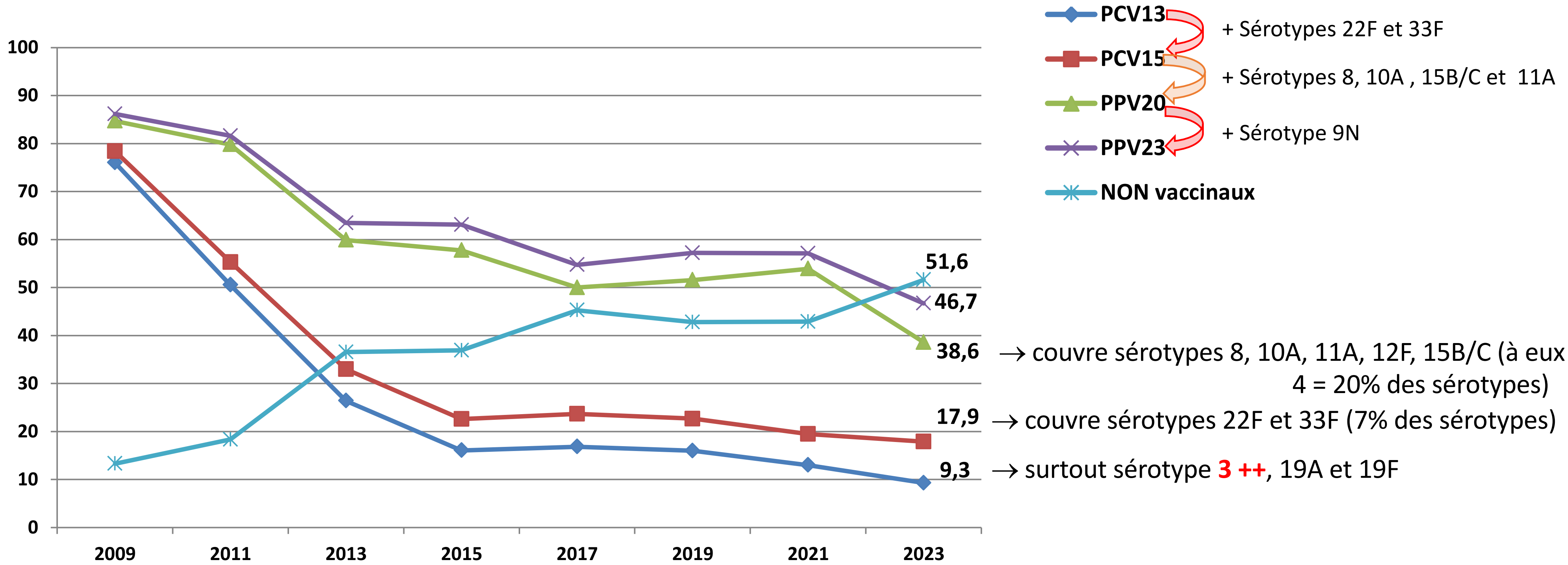


p < 0,05

Evolution de la part des sérotypes vaccinaux dans les LCR + HEM Enfants

n= 2060 souches

CNRP



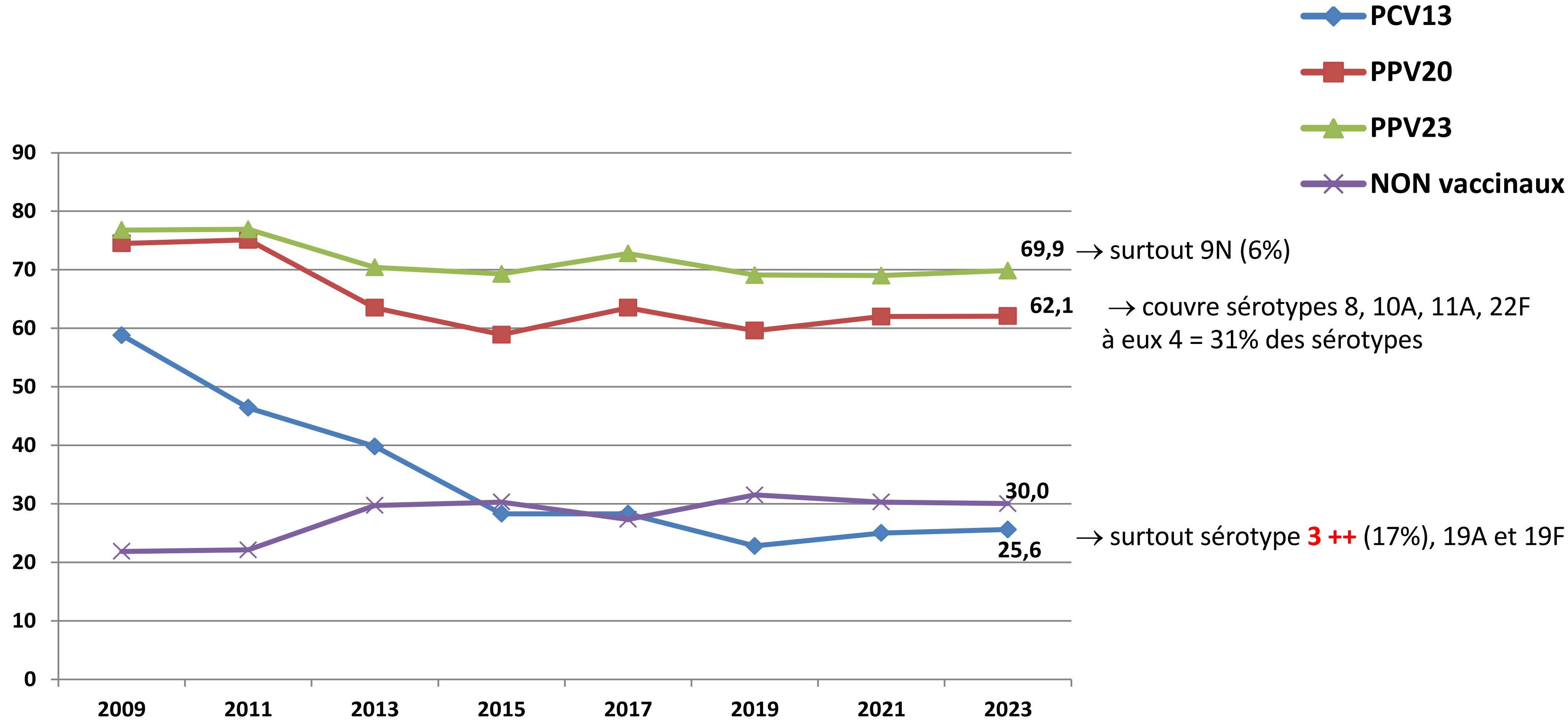
→ couvre sérotypes 8, 10A, 11A, 12F, 15B/C (à eux 4 = 20% des sérotypes)

→ couvre sérotypes 22F et 33F (7% des sérotypes)

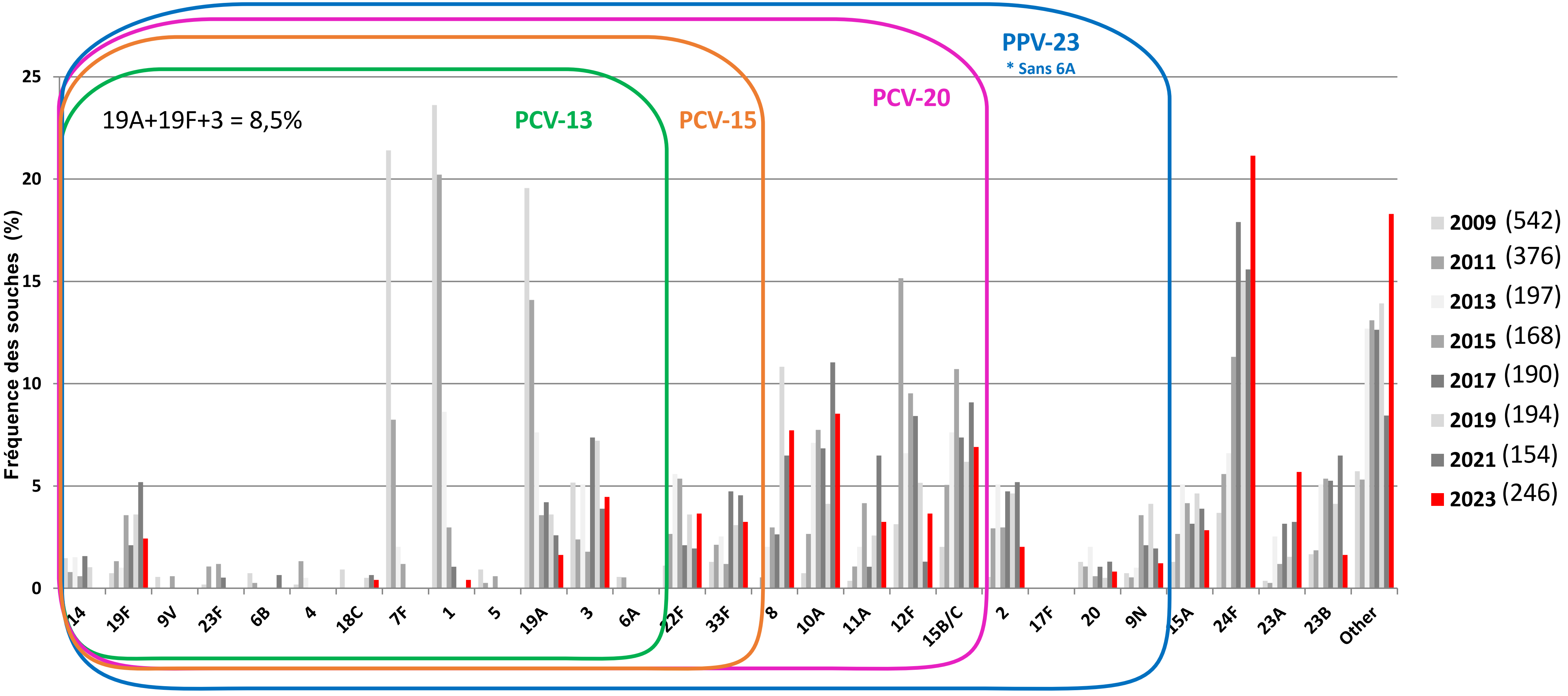
→ surtout sérotype **3 ++**, 19A et 19F

Evolution de la part des sérotypes vaccinaux dans les LCR + HEM Adultes

n= 7053 souches

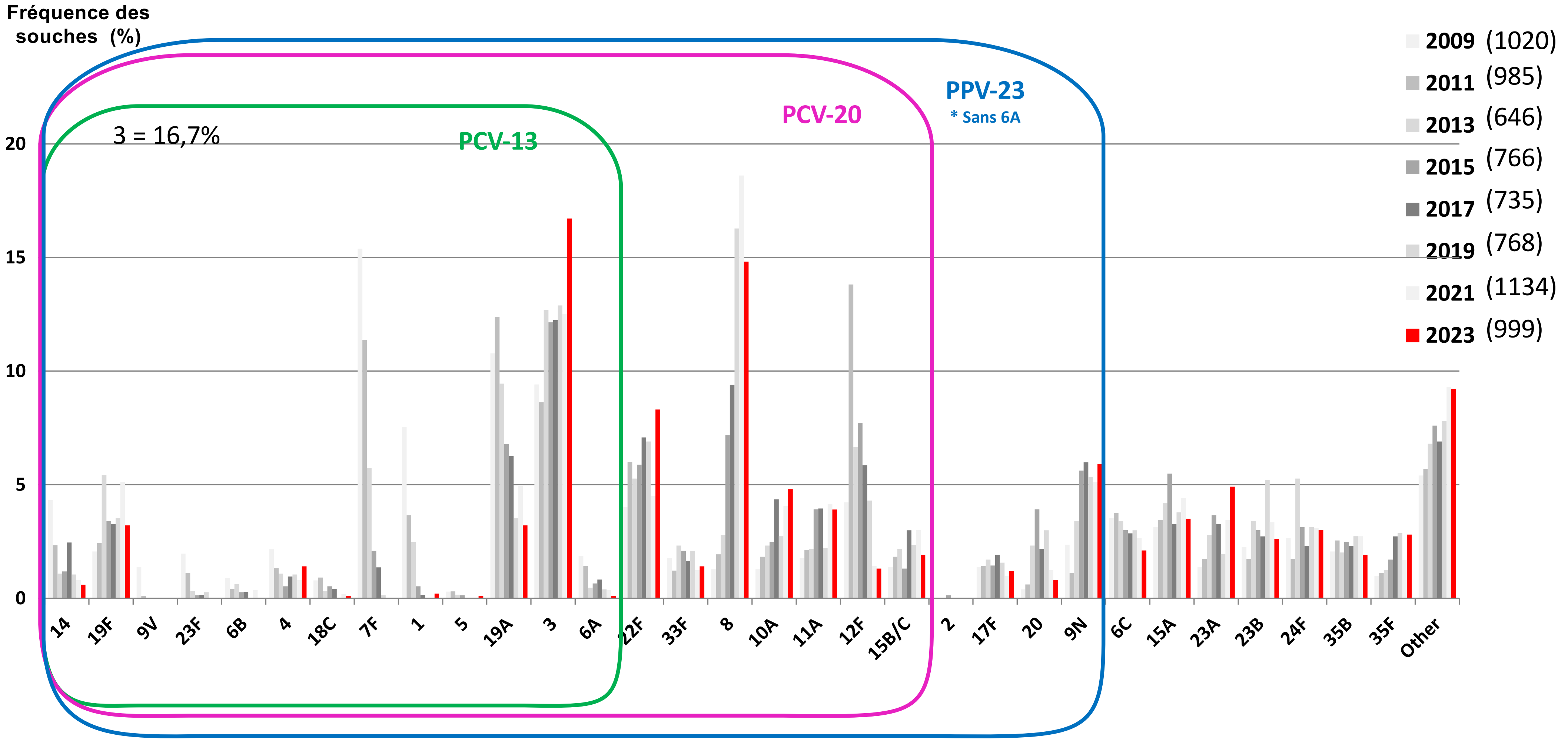


Evolution de la distribution des sérotypes – LCR + HEM enfants *(n= 2067)*



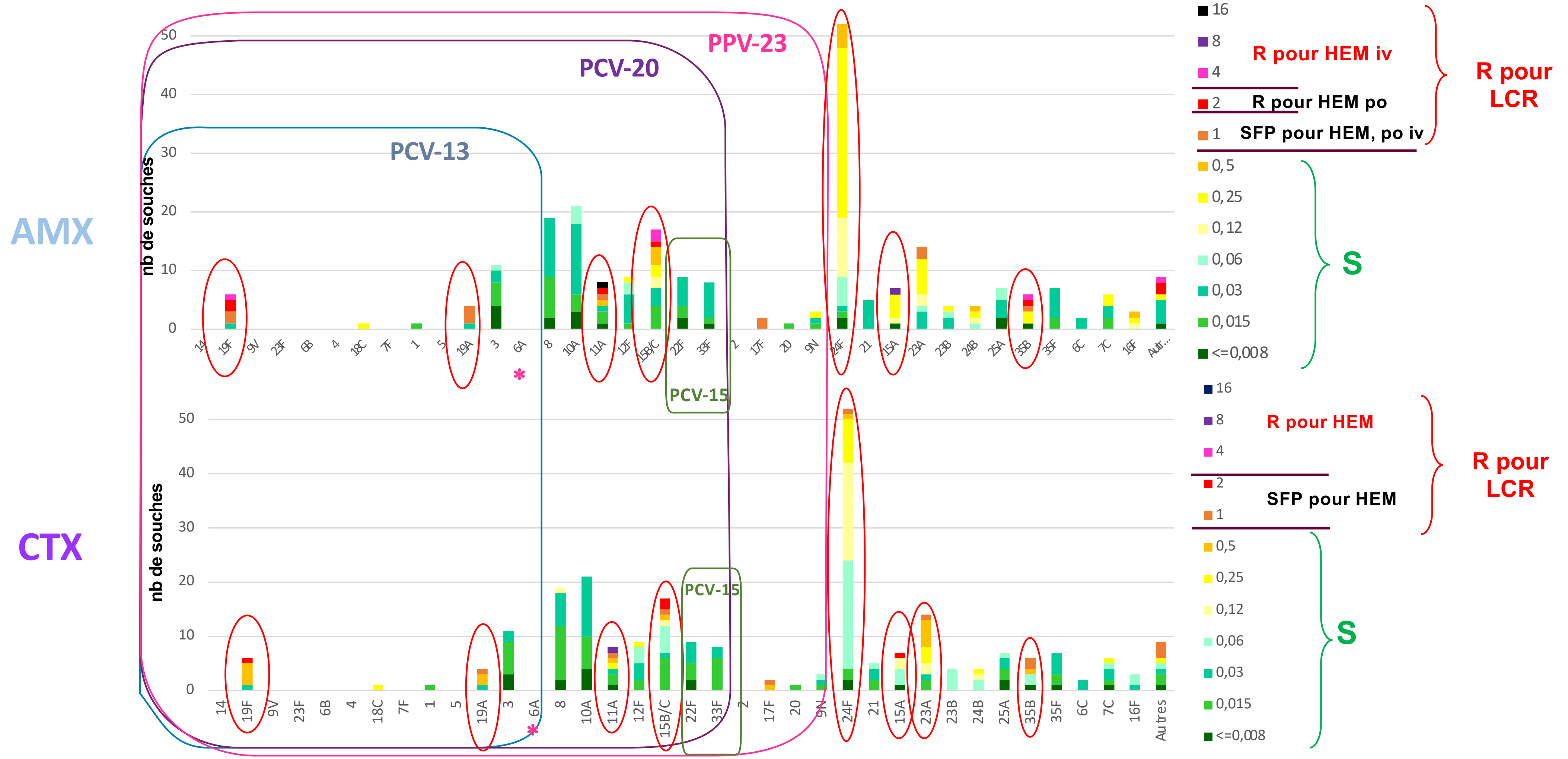
Evolution de la distribution des sérotypes – LCR + HEM adultes *(n= 7053)*

CNRP



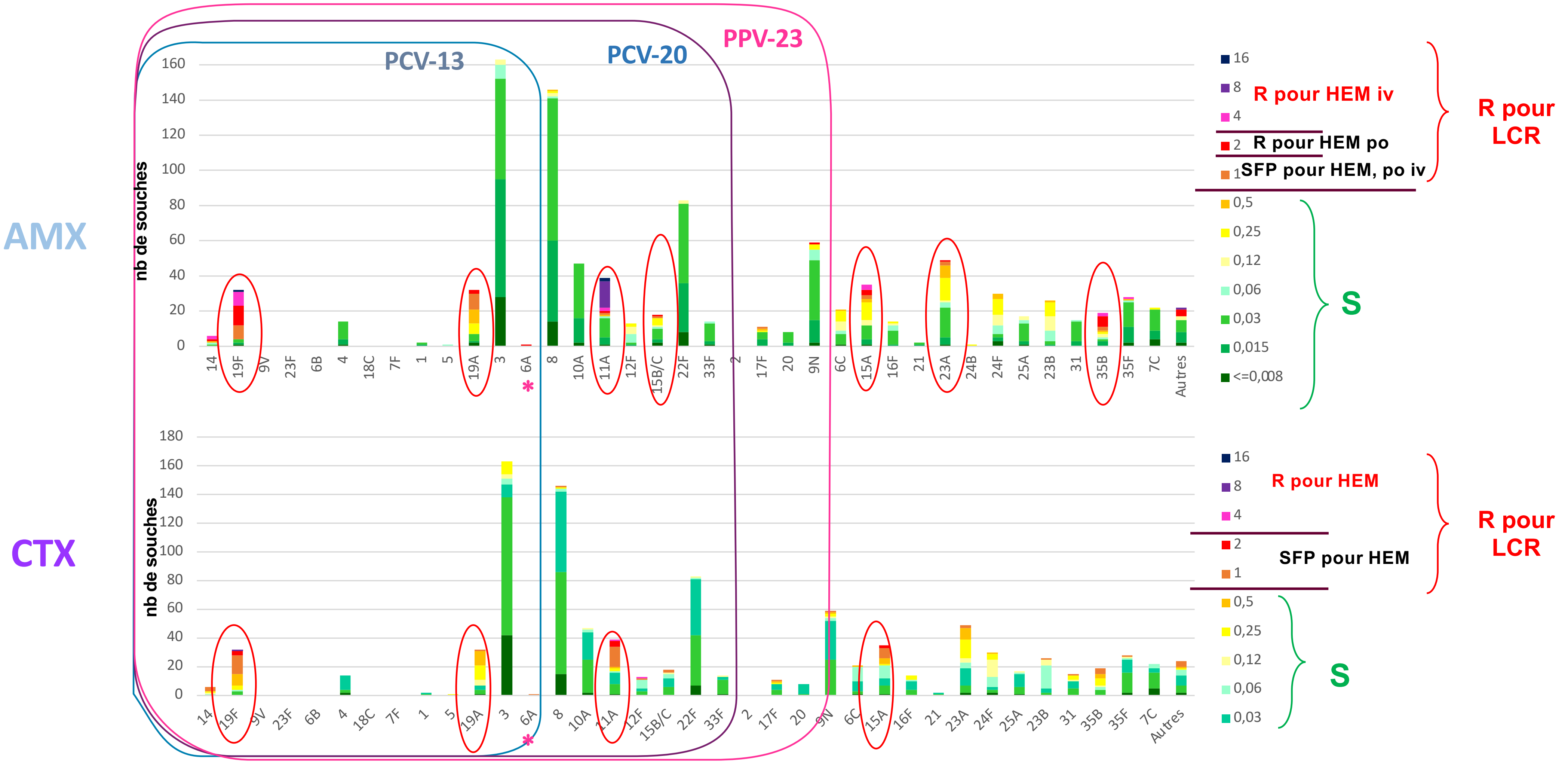
Relation entre sérotype et résistance, 2023 - LCR+HEM enfants

n= 246 souches



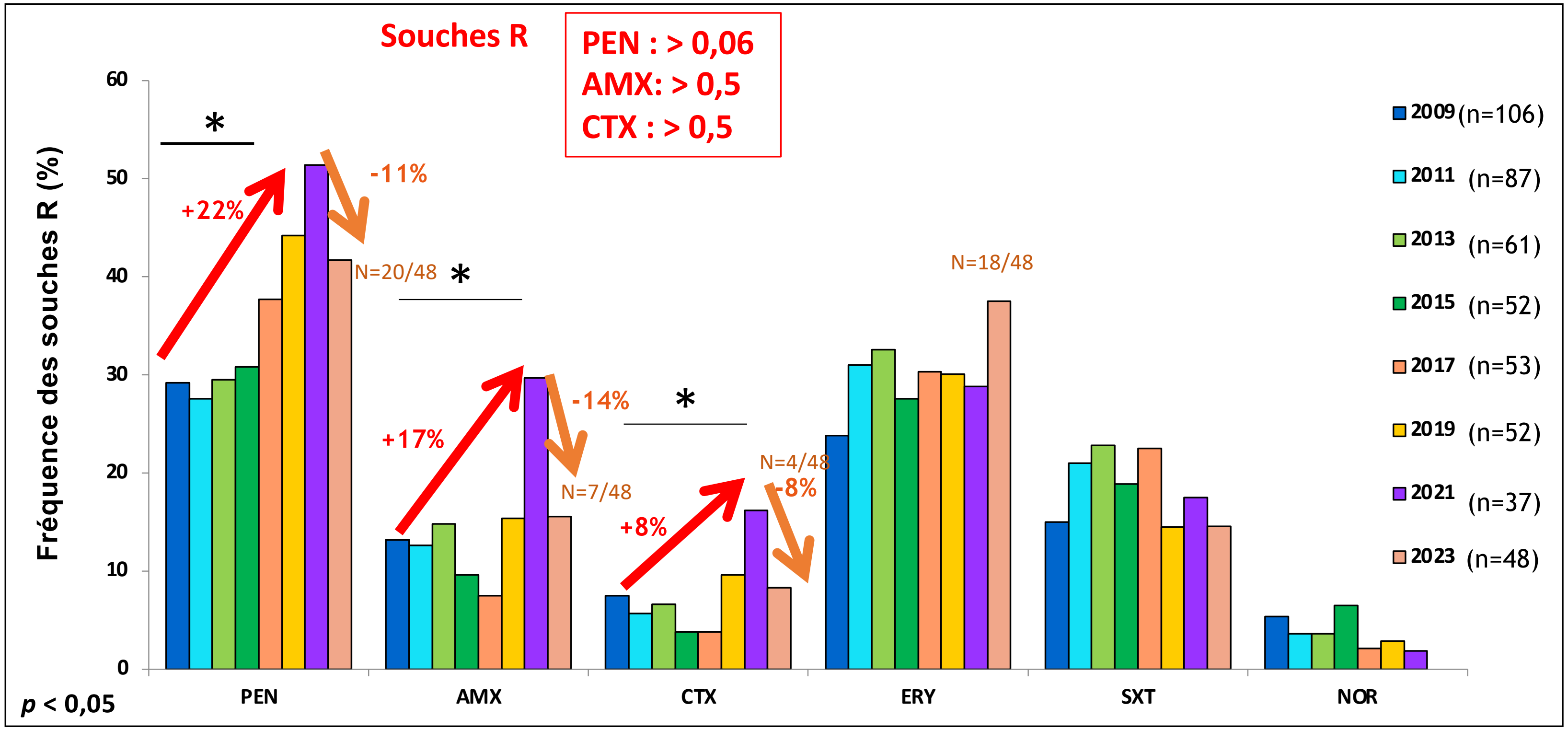
Relation entre sérotype et résistance, 2023 - LCR+HEM adultes

n= 999 souches



Résultats – Evolution de la résistance des souches de LCR chez l'enfant (n= 496)

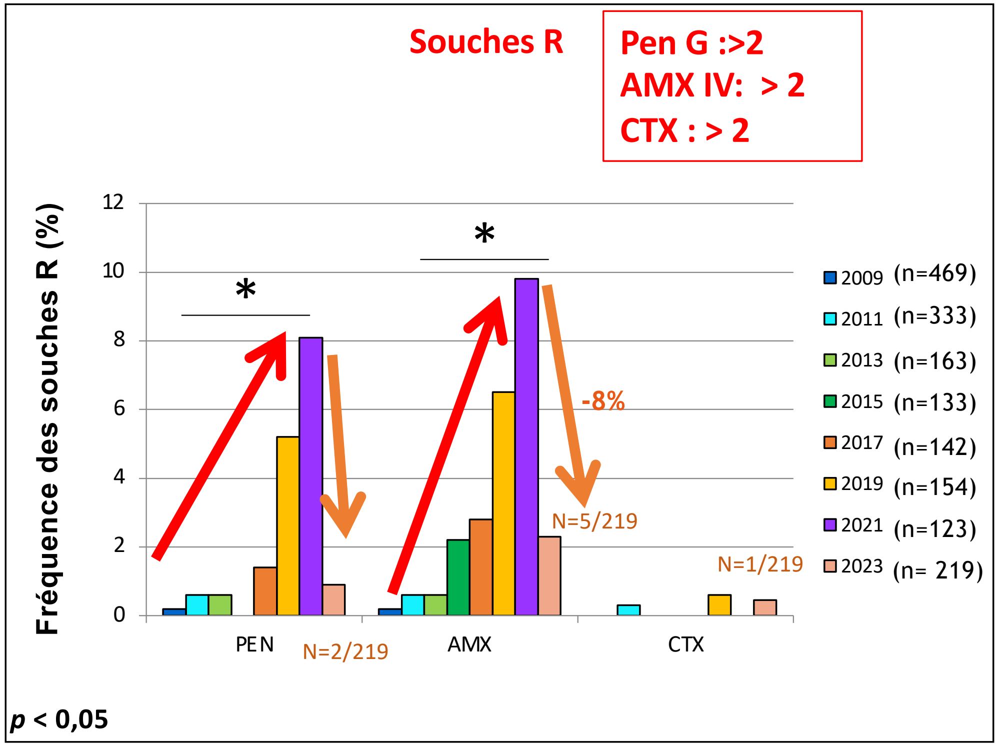
Interprétations selon le CA-SFM de juin 2023

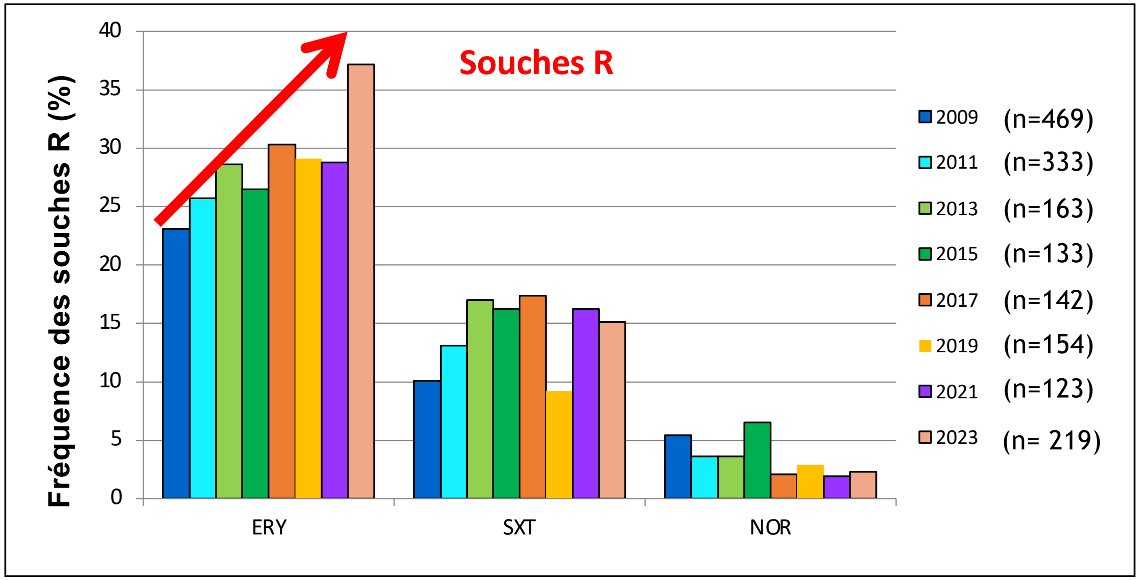


En 2023 : 7 souches R. à l'Amox (sérotypes 23A, 15B/C, 19F)
4 souches R. au CTX (sérotypes 23A, 15B/C)

Résultats – Evolution de la résistance des souches d'hémocultures chez l'enfant (n= 1736)

Interprétations selon la CA-SFM de juin 2023



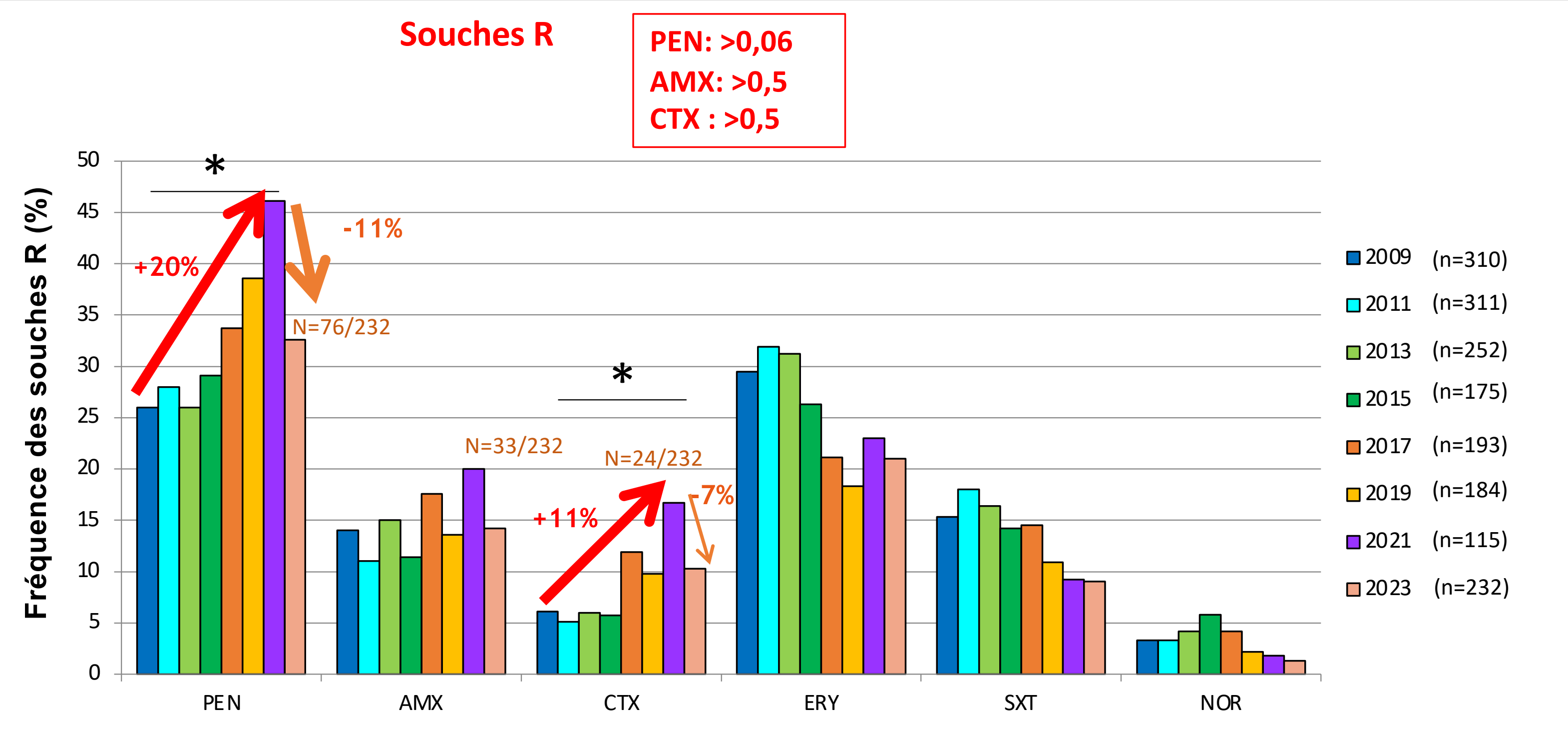


2023 : **5** souches **R. AMX iv** : dont 1 souche avec CMI = **8** mg/l (15A)
et 1 souche avec CMI = **16** mg/l (**11A**)

1 souche **R CTX** (avec CMI =**8** mg/L) (**11A**)

Résultats – Evolution de la résistance des souches de LCR chez l'adulte (n= 1540)

Interprétations selon le CA-SFM de juin 2023

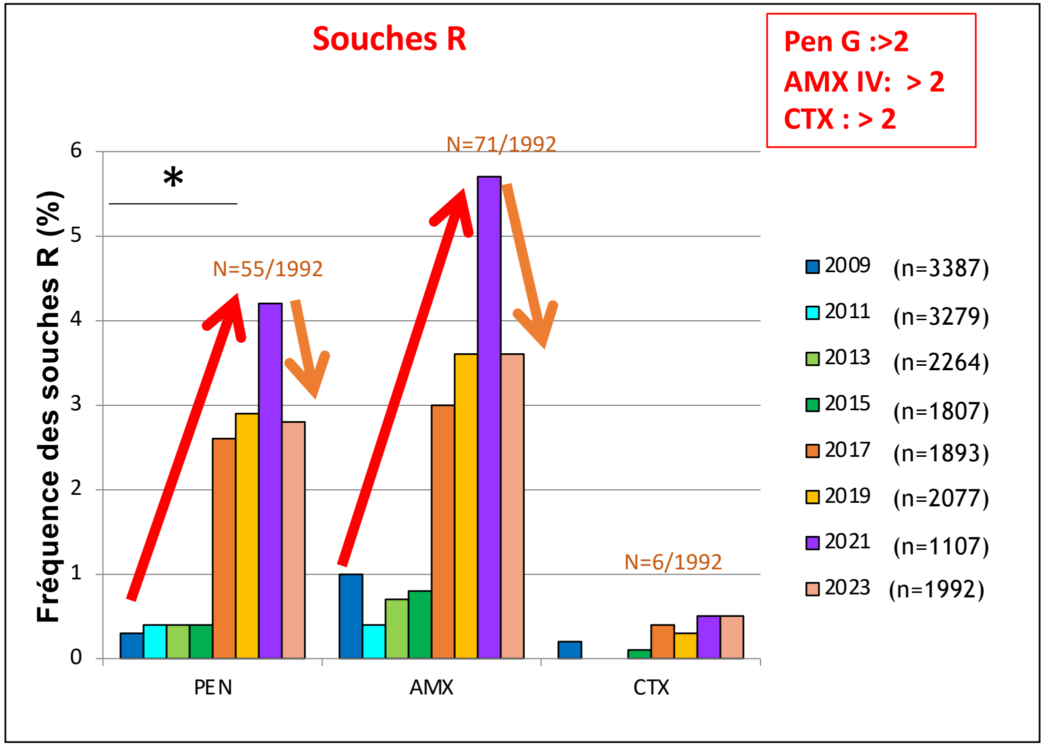


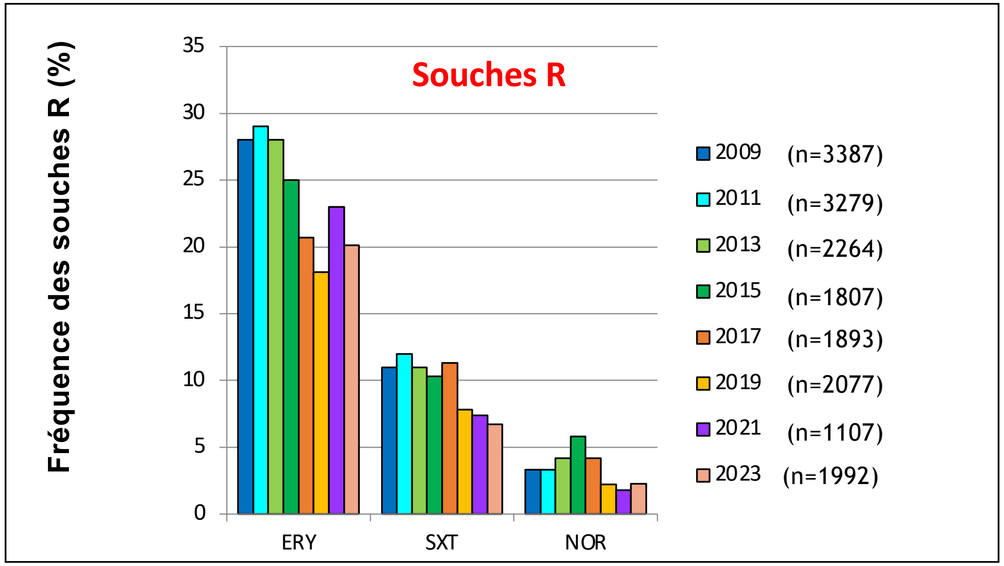
2023 : 33 souches R. AMX : dont 3 souches avec CMI = 8 mg/l (11A)
et 2 souches avec CMI = 16 mg/l (11A)

24 souches R CTX dont 1 avec CMI = 4 mg/L (12F)

Résultats – Evolution de la résistance des souches d'hémocultures chez l'adulte (n= 17 806)

Interprétations selon le CA-SFM de juin 2023





2023 : 71 souches R. AMX iv : dont 24 souches avec CMI = 8 mg/l (**11A** +++)
et 9 souches avec CMI = 16 mg/l (19F)

6 souches R CTX (CMI =8 mg/L) (19 F et **11A**)

Perspectives de développement

Microorganism	Number of vaccines in the pipeline	Status	Trial population	Technology Platform
C. difficile	3	Phase I (1) Phase II (1) Phase III (1)	Adults, Older Adults	Toxoid vaccine Protein subunit
***E. coli* (ExPEC)**[15]	1	Phase III	Older Adults	Glycoconjugate vaccine
K. pneumoniae	1	Phase I	Adults, Older Adults	Glycoconjugate vaccine
Shigella spp.	1	Phase II	Paediatric, Adults	Glycoconjugate vaccine
S. aureus	1	Phase II	Adults	Glycoconjugate vaccine
S. pneumoniae	4	Phase II (3) Phase III (1)	Paediatric, Adults, Older Adults	Protein subunit Glycoconjugate vaccine

Fig 1 – Vaccines under development tackling AMR

Micoli et al, Nature Reviews Microbiology, 2021
Vaccines Europe report, 2024

Vaccines and AMR: issues for the development

1. **Vaccine R&D is limited by the state of scientific knowledge and** insufficient bacterial genotype and serotype surveillance

- lack of immunological correlates of protection for some diseases
- complexity and high costs of target validation and proof of concept,
- absence of good animal models for research

2. R&D for vaccines is long, complex and carries high investments and risks, while market demand is sometimes limited

3. Clinical research is challenging for diseases that occur in specific risk groups or environments

- hospitalised elderly, immunocompromised individuals, neonates
- lack of clarity on the target population. For example, in HICs, K. pneumoniae is more likely to affect older and immunocompromised people, while in LMICs, it is neonates who are more likely to be affected by this infection

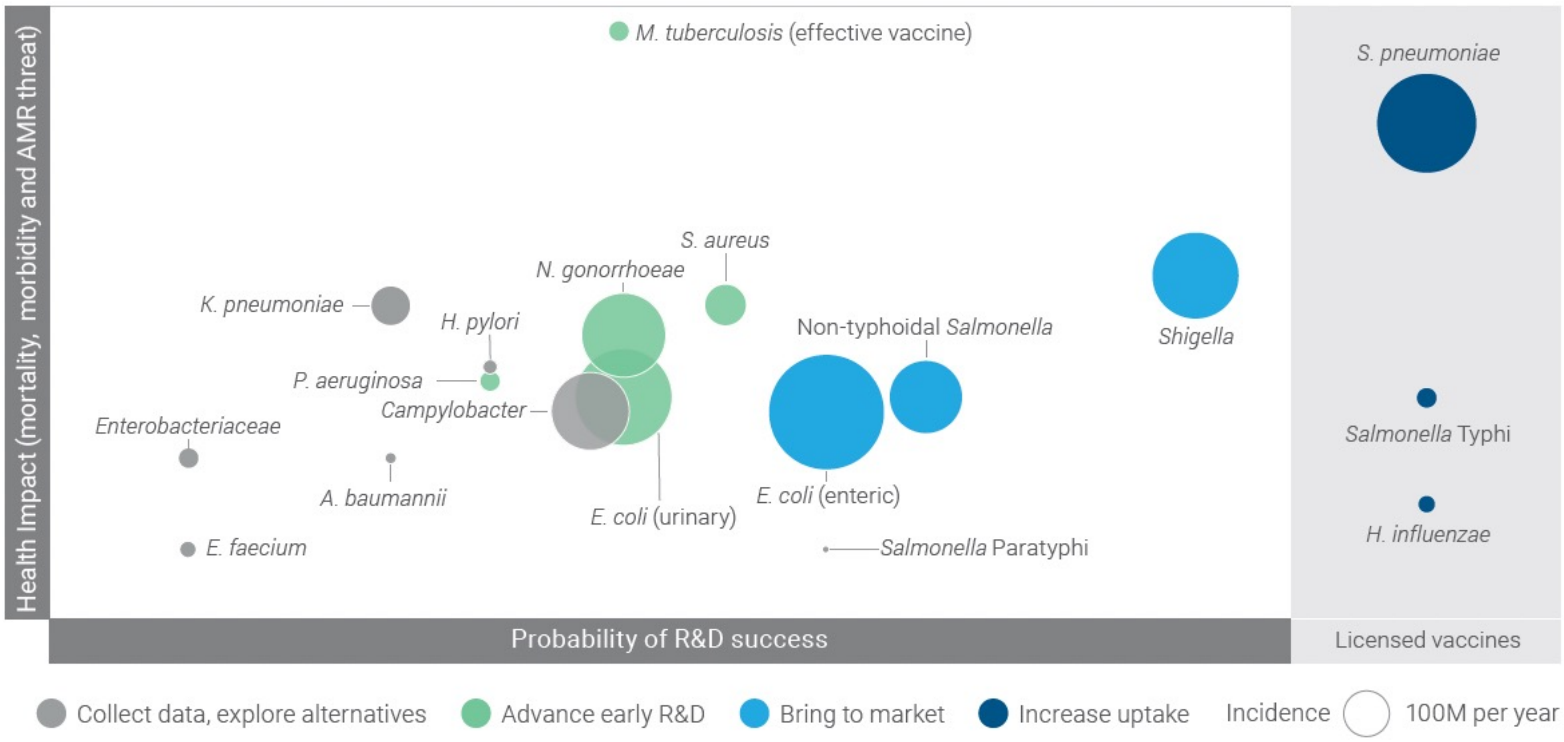
4. The technical, regulatory and HTA requirements are complex and contribute to higher investment needs and risks

- → **incentives tailored for AMR vaccines**

Vaccines Europe report, 2023

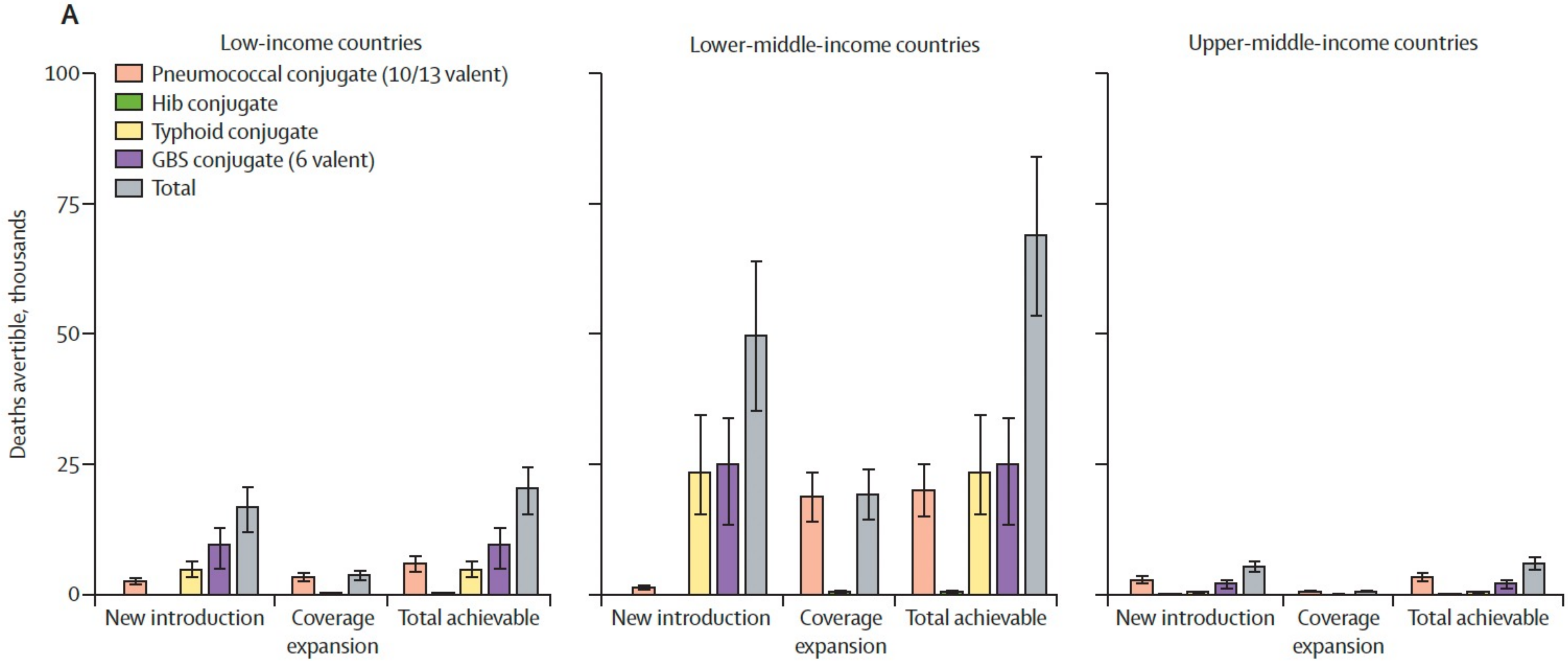
One Health Surveillance to prioritise interventions

PATHOGEN SEGMENTATION BASED ON ASSESSMENT CREATES CLUSTERS THAT CAN HELP PRIORITISE INTERVENTIONS



Vaccination against viruses and impact on AMR

- Vaccination against rotavirus → prevents 13.6 million antibiotic-treated disease episodes in children under the age of 5 in LMICs every year.
- Vaccination against influenza, varicella and dengue also have been shown to reduce antibiotic use
- Recent findings show that the administration of an RSV vaccine to pregnant mothers would reduce antimicrobial prescribing among their infants by 12.9% over the first 3 months of life
- Influenza vaccination → reduce use of antibiotics by as much as 64% in vaccinated individuals,



Lenward et al, 2024

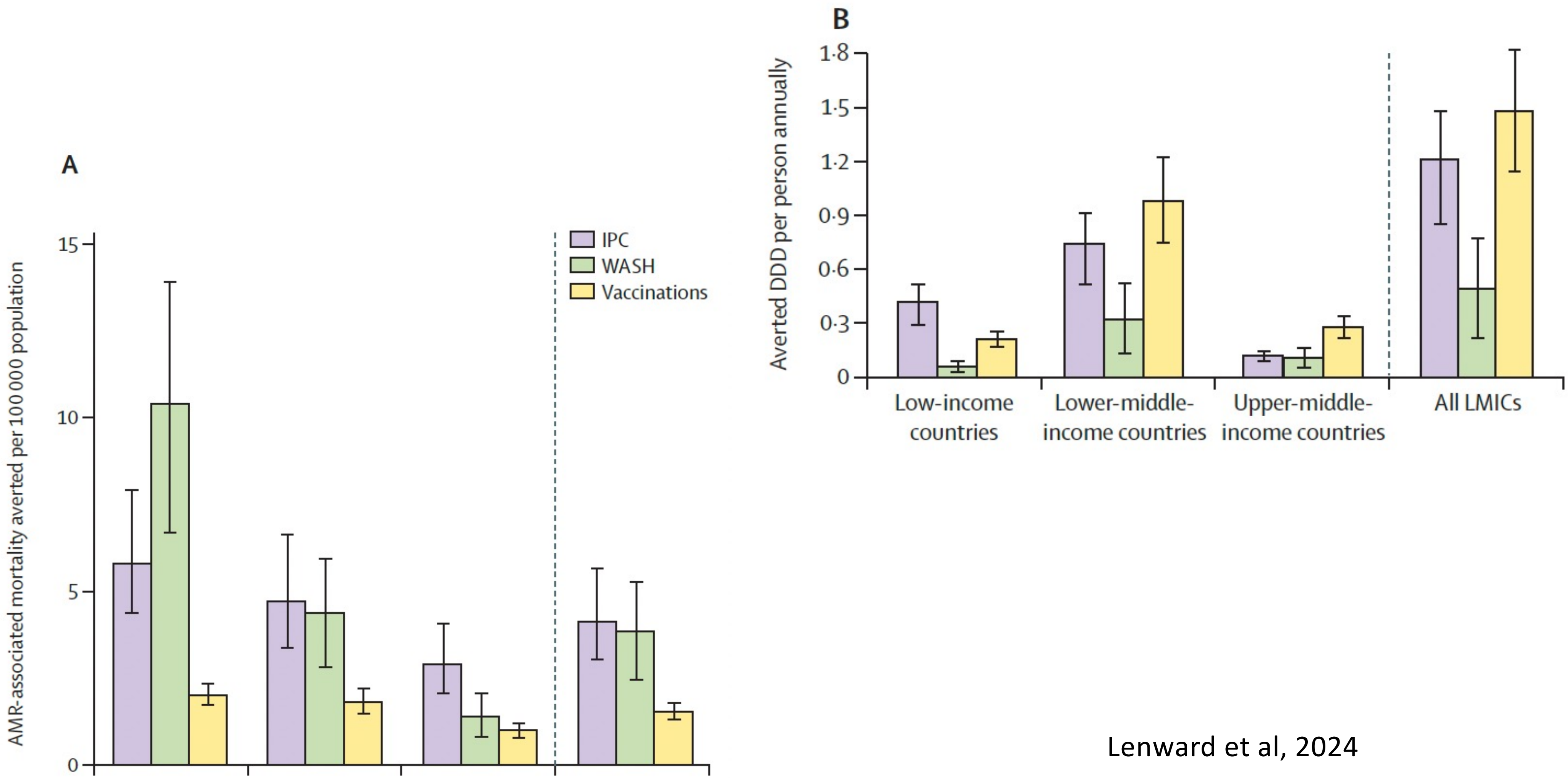
Lack of sanitation infrastructure and access to safe water

AMR is closely linked to poverty, lack of sanitation, poor hygiene and pollution.

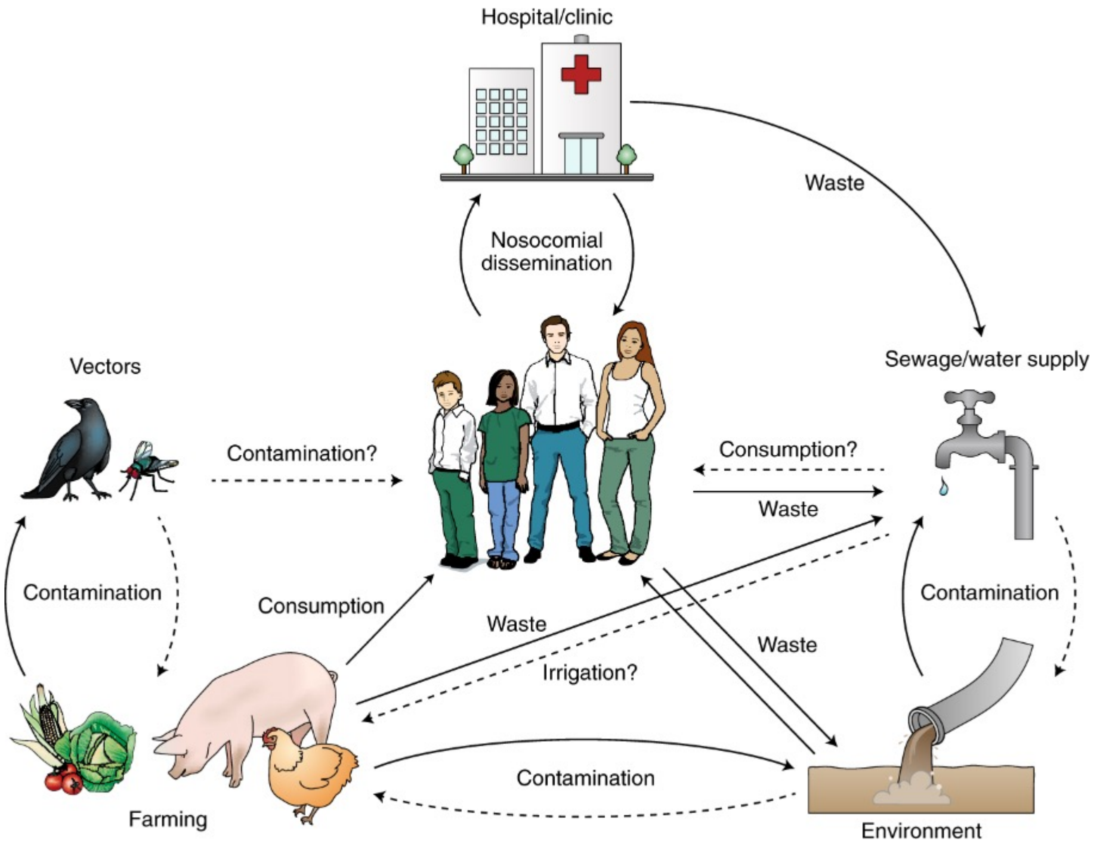
Low-income and lower-middle-income countries are the worst affected by AMR.

AMR also exacerbates inequities within societies.
Groups including women, children, migrants, refugees, people employed in certain sectors (e.g. agriculture or healthcare) and those living in poverty may be particularly vulnerable and/or more exposed to drug-resistant infections

UNEP report 2023



Lenward et al, 2024

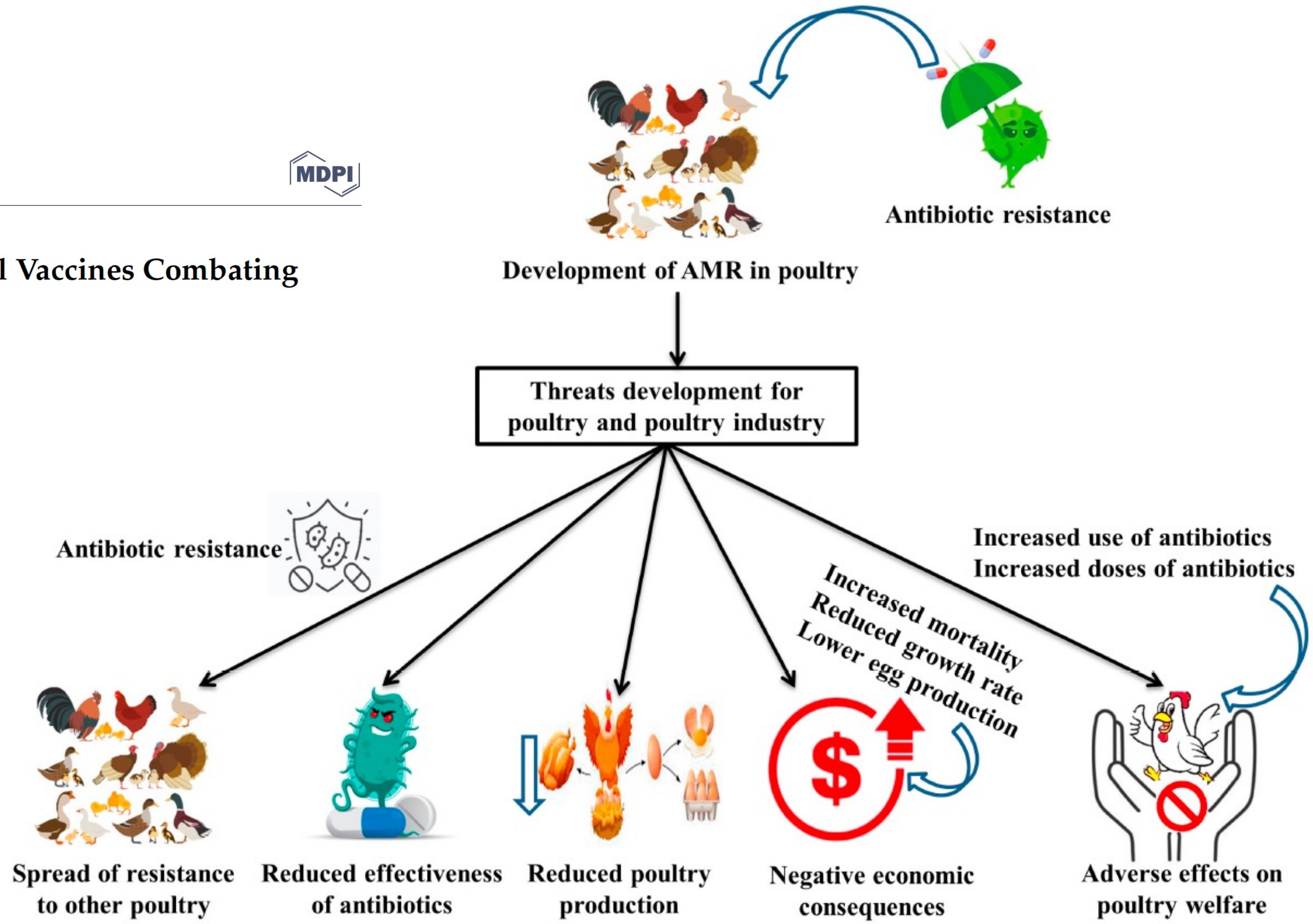

Hospital/clinic
Nosocomial dissemination
Waste
Sewage/water supply
Vectors
Contamination?
Consumption?
Waste
Contamination
Consumption
Waste
Irrigation?
Waste
Contamination
Contamination
Farming
Environment

vaccines

Review

A Comprehensive Review on Bacterial Vaccines Combating Antimicrobial Resistance in Poultry

Md. Saiful Islam and Md. Tanvir Rahman *



Practical Guidelines for National Procurement of Veterinary Vaccines

February 2024

World Organisation for Animal Health
Founded as OIE

https://www.woah.org/en/what-we-offer/veterinary-products/

Estimating the impact of vaccines in reducing antimicrobial resistance and antibiotic use

World Health Organization

WHO report 2024

High impact | Moderate impact | Low impact | Not assessed | No direct impact

Vaccine and its characteristics		Vaccine-averted deaths associated with AMR	Vaccine-averted DALYs associated with AMR	Vaccine-averted antibiotic use	Vaccine-averted hospital costs associated with AMR	Vaccine-averted productivity losses associated with AMR
SP_3	Serotype-specific vaccine against ***S. pneumoniae***, given to 90% of infants and the elderly, with 5-year efficacy of 25% for LRI and 58% for invasive pneumococcal disease	High impact	High impact	High impact	High impact	Moderate impact
SP_2	Serotype-specific vaccine against ***S. pneumoniae***, given to 90% of infants, with 5-year efficacy of 25% for LRI and 58% for invasive pneumococcal disease	High impact	High impact	Moderate impact	Moderate impact	Moderate impact
SP_1	Serotype-specific vaccine against ***S. pneumoniae***, given to 51% of infants (2019 coverage), with 5-year efficacy of 25% for LRI and 58% for invasive pneumococcal disease	Moderate impact	Moderate impact	Moderate impact	Moderate impact	Moderate impact
TB_1	Vaccine against pulmonary ***M. tuberculosis***, given to 70% of infants, with 10-year efficacy of 80% and subsequent boosting for lifelong protection	High impact	Moderate impact	High impact	High impact	Moderate impact
TB_2	Vaccine against pulmonary ***M. tuberculosis***, given to 70% of 10-year-olds, with 10-year efficacy of 50% and subsequent boosting for lifelong protection	High impact	Moderate impact	High impact	Moderate impact	Moderate impact
ST	Vaccine against ***S.* Typhi**, given to 70% of infants in high typhoid burden countries, with 15-year efficacy of 85%	Moderate impact	Moderate impact	High impact	Low impact	High impact
Hib_1	Vaccine against **Hib**, given to 74% of infants (2019), with 5-year efficacy of 93%	Low impact	Low impact	Moderate impact	Low impact	Low impact
Hib_2	Vaccine against **Hib**, given to 90% of infants, with 5-year efficacy of 93%	Low impact	Moderate impact	Moderate impact	Low impact	Low impact

High impact | Moderate impact | Low impact | Not assessed | No direct impact

Vaccine and its characteristics		Vaccine-averted deaths associated with AMR	Vaccine-averted DALYs associated with AMR	Vaccine-averted antibiotic use	Vaccine-averted hospital costs associated with AMR	Vaccine-averted productivity losses associated with AMR
Influenza_1	Seasonal maternal vaccine against **influenza**, given to 70% of pregnant women to protect neonates and infants, with 1-year efficacy of 70%	No direct impact	No direct impact	Moderate impact	Not assessed	No direct impact
Malaria	Vaccine against clinical ***P. falciparum***, given to 70% of infants, with 4-year efficacy of 40%	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
Rotavirus	Oral, live attenuated vaccine against **rotavirus**, given to 90% of infants, with 2-year efficacy of 60%	No direct impact	No direct impact	Moderate impact	No direct impact	No direct impact
RSV_2	Vaccine against severe **RSV**, given to 70% of infants, with 2-year efficacy of 70%	No direct impact	No direct impact	Moderate impact	No direct impact	No direct impact
RSV_1	Vaccine against severe **RSV**, given to 70% of infants through maternal vaccination, with 6-month efficacy of 70%	No direct impact	No direct impact	Low impact	No direct impact	No direct impact
NG	Vaccine against ***N. gonorrhoeae***, given to 70% of adolescents, with 10-year efficacy of 70%	Not assessed	Low impact	Not assessed	Not assessed	Not assessed

Fig. B. The estimated and potential annual impact on AMR of vaccines with medium feasibility of development and implementation

High impact · Not assessed · Moderate impact · No direct impact · Low impact

Vaccine and its characteristics		Vaccine-averted deaths associated with AMR	Vaccine-averted DALYs associated with AMR	Vaccine-averted antibiotic use	Vaccine-averted hospital costs associated with AMR	Vaccine-averted productivity losses associated with AMR
ExPEC_3	Vaccine against urinary tract **ExPEC**, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Low impact	Low impact	High impact	High impact	Low impact
ExPEC_1	Vaccine against bloodstream **ExPEC**, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Low impact	Low impact	Low impact	Low impact	Low impact
KP_1	Vaccine against bloodstream ***K. pneumoniae***, given to 70% of infants through maternal vaccination, with 6-month efficacy of 70%	Moderate impact	Moderate impact	Low impact	Moderate impact	Moderate impact
GAS	Vaccine against **GAS**, given to 70% of infants, with 5-year efficacy of 70%	Low impact	Low impact	High impact	High impact	Low impact
Shigella	Vaccine against moderate to severe diarrhoea caused by ***Shigella***, given to 70% of infants, with 5-year efficacy of 60%	Low impact	Low impact	Moderate impact	High impact	Low impact
ETEC	Vaccine against moderate to severe diarrhoea caused by **ETEC**, given to 70% of infants, with 5-year efficacy of 60%	Low impact	Low impact	Moderate impact	High impact	Low impact
PA_1	Vaccine against bloodstream and lower respiratory tract ***P. aeruginosa***, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Low impact	Low impact	Moderate impact	Moderate impact	Low impact
NTS	Vaccine against **nontyphoidal *Salmonella***, given to 70% of infants, with 5-year efficacy of 80%	Low impact	Low impact	Low impact	High impact	Low impact
CJ	Vaccine against ***C. jejuni***, given to 70% of infants, with 5-year efficacy of 70%	Not assessed	Not assessed	Low impact	Not assessed	Not assessed
HP	Vaccine against ***H. pylori***, given to 70% of infants, with 5-year efficacy of 70%	Not assessed	Not assessed	Low impact	Not assessed	Not assessed
Norovirus	Vaccine against **norovirus**, given to 70% of infants, with 5-year efficacy of 50%	No direct impact	No direct impact	Low impact	No direct impact	No direct impact

High impact · Not assessed · Moderate impact · No direct impact · Low impact

Fig. C. Estimated and potential annual impact on AMR of vaccines with a low feasibility of development and implementation

High impact | Not assessed | Moderate impact | No direct impact | Low impact

	Vaccine and its characteristics	Vaccine-averted deaths associated with AMR	Vaccine-averted DALYs associated with AMR	Vaccine-averted antibiotic use	Vaccine-averted hospital costs associated with AMR	Vaccine-averted productivity losses associated with AMR
KP_3	Vaccine against ***K. pneumoniae***, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	High impact	High impact	High impact	High impact
KP_2	Vaccine against ***K. pneumoniae***, given to 70% of infants and the elderly, with 5-year efficacy of 70%	High impact	Moderate impact	High impact	High impact	Moderate impact
ExPEC_6	Vaccine against **ExPEC**, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	High impact	High impact	High impact	High impact
ExPEC_5	Vaccine against **ExPEC**, given to 70% of infants and the elderly, with 5-year efficacy of 70%	High impact	Moderate impact	High impact	High impact	Moderate impact
ExPEC_2	Vaccine against bloodstream **ExPEC**, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	Moderate impact	Moderate impact	High impact	Moderate impact
ExPEC_4	Vaccine against urinary tract **ExPEC**, given to 70% of all at risk of infection, with 5-year efficacy of 70%	Moderate impact	Moderate impact	High impact	High impact	Moderate impact
SP_4	Non-serotype-specific vaccine against ***S. pneumoniae***, given to 90% of infants and the elderly, with 5-year efficacy of 50% for LRI and 70% for invasive pneumococcal disease	High impact	High impact	High impact	High impact	High impact
SA_2	Vaccine against ***S. aureus***, given to 70% of all at risk of ww, with 5-year efficacy of 60%	High impact	High impact	High impact	High impact	High impact
SA_1	Vaccine against ***S. aureus***, given to 70% of infants and the elderly, with 5-year efficacy of 60%	High impact	Moderate impact	High impact	High impact	Moderate impact
AB_4	Vaccine against ***A. baumannii***, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	High impact	High impact	High impact	High impact
AB_2	Vaccine against bloodstream ***A. baumannii***, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	Moderate impact	Moderate impact	High impact	High impact

High impact | Not assessed | Moderate impact | No direct impact | Low impact

	Vaccine and its characteristics	Vaccine-averted deaths associated with AMR	Vaccine-averted DALYs associated with AMR	Vaccine-averted antibiotic use	Vaccine-averted hospital costs associated with AMR	Vaccine-averted productivity losses associated with AMR
AB_3	Vaccine against ***A. baumannii***, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Moderate impact	Moderate impact	Moderate impact	Moderate impact	Low impact
AB_1	Vaccine against bloodstream ***A. baumannii***, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Low impact	Low impact	Low impact	Low impact	Low impact
PA_2	Vaccine against bloodstream and LRI ***P. aeruginosa***, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	Moderate impact	High impact	High impact	High impact
EF_2	Vaccine against ***E. faecium***, given to 70% of all at risk of infection, with 5-year efficacy of 70%	High impact	Moderate impact	High impact	High impact	Moderate impact
EF_1	Vaccine against ***E. faecium***, given to 70% of infants and the elderly, with 5-year efficacy of 70%	Low impact	Low impact	Low impact	High impact	Moderate impact
SPara	Vaccine against ***S.* Paratyphi A**, given to 70% of infants in high typhoid burden countries, with 5-year efficacy of 70%	Low impact	Low impact	Low impact	Low impact	Low impact
Influenza_2	Universal vaccine against **type A influenza**, given to 70% of infants and the elderly, with 5-year efficacy of 70%	No direct impact	No direct impact	High impact	Not assessed	No direct impact
CD	Vaccine against ***C. difficile***, given to 70% of adults aged 45 years, with 5-year efficacy of 70%	Not assessed	Not assessed	Low impact	Not assessed	Not assessed

Fig. 5. Visuals from the International Vaccine Institute's advocacy campaign about the contribution of vaccines in the fight against AMR[a]

[a] International Vaccine Institute. IVI: World antibiotic awareness week 2019 [Internet]. 2019 [cited 2020 Feb 26]. Available from: https://www.ivi.int/world-antibiotic-awareness-week-2019/

Conclusion

1. Expanding use of licensed vaccines to maximize impact on AMR

2. Developing new vaccines that contribute to prevention and control of AMR

3. Expanding and sharing knowledge of vaccine impact on AMR