

Ruolo e importanza delle vaccinazioni dell'anziano e del fragile per contrastare l'AMR

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21 novembre 2024
Ministero della Salute

Il Forum Prevenzione vaccinale dell'anziano e del fragile
Programmi e obiettivi governativi, modelli organizzativi sul territorio, strategie di comunicazione

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Conflitti di interesse



Nessuno

La resistenza agli antimicrobici (AMR) è una minaccia per la salute globale

Strategie globali di contrasto dell'AMR:

- Uso appropriato degli antibiotici
- uso di test diagnostici rapidi ed efficaci
- implementazione della sorveglianza e dei sistemi di monitoraggio
- riduzione degli antibiotici in agricoltura e nell'ambiente
- riduzione della trasmissione di agenti patogeni e di infezioni
 - misure di prevenzione e controllo delle infezioni
 - **aumento della copertura vaccinale dei vaccini esistenti**
 - **sviluppo di vaccini futuri contro ceppi batterici resistenti**

Due facce ...

Prevenzione



Infezione da trattare

Non è un tema così nuovo

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Review

Impact of vaccines on antimicrobial resistance

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A B S T R A C T

Drivers of antimicrobial resistance: Antibiotic use drives the development and spread of resistant bacterial infections. Antimicrobial resistance (AMR) has become a prolific global issue, due to significant increases in antibiotic use in humans, livestock and agriculture, inappropriate use (under-dosing and over-prescribing), and misuse of antibiotics (for viral infections where they are ineffective). Fewer new antibiotics are being developed.

The problem of AMR: AMR is now considered a key threat to global health, leading to more mortality and increased healthcare costs threatening future conduct of routine medical procedures. Traditional approaches to address AMR include antibiotic stewardship, better hygiene/infection control, promoting antibiotic research and development, and restricting use for agricultural purposes.

Vaccines as a tool to reduce AMR: While antibiotic development is declining, vaccine technology is growing. This review shows how vaccines can decrease AMR by preventing bacterial and viral infections, thereby reducing the use/misuse of antibiotics, and by preventing antibiotic-resistant infections. Vaccines are less likely to induce resistance. Some future uses and developments of vaccines are also discussed.

Conclusions: Vaccines, along with other approaches, can help reduce AMR by preventing (resistant) infections and reducing antibiotic use. Industry and governments must focus on the development of novel vaccines and drugs against resistant infections to successfully reduce AMR. A graphical abstract is available online.



Review > Front Immunol. 2020 Jun 3;11:1048. doi: 10.3389/fimmu.2020.01048. eCollection 2020.

Vaccines Against Antimicrobial Resistance

Roberto Rosini¹, Sonia Nicchi^{1,2}, Mariagrazia Pizza¹, Rino Rappuoli^{1,3,4}

Affiliations + expand

PMID: 32582169 PMCID: PMC7283535 DOI: 10.3389/fimmu.2020.01048

Erratum in

Corrigendum: Vaccines Against Antimicrobial Resistance.

Rosini R, Nicchi S, Pizza M, Rappuoli R.

Front Immunol. 2020 Jul 21;11:1578. doi: 10.3389/fimmu.2020.01578. eCollection 2020.

PMID: 32849536 Free PMC article.

Abstract

In the last century, life expectancy has increased considerably, thanks to the introduction of antibiotics, hygiene and vaccines that have contributed to the cure and prevention of many infectious diseases. The era of antimicrobial therapy started in the nineteenth century with the identification of chemical compounds with antimicrobial properties. However, immediately after the introduction of these novel drugs, microorganisms started to become resistant through different strategies. Although resistance mechanisms were already present before antibiotic introduction, their large-scale use and mis-use have increased the number of resistant microorganisms. Rapid spreading of mobile elements by horizontal gene transfer such as plasmids and integrative conjugative elements (ICE) carrying multiple resistance genes has dramatically increased the worldwide prevalence of relevant multi drug-resistant human pathogens such as *Staphylococcus aureus*, *Neisseria gonorrhoeae*, and *Enterobacteriaceae*. Today, antimicrobial resistance (AMR) remains one of the major global concerns to be addressed and only global efforts could help in finding a solution. In terms of magnitude the economic impact of AMR is estimated to be comparable to that of climate global change in 2030. Although antibiotics continue to be essential to treat such infections, non-antibiotic therapies will play an important role in limiting the increase of antibiotic resistant microorganisms. Among non-antibiotic strategies, vaccines and therapeutic monoclonal antibodies (mAbs) play a strategic role. In this review, we will summarize the evolution and the mechanisms of antibiotic resistance, and the impact of AMR on life expectancy and economics.

Keywords: antimicrobial resistance (AMR); infectious diseases; mechanisms of antibiotic resistance; vaccine development; vaccines; vaccinology.

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 9, 2142–2149
<https://doi.org/10.1080/21645515.2018.1476814>

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Taylor & Francis Group

MINI-REVIEW

OPEN ACCESS



The role of vaccines in fighting antimicrobial resistance (AMR)

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ABSTRACT

The problem of antimicrobial resistance (AMR) and the associated morbidity and mortality due to antibiotic resistant bacterial pathogens is not new. However, AMR has been increasing at an alarming rate with appearances of diseases caused by bacteria exhibiting resistance to not just one but multiple classes of antibiotics. The World Health Organization (WHO) supported by governments, health ministries and health agencies has formulated global action plans to combat the rise in AMR, supporting a number of proven initiatives such as antimicrobial stewardship, investments in development of new classes of antibiotics, and educational programs designed to eliminate inappropriate antibiotic use. Vaccines as tools to reduce AMR have historically been under-recognized, yet the positive effect in reducing AMR has been well established. For example *Haemophilus influenzae* type B (Hib) as well as *Streptococcus pneumoniae* (pneumococcal) conjugate vaccines have impressive track records in not only preventing life threatening diseases caused by these bacteria, but also reducing antibiotic use and AMR. This paper will describe the drivers of antibiotic use and subsequent development of AMR; it will make the case how existing vaccines are already participating in combatting AMR, describe future prospects for the role of new vaccines in development to reduce AMR, and highlight challenges associated with future vaccine development to combat AMR.

ARTICLE HISTORY

Received 15 March 2018
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KEYWORDS

antimicrobial resistance; vaccines; *Streptococcus pneumoniae*; *Staphylococcus aureus*; *Clostridium difficile*; Group B streptococcus



MINIREVIEW



How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem?

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ABSTRACT There is a growing appreciation for the role of vaccines in confronting the problem of antimicrobial resistance (AMR). Vaccines can reduce the prevalence of resistance by reducing the need for antimicrobial use and can reduce its impact by reducing the total number of cases. By reducing the number of pathogens that may be responsible for a particular clinical syndrome, vaccines can permit the use of narrower-spectrum antibiotics for empirical therapy. These effects may be amplified by herd immunity, extending protection to unvaccinated persons in the population. Because much selection for resistance is due to selection on bystander members of the normal flora, vaccination can reduce pressure for resistance even in pathogens not included in the vaccine. Some vaccines have had disproportionate effects on drug-resistant lineages within the target species, a benefit that could be more deliberately exploited in vaccine design. We describe the effects of current vaccines in controlling AMR, survey some vaccines in development with the potential to do so further, and discuss strategies to amplify these benefits. We conclude with a discussion of research and policy priorities to more fully enlist vaccines in the battle against AMR.



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OMS: pacchetto degli interventi chiave per gestire l'AMR nella salute umana

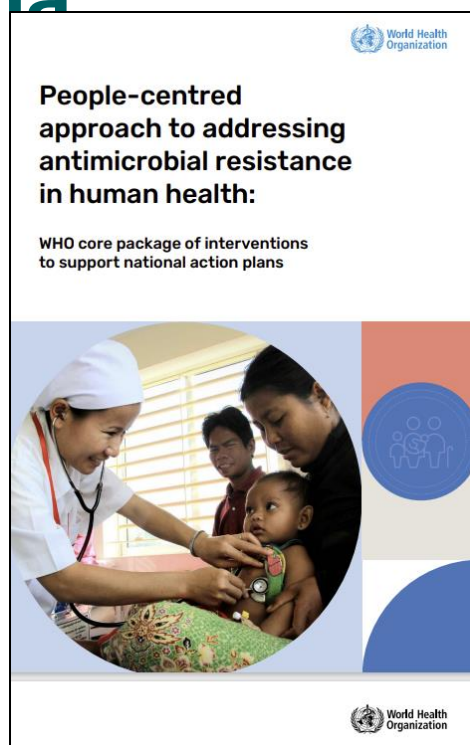
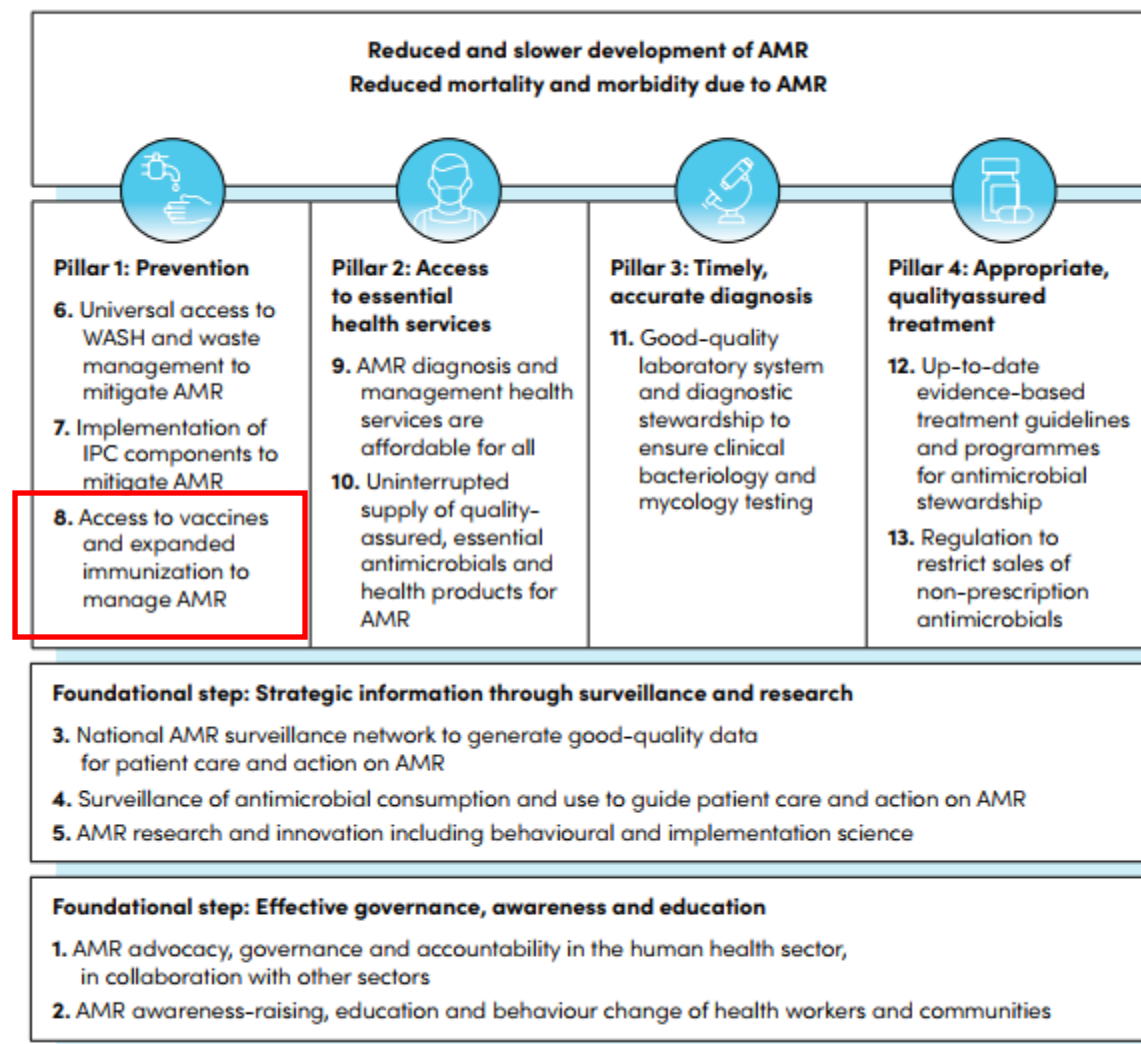


Fig. 1.1. The WHO core package of interventions to manage AMR in human health



AMR: antimicrobial resistance; IPC: infection prevention and control; WASH: water, sanitation and hygiene; WHO: World Health Organization.

La visione OMS del contrasto AMR include ormai stabilmente la vaccinazione nell'approccio persona-centrico

(19/10/2023)



World Health Organization

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

WHO core package of interventions to support national action plans

World Health Organization



Intervention 8:

Access to vaccines and expanded immunization to manage AMR

Priority actions

National and/or subnational level

- Expand national immunization programmes and ensure that developed and licensed vaccines are available and accessible to prevent infections and subsequent use of antibiotics (and thus the emergence of AMR).
- Update national recommendations and normative guidance to include the role of vaccines in controlling AMR.

All health-care levels

- Ensure that health workers are vaccinated and trained to meet national immunization programme targets for vaccines that impact AMR.

Community

- Raise awareness of the role of vaccines in limiting the emergence of AMR and use of antibiotics.

Il contrasto va fatto con un approccio larghi



Sustainable Access to Antibiotics 3

Expanding antibiotic, vaccine, and diagnostics development and access to tackle antimicrobial resistance

Ramanan Laxminarayan, Isabella Impalli, Radha Rangarajan, Jennifer Cohn, Kavi Ramjeet, Betsy Wonderly Trainor, Steffanie Strathdee, Nithima Sumpradit, Daniel Berman, Heiman Wertheim, Kevin Outterson, Padmini Srikantiah, Ursula Theuretzbacher

Lancet 2024; 403: 2534–50

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[https://doi.org/10.1016/S0140-6736\(24\)00878-X](https://doi.org/10.1016/S0140-6736(24)00878-X)

See [Comment](#) *Lancet* 2024; 403: 2355–57

See [Perspectives](#) *Lancet* 2024; 403: 2367

This is the third in a [Series](#) of four papers on sustainable access to antibiotics. All papers in the Series can be found at [thelancet.com/series/antibiotic-resistance](https://www.thelancet.com/series/antibiotic-resistance)

One Health Trust, Bengaluru, India (Prof R Laxminarayan PhD, I Impalli BSE); High Meadows Environmental Institute, Princeton University.

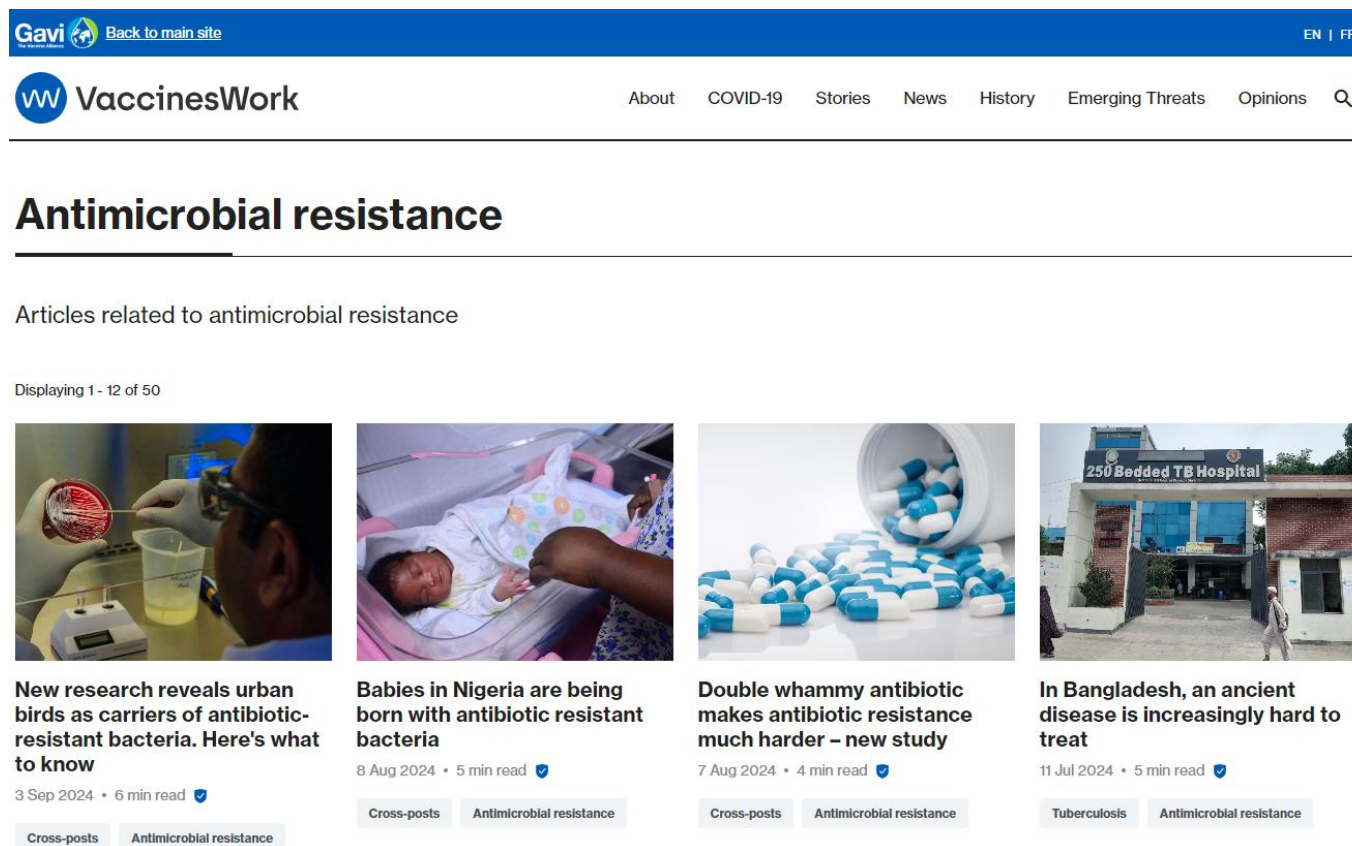
The increasing number of bacterial infections globally that do not respond to any available antibiotics indicates a need to invest in—and ensure access to—new antibiotics, vaccines, and diagnostics. The traditional model of drug development, which depends on substantial revenues to motivate investment, is no longer economically viable without push and pull incentives. Moreover, drugs developed through these mechanisms are unlikely to be affordable for all patients in need, particularly in low-income and middle-income countries. New, publicly funded models based on public–private partnerships could support investment in antibiotics and novel alternatives, and lower patients’ out-of-pocket costs, making drugs more accessible. Cost reductions can be achieved with public goods, such as clinical trial networks and platform-based quality assurance, manufacturing, and product development support. Preserving antibiotic effectiveness relies on accurate and timely diagnosis; however scaling up diagnostics faces technological, economic, and behavioural challenges. New technologies appeared during the COVID-19 pandemic, but there is a need for a deeper understanding of market, physician, and consumer behaviour to improve the use of diagnostics in patient management. Ensuring sustainable access to antibiotics also requires infection prevention. Vaccines offer the potential to prevent infections from drug-resistant pathogens, but funding for vaccine development has been scarce in this context. The High-Level Meeting of the UN General Assembly in 2024 offers an opportunity to rethink how research and development can be reoriented to serve disease management, prevention, patient access, and antibiotic stewardship.



DIPARTIMENTO
MALATTIE INFETTIVE

L'utilità dei vaccini come strumento per combattere la resistenza antimicrobica è stata ampiamente riconosciuta





- Gli Stati Uniti considerano la ricerca per lo sviluppo di nuovi vaccini tra i principali obiettivi strategici contro l'AMR
- l'impatto della vaccinazione sulla resistenza antimicrobica è ora incluso anche nei criteri di valutazione della Global Alliance for Vaccines and Immunization (GAVI).



The screenshot shows the VaccinesWork website interface. At the top, there is a blue navigation bar with the Gavi logo and a 'Back to main site' link on the left, and 'EN | FR' on the right. Below the navigation bar is the 'VaccinesWork' logo and a menu with links for 'About', 'COVID-19', 'Stories', 'News', 'History', 'Emerging Threats', and 'Opinions'. The main content area is titled 'Antimicrobial resistance' and lists 'Articles related to antimicrobial resistance'. It indicates 'Displaying 1 - 12 of 50' articles. Four article cards are visible, each with a thumbnail image, a title, a date, a read time, and tags for 'Cross-posts' and 'Antimicrobial resistance'.

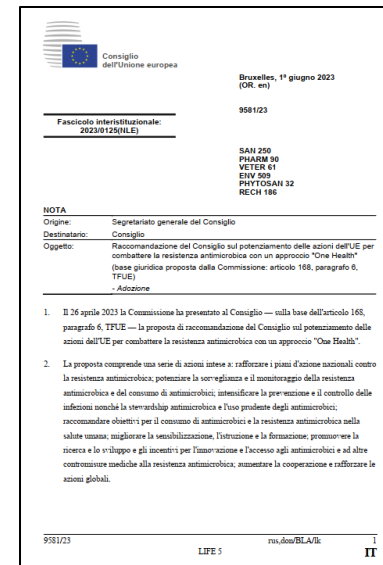
Articles related to antimicrobial resistance

Displaying 1 - 12 of 50

- **New research reveals urban birds as carriers of antibiotic-resistant bacteria. Here's what to know**
3 Sep 2024 • 6 min read
- **Babies in Nigeria are being born with antibiotic resistant bacteria**
8 Aug 2024 • 5 min read
- **Double whammy antibiotic makes antibiotic resistance much harder – new study**
7 Aug 2024 • 4 min read
- **In Bangladesh, an ancient disease is increasingly hard to treat**
11 Jul 2024 • 5 min read

Raccomandazione del Consiglio sul potenziamento delle azioni dell'UE per combattere l'AMR con un approccio "One Health« (13 giugno 2023)

- promuovere lo sviluppo e l'accessibilità di contromisure mediche pertinenti per combattere la resistenza antimicrobica, compresi antimicrobici vecchi e nuovi, diagnostiche e vaccini contro gli agenti patogeni resistenti.
- promuovere il ricorso alla vaccinazione come pure lo sviluppo e la disponibilità dei vaccini e l'accesso agli stessi
- garantire le misure di prevenzione e controllo delle infezioni attuando programmi nazionali di vaccinazione
- Attuare la vaccinazione anche in zootecnia



G7 Italia, il comunicato conclusivo della Riunione dei Ministri della Salute (10-11 ottobre 2024)



“È una dichiarazione politica ambiziosa, che include e riassume le posizioni comuni su tutte le tematiche affrontate durante questi mesi”. Così il Ministro della Salute Orazio Schillaci, ha commentato la dichiarazione finale adottata dai Paesi del G7 Salute che si è tenuto ad Ancona dal 9 all’11 ottobre.

Schillaci ha sottolineato che il vertice si è occupato “di problematiche che impattano sulla vita di ognuno di noi. A questi temi abbiamo iniziato a dare risposte concrete”.

A partire dal contrasto all’antimicrobico resistenza: “Nella riunione congiunta con i Ministri delle Finanze, l’Italia ha annunciato un finanziamento di 21 milioni di dollari nel prossimo

triennio a favore di CARB-X, una partnership globale senza scopo di lucro che sostiene lo sviluppo di nuovi antibiotici. Con questa scelta chiara l’Italia è in prima linea per gestire la crisi dell’antibiotico-resistenza”.

Un altro risultato significativo riguarda l’approvazione per la prima volta, nell’ambito della Presidenza del G7, di una di un policy brief su Intelligenza Artificiale e Salute.

Guarda

- › [Video della Conferenza stampa conclusiva del Ministro Schillaci](#)
- › [Video riassuntivo dell’evento](#)

Leggi

il documento conclusivo della Riunione dei Ministri della Salute in lingua inglese

- › [G7 Health Ministers’ Communiqué - Ancona, October 10-11, 2024](#)
- › [G7 Policy brief on Artificial Intelligence: opportunities and challenges for the Health Sector](#) (allegato)



- Alcuni dei punti di una lunga lista:
 - condivisione volontaria dei dati sulla resistenza antimicrobica
 - strumenti diagnostici AMR affidabili, rapidi, efficaci e accessibili
 - migliorare l'interoperabilità dei sistemi per la microbiologia epidemiologica, compresi i dati genomici e clinici
 - Finanziamenti per incentivi PUSH, compreso il contributo agli sforzi congiunti globali esistenti per accelerare la ricerca e lo sviluppo di nuovi antimicrobici, vaccini, diagnostici e terapie alternative



www.iss.it/malattie-infettive

https://www.salute.gov.it/portale/news/p3_2_1_1_1.jsp?lingua=italiano&menu=notizie&p=dalministero&id=6666



Riferimenti sulla vaccinazione come misura di contrasto dell'ABR sono inseriti in PNCAR, PNPV e PNP



Documento strategico contenente le indicazioni operative per affrontare l'emergenza dell'ABR, seguendo un approccio multidisciplinare e una visione One Health

Piano Nazionale Prevenzione Vaccinale

PNPV 2023-2025

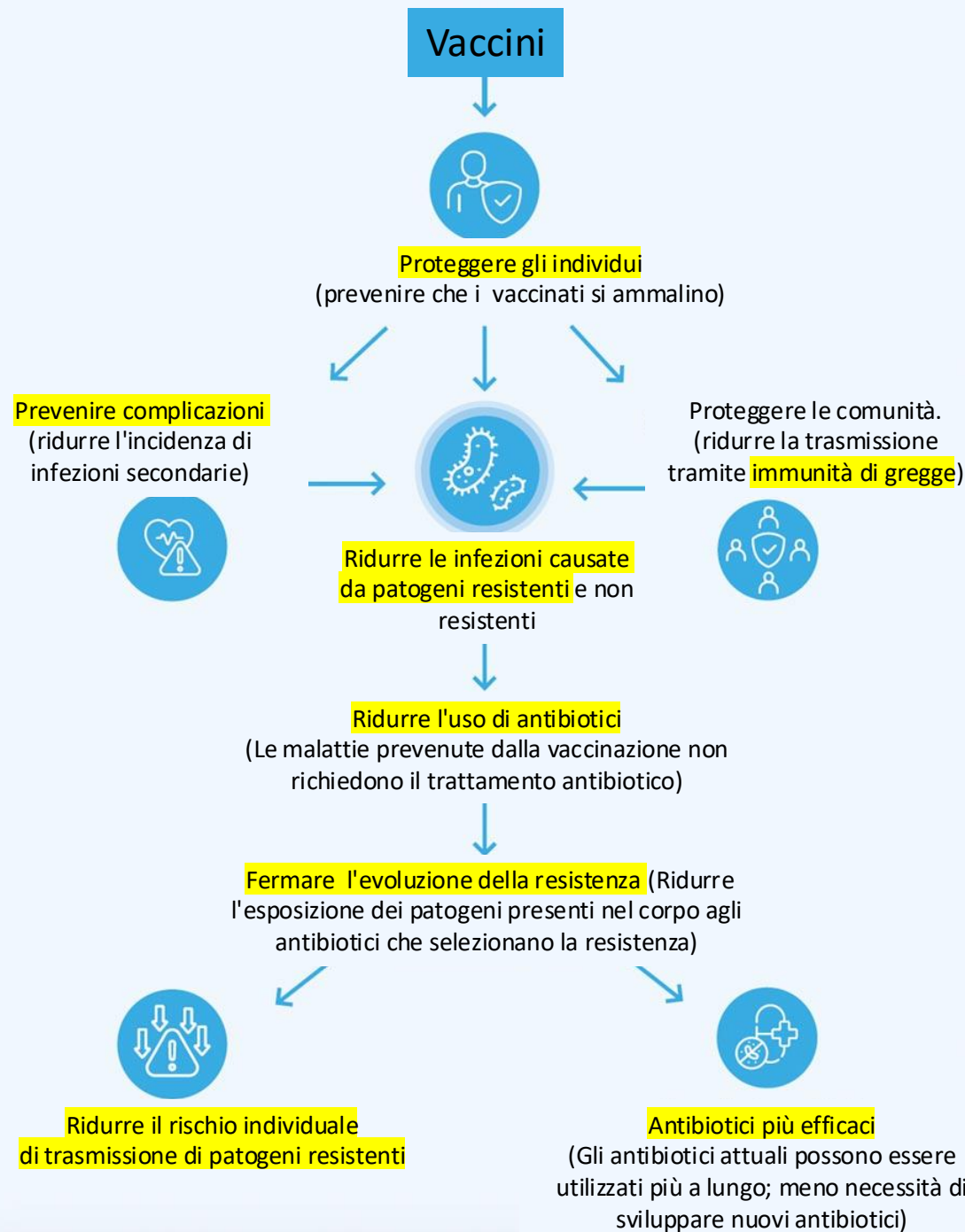
21 marzo 2023

Va ad integrare il Piano Nazionale di Prevenzione 2020-2025, rappresentando un punto di riferimento nell'ambito delle politiche vaccinali



Perché i vaccini sono vitali nel combattere l'AMR

Adattata da Insight paper
May 2024 | gavi.org
<https://www.gavi.org/news/document-library/insight-paper-vaccines-key-tool-tackle-antimicrobial-resistance-amr>



Il ruolo dei vaccini

L'utilità dei vaccini come strumento per combattere la resistenza antimicrobica è stata ampiamente riconosciuta.

I vaccini:

- contro i batteri: riducendo l'incidenza delle infezioni, limitano l'uso di antibiotici (**effetto diretto**).
- contro i virus: diminuiscono le prescrizioni inappropriate di antibiotici (**effetto indiretto**)

Ricordiamo che **nel settore umano il 90% del consumo degli antibiotici è in comunità**

I vaccini sono importanti anche in contesti veterinari e agricoli, dove l'uso di antibiotici è eccessivo (quasi il 50% del consumo totale) ma bene regolamentato e in netto calo

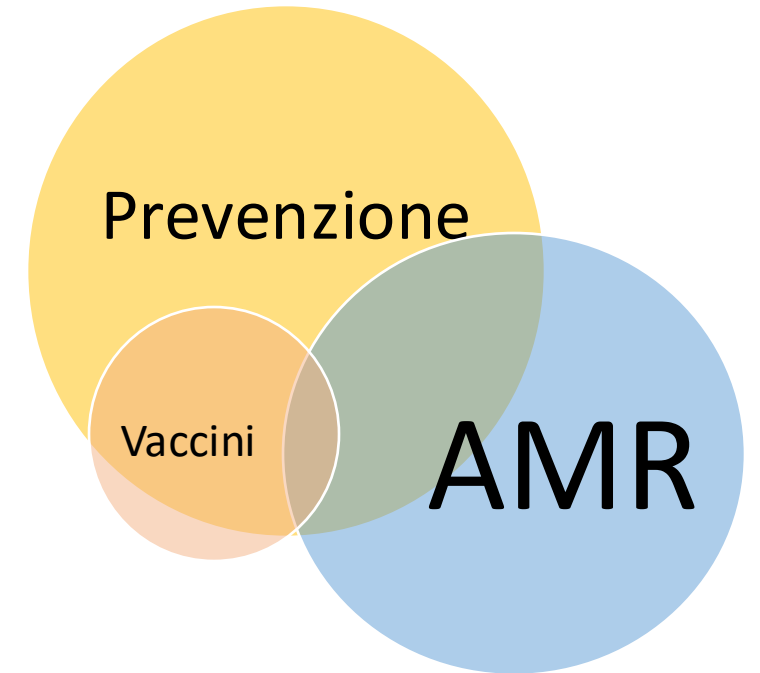


Fig 4. WHO Bacterial Priority Pathogens List, 2024

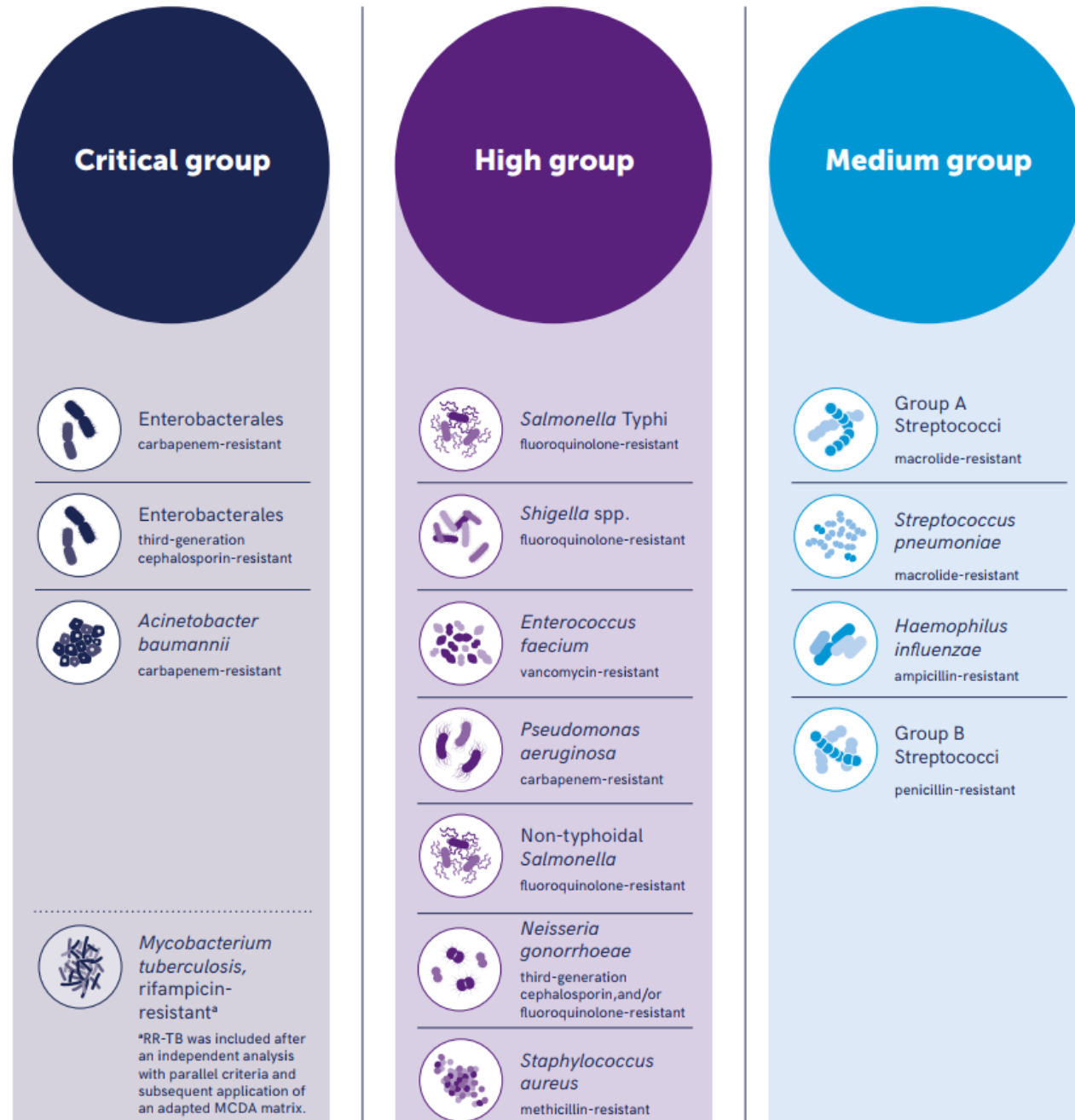
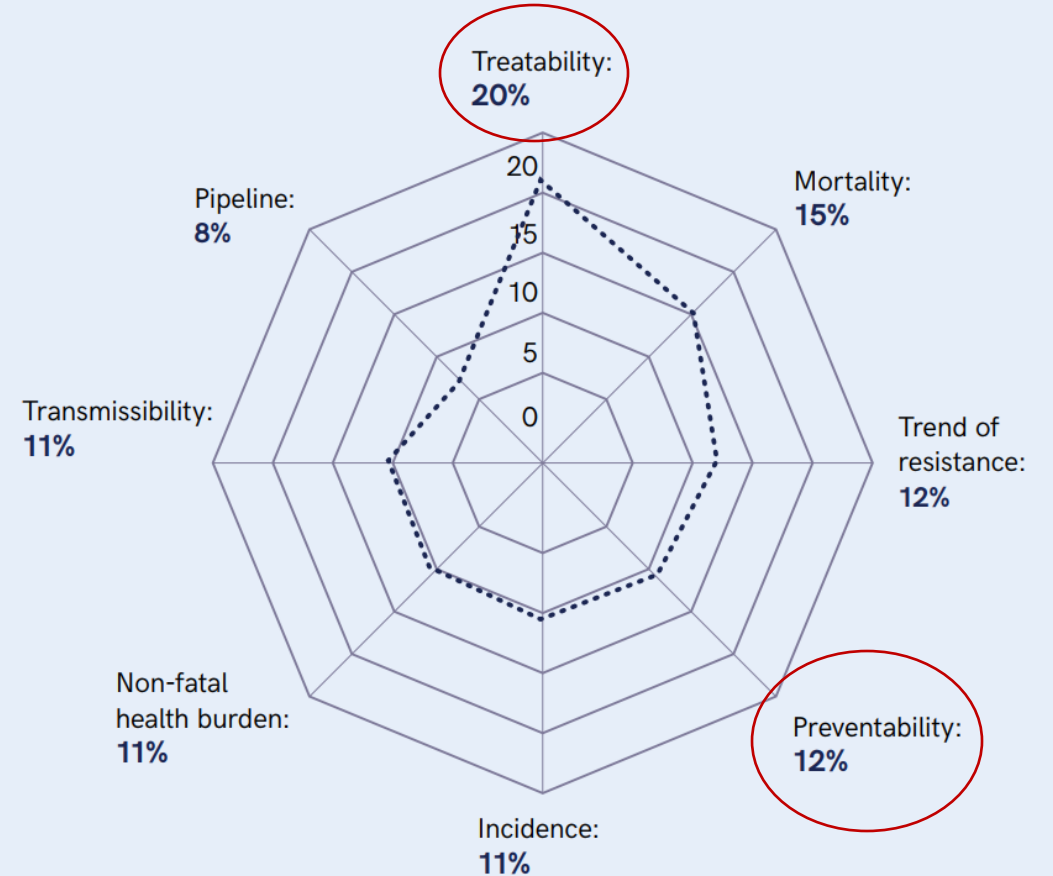


Fig. 3. Pooled criteria weights (results from the Global PAPRIKA^a survey)



Spearman rank correlation = 0.9

Kendall's W = 0.871

^a PAPRIKA (Potentially All Pairwise RanKings of all possible Alternatives) is a robust decision-making approach for systematic evaluation and ranking of all conceivable pairwise alternatives to ensure comprehensive decision analysis. The method is a structured, thorough means of comparing and prioritizing diverse alternatives in making complex decisions.

I vaccini in pipeline correlati all' AMR

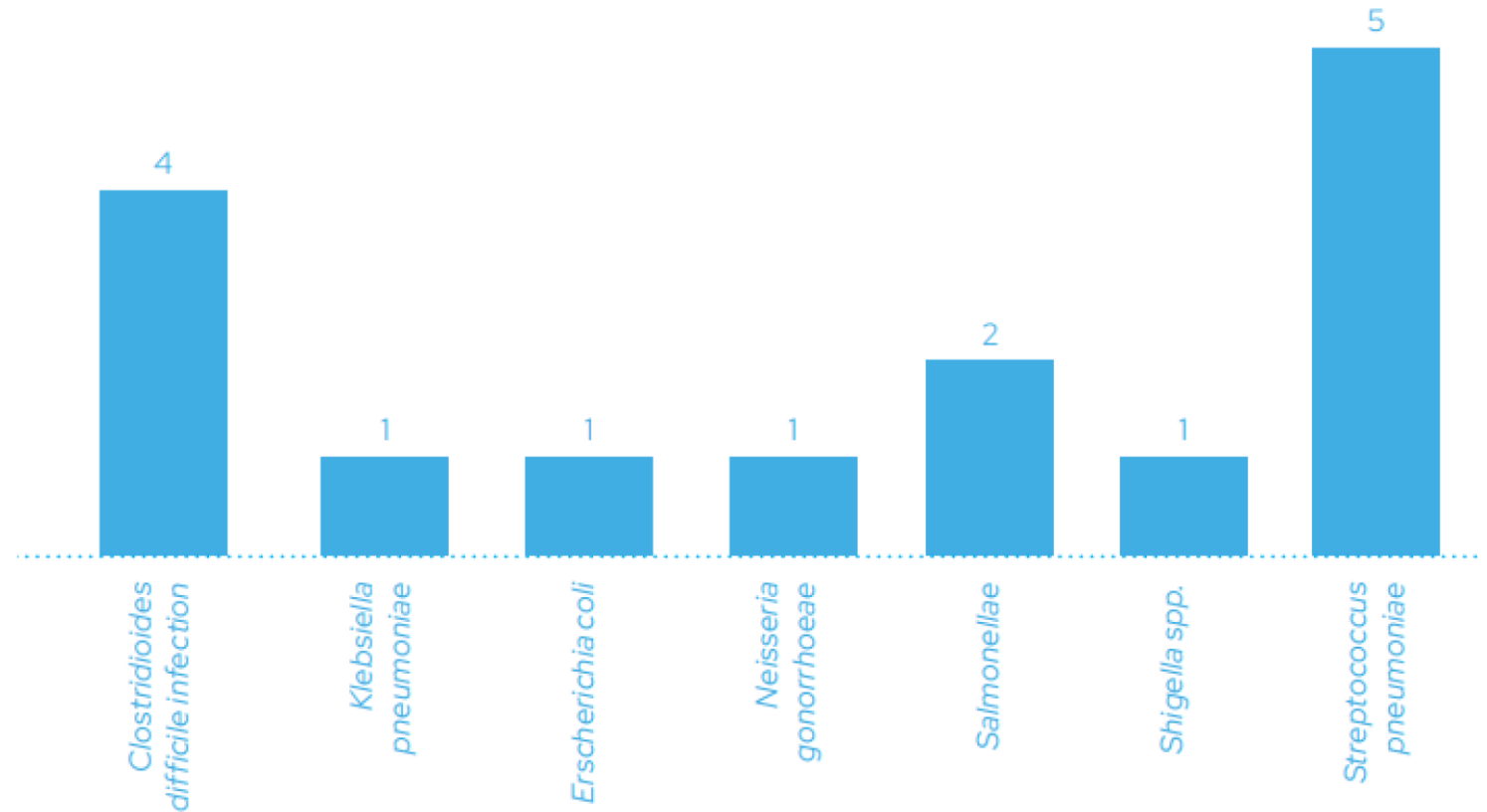
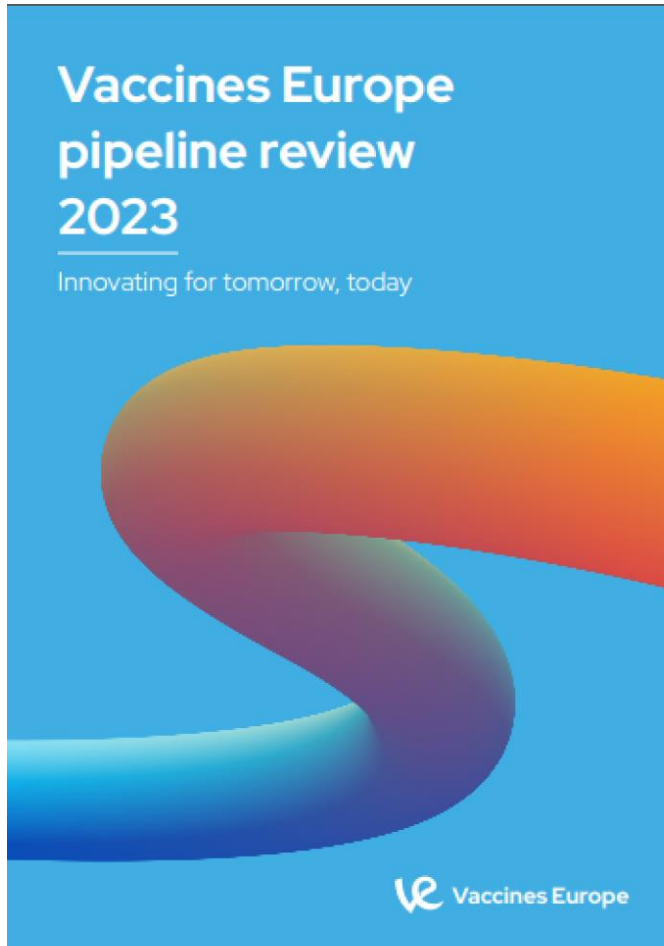


Figure 10. Number of vaccine candidates addressing antibiotic-resistant microorganisms.

Raggiungimento degli obiettivi dell'Agenda di Immunizzazione 2030 e dell'OMS

IMPLEMENTING THE IMMUNIZATION AGENDA 2030:

A Framework for Action through Coordinated Planning, Monitoring & Evaluation, Ownership & Accountability, and Communications & Advocacy

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



- Raggiungere l'obiettivo dell'Immunizzazione 2030 (IA2030) e dell'Organizzazione Mondiale della Sanità (OMS) per la copertura globale di *Streptococcus pneumoniae* nei bambini (90%) e negli anziani potrebbe:
 - evitare **27.100 morti** in più all'anno
 - evitare **1,5 milioni di DALYs**
 - prevenire **507 milioni di dollari** di costi ospedalieri e **879 milioni di dollari** di produttività



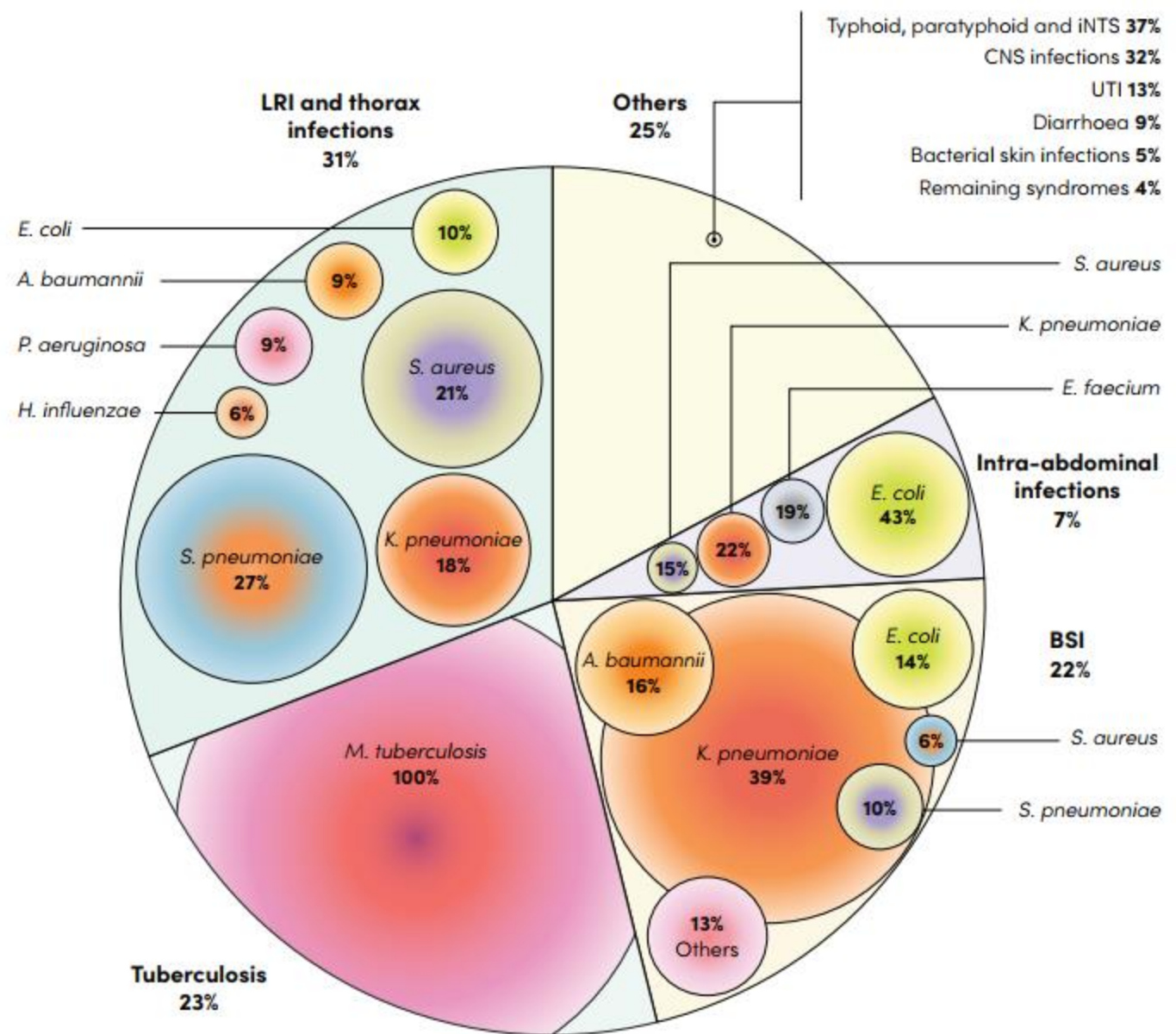
Nuovo report OMS: il ruolo dei vaccini nella riduzione dell'AMR e raccomandazioni per migliorarne l'impatto (10 ottobre 2024)

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

- I vaccini (inclusi quelli in sviluppo) possono potenzialmente evitare circa **515.000** di **5 milioni** di morti associate all'AMR ogni anno, riducendo l'incidenza di infezioni, la trasmissione di agenti patogeni, l'uso di antibiotici e l'evoluzione di geni resistenti.

Stima dei potenziali decessi prevenibili da vaccino associati alla resistenza antimicrobica da infettive Sindrome e patogeno nel 2019

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



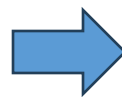
L'impatto dei vaccini in fase di sviluppo clinico precoce nel contrasto all'AMR

Il rapporto stima che i vaccini che sono ancora nelle prime fasi di sviluppo clinico potrebbero:

- evitare ogni anno fino a 408.000 morti, 23,0 milioni di DALY, 30,0 miliardi di dollari di costi ospedalieri e 17,7 miliardi di dollari di perdita di produttività associati alla resistenza antimicrobica
- Ridurre l'uso di antimicrobici di 548 milioni di DDD all'anno.

Ad esempio, un vaccino per le madri contro *Klebsiella pneumoniae*, mirato a proteggere i neonati e gli anziani dalle infezioni del flusso sanguigno potrebbe prevenire circa 64.500 decessi, 3,7 milioni di DALY, legati alla resistenza antimicrobica.

Pathogen	Vaccine description and short name	Vaccine-averted deaths associated with AMR in 2019 (95% UI)	Vaccine-averted DALYs associated with AMR in 2019 (95% UI)
<i>Klebsiella pneumoniae</i>	A vaccine against bloodstream <i>K. pneumoniae</i> infection given to 70% of infants through maternal vaccination , with 6-month efficacy of 70% [KP_1] ^b	27 500 (22 000–35 000)	2.4 (2.0–3.1) million
	A vaccine against <i>K. pneumoniae</i> infection given to 70% of infants and elderly people , with 5-year efficacy of 70% [KP_2] ^b	64 500 (58 500–72 000)	3.7 (3.3–4.1) million
	A vaccine against <i>K. pneumoniae</i> infection given to 70% of all people at risk of infection , with 5-year efficacy of 70% [KP_3]	321 000 (309 000–336 000)	13.7 (12.8–14.7) million



Conclusioni e prospettive future

- Un chiaro riferimento al tema AMR e vaccini è trattato in diversi documenti nazionali e internazionali per favorire la coerenza delle azioni.
- La resistenza antimicrobica è **un'urgente minaccia** per la salute globale, e lo sviluppo di vaccini contro agenti patogeni con un profilo di resistenza complesso e un'alta incidenza di infezioni gravi può essere una soluzione promettente.
- **Per massimizzare l'impatto dei vaccini nel ridurre l'emergere di AMR, la maggior parte della popolazione a rischio di infezione dovrebbe essere vaccinata.**
- Sfortunatamente, **per la maggior parte dei principali agenti patogeni resistenti agli antimicrobici, i vaccini non sono ancora disponibili**, ma in fase di sviluppo.
- **I vaccini attuali devono essere usati al meglio per ridurre le infezioni, ma ci vuole un «arsenale» più mirato**



Grazie per l'attenzione !!!

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