VACCINES BEAT

# THE POLIO ENDGAME

An exquisite deep dive into poliomyelitis with **Dr. Ananda Bandyopadhyay**

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*"IMMUNIZATION IS A GLOBAL HEALTH AND DEVELOPMENT SUCCESS STORY SAVING MILLIONS OF LIVES EVERY YEAR"*

WORLD HEALTH ORGANIZATION



# The polio endgame

## An exquisite deep dive into poliomyelitis with Dr. Ananda Bandyopadhyay

The unequivocal global authority in polio, Dr. Ananda Sankar Bandyopadhyay has led disease control initiatives in diverse settings across the globe. He began his career as a surveillance medical officer with the World Health Organization's National Polio Surveillance Project in India, where he played a key role in the country's polio elimination and measles surveillance efforts. In a career spanning more than 15 years, he also served as a medical epidemiologist at the Rhode Island Department of Health in the United States, coordinating public health surveillance and response activities. Ananda, as he is affectionately known by his colleagues, grew up in Kolkata, India, and earned his medical degree from Calcutta National Medical College and Hospital, graduating with a gold medal and numerous honors. He later earned a Master of Public Health (MPH) from the Harvard T.H. Chan School of Public Health and is currently a guest faculty in several prestigious global programs focused on public health and vaccinology. Currently, as the Deputy Director of Technology, Research and Analytics of the Polio Team at the Bill & Melinda Gates Foundation, Dr. Bandyopadhyay leads global research efforts aimed at achieving and sustaining polio eradication. His work includes the development of novel polio vaccines, the generation of data to inform immunization policies, and the advancement of effective detection and surveillance tools. His contributions to public health have reverberated across the globe as he continues to build a remarkable legacy along his ever evolving and prolific career.
Full Bio

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# LETTER FROM EDITORS

Welcome to our fifth issue of Vaccines Beat. We are excited to continue our mission of communicating, educating, and promoting knowledge in the fields of vaccinology and vaccination.

In our 'Coffee with an Expert' section, we are deeply honored to feature an interview with Dr. Ananda Bandyopadhyay, a renowned global expert in Polio. Dr. Bandyopadhyay grew up in Kolkata, India and completed his medical graduation from Calcutta National Medical College & Hospital (2005) with a gold medal and several honors certificates. He received his Master of Public Health (MPH) degree in Global Health from Harvard School of Public Health (2010).

In his professional career spanning more than 15 years, Ananda has worked in diverse settings and has led disease control initiatives across the globe. He worked as a Surveillance Medical Officer with National Polio Surveillance Project, WHO and contributed to India's polio elimination effort and measles surveillance initiatives. Based out of Seattle, United States, Ananda in his current role as a Deputy Director at the Bill and Melinda Gates Foundation coordinates global research to facilitate polio eradication. His work on clinical development of novel vaccines and polio endgame vaccination schedules along with his research to enhance polio environmental surveillance have been impactful in global policy formulation and have been published in leading peer-reviewed journals.

Ananda is associated with advanced degree programs in public health and vaccinology in several globally renowned teaching venues as a guest faculty.

Our Editor's Corner explores how vaccines play a vital role in combating antimicrobial resistance (AMR). It provides an overview of AMR mechanisms, its overall impact, also explains how vaccines contribute to its prevention, and highlights the current WHO priority vaccines aimed at addressing this global challenge.

Our Best Practice section delves into the current and somewhat controversial 1+1 pneumococcal vaccination schedule for children in the United Kingdom.

In the "Guest Contributors" section we have an article that features a groundbreaking initiative from the Middle East and North Africa (MENA) region. In response to the World Health Organization (WHO), the Medicines Patent Pool (MPP) and their mRNA Technology Transfer Hub Program, this initiative aims at reducing reliance on limited vaccine suppliers by enabling local manufacturers in LMICs by establishing a sustainable framework for developing vaccines against infectious diseases independently.

As always, this issue features carefully curated and up-to-date information on the 'Latest Scientific Publications' along with the most recent and important 'News and Alerts'.

We hope you find this November issue informative and engaging, and we look forward to continuing this unique effort in support of a healthier planet.

Javier Casellas, M.D., Ph.D.

Chief Editor

Enrique Chacon-Cruz, M.D., MSc

Chief Editor

## Javier Casellas

Well-recognized Argentinian Pediatrician and Infectious Diseases Specialist with more than 17 years of experience on Medical Affairs & Clinical Research on Vaccines field within different multinatinational & recognized Pharmaceutical Companies. (GSK and Novartis Vaccines)

From 2005 to 2015 Dr. Casellas worked as Vaccines Medical Affairs / Clinical Research Director (GSK and Novartis vaccines in Latam Region) with experience on vaccine clinical research, medical affairs activities, vaccine pharmacovigilance, public & private vaccine market access, strong relationship with MoHs across Latam and supranational organizations (such as PAHO, and Sabin Institute), and has published several scientific papers and posters in international journals and meetings, among the most relevant medical activities.

Since 2016 Dr. Casellas became an Independent Vaccine Consultant. From 2016 to 2018, Dr. Casellas joined an NPO (FIDEC, Miami, FL, USA) as Medical Manager working on vaccine clinical trials along with Bill and Melinda Gates Foundation. Currently, Dr. Casellas works on global & regional Vaccine and Infectious Diseases (IDs) trials at IQVIA as Global Medical Director within the Infectious Diseases and Vaccines Team.

## Enrique Chacon Cruz

Enrique Chacon-Cruz, M.D., MSc, Mexican-born medical doctor with a degree from Guadalajara, Mexico, and further specializations in Pediatrics and Infectious Diseases from institutions in Mexico City and the USA (Eastern Virginia Medical School). He also holds a Master's degree in Vaccinology and Drug Development from the University of Siena, Italy.

He is an Overseas Fellow of the Royal Society of Medicine of the United Kingdom and a member of several international associations in Infectious Diseases. Currently, he is the CEO and Founder of "Think Vaccines" (Research, Education, and Consultancy for Vaccines and Vaccinology) based in Houston, Texas.

With over 140 research items published and/or presented at international meetings and more than 500 international lectures, all focused on vaccines, vaccination, clinical trials, and vaccine-preventable diseases. The latter conducted independently or in association with the Centers for Disease Control and Prevention (CDC), the University of California in San Diego, Eastern Virginia Medical School, and several other institutions.

Additionally, he is a member of the Mexican Committee for the Elimination of Measles, Rubella, and Congenital Rubella, and the Scientific Committee on Health Issues of the Mexican Government in Baja-California. He is also the former Director of the Mexican Active Surveillance Network for Bacterial Meningitis and the former Head of the Pediatric Infectious Diseases Department and the Research Department at the General Hospital of Tijuana, Baja-California, Mexico.

Coffee with the Expert

# THE POLIO ENDGAME

## An exquisite deep dive into poliomyelitis with Dr. Ananda Bandyopadhyay

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*Javier Casellas, M.D., Ph.D.*
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The unequivocal global authority in polio, Dr. Ananda Sankar Bandyopadhyay has led disease control initiatives in diverse settings across the globe. He began his career as a surveillance medical officer with the World Health Organization's National Polio Surveillance Project in India, where he played a key role in the country's polio elimination and measles surveillance efforts. In a career spanning more than 15 years, he also served as a medical epidemiologist at the Rhode Island Department of Health in the United States, coordinating public health surveillance and response activities.

Ananda, as he is affectionately known by his colleagues, grew up in Kolkata, India, and earned his medical degree from Calcutta National Medical College and Hospital, graduating with a gold medal and numerous honors. He later earned a Master of Public Health (MPH) from the Harvard T.H. Chan School of Public Health and is currently a guest faculty in several prestigious global programs focused on public health and vaccinology.

Currently, as the Deputy Director of Technology, Research and Analytics of the Polio Team at the Bill & Melinda Gates Foundation, Dr. Bandyopadhyay leads global research efforts aimed at achieving and sustaining polio eradication. His work includes the development of novel polio vaccines, the generation of data to inform immunization policies, and the advancement of effective detection and surveillance tools.

His contributions to public health have reverberated across the globe as he continues to build a remarkable legacy along his ever evolving and prolific career.

### Formative years

When Dr. Bandyopadhyay was in medical school, India was grappling with a heavy burden of diseases, many of which were vaccine preventable. In his quest to understand the science behind these diseases, his mission was not only to study their development but also to explore how they could be prevented and treated. Reflecting on his journey, he often says that he did not choose polio, rather, polio chose him.

"I was looking for something more challenging, something different from the clinical studies that I was already doing," he recollects. "So, post the medical graduation, I got selected for the WHO polio surveillance project in India as a surveillance medical officer. And I thought this was a great opportunity to do applied epidemiology," he recollects it was a post that took him away from his hometown and deployed him around many locations within the country doing polio outbreak investigations, while coordinating large-scale vaccination campaigns.

What initially was supposed to be a year-long association, in an era when India was intensely endemic with polio, happened to be a career long effort. After his training at the Harvard T.H. Chan School of Public Health, Dr. Bandyopadhyay started to focus almost exclusively on polio research at a global scale.

## The basics about polio

Dr. Bandyopadhyay explains that, broadly speaking, polio has three naturally occurring or 'wild' serotypes: types 1, 2 and 3. Depending on its origin, whether from a naturally occurring polio virus or derived from a vaccine strain, it can be further subdivided. Wild types 2 and 3 have already been certified as eradicated, meaning that two-thirds of wild polio disease has been effectively wiped out of the planet. What remains is wild type 1, which is only endemic in Pakistan and Afghanistan.

On the other hand, there is a burden of vaccine-derived polio viruses (VDPVs) or variant polio viruses. These viruses are essentially derived from the oral poliovirus vaccine (OPV), a live attenuated vaccine. In settings with persistently low immunization coverage, the population remains vulnerable to virus circulation, allowing the live attenuated strains of the vaccine virus to evolve into forms capable of causing paralytic outbreaks.

"So, if you ask me, it's more poor vaccination derived polio viruses than really vaccine derived polio viruses, because if vaccination coverage is uniformly high and high over time, then the risk of such strains is essentially negligible," asserts Dr. Bandyopadhyay.

This phenomenon occurs primarily in areas where immunization coverage remains low for extended periods. In such settings, the oral polio vaccine (OPV) strains can lose the attenuating mutations that were originally present in the vaccine virus. As a result, the vaccine virus can replicate in unvaccinated or inadequately vaccinated children. Through this replication process, the virus can spread from one susceptible child to another, regaining the ability to cause paralytic outbreaks.

## Why vaccination coverage is not optimal?

Dr. Bandyopadhyay explains that there are three main factors that can disrupt or hinder optimal vaccination coverage. One major factor in today's world is geopolitical unrest, which takes many forms. In extreme situations, such as active conflicts or wars, healthcare and immunization services are often severely disrupted. In other cases, civil unrest or political instability can also interfere with or halt vaccination efforts.

"And, unfortunately, that's in a way growing in today's world. And that is concerning because it eventually impacts vulnerable children who are not receiving the lifesaving vaccines or other lifesaving interventions," he points out with clear concern.

Another factor affecting vaccination coverage is vaccine acceptance, which can be suboptimal in some communities. Dr. Bandyopadhyay suggests that improving health communication is key—this involves reaching out to these communities with accurate, science-based information about the safety and effectiveness of vaccines.

A third challenge is disruptions in vaccine supply, which became especially prominent during the COVID-19 pandemic. The interruption of global supply chains led to sporadic shortages of vaccines.

It is also important to note that the majority of cases of circulating vaccine-derived polioviruses (cVDPVs) stem from the oral polio vaccine (OPV) targeting serotype 2, rather than vaccines for other serotypes. In response, the Global Polio Eradication Initiative (GPEI), in collaboration with several partners, developed novel oral poliovirus vaccines (nOPVs). These vaccines are now being deployed worldwide. The partnership also worked together to clinically develop these new vaccines and navigate the World Health Organization's unique regulatory pathway, known as the Emergency Use Listing (EUL) process.

"So, this overall journey has been quite fascinating in terms of developing the idea, then getting into pre-clinical studies, clinical studies, down selection between candidates, and then, as I said, the regulatory pathway that was applied," commented Dr. Bandyopadhyay.

This vaccine is reserved for outbreak response and is only used in areas where circulating vaccine-derived polioviruses of type 2 variants have been detected. To date, approximately about 1.3 billion doses of nOPV2 have been administered across about 240 mass vaccination campaigns in 41 countries.

## Sewage surveillance

Polio is a notoriously elusive virus and knows 'how to hide', which is why sewage surveillance was added to complement acute flaccid paralysis (AFP) surveillance. Dr. Bandyopadhyay explains that polio behaves in a way that makes it difficult to detect: of 100 infected individuals, only one may show the classic signs of paralytic disease. The others may have no symptoms or exhibit only mild, atypical ones.

"So that means, when we have to search for the virus, we really have to be smart. So, one component of that was the focus on not polio paralysis surveillance, but acute flaccid paralysis surveillance, where you are essentially broadening your net," he says, noting that even a rare case could be caused by polio.

As they gained a deeper understanding of how polio circulates, sewage surveillance was introduced, not to replace AFP surveillance but to complement it. The goal is to collect wastewater samples from strategically selected locations to detect whether the polio virus is circulating. Because polio is often subclinical, even the best AFP surveillance may miss that one paralytic case.

"With sewage surveillance, you are not only focusing on the disease part of the spectrum, but you're actually focusing on the existence of the virus itself. And that, actually, is the essence of the idea of eradication. Because with polio eradication, we are not only talking about stopping the disease. But we are talking about wiping the world out of the polio virus," he asserts adding that there are around 140 specialized laboratories globally trained to detect polioviruses.

Dr. Bandyopadhyay notes that over the past five years, sewage surveillance networks have expanded significantly. However, he emphasizes that there is still more to be done, particularly in strategically locating sewage surveillance sites to track polioviruses more effectively.

## The future of polio

Dr. Bandyopadhyay outlines two primary goals for the near future in the fight against polio: to **stop the wild poliovirus type 1** once and for all, and to **halt the spread of circulating vaccine-derived poliovirus type 2 (cVDPV-2)**. Both are significant challenges, but they are not insurmountable.

To put it in perspective, it's important to note that while there were initially more than 10 sub-lineages of wild type 1, this number has now dwindled to just two, primarily in the border areas between Pakistan and Afghanistan. Unfortunately, ongoing geopolitical unrest is complicating efforts to reach these areas. Despite this, the progress made so far offers strong evidence that wild type 1 can be eradicated decisively and permanently.

"So that is a definitive indication, if you ask me, that the virus is gasping in these last corridors. That's exactly what you see from a molecular epidemiology perspective everywhere," he asserts. "And we know this through genetic sequencing."

The second major goal is to stop the circulation of cVDPV-2, which is primarily circulating in the WHO AFRO Region, but spread to several other countries in recent years, and was detected in the UK, Israel, the US, and Canada, underscoring how easily polio can travel. "Polio is just a plane ride away," Dr. Bandyopadhyay points out, highlighting the global risk.

"So, there are huge challenges to stop the spread of the variant type 2 poliovirus or the circulating vaccine-derived poliovirus. But on the other hand, we just discussed there is also the promise of a tool like the novel OPV2, the nOPV2, which has significantly more genetic stability," Dr. Bandyopadhyay notes.

He emphasizes that the introduction of nOPV2 in outbreak response has reduced the risk of new cVDPV-2 emergence by about 75% to 80%, providing a crucial opportunity to break the cycle of new outbreaks. Looking further into the future, Dr. Bandyopadhyay points out the ongoing need to develop policies for long-term polio vaccination.

"As of now, SAGE (Strategic Advisory Group of Experts) has recommended that post-certification of eradication, countries continue using polio vaccines. And in this case, post-eradication polio vaccine, we understand, will be the inactivated polio vaccine (IPV) given by injection. That's going to be kind of the exclusive use era of IPV post-certification of eradication," he confirms. "And the duration of such use is at least 10 years post-eradication," he explains that, for countries with polio-essential facilities, places where polioviruses are still studied or used for vaccine production, the period of vaccination could be longer.

In short, while the immediate goals are to end wild poliovirus type 1 and halt cVDPV-2 circulation, the long-term success of polio eradication will depend on continuing to vaccinate and fine-tune strategies to keep the virus from resurfacing.

## Eradication of polio

One key factor that makes poliovirus an eradicable disease is the absence of a known carrier state in immunocompetent individuals. In contrast, immunocompromised individuals, especially those with B-cell related immunodeficiencies, can be exposed to the live attenuated poliovirus strains in the OPV, allowing the virus to replicate and be shed for an extended period. This prolonged shedding poses a potential risk for the reintroduction of poliovirus into the community.

"Now, there are two issues to understand here," Dr. Bandyopadhyay explains. "One, we have not really seen definitive evidence of such prolonged shedding from individuals with immunodeficiency disorders leading to community outbreaks," he continues. "So, that's one thing to note. But there is a theoretical risk for sure that the community around such individuals will be exposed. And for that, we are trying to develop polio antivirals."

The development of polio antivirals is part of the global polio research agenda. These antivirals, if proven effective, could stop prolonged replication and shedding if administered in time. Several antiviral candidates are currently in clinical trials or at the preclinical stage and, if successful, they will eventually be introduced to the market.

"I also must note, as I just mentioned to your previous question, if the world moves to an all IPV schedule, eventually the continuous risk that comes in with OPV use for immunocompromised individuals being infected and then starting to shed for a long time, that trigger will also not be there once you move to all IPV. So, you'll also have to consider that even without polio antivirals, probably the risk gradient will go down over time as more and more countries move to an exclusive IPV schedule," he concludes.

## Polio and migration

In countries with large immigrant populations, relying solely on IPV, which provides only direct protection and no indirect protection and limited mucosal immunity, can present a complex epidemiological challenge.

Dr. Bandyopadhyay explains that in developed settings like the United States, IPV is an effective tool. While it doesn't induce strong mucosal intestinal immunity, it provides robust humoral immunity after an adequate number of doses, offering good protection against paralytic disease. However, IPV can also help reduce person-to-person transmission by impacting oropharyngeal mucosal immunity. In environments with good sanitation and hygiene, oropharyngeal immunity plays a role in preventing transmission.

But this is just one piece of the puzzle. In certain settings, even with only IPV, there could still be protection against transmission. However, in areas with high population density and suboptimal sanitation, the need for a live attenuated vaccine like OPV becomes critical. OPV protects the gut by inducing mucosal immunity, which is vital in settings with high force of infection. This is why the policy is to continue using OPV until wild poliovirus type 1 is eradicated globally.

"And also, there are other indicators to move eventually to IPV only if the OPV coverage in a particular country is maintained at a recommended threshold for a period of time. So, there are these checks and balances, which probably gets you to that optimum timeframe that you can consider getting to an all IPV schedule. It's not an all or none policy where we just move, you know, not considering all these epidemiologic factors," he adds.

Dr. Bandyopadhyay emphasizes that the true risk of polio transmission related to migration is not population movement itself, but rather the adequacy of vaccination coverage.

"If the people who are moving in and out are adequately covered with vaccines that they need, and also, you know, the places where the people are moving into, if those places have adequate coverage, then it's not really an epidemiologic risk," he explains.

Rather than focusing solely on population movement, Dr. Bandyopadhyay suggests the key is maintaining robust surveillance systems to detect any new outbreaks and improving vaccination coverage with the most appropriate vaccine for each setting—whether IPV, OPV, or a combination of both.

## News & Alerts

# MOST RELEVANT MONTHLY NEWS ON VACCINATION AND EMERGING DISEASES WITH BIBLIOGRAPHIC ALERTS

*A summary of the latest News & Alerts in the fields of vaccinology, vaccines, vaccination, and vaccine-preventable diseases. We curate the latest information on regulatory updates, emerging trends, breakthroughs in vaccine technology, vaccine safety and efficacy, global immunization developments and outbreak alerts, as a resource to keep our community informed.*

**"What to Know About XEC, the New SARS-CoV-2 Variant Expected to Dominate Winter's COVID-19 Wave".**
Published: JAMA (Nov 22nd, 2024): 10.1001/jama.2024.24481.

https://jamanetwork.com/journals/jama/fullarticle/2827145

Note: What to Know About XEC, the New SARS-CoV-2 Variant Expected to Dominate Winter's COVID-19 Wave XEC, the up-and-comer among circulating SARS-CoV-2 viruses, arose from the recombination of 2 other variants. Fortunately, all 3 are descendants of the original Omicron virus and are closely related to the variants targeted by the latest COVID-19 vaccines, which are JN.1 and KP.2. Fortunately, XEC is similar enough to other circulating variants that it's not expected to cause worse symptoms or undermine the latest COVID-19 vaccines' ability to prevent severe disease. There's no evidence that it's making people sicker.

**"California confirms first clade I mpox case".**
Published: November 16th, 2024. CDC

https://www.cdc.gov/media/releases/s1116-california-first-clade.html

**"WHO Global Health Emergency Corps sets out actions to save lives during health emergencies".**
Published: November 14th, 2024.

https://www.who.int/news/item/14-11-2024-who-global-health-emergency-corps-sets-out-actions-to-save-lives-during-health-emergencies

Note: Since the launch of the Global Health Emergency Corps (GHEC) in May 2023, WHO, ministries of health and partners have worked to consolidate a vision of an interoperable and globally connected health emergency workforce that can work together on health emergencies. GHEC will enable countries to strengthen their emergency workforce capacities, streamline

coordination mechanisms during response efforts and ultimately save lives. To foster broadened ownership of GHEC, WHO is now rolling out implementation guidance that can be adapted and used at national, regional and global levels. WHO gathered country representatives and partners, from 30 October–1 November 2024, to test the design of the Global Health Emergency Corps through a scenario-based exercise and to discuss concrete steps for implementation.

**"Register: Virtual Update on Polio Eradication, 13 November".**
Published: November 12th, 2024.

https://polioeradication.org/news/register-virtual-update-on-polio-eradication-13-november/

Note: An update on polio eradication achievements, including vaccination in Gaza, sponsored by the Polio Global Eradication Initiative.

**"Weekly Special Press Briefing on the Mpox Outbreak and other Health Emergencies in Africa".**
Published: November 11th, 2024.

https://africacdc.org/news-item/weekly-special-press-briefing-on-the-mpox-outbreak-and-other-health-emergencies-in-africa-6/

**European CDC "Communicable disease threats report, 2-8 November 2024, week 45".**
https://www.ecdc.europa.eu/en/publications-data/communicable-disease-threats-report-2-8-november-2024-week-45

**"Situation Report No 42 - Dengue Epidemiological Situation in the Region of the Americas - Epidemiological Week 42, 2024."**
Published: November 7th, 2024.

https://www.paho.org/en/documents/situation-report-no-42-dengue-epidemiological-situation-region-americas-epidemiological

Note: Between epidemiological weeks (EW) 1 and 42 of 2024, a total of 12,261,165 suspected cases of dengue were reported, resulting in a cumulative incidence of 1,284 per 100,000 population. This represents an increase of 209% compared to the same period in 2023 and 387% compared to the average of the last 5 years. Figure 1 shows the trend of suspected dengue cases as of EW 42.

**"Pertussis Surveillance and Trends"**
Published: November 7th, 2024.

https://www.cdc.gov/pertussis/php/surveillance/index.html#:~:text=In%202024%2C%20reported%20cases%20of,the%20same%20time%20in%202023

Note: In 2024, reported cases of pertussis increased across the United States, indicating a return to more typical trends. Preliminary data show that more than five times as many cases have been reported as of week 44, reported on November 2, 2024, compared to the same time in 2023. The number of reported cases this year is higher than what was seen at the same time in 2019, prior to the pandemic.

**"Marburg virus disease - Rwanda" - WHO.**
Published: November 1, 2024.

https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON543

Note: It has been over a month since the declaration of the Marburg virus disease (MVD) outbreak in Rwanda on 27 September 2024. As of 31 October 2024, 66 confirmed cases, including 15 deaths (CFR: 23%), have been reported including two new confirmed cases since the previous Disease Outbreak News report.

**"Oropouche virus disease update"**
Published: October 22nd, 2024.

https://www.who.int/news-room/fact-sheets/detail/oropouche-virus-disease#:~:text=In%202024%20concerns%20arose%20about,that%20requires%20further%20investigation%20and

**"WHO Approves Another HPV Vaccine for Single-Dose Use".**
Published: October 4th, 2024.

https://www.who.int/news/item/04-10-2024-who-adds-an-hpv-vaccine-for-single-dose-use

Note: In early October, the World Health Organization (WHO) prequalified a fourth human papillomavirus (HPV) vaccine, Cecolin, for single-dose use. The shift from a 2-dose

HPV vaccine regimen to an alternative, off-label 1-dose injection schedule, recommended by the WHO in 2022, will help address the global supply shortages that have historically left individuals from low- and middle-income countries unprotected, the organization said.

**"WHO South-East Asia Region Epidemiological Bulletin, 21st edition (2024), 16 October 2024. Reporting period: 30 September to 13 October 2024".**
https://reliefweb.int/report/myanmar/who-south-east-asia-region-epidemiological-bulletin-21st-edition-2024-16-october-2024-reporting-period-30-september-13-october-2024

**First pediatric flu death of the season reported | AAP News | American Academy of Pediatrics**
https://publications.aap.org/aapnews/news/30721?autologincheck=redirected

Note: The CDC reported the first pediatric flu death of the season. The child was infected with influenza A and died in mid-October. Last flu season, 204 children died of flu. Flu activity is still low nationally, but there have been slight increases among children and teens. CDC and AAP recommend everyone 6 months and older get vaccinated against flu and COVID.

**Hidden in plain sight: the threat of mpox to children and adolescents - The Lancet Child & Adolescent Health**
https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(24)00298-0/abstract

Note: Of the 7851 individuals with mpox notified to WHO by the Democratic Republic of the Congo Ministry of Health from January to May, 2024, 5254 (70%) were younger than 15 years, including 321 people who died (83% of total fatalities due to mpox).2 Young children are at particular risk of severe outcomes from mpox due to malnutrition and co-infections, underscoring the urgent need for a targeted response in children

**Latest update on cases of Clade Ib mpox - GOV.UK**
https://www.gov.uk/government/news/ukhsa-detects-first-case-of-clade-ib-mpox

Note: The first detection of mpox Clade Ib in the UK has occurred. It is different from mpox Clade II that has been circulating at low levels in the UK since 2022.

Clades Ia and Ib are causing outbreaks in the Democratic Republic of the Congo and other African nations. Recently, clade Ib has been detected outside of Africa.

"It is thanks to our surveillance that we have been able to detect this virus. This is the first time we have detected this Clade of mpox in the UK, though other cases have been confirmed abroad." - Professor Susan Hopkins, Chief Medical Adviser at UKHSA

Emergency operations are intact. However, this calls for different countries to strengthen surveillance and contact tracing where necessary.

**"Second round of polio campaign in Gaza completed amid ongoing conflict and attacks: UNICEF and WHO".**
https://www.who.int/news/item/06-11-2024-second-round-of-polio-campaign-in-gaza-completed-amid-ongoing-conflict-and-attacks--unicef-and-who

## Latest Relevant Publications

# LATEST PUBLISHED PAPERS AND COMMENTARIES FROM THE CHIEF EDITORS

*Latest impactful scientific publications that stand out for their potential bearing on healthcare. We introduce groundbreaking research findings, innovative treatment modalities, results from phase 1 to 3 vaccine clinical trials, or paradigm-shifting discoveries that redefine our understanding of infectious diseases and therapeutic approaches for all vaccine-preventable diseases.*

01

"An Improved Alert System for Emerging Infectious Diseases".
**Published:** JAMA 2024; Nov 6. https://doi.org/10.1001/jama.2024.22023

**Editorial comment:** Based on the author, current epidemiological alerts are inadequate because they do not account for uncertainty or provide actionable guidance needed if the situation evolves. An improved outbreak alert system is needed to ensure a coordinated response across health care and public health sectors, this viewpoint publication emphasizes on those defects, and proposes new methods to improve alert systems confronting a future outbreaks, and even new pandemic.

02

Identifying WHO global priority endemic pathogens for vaccine research and development (R&D) using multi-criteria decision analysis (MCDA): an objective of the Immunization Agenda 2030
**Published:** EbioMedicine 2024; November 4th: https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(24)00460-2/fulltext

**Editorial comment:** A must-read publication. The World Health Organization's (WHO) Immunization Agenda 2030 (IA2030) has established a structured approach to prioritize vaccine R&D for endemic pathogens based on regional and country-specific health needs. Through surveys conducted with policymakers and immunization stakeholders across WHO regions, eight criteria were used to assess pathogens, with two—annual deaths in children under five and contribution to antimicrobial resistance—emerging as top priorities in five of the six regions.

The survey responses revealed that these priority criteria did not significantly vary by region, demographic background, or expertise area of respondents. This consistency helped identify five pathogens—Mycobacterium tuberculosis, HIV-1, Klebsiella pneumoniae, Staphylococcus aureus, and extra-intestinal pathogenic Escherichia coli—as shared priorities across all regions. Additionally, six pathogens were uniquely prioritized in individual regions, reflecting localized health needs.

By merging the top ten pathogen lists from each region, WHO derived a global priority list of 17 pathogens for targeted vaccine R&D. To support this agenda, 34 distinct R&D use cases were identified, divided into categories based on necessary actions: Advance product development (the majority), Research, and Prepare to implement. This categorization helps streamline efforts to accelerate vaccine development and implementation for priority pathogens globally.

03

"Global landmark: 2023 marks the worst year for dengue cases with millions infected and thousands of deaths reported".
**Published:** IJID Regions 2024; Dec: 100459. https://doi.org/10.1016/j.ijregi.2024.100459

**Editorial comment:** The authors collected data on reported Dengue cases and deaths from various countries submitted to the World Health Organization (WHO) and its regional offices. They estimated the incidence per million population and the case fatality ratio (CFR) among confirmed cases reported by each country. In 2023, over 6.5 million cases and more than 6,800 Dengue-related deaths were recorded globally, marking a historic high. South America and Southeast Asia showed the highest levels of endemicity and CFRs.

04

"Impact of the 100 days mission for vaccines on COVID-19: a mathematical modelling study.
**Published:** Lancet Glob Health 2024; 12: e1764-74 (November-2024). https://doi.org/10.1016/S2214-109X(24)00286-9

**Editorial comment:** In this study, the authors used a previously published model of SARS-CoV-2 transmission dynamics, calibrated to excess mortality data from the COVID-19 pandemic, to project outcomes under three investment strategies: rapid vaccine development and manufacturing, expanded manufacturing capacity to overcome supply constraints, and strengthened health systems for faster vaccine distribution and global equity. Each scenario was evaluated against the actual COVID-19 pandemic to estimate both public health and economic impacts.

The findings indicate that, assuming countries implemented non-pharmaceutical interventions (NPIs) as they did historically, the "100 Days Mission" could have prevented an estimated 8.33 million deaths worldwide, primarily in lower-middle-income countries, translating to a potential economic savings of US$14.35 trillion. Further investments in manufacturing and health systems could increase the total deaths averted to 11.01 million. In an alternative scenario, where NPIs are lifted earlier based on vaccine coverage, the 100 Days Mission alone could have reduced global restriction days by 12,600 while still averting 5.76 million deaths.

05

"Real-World Assessment of Economic and Clinical Outcomes in Thai Patients With Respiratory Syncytial Virus Infection Across Age Groups: A Retrospective Cohort Analysis."
**Published:** Influenza and other respiratory viruses – Wiley; November 4th, 2024. https://doi.org/10.1111/irv.70039

**Editorial comment:** In this study conducted in Thailand, among RSV-positive patients, younger children experienced the highest disease burden, while older adults faced poorer health outcomes. Older age, comorbidities, and critical care needs were associated with increased healthcare costs. Understanding the economic burden of RSV is essential for evaluating the cost-effectiveness and public health impact of vaccination programs that prioritize at-risk groups to reduce RSV's overall impact on public health.

06

"Excess mortality associated with chikungunya epidemic in Southeast Brazil, 2023."
**Published:** Front Trop Dis 2024; 5 (October). https://doi.org/10.3389/fitd.2024.1466207

**Editorial comment:** In 2023, a significant chikungunya epidemic struck Minas Gerais, one of Brazil's most populous states. The authors focused on the North and Northeast Health Macroregions of Minas Gerais, covering 2.5 million residents. Using epidemiological data from the Ministry of Health's laboratory surveillance, disease notification, and mortality systems, they developed a robust Poisson regression model to estimate expected monthly mortality. Excess deaths were determined by comparing observed deaths to model estimates during the epidemic period. The analysis revealed 890 excess deaths attributed to chikungunya, resulting in a mortality rate of 35.1 per 100,000 inhabitants—approximately 60 times higher than the 15 deaths officially reported by surveillance. This study underscores the need for complementary tools to traditional surveillance to better assess the true impact of outbreaks on morbidity and mortality and to inform public health priorities and interventions more effectively.

07

## Arbovirosis in Europe

**Published:** Enfermedades infecciosas y microbiologia clinica (English ed.), Volume 42, Issue 9, 2024, https://doi.org/10.1016/j.eimce.2024.09.008

**Editorial Comment:** This review highlights the ecological and epidemiological aspects of arboviruses, emphasizing the roles of diverse hosts and reservoirs, including humans, animals, and vectors, in their life cycles. The influence of climate change on the ecology of the vector, which potentially favors the arbovirus transmission, is also reviewed. Focusing on diagnosis, prevention and in the absence of specific treatments, the importance of understanding vector–host interactions and environmental impacts to develop effective control and prevention strategies is emphasized.

08

## Lassa fever research priorities: towards effective medical countermeasures by the end of the decade

**Published:**The Lancet Infectious Diseases, Volume 24, Issue 11, e696 - e706 https://doi.org/10.1016/S1473-3099(24)00229-9

**Editorial Comment:** In 2016, WHO designated Lassa fever a priority disease for epidemic preparedness as part of the WHO Blueprint for Action to Prevent Epidemics. One aspect of preparedness is to promote development of effective medical countermeasures (ie, diagnostics, therapeutics, and vaccines) against Lassa fever. Diagnostic testing for Lassa fever has important limitations and key advancements are needed to ensure rapid and accurate diagnosis. Additionally, the only treatment available for Lassa fever is ribavirin, but controversy exists regarding its effectiveness. Finally, no licensed vaccines are available for the prevention and control of Lassa fever.

09

## Current Epidemiological Status of Chikungunya Virus Infection in East Africa: A Systematic Review and Meta-Analysis

**Published:** Journal of Tropical MedicineVolume 2024, Article ID 7357911 https://onlinelibrary.wiley.com/doi/10.1155/2024/7357911

**Editorial Comment:** This study highlights the significant burden of chikungunya in East Africa, and the findings underscore the need for targeted public health interventions and improved surveillance to manage and control chikungunya outbreaks in the region.

10

## Clinical characteristics and in-hospital outcomes associated with RSV-ALRI compared to other viral ALRI in hospitalised children under two years old

**Published:** The Journal of Infectious Diseases, 2024; jiae543 https://doi.org/10.1093/infdis/jiae543

**Editorial Comment:** Children with RSV-ALRI exhibited more severe symptoms, received more antibiotics, and had longer hospital stays compared to those with other viral ALRIs, underscoring the need for effective prevention and treatment strategies for RSV.

11

## Long-term dynamics of measles virus-specific neutralizing antibodies in children vaccinated before 12 months of age

**Published:** Clinical Infectious Diseases, 2024;, ciae537. https://doi.org/10.1093/cid/ciae537

**Editorial Comment:** Children vaccinated before 8·5 months of age exhibited a markedly faster antibody decay and lost their protective neutralizing antibody levels over 6 years.

Routine vaccination of infants under 8·5 months of age may lead to blunted MeV-specific antibody responses to subsequent MMR vaccination. Early MMR vaccination should only be considered during measles outbreaks or in other situations of increased risk of MeV infection.

12

## Hajj vaccination strategies: Preparedness for risk mitigation

**Published:** Journal of Infection and Public Health,Volume 17, Issue 11, 2024. https://doi.org/10.1016/j.jiph.2024.102547

**Editorial Comment:** On top of meningococcal vaccines much more much more vaccines are recommended for Hajj pilgrims. Drawing from the collective experience, the annual planning process emphasizes the importance of adapting vaccination approaches to address new threats and emerging public health concerns.

13

## The role of antibody-dependent enhancement in dengue vaccination

**Published:** Trop Dis Travel Med Vaccines 10, 22 (2024). https://doi.org/10.1186/s40794-024-00231-2

**Editorial Comment:** Antibody-dependent enhancement is a phenomenon causing worldwide morbidity and mortality in dengue virus infections. Additionally, in the search for a vaccine against DENV, vaccine-induced ADE has caused several setbacks for the use of a vaccine on a larger scale. Despite this, a recently licensed live attenuated vaccine (Qdenga, TAK-003, Takeda) has not shown signs of ADE. Long-term data has yet to show whether new candidates in phase 2 and 3 trials such as TV003/TV005 with both structural as well as non-structural proteins have a higher efficacy. Another big question remaining is if vaccine efficacy is waning, could that result in more ADE?

14

## "Effect of COVID-19 vaccination on the risk of developing post-COVID conditions: The VENUS study".

**Published:** Vaccine 2025; 43: 126497. https://doi.org/10.1016/j.vaccine.2024.126497

**Editorial comment:** This retrospective cohort study analyzed a database containing medical claims, COVID-19 case data, and vaccination records from residents of four Japanese municipalities. Among 84,464 participants, 9,642 (11.4%) developed post-COVID-19 conditions over an 8-month period. The risk of developing 28 out of 36 targeted conditions—including various respiratory, cardiovascular, inflammatory, immune, physical, psychiatric, and endocrine disorders—was significantly lower for individuals who had received a COVID-19 vaccination within 14 to 149 days prior to infection. These findings suggest that COVID-19 vaccination, particularly when administered within 5 months before infection, can reduce the incidence and risk of post-COVID-19 conditions. Notably, despite having the highest mean age and prevalence of comorbidities, those most recently vaccinated experienced a lower risk of developing post-COVID-19 conditions. These results offer valuable insights for shaping future COVID-19 vaccination strategies.

15

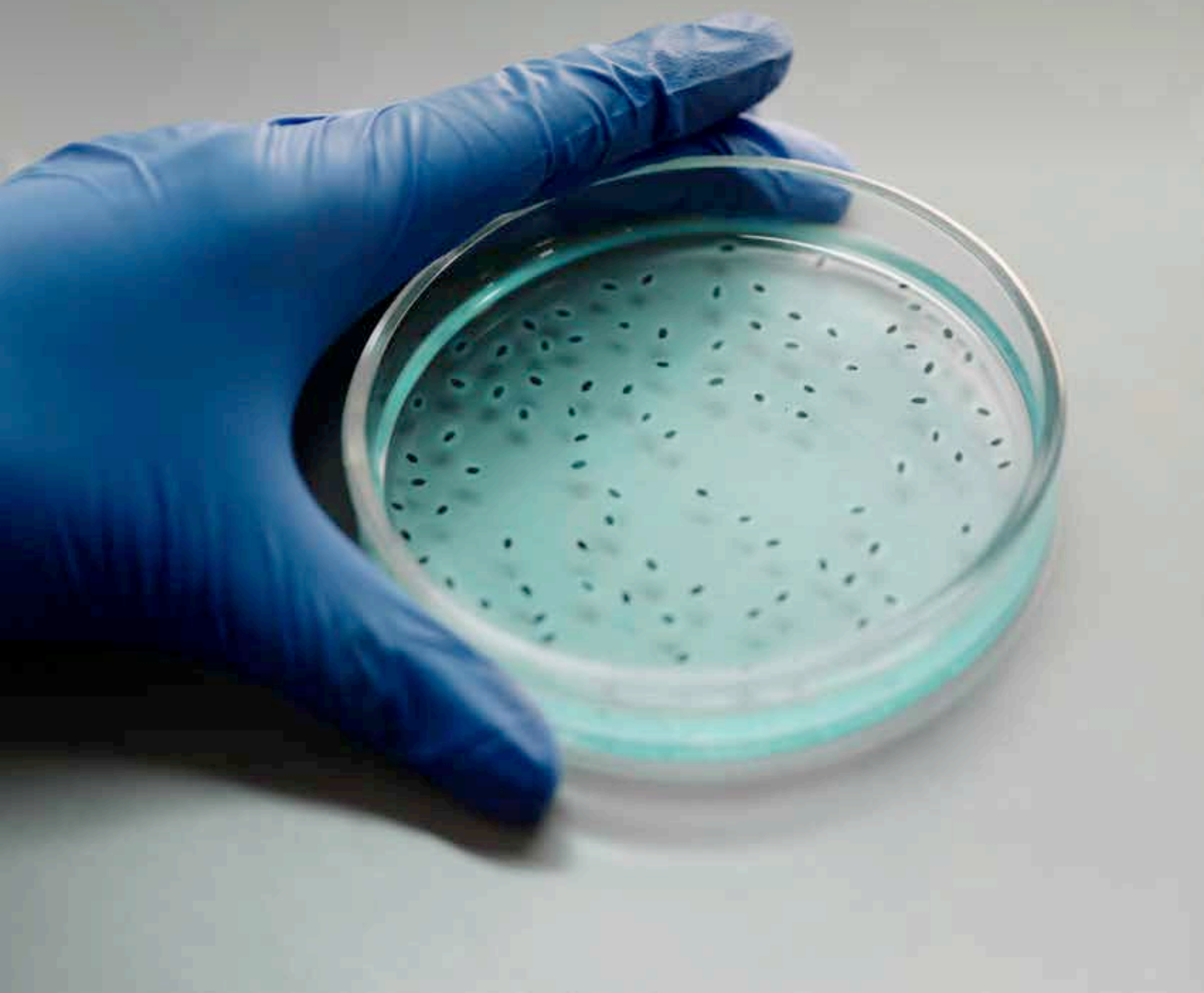
## "Does Tobacco Smoking Affect Vaccine-Induced Immune Response? A Systematic Review and Meta-Analysis"

**Published:** Vaccines 2024; 12: 1260. https://doi.org/10.3390/vaccines12111260

**Editorial comment:** This review provides a comprehensive overview of the literature on how smoking diminishes the effectiveness of active immunization by impairing vaccine-induced immune responses. Thirty-four studies were included in the analysis. Overall, smoking was associated with reduced antibody levels and avidity, as well as lower immune cell production. The meta-analysis revealed a weighted mean difference of 0.65 (95% CI: 0.10–1.19, p = 0.02) in vaccine effectiveness between smokers and non-smokers for vaccines against COVID-19, influenza, pneumococcus, HBV, HPV, tetanus, pertussis, polio, Haemophilus influenzae type b, measles-mumps-rubella, and recurrent urinary tract infections. The findings suggest that smoking cessation programs should be integrated into vaccination strategies to enhance vaccine effectiveness and improve public health outcomes, and maybe vaccination schemes should be different between smokers and non-smokers.

Editors Corner

# VACCINATION AS A TOOL TO DECREASE ANTIMICROBIAL RESISTANCE



Since the introduction of penicillin, bacteria have gradually developed mechanisms to resist its effects. To date, hundreds of antibacterial agents have been developed, and bacteria have evolved various mechanisms of antimicrobial resistance (AMR). Some of the key mechanisms include:

1. **Reduced Permeability**: Mutations in bacterial porins decrease the entry of the antibacterial agent. A well-known example includes penicillin-resistant *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* (Shown as Mechanism 1, in Figure-1).
2. **Efflux Pumps**: Once the antibacterial agent enters the bacterial cell, efflux pumps can be activated to expel the drug. This is a common mechanism, particularly in *Enterobacteriaceae* against aminoglycosides, though not exclusive to them. (Shown as Mechanism 2, in Figure-1).
3. **Receptor Modification**: Bacteria can alter the receptors on their ribosomes, thereby reducing the binding effectiveness of protein synthesis inhibitors, such as aminoglycosides, tetracyclines, and macrolides. (Shown as Mechanism 3, in Figure-1).
4. **Enzymatic Inactivation**: Perhaps the most widespread mechanism, enzymatic inactivation involves the production of enzymes like beta-lactamases, which break down drugs such as beta-lactam antibiotics. (Shown as Mechanism 4, in Figure-1).

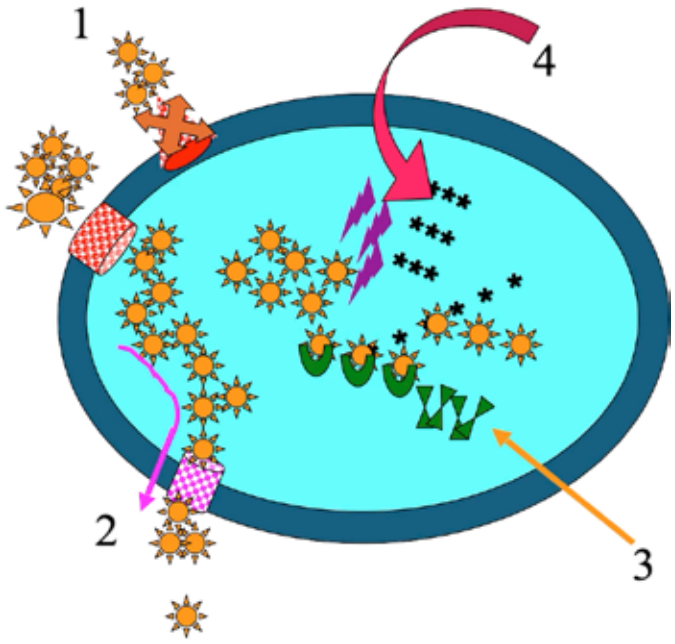



Figure-1: Mechanisms of AMR:

AMR can be rapidly transmitted between bacteria through horizontal gene transfer, primarily via conjugation (bacteriophages). This efficient spread has led to the rapid global dissemination of resistant strains, making antimicrobial resistance a major health threat. In 2019 alone, AMR was responsible for an estimated 4.9 million deaths worldwide.

The use of antimicrobial agents in animals is the largest contributor to global antimicrobial consumption. In 2019, the World Organization for Animal Health (WOAH) estimated that 84,500 tons of antimicrobials were used in the animal sector, although this represented a 13% decrease compared to 2017. In contrast, global antibiotic consumption in humans increased by 65% between 2000 and 2015, with the most significant rise occurring in low- and middle-income countries (LMICs). This trend is expected to triple by 2030, compared to 2015 levels, unless effective interventions are implemented. A major challenge is ensuring equitable access to antimicrobials, particularly in LMICs, where the lack of access to effective treatments may pose a greater risk to public health than antimicrobial resistance itself.

Indeed, regulating and restricting the use of antibacterials are crucial measures to prevent the spread of AMR. However, as illustrated in the figure below (Figure 2), several other interventions can complement these efforts. These include the development of better, faster, and cost-effective diagnostic tools to accurately distinguish viral infections and avoid unnecessary antibacterial prescriptions; strategies to maintain microbiota balance (the best example is how gut microbiota influences the growth of *Clostridium difficile*); the use of more selective antibacterials; the development of monoclonal antibodies; bacteriophages engineered with counteracting genetic information against AMR; and the use of vaccines.

Figure-2: Interventions to prevent AMR (Reproduced with permission of Micoli F, Bagnoli F, Rappuoli R, Nature Rev 2021; 19: 287-302).

Now, how can vaccination help prevent the dissemination of AMR?

As illustrated in Figure 3, from an individual perspective, an unvaccinated person with a bacterial infection would typically require one or more antibiotics, so called first - and second - line

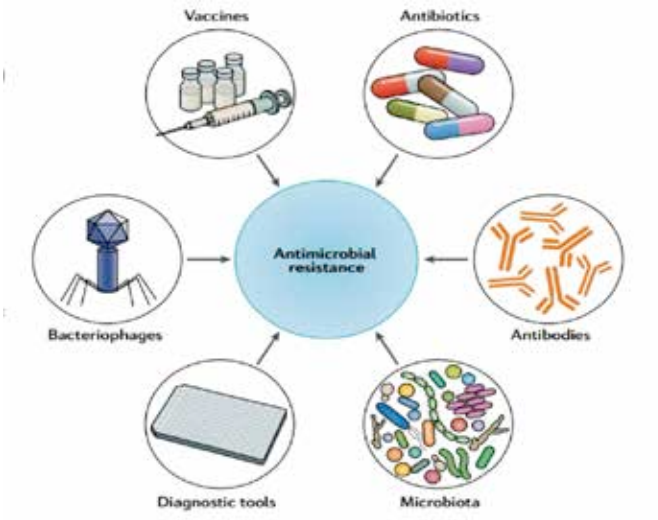



Figure-2: Interventions to prevent AMR (Reproduced with permission of Micoli F, Bagnoli F, Rappuoli R, Nature Rev 2021; 19: 287-302).

antibacterials. Now, in a population with many unvaccinated individuals, increased prescription of antibiotics would lead to the rapid spread of both bacterial infections and AMR in the community, with a range of negative consequences.

However, when individuals are vaccinated, both on a personal and population level, vaccination helps prevent infection. As a result, the need for first- or second - line antibiotics becomes rare, as shown in Figure 4.

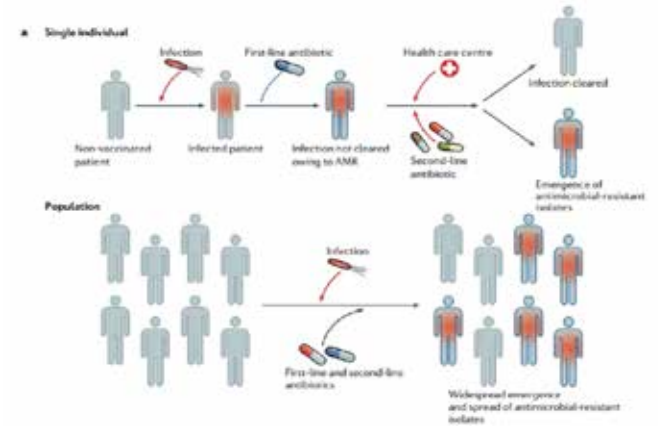



Figure 3. AMR transmission without vaccination (Reproduced with permission of Micoli F, Bagnoli F, Rappuoli R, Nature Rev 2021; 19: 287-302).

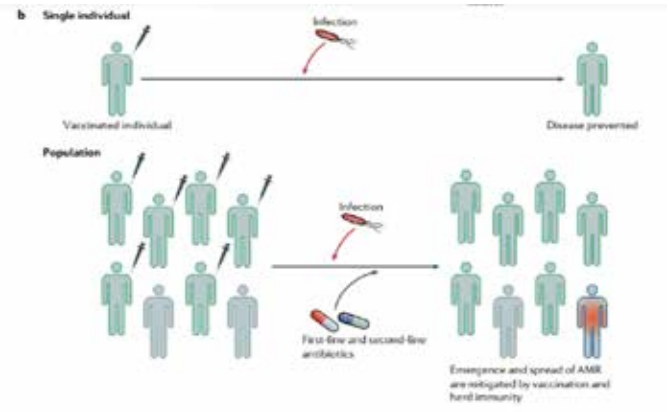



Figure 4. AMR prevention thru vaccination (Reproduced with permission of Micoli F, Bagnoli F, Rappuoli R, Nature Rev 2021; 19: 287-302).

Pneumococcal vaccination, particularly with the current pneumococcal polysaccharide-protein conjugate vaccines (PCVs), provides a clear example of how vaccination can reduce antibiotic prescriptions and, consequently, decrease pneumococcal AMR. This effect is observed both in terms of nasopharyngeal colonization and in cases of disease, with a reduction of up to 62%, especially against penicillins, cephalosporins, and macrolides.

In addition, the meningococcal B vaccine is estimated to provide 33–47% protection against gonorrhea, potentially helping to reduce AMR associated with this widely spread pathogen.

On the other hand, viral infections often result in the inappropriate overprescription of antibiotics, which contributes to the spread of antimicrobial resistance (AMR). Accordingly, vaccination against both influenza and SARS-CoV-2 has been shown to reduce the need for antibacterial prescriptions, thereby helping to mitigate the rise of AMR.

In 2024, the World Health Organization has published a report entitled **"Estimating the impact of vaccines in reducing antimicrobial resistance and antibiotic use".**

Globally, vaccines and vaccination could annually avert up to 408 000 deaths, 23.0 million DALYs, US$ 30.0 billion in hospital costs and US$ 17.7 billion in productivity losses, all associated with AMR.

The report evaluates the impact of both already licensed vaccines and those currently in development.

Each year, vaccines against the following diseases could significantly reduce antibiotic use:

- ***Streptococcus pneumoniae***: Vaccinating 90% of the world's children, as targeted by the Immunization Agenda 2030, along with older adults, could save up to 33 million antibiotic doses.
- **Typhoid**: Accelerating the introduction of typhoid vaccines in high-burden countries could save 45 million antibiotic doses.
- **Malaria (***Plasmodium falciparum***)**: The malaria vaccine could prevent up to 25 million antibiotic doses, which are often misused in attempts to treat malaria.
- **Tuberculosis (TB)**: Once developed, TB vaccines could have the greatest impact, saving between 1.2 and 1.9 billion antibiotic doses — a significant portion of the 11.3 billion doses used annually to treat the diseases covered in this report.

The WHO report also assesses the role of vaccines in mitigating AMR and provides actionable recommendations for key stakeholders on how to enhance vaccines' effectiveness in addressing AMR. The analysis covers 44 vaccines targeting 24 pathogens, including 19 bacterial species, four viruses, and one parasite. Given that infections can cause multiple syndromes and impact different age groups, several vaccines targeting the same pathogen were evaluated for their potential to reduce AMR.

The pathogens examined in the report include: *Acinetobacter baumannii, Campylobacter jejuni, Clostridioides difficile, Enterococcus faecium, Enterotoxigenic Escherichia coli* (ETEC), *Extraintestinal Pathogenic Escherichia coli* (ExPEC), *Group A Streptococcus* (GAS), *Haemophilus influenzae* type B (Hib), *Helicobacter pylori, Klebsiella pneumoniae, Mycobacterium tuberculosis, Neisseria gonorrhoeae,* nontyphoidal *Salmonella, Pseudomonas aeruginosa, Salmonella paratyphi A, Salmonella typhi, Shigella, Staphylococcus aureus, Streptococcus pneumoniae, Plasmodium falciparum* (malaria), influenza, norovirus, rotavirus, and respiratory syncytial virus (RSV).

Indeed, vaccines offer numerous opportunities to prevent diseases, reduce hospitalizations, save lives, and lower healthcare costs. By helping to reduce AMR, vaccines play an additional critical role in improving global health, making them essential for human well-being and long-term survival.

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Best Practice

# PNEUMOCOCCAL CONJUGATED VACCINES (PCVS) SHORT SCHEMES: THE UK EXPERIENCE

In 2006, the UK introduced the 7-valent PCV (PCV7) into the infant immunization program with a 2+1 schedule, alongside a 12-month catch-up for all children up to 2 years of age. This program achieved a high vaccine coverage (>90%), resulting in a rapid and sustained reduction of Invasive Pneumococcal Disease (IPD) due to the PCV7 serotypes across all age groups. This impact was due to the direct protection from vaccination as well as indirect (herd immunity) protection achieved through the prevention of pneumococcal carriage in the vaccinated child's nasopharynx and onward transmission to others. This decline was partially offset by small increases in non-PCV7 type IPD across all age groups.

In April 2010, PCV13 replaced PCV7, which led to further reductions in IPD due to the additional PCV13 serotypes. Since 2013/14 an increase in overall incidence of IPD has been observed, largely due to increases in non-PCV13 vaccine serotypes (especially serotypes 8, 12F and 9N) and mainly in older age groups.

In early 2020, the UK moved to a 1+1 infant schedule, with vaccinations given at 12 weeks and 1 year of age. Due to COVID-19 pandemic lockdown and subsequent restrictions since March 2020, IPD incidence decreased by 65% across all age groups in 2020/21 (see figure below). As restrictions were eased, IPD incidence gradually increased, initially in young children followed by older children and adults.

In 2022, PCV15, which protects against the PCV13 pneumococcal serotypes as well as serotypes 22F and 33F, was licensed for use from 6 weeks of age. UKs Joint Committee on Vaccination and Immunisation (JCVI) considered the use of PCV15 in a 1+1 schedule and agreed that the current evidence indicated

it could be used in a 1+1 schedule. On the other hand, PCV20 which protects against 20 pneumococcal serotypes became available too but not yet included in UKs NIP.

Recent modeling suggests that PCV15 might increase overall invasive pneumococcal disease as the reduction in vaccine-type invasive pneumococcal disease would be counterbalanced by an increase in non-PCV15 invasive pneumococcal disease. By contrast, PCV20 is projected to have a substantial impact on overall invasive pneumococcal disease due to higher invasiveness of the additional serotypes covered by PCV20 than the replacing non-vaccine serotypes. Reduced carriage protection against PCV13 serotypes with higher valency vaccines would amplify these effects. (see PCVs table)

Replacing PCV13 with PCV20 is likely to have a substantial public health benefit, but PCV15 could potentially increase the overall burden of disease since it does not cover PCV20 STs

The decision to replace current PCVs with higher valency vaccines in pediatric vaccination programs requires careful evaluation, considering the complexity of the dynamic changes in pneumococcal transmission and the relative invasiveness of emerging serotypes in carriage. Multivalent vaccine formulations that preserve immunogenicity with increasing valency or the development of PCVs that complement existing PCVs by including only the main highly invasive non-vaccine serotypes could offer additional public health benefit.

## Final Remarks

Adding more STs to PCVs decreases protein-polysaccharide conjugations, leading to decreased immunogenicity.

UK experience should be closely followed up to measure its impact and, in this way, evaluate if countries with similar epidemiology and PCV schedule history can switch to a shortened scheme such as the 1+1.

## UK PCV Vaccines

| Type | Trade Mark | Serotypes included |
|---|---|---|
| Pneumococcal con-jugate vaccine (PCV20) | Apexxnar® | 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F |
| Pneumococcal con-jugate vaccine (PCV15) | Vaxneuvance® | 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F |
| Pneumococcal conjugate vaccine (PCV13) | Prevenar 13® | 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F |
| Pneumococcal conjugate vaccine (PCV10) | Synflorix® | 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F. |

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Guest Contributors

# ADVANCING VACCINE MANUFACTURING IN LOW- AND MIDDLE-INCOME COUNTRIES: INSIGHTS FROM THE WHO/ MPP MRNA TECHNOLOGY TRANSFER HUB PROGRAM

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## Introduction

The COVID-19 pandemic illuminated the stark inequities in global vaccine distribution, especially for low- and middle-income countries (LMICs). While wealthier nations secured early access to vaccines, many LMICs struggled to obtain enough doses, prolonging the pandemic and contributing to the rise of new variants. This disparity underscored the urgent need for more equitable vaccine access, especially in the context of global health security.

In response to these challenges, the World Health Organization (WHO) and the Medicines Patent Pool (MPP) launched the **mRNA Technology Transfer Hub Program**. This ambitious initiative aims to reduce dependency on global vaccine suppliers by enabling local manufacturers in LMICs to independently produce mRNA vaccines. While this effort directly addresses COVID-19, it also lays the groundwork for future vaccine production against other infectious diseases. One of the key players in this initiative is Egypt, which has become a leader in mRNA vaccine production in the Middle East and North Africa (MENA) region.

This article explores the progress, challenges, and future potential of the WHO/MPP mRNA Technology Transfer Hub, with a focus on Egypt's role in reshaping vaccine manufacturing in LMICs.

## The WHO/MPP mRNA Technology Transfer Hub: Goals and Importance

The WHO/MPP mRNA Technology Transfer Hub was designed to empower LMICs by sharing mRNA vaccine technology with qualified local manufacturers. The initiative seeks to democratize vaccine production, allowing countries to meet their own vaccine needs and reduce reliance on external suppliers. mRNA vaccines, which were first developed to combat COVID-19, represent a breakthrough in vaccinology due to their

flexibility, rapid development timeline, and potential to tackle a wide range of pathogens.

Egypt recognized the transformative potential of mRNA technology early on. In addition to addressing COVID-19, the government and healthcare stakeholders in Egypt understood that local mRNA manufacturing could help protect against other diseases, such as seasonal influenza, rabies, and polio. These diseases, traditionally difficult to tackle in LMICs, could potentially be controlled using mRNA-based vaccines.

As a key partner in the program, Egypt has worked closely with WHO, MPP, and other stakeholders to ensure the successful transfer and application of mRNA technology. The project's impact has been significant, not just for Egypt, but for the entire MENA region. Through collaboration and technical exchanges, Egypt is laying the foundation for a future of self-sufficient vaccine production.

## Scope and Implementation: Establishing an mRNA Vaccine Manufacturing Facility in Egypt

The journey to establishing an mRNA vaccine production facility in Egypt began with a comprehensive needs assessment. In partnership with WHO and MPP, Egypt conducted an in-depth evaluation of its infrastructure, workforce, and regulatory environment. This assessment was vital in determining the feasibility of setting up such a facility, as well as identifying gaps in technology and capacity that needed to be addressed.

To build the necessary expertise, Egypt's healthcare professionals, along with representatives from the Egyptian Drug Authority (EDA), were trained at South Africa's mRNA training center. This training covered essential aspects of mRNA production, such as sequencing, formulation, and quality control, enabling the team to gain hands-on experience in laboratory-scale production.

Returning to Egypt, the team began establishing pilot production facilities to adapt the lessons learned in South Africa to local conditions. Collaboration with the Ministry of Health's Preventive Affairs Sector and WHO's Eastern Mediterranean Regional Office (EMRO) was critical in ensuring that Egypt's vaccine production capabilities aligned with both national and regional needs.

A major milestone was reached when Egypt successfully established a functional pilot production line capable of producing test batches of mRNA vaccine material. This achievement marked Egypt's entry into mRNA vaccine production, setting the stage for future advancements in local vaccine manufacturing. With continued support from WHO and MPP, Egypt is on track to scale these efforts into a full-fledged manufacturing facility that could meet both national and regional vaccine needs.

## Overcoming Challenges in the Technology Transfer Process

Building a local mRNA vaccine manufacturing facility is not without its challenges, particularly in LMICs where infrastructure and regulatory systems may not be fully equipped to support such advanced technologies. In Egypt, navigating the regulatory landscape for mRNA vaccines presented a significant hurdle. Unlike traditional vaccines, mRNA vaccines require specialized equipment and stringent storage and transport conditions to maintain stability and efficacy. These requirements necessitated a complete overhaul of existing regulatory frameworks to ensure they were aligned with global standards.

To address this, Egypt worked closely with the Egyptian Drug Authority (EDA) to develop a regulatory framework that would accommodate the unique needs of mRNA vaccine production. This involved a series of technical consultations and iterative adjustments to meet both local and WHO standards. While time-consuming, this process has helped ensure that Egypt's vaccine production meets the highest standards of quality and safety.

In addition to regulatory challenges, securing sustained funding and resources has been another major obstacle. Although the WHO/MPP provided initial funding, the costs associated with infrastructure development, staff training, and equipment procurement quickly exceeded initial estimates. As Project Manager, I oversaw resource allocation, managed budgets, and engaged with potential investors to explore alternative funding sources to ensure the financial sustainability of the project.

Logistical challenges also arose, particularly in the international shipping of specialized equipment. Key components, such as bioreactors and purification systems, had to be imported, which

required navigating complex trade regulations and supply chain disruptions. Despite these obstacles, Egypt's commitment to overcoming these challenges has paved the way for significant progress in local mRNA vaccine production.

## Regional and Global Impact of Local mRNA Production

The establishment of an mRNA vaccine manufacturing facility in Egypt has wide-reaching implications for both the MENA region and the global health landscape. By reducing its reliance on external suppliers, Egypt is enhancing its health security and establishing itself as a regional leader in vaccine production. This capability will not only improve Egypt's ability to respond to future pandemics but will also help mitigate the impact of infectious disease outbreaks in neighboring LMICs.

The success of the mRNA Technology Transfer Hub also demonstrates the power of international cooperation in health technology transfer. Through partnerships with organizations like WHO and MPP, Egypt is showing that LMICs can play a crucial role in addressing global health challenges. This collaborative model may inspire similar programs in other regions, creating a network of self-sustaining vaccine manufacturers capable of responding to emerging health threats.

Beyond COVID-19, mRNA vaccines have the potential to address a wide array of diseases. Egypt's growing expertise in mRNA technology positions it to expand its vaccine portfolio, including vaccines for influenza, rabies, and even certain types of cancer. As Egypt builds on its mRNA capabilities, it is also contributing to the regional economic growth and improving public health outcomes, making healthcare systems more resilient in the face of future challenges.

## Future Prospects and Next Steps

Looking ahead, Egypt plans to continue expanding its mRNA production capacity. The progress achieved so far has laid a strong foundation, but scaling up production, optimizing manufacturing processes, and exploring new vaccine targets are key priorities. To achieve this, Egypt is actively seeking new partnerships and funding opportunities to support its continued growth in mRNA vaccine production.

Collaborations with global health organizations like the Serum Institute of India and Sinopharm are instrumental in diversifying Egypt's vaccine production capabilities. These partnerships will help Egypt localize additional vaccine technologies, such as viral vector and recombinant vaccines, which will further enhance its ability to respond to diverse health threats in the region.

Additionally, Egypt aims to become a regional training hub, offering technical support and capacity-building services to other LMICs interested in developing their own vaccine manufacturing capabilities. By sharing knowledge and expertise, Egypt can help other nations achieve self-sufficiency in vaccine production, contributing to a more equitable global health ecosystem.

## Conclusion

The WHO/MPP mRNA Technology Transfer Hub Program represents a transformative step toward global vaccine equity, and Egypt is proud to be at the forefront of this initiative. Through the transfer of mRNA technology, Egypt is building a self-sufficient healthcare system capable of addressing its own vaccine needs and contributing to regional health security. The progress made thus far highlights the importance of international cooperation, regulatory adaptability, and financial sustainability in establishing resilient vaccine production infrastructures.

As Egypt continues to expand its mRNA capabilities and form new partnerships, it is playing a pivotal role in reshaping the future of vaccine manufacturing in LMICs. The path toward vaccine self-reliance is challenging, but with continued support from WHO, MPP, and other international stakeholders, Egypt is on track to achieve a sustainable and resilient healthcare ecosystem that can respond to both current and future health challenges.

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VACCINES BEAT

## Who we are

At Vaccines Beat, we understand that vaccines and immunization have become a crucial topic of discussion at the center of any public health analysis. Therefore, timely, relevant, accessible, and well-curated information for all vaccine preventable diseases is key to advancing better health policies.

For this reason, a team of passionate vaccine professionals has created Vaccines Beat and each month diligently works to share with the healthcare ecosystem information, knowledge, and insights to improve global health.

## Vision

Vaccines Beat aims to become the beacon of insight in the public health ecosystem through its distinctive monthly newsletter. With an in-depth 360 perspective, carefully curated information and expert analysis, this novel platform fosters collaboration among a diverse global network of stakeholders.

## Mission

Vaccines Beat's main task is to inform through the review of the most recent developments in vaccines, immunization, and vaccine preventable diseases. Our mission extends to sharing best practices from successful initiatives worldwide while building bridges through editorial collaboration with regional and international stakeholders.

Vaccines Beat highlights the importance of information sharing & collaborative efforts within the public health community to boost vaccination campaigns, R&D, public policy, access, awareness, and equity.

Vaccines Beat encourages stakeholders to take action and promote sustainable commitment with continued support through multi-stakeholder synergies.



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