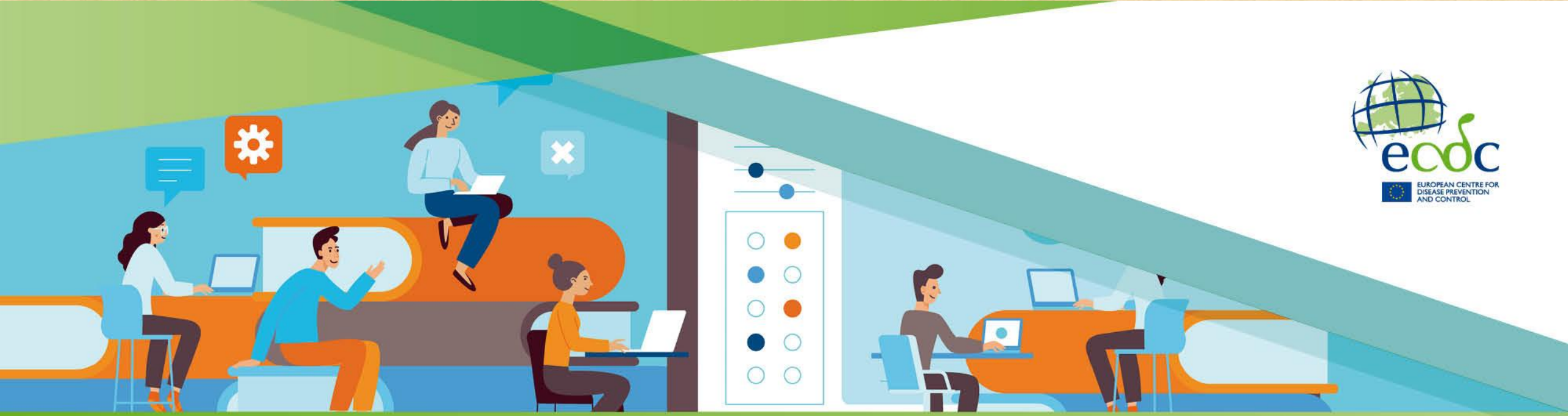

GenEpi-BioTrain - Virtual Training 28 - Genomics and epidemiology of polioviruses: How a virus resists eradication

Vaccination and Evolution of Vaccine-Derived Strains

20 July 2026

Dr. Corey Peak, Gates Foundation

Aim and learning objectives

Aim

Understand how poliovirus genomics and vaccination strategy interact to drive emergence and eradication of vaccine-derived strains, and what this means for global poliovirus eradication.

Specific learning objectives

At the end of this session, you will be able to:

1. Differentiate wild-type poliovirus, oral polio vaccine strains, and vaccine-derived polioviruses
2. List the risk factors for vaccine-derived poliovirus emergence and evolution
3. Describe the key factors and milestones for the transition from oral polio vaccine to inactivated polio vaccine

Outline

This session consists of the following elements:

1. Overview of diverse types of polioviruses slated for eradication and their inter-relationships
2. Review of steps and plans to reduce emergence risk (eg, cessation and novel oral polio vaccines)
3. Q&A

Types of polioviruses

	Serotype 1	Serotype 2	Serotype 3
Wild	**WPV1**: Endemic in Afghanistan and Pakistan	**WPV2**: Eradicated globally; last detected in 1999 in India	**WPV3**: Eradicated globally; last detected in 2012 in Nigeria

- Global Polio Eradication Initiative (GPEI) launched in 1988 with the aim to eradicate polio by 2000
- Three serotypes of wild poliovirus were identified, against which we had trivalent oral polio vaccines (OPV) and inactivated polio vaccines (IPV)
  - OPV and IPV tools developed >60 years ago overall continue to protect against respective serotypes [1,2]

[1] Sun M, et al. Immune Serum From Sabin Inactivated Poliovirus Vaccine Immunization Neutralizes Multiple Individual Wild and Vaccine-Derived Polioviruses, *Clinical Infectious Diseases*, Volume 64, Issue 10, 15 May 2017, Pages 1317–1325, https://doi.org/10.1093/cid/cix110
[2] Alam MM, et al. Structure of Contemporary Wild Poliovirus Type 1 Strains Endemic in Pakistan, *The Journal of Infectious Diseases*, Volume 226, Issue 5, 1 September 2022, Pages 843–851, https://doi.org/10.1093/infdis/jiab555

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Wild	**WPV1**: Endemic in Afghanistan and Pakistan	**WPV2**: Eradicated globally; last detected in 1999 in India	**WPV3**: Eradicated globally; last detected in 2012 in Nigeria
Vaccine-Like	**Sabin-Like Type 1**: Commonly seen; indicative of bOPV use	**Sabin-Like Type 2**: No longer seen since last use of Sabin OPV2 in 2023 **Novel-Like Type 2**: Commonly seen; indicative of nOPV2 use	**Sabin-Like Type 3**: Commonly seen; indicative of bOPV use

- Sabin-Like vaccine viruses are genetically identical to, or nearly identical to, the live-attenuated strains Albert Sabin developed for his OPV product in the 1950s

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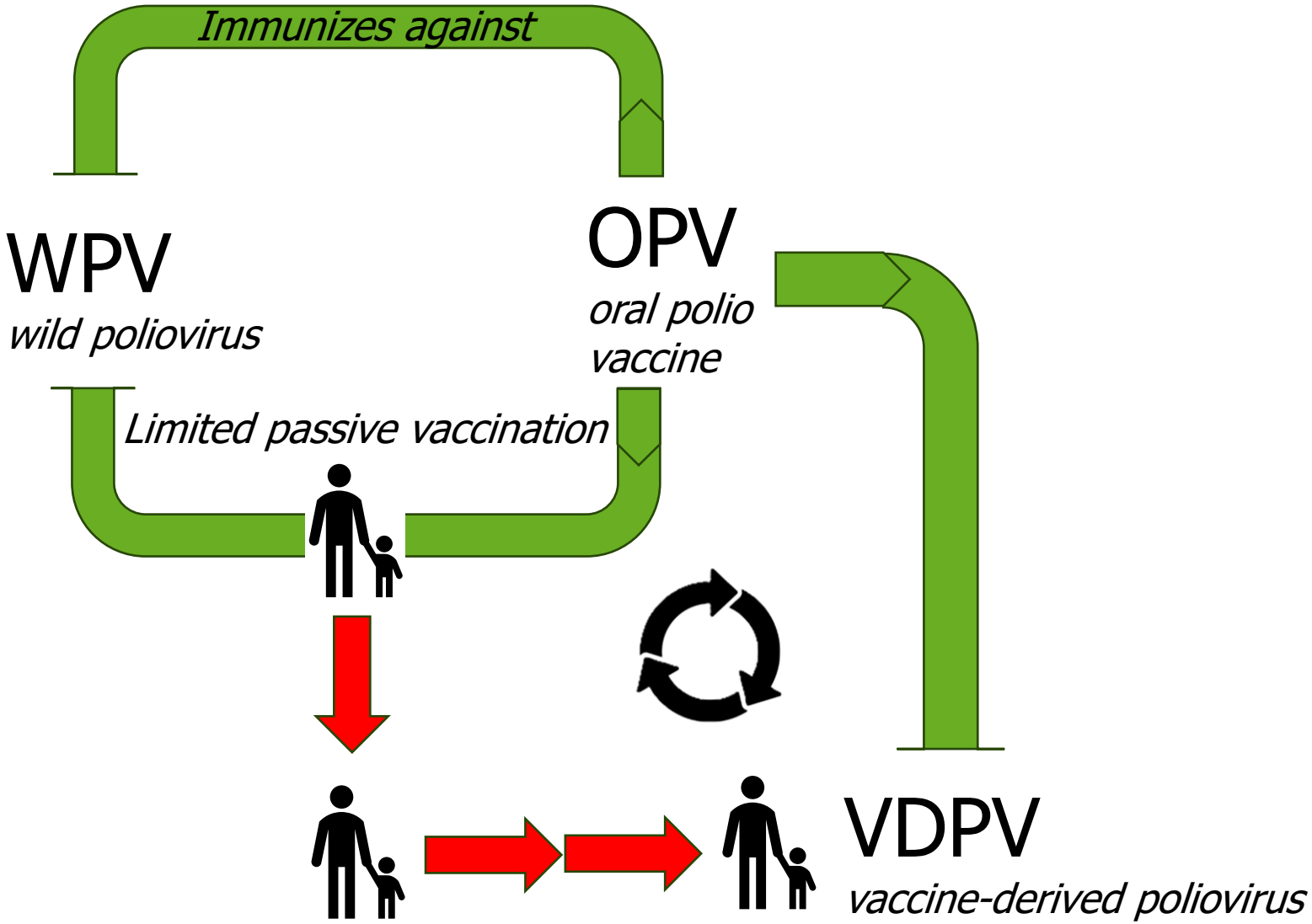
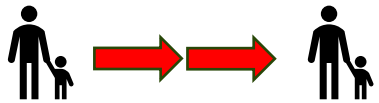
Vaccine-Derived	**VDPV1**: Uncommonly seen	**VDPV2**: Outbreaks in 13 countries; dominant source of paralytic poliomyelitis	**VDPV3**: Uncommonly seen

Catch 22

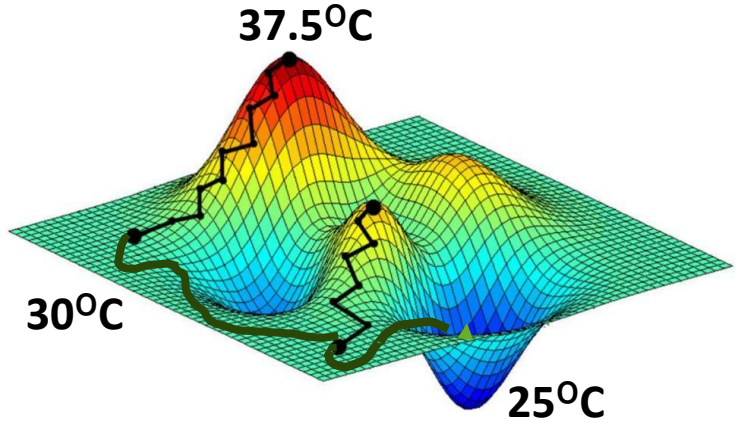

Immunizes against
WPV
wild poliovirus
OPV
oral polio vaccine
Limited passive vaccination
VDPV
vaccine-derived poliovirus

Genetic changes on the road to and from attenuation



VDPV
vaccine-derived poliovirus

- Attenuation of Sabin strains performed via serial passage (~37) with cold adaptation (33ºC → 30ºC → 25ºC) [1]
- Sites under strong selection vary by serotype; some emerge <1 month after vaccination [2]
  - Each serotype includes a major attenuation mutation in IRES domain V: Sabin 1 position 480, Sabin 2 position 481, or Sabin 3 position 472
- Capsid sequence, including Virus Protein 1 (VP1), of VDPVs still more closely related to the Sabin strain than to WPV, though the paralysis induced is clinically indistinguishable [3]
  - A poliovirus is classified as a VDPV once VP1 diverges from the parent Sabin strain by ≥10 nucleotides (types 1 and 3) or ≥6 nucleotides (type 2) — roughly ≥1% and ≥0.6% divergence



Temperature tolerant viruses observed in vaccinee stool samples soon after vaccination, leading to loss of attenuation [1]

TABLE 3 Sabin type 2 sites under strong selection[f]

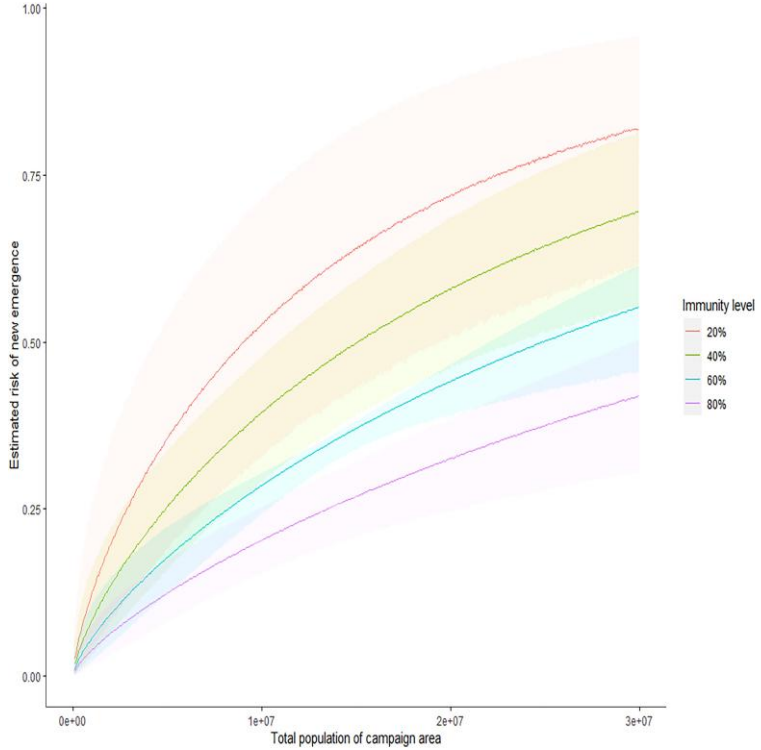
Nucleotide[a]	Amino acid[b]	Consensus circulating nucleotide[c]	No. of fixed variants (n = 43)	Mean rate (10^{-3} nt/day)
U-398-C[d]		C[e]	4	21
A-481-G		G	17	154
U-2909-C	**I-1143-T**	C (T)	8	47

[1] Raul Andino, July 2026 adaptation of Stern A, Yeh MT, Zinger T, Smith M, Wright C, Ling G, Nielsen R, Macadam A, Andino R. The Evolutionary Pathway to Virulence of an RNA Virus. Cell. 2017 Mar 23;169(1):35-46.e19. https://doi.org/10.1016/j.cell.2017.03.013
[2] Famulare M, Chang S, Iber J, Zhao K, Adeniji JA, Bukbuk D, Baba M, Behrend M, Burns CC, Oberste MS. 2016. Sabin Vaccine Reversion in the Field: a Comprehensive Analysis of Sabin-Like Poliovirus Isolates in Nigeria. J Virol 90:. https://doi.org/10.1128/jvi.01532-15
[3] Burns CC, Diop OM, Sutter RW, Kew OM. Vaccine-Derived Polioviruses. Journal of Infectious Diseases. 2014;210(Suppl 1):S283–S293. https://doi.org/10.1093/infdis/jiu295

Epidemiologic Risk Factors

A Constellation of factors increase VDPV emergence risk:

- **Larger campaign size** (though sub-linearly so per-dose risk decreases)
- **Lower pre-campaign immunity** (particularly intestinal mucosal immunity)
- **"Singleton" campaigns** (ie, campaigns not part of a sequence)
- **Sabin**, compared with novel, OPVs
- **Low campaign coverage** (however, limited by measurement error; frontier effects)
- **Non-polio enterovirus (NPEV) co-infection** (influencing vaccine take and recombination)
- **Poor sanitation and hygiene** (hence higher R_0)
- **Surveillance** (influencing detection of emergence)

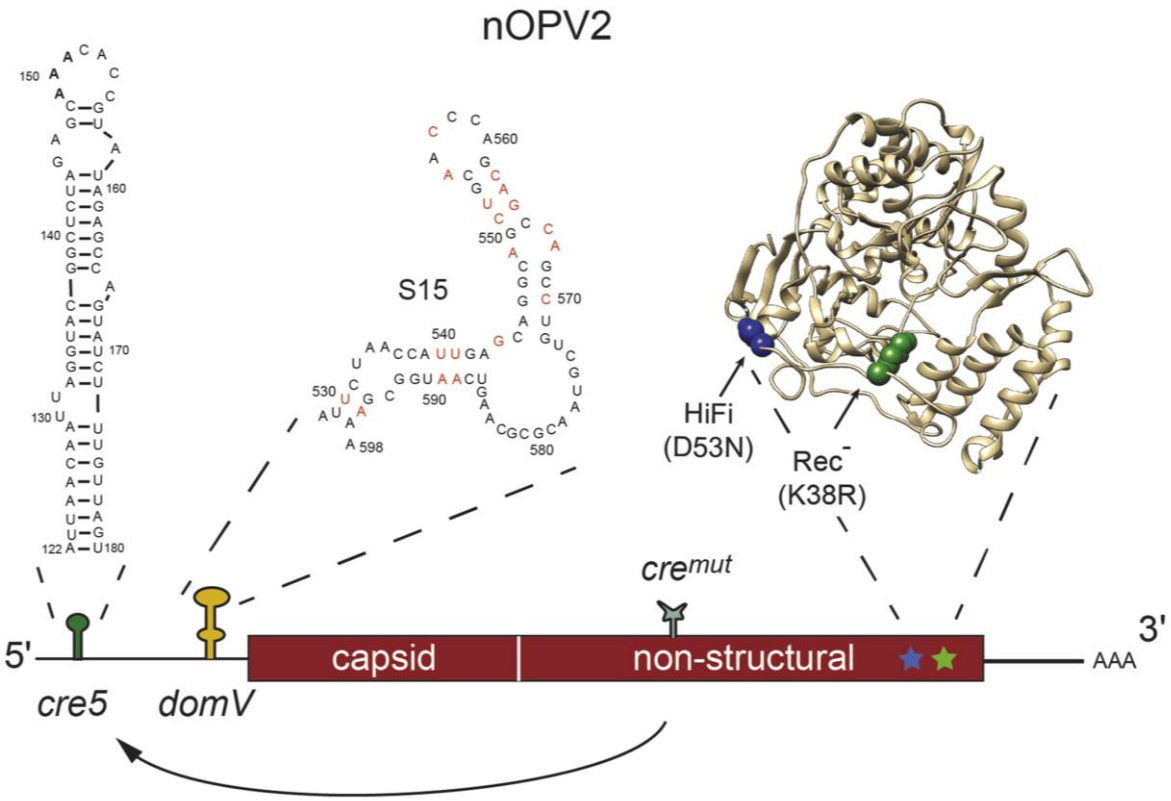


Estimated risks of new emergences, with 95% credible intervals, shown in the shaded areas, given population and immunity levels in children younger than 5 years [1].

[1] Gray EJ, Cooper LV, Bandyopadhyay AS, Blake IM, Grassly NC. The Origins and Risk Factors for Serotype-2 Vaccine-Derived Poliovirus Emergences in Africa During 2016-2019. J Infect Dis. 2023 Jun 28;228(1):80-88. https://doi.org/10.1093/infdis/jiad004

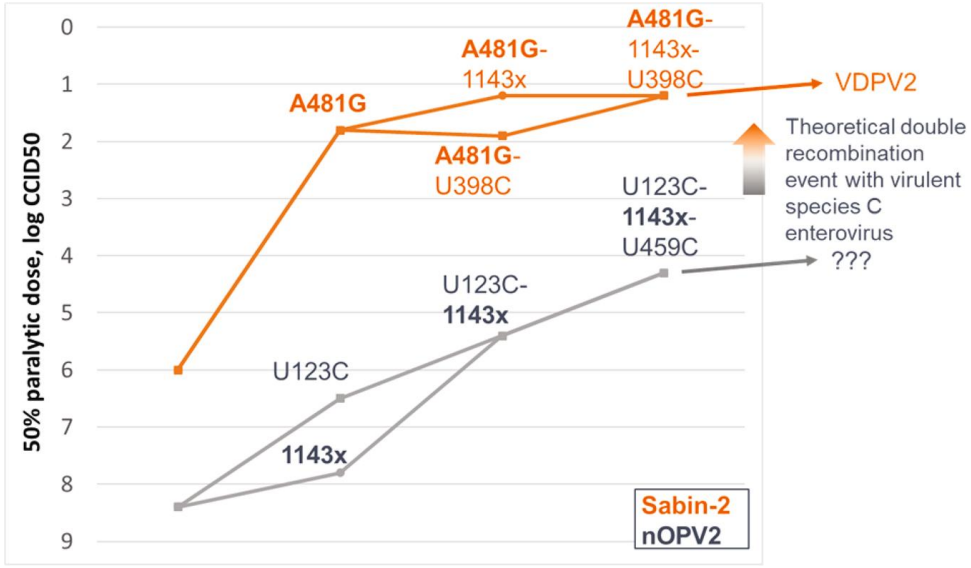
Strategies to reduce emergence risk: nOPV

- Novel oral polio vaccines (nOPV) were engineered to preserve immunogenicity while reducing reversion
- ***domV***: major attenuation determinant genetically stabilized
- ***cre***: relocated to resist *domV* replacement via recombination
- ***3D^{pol}***: two mutations to reduce mutation and recombination rate



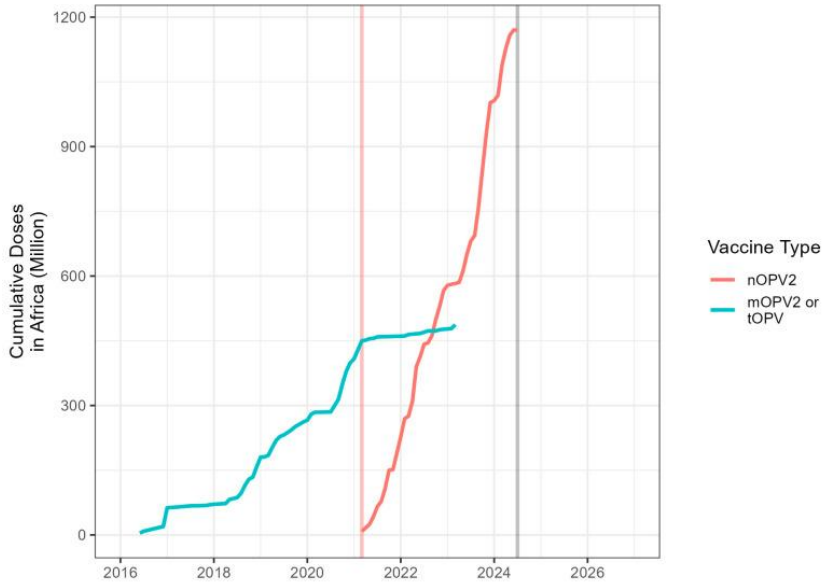
Yeh M, et al. Engineering the Live-Attenuated Polio Vaccine to Prevent Reversion to Virulence. Cell Host & Microbe. 2020; 27: 736-751 e8

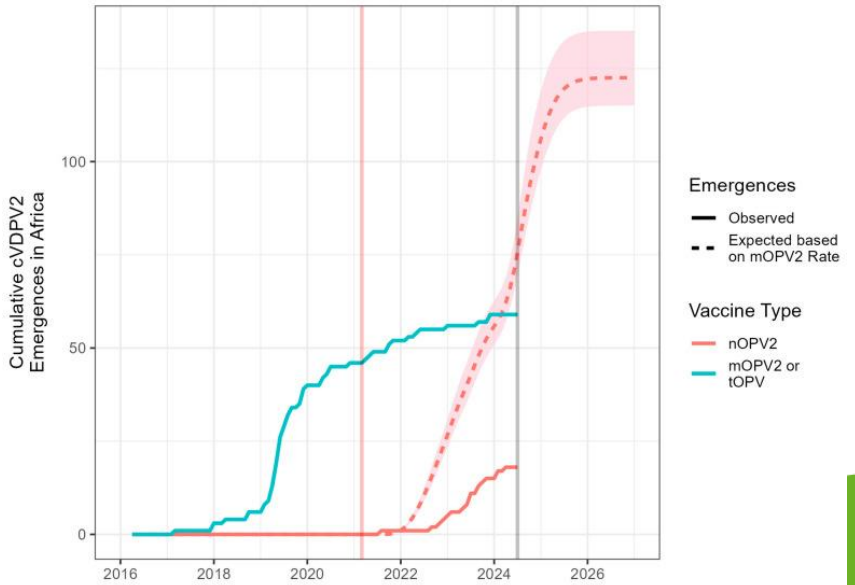
Strategies to reduce emergence risk: nOPV



Left. Framework of genetic evolution of Sabin-2 and nOPV2-c1 in humans and impact on neurovirulence in Tg66 mice. 1143x refers to mutations in VP1-143 (isoleucine to threonine or valine) [1]

Right. Cumulative doses of nOPV2 and mOPV2 or tOPV in Africa; (bottom) cumulative observed and expected cVDPV2 emergences derived from nOPV2 and mOPV2 or tOPV in Africa by virus date of index isolate. Vertical lines indicate date of first nOPV2 use (red) and August 2024 (grey) [2]



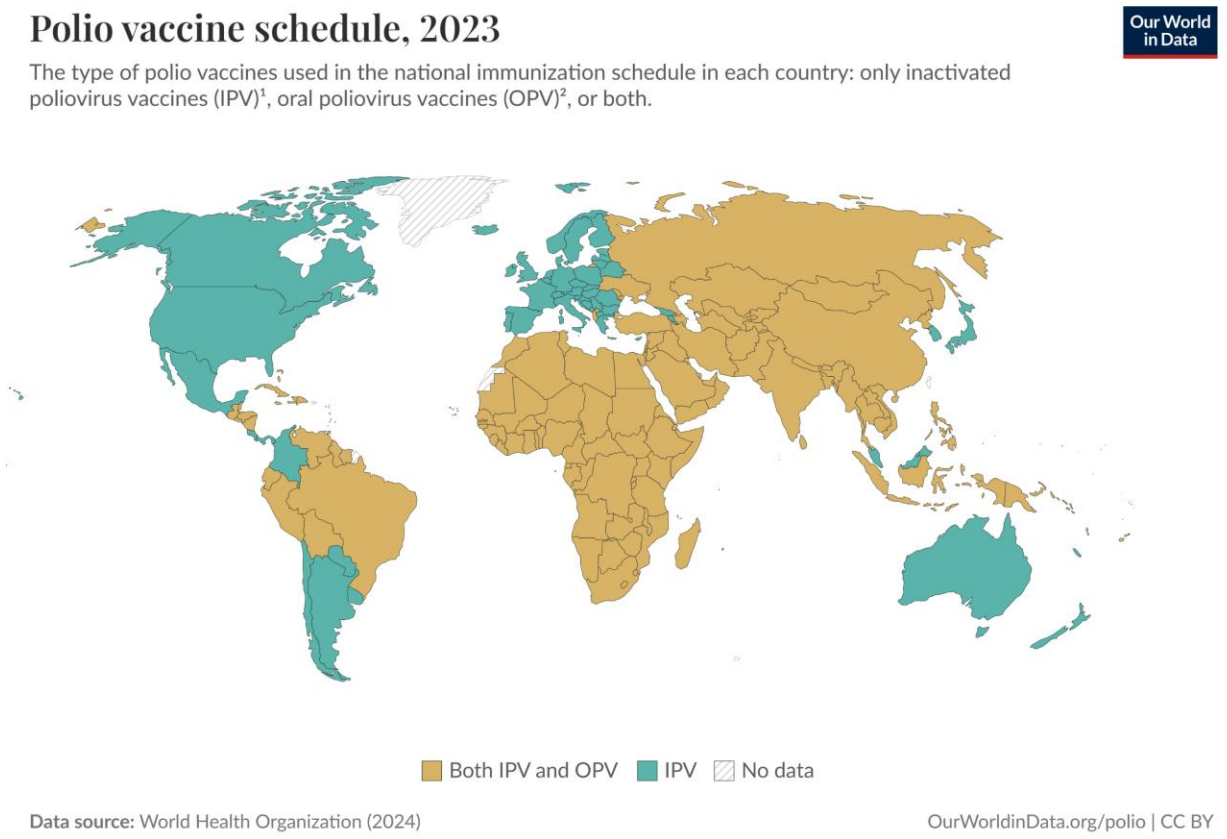


[1] Wahid, R., Mercer, L., Gast, C. *et al.* Evaluating stability of attenuated Sabin and two novel type 2 oral poliovirus vaccines in children. *npj Vaccines* **7**, 19 (2022). https://doi.org/10.1038/s41541-022-00437-5

[2] Peak CM, Lyons H, Voorman A, Gray EJ, Cooper LV, Blake IM, Hawes KM, Bandyopadhyay AS. Monitoring the Risk of Type-2 Circulating Vaccine-Derived Poliovirus Emergence During Roll-Out of Type-2 Novel Oral Polio Vaccine. Vaccines (Basel). 2024 Nov 22;12(12):1308. https://doi.org/10.3390/vaccines12121308

Strategies to reduce emergence risk: cessation

- Rebalancing of risks: WPV and VDPV/VAPP
- Switch to non-live vaccines (eg, IPV) done gradually already by many countries. Consider:
  - RI coverage – fraction of population protected via direct immunization with at least IPV2
  - Sanitation – local Ro
  - Surveillance – capacity to detect and respond
    - Sometimes IPV-only response (eg, US, UK)
    - Sometimes requires OPV (eg, Israel)
  - Importation risk – neighboring schedules and circulation

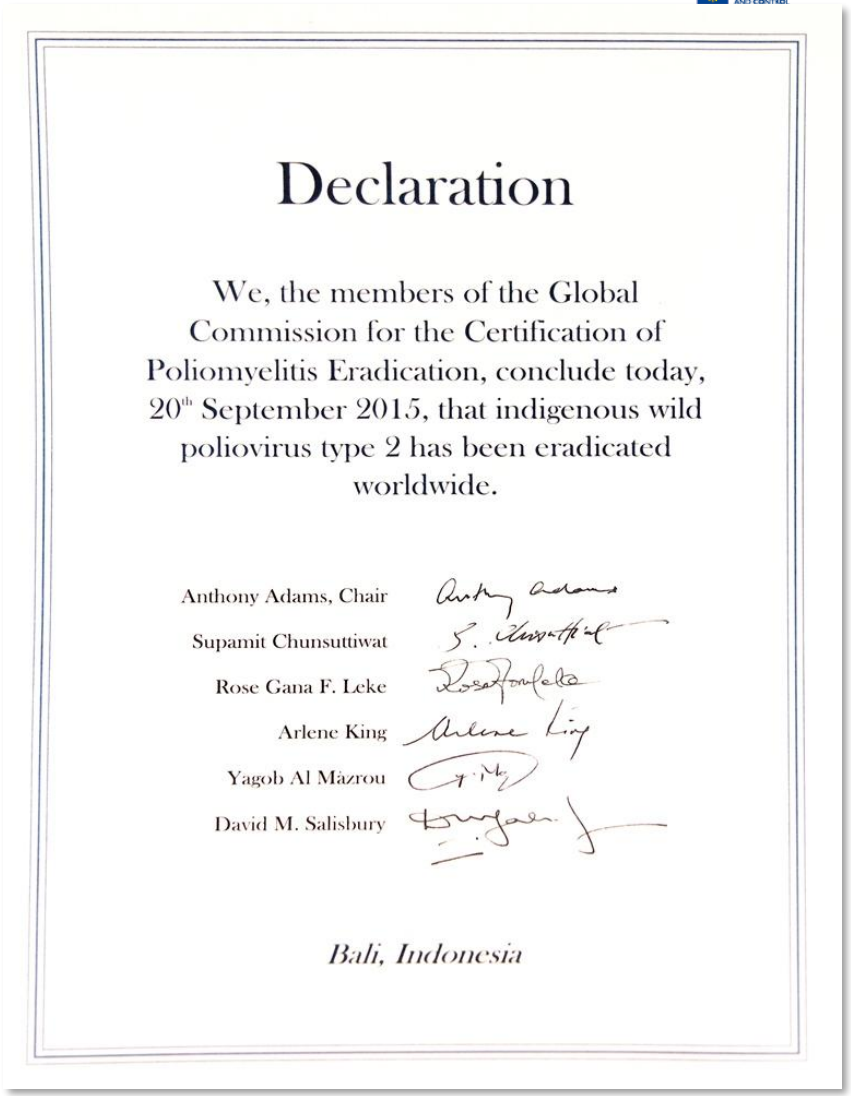


The Switch

- Global eradication of WPV2 was declared in 2015; 16 years after the last detection
- Eradication was one prerequisite for the phased removal of OPVs, beginning with "The Switch" from trivalent OPV to bivalent OPV (bOPV; types 1 and 3)
  - Other criteria included introducing IPV in RI, stockpiling OPV, and containment of type 2 viruses at laboratories and manufacturers

Motivations:

- Burden. Type 2 caused 90% of cVDPV outbreaks and 38% of VAPP cases [1]
- Interference. Type 1 and 3 immune response elicited by bOPV superior to tOPV [2]



Declaration

We, the members of the Global Commission for the Certification of Poliomyelitis Eradication, conclude today, 20th September 2015, that indigenous wild poliovirus type 2 has been eradicated worldwide.

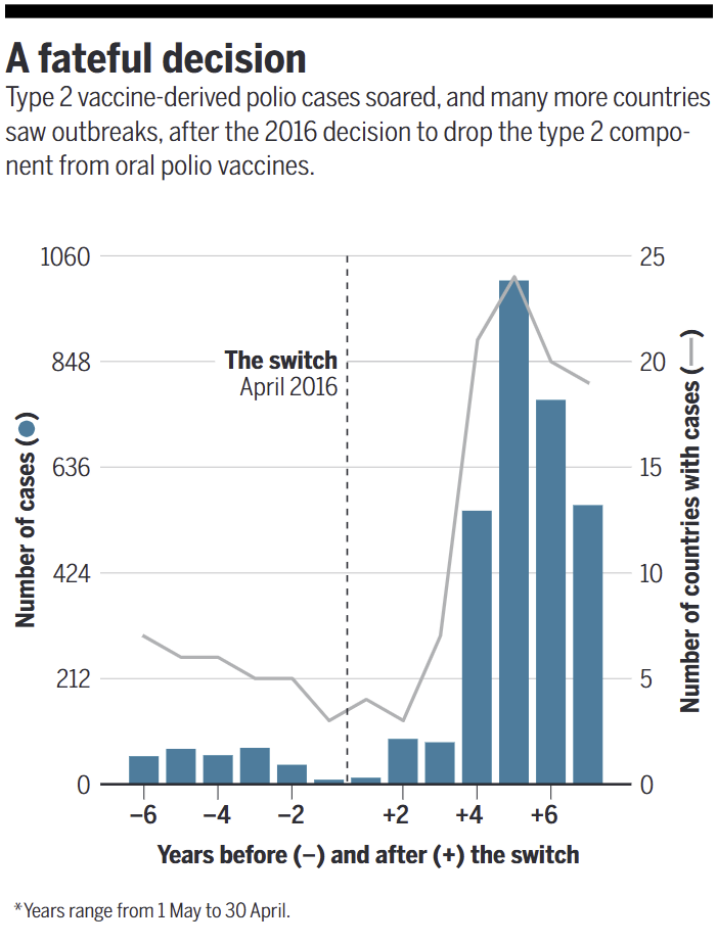
Anthony Adams, Chair
Supamit Chunsuttiwat
Rose Gana F. Leke
Arlene King
Yagob Al Mazrou
David M. Salisbury

Bali, Indonesia

[1] https://polioeradication.org/news/global-eradication-of-wild-poliovirus-type-2-declared/
[2] Estívariz CF, et al. Immunogenicity of three doses of bivalent, trivalent, or type 1 monovalent oral poliovirus vaccines with a 2 week interval between doses in Bangladesh: an open-label, non-inferiority, randomised, controlled trial. The Lancet Infectious Diseases. Volume 15, Issue 8. 2015. https://doi.org/10.1016/S1473-3099(15)00094-8

Shortcomings of The Switch

- "The largest coordinated public health effort in history" [1]
  - 155 countries over 2 weeks
- Challenges include:
  - Insufficient IPV immunity: 26 countries had zero does; 83 had only 1 dose; low coverage even if IPV 'scheduled'
  - Risk of post-cessation OPV2 use recognized by modeling in advance [2] paper)
    - mOPV2 responses of limited scope, delayed, evidently insufficient coverage



[1] https://www.science.org/content/article/unqualified-failure-polio-vaccine-policy-left-thousands-kids-paralyzed
[2] McCarthy KA, Chabot-Couture G, Famulare M, Lyons HM, Mercer LD. The risk of type 2 oral polio vaccine use in post-cessation outbreak response. BMC Med. 2017 Oct 4;15(1):175. https://doi.org/10.1186/s12916-017-0937-y

Preparing for bOPV cessation

Those who cannot remember the past are condemned to repeat it.
– George Santayana

Triggers [1]

- Certification of Global WPV1 Eradication
- Certification of Global VDPV2 Elimination
  - *as proof that OPV cessation is possible*
- No persistent (>6 months) circulation of VDPV1/3
- Sufficient type 1/3 OPV stockpiles
- At least 2-dose IPV RI schedule in all countries
  - *established at least 2 years prior to cessation*

Enablers of Success [2]

- High population immunity
  - *including pre-cessation campaigns*
- Sufficient Vaccines
- Surveillance
- Outbreak response capacity

[1] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, March 2024: conclusions and recommendations Wkly Epidemiol Rec, 99 (22) (2024), pp. 285-306. https://www.who.int/publications/i/item/WER-9922-285-306
[2] Sun Y, et al. Global cessation of bivalent oral polio vaccine (bOPV): A comprehensive review of modeling studies from 2000 to 2025. Vaccine. Volume 86, 2026. https://doi.org/10.1016/j.vaccine.2026.128707

In summary

Rather than immune-evasion through genetic and antigenic drift (eg, HIV, influenza)…

…the primary genomic driver which "resists eradication" of polio is VDPV emergence…

…hence we must stop emergence to achieve and maintain eradication.

As evidenced by successful eradication of WPV2 and WPV3 and continued efficacy of >60 year-old vaccines

OPV is both the workhorse and Achilles heel of eradication

Eventual need to stop use of vaccines with any emergence risk

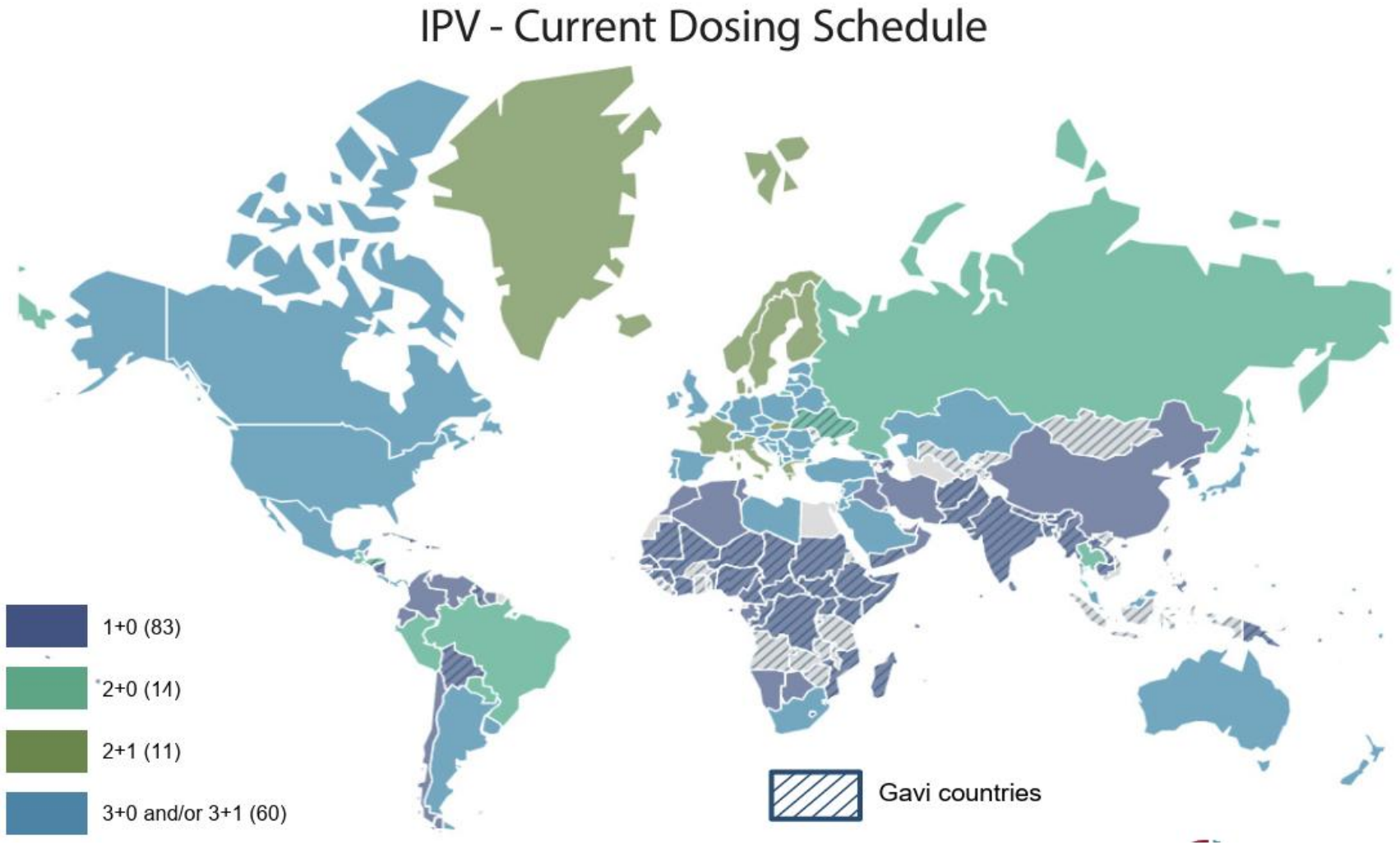
Thank you

Reusing this content

Appendix

IVAC 2016 report

"61% of worlds infants (82.1 million) are not receiving IPV"



https://view-hub.org/sites/default/files/2020-05/IVAC_VIEW-hub_Report%202016Jun_public.pdf