Cholera and cholera vaccines

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Facultad de Medicina,
Universidad Nacional Autónoma de México
ARVAC course, June 2023

FOUR HORSEMEN OF THE APOCALYPSE

by Rina Prince

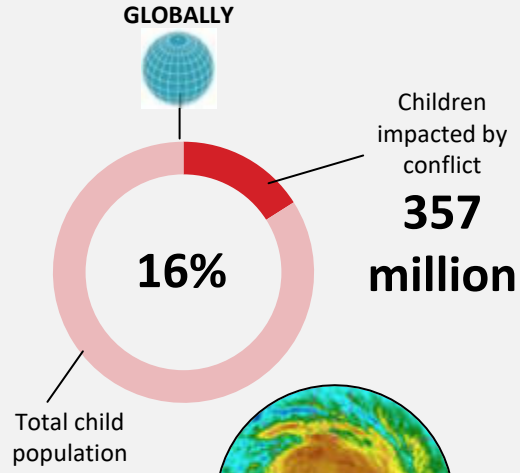
WAR FAMINE PESTILENCE DEATH

VUCA world

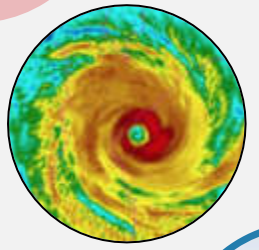
Volatile
Uncertain
Complex
Ambiguous

We are in a ‘VUCA’ world

Conflict and Displacement



Climate Change



2 billion people living in slums by 2030

Outbreaks

icddr,b

KNOWLEDGE FOR GLOBAL LIFESAVING SOLUTIONS

Table 1. Cholera cases and deaths reported to WHO from WHO regions, as of 20 March 2023**

Country, area, territory	Suspected/confirmed cases[1]	Total deaths	Cases per 100 000	CFR (%)	Reporting period (DD/MM/YYYY)
Burundi	193	1	2	<1%	08/12/2022 – 19/03/2023
Cameroon	15 309	311	55	2.0	01/10/2021 – 12/03/2023
Democratic Republic of the Congo	24 657	334	26	1.4	01/01/2022 – 2003/2023
Ethiopia	2095	44	2	2.1	01/08/2022 – 20/03/2023
Kenya	7235	116	14	1.6	08/10/2022 – 20/03/2023
Malawi	54 841	1684	272	3.1	01/03/2022 – 20/03/2023
Mozambique	10 854	75	34	<1%	01/09/2022 – 20/03/2023
Nigeria	922	32	<1	3.5	01/01/2023 – 05/03/2023
South Africa	6	1	<1	16.7	01/02/2023 – 04/03/2023
South Sudan	307	1	2	<1%	22/02/2023 – 16/03/2023
United Republic of Tanzania	72	3	<1	4.216	01/02/2023 – 13/03/2023
Zambia	268	7	1	2.6	21/01/2023 – 20/03/2023
Zimbabwe	121	1	1	<1%	12/02/2023 - 19/03/2023
Afghanistan*	22 848	7	57	<1%	01/01/2023 – 20/03/2023
Lebanon	1060	0	19	0	01/1/2023 - 20/03/2023
Somalia	2573	7	101	<1%	01/01/2023 – 12/03/2023
Syrian Arab Republic	21 427	5	101	<1%	01/01/2023 – 11/03/2023
North-west Syria	57 947	23	1252	<1%	16/09/2023 – 18/03/2023
Yemen	1724	3	6	<1%	01/01/2023 – 12/03/2023
Pakistan***	77 714	0	34	0	01/01/2023 – 12/03/2023
Dominican Republic	96	0	<1	0	17/10/2022 – 19/03/2023
Haiti	36 544	632	317	1.7	02/10/2022 – 16/03/2023
Bangladesh (Cox's Bazar)	19	0	-	0	01/01/2023 – 15/03/2023

Figure-1: Global situation of active epidemics of cholera and acute watery diarrhea as of 20 March 2023

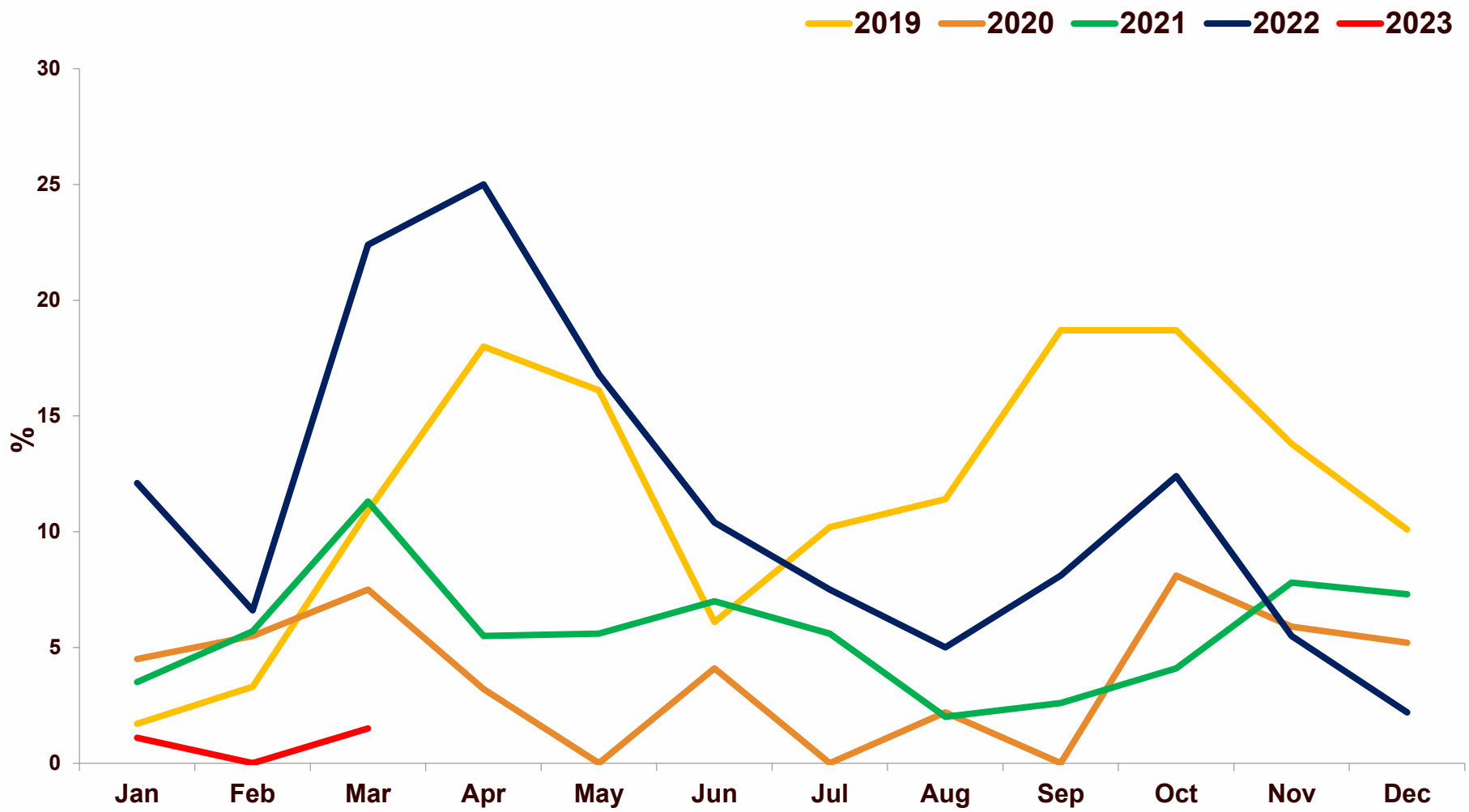
The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 20 March 2023

World Health Organization


icddr,b
DHAKA HOSPITAL
BRAC BANK
Short Stay Ward
icddr,b

Yearly isolation of *V. cholerae* in 2019-2023
Hospital Surveillance, Dhaka Hospital, icddr,b



Introduction: *Vibrio cholerae*

Vibrio cholerae is a Gram-negative rod comma shaped bacterium with a single flagellum

- Classified by the composition of its lipopolysaccharide **major surface antigen** (O) into over 206 serogroups; with
- **Only two serogroups of *V. cholerae*, O1 and O139, proven as causative agents of epidemic cholera** (Sharma *et al*. Indian J. Med. Res. 2007;125:633–40)

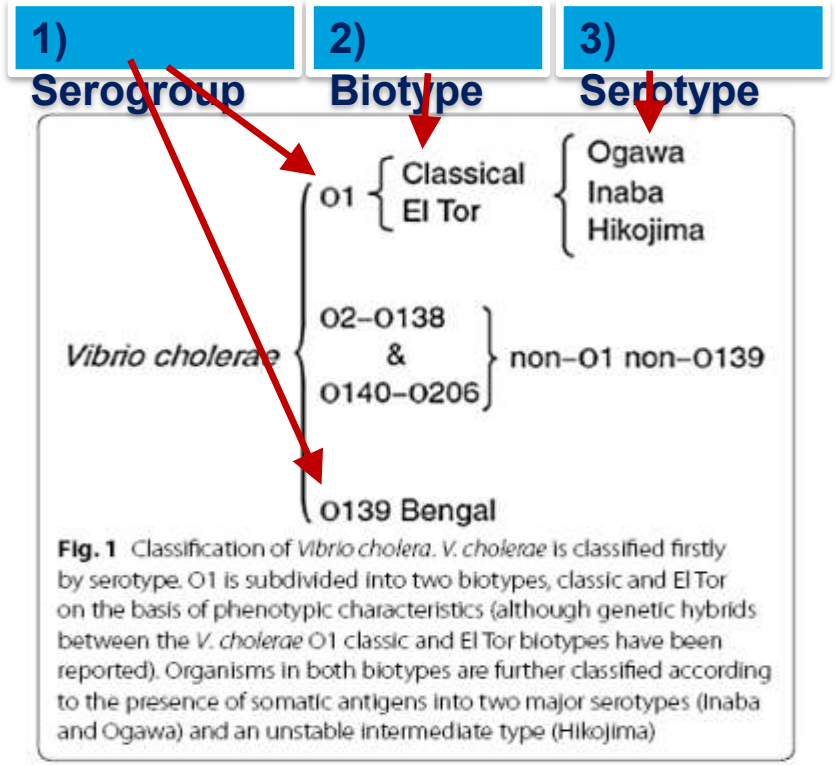
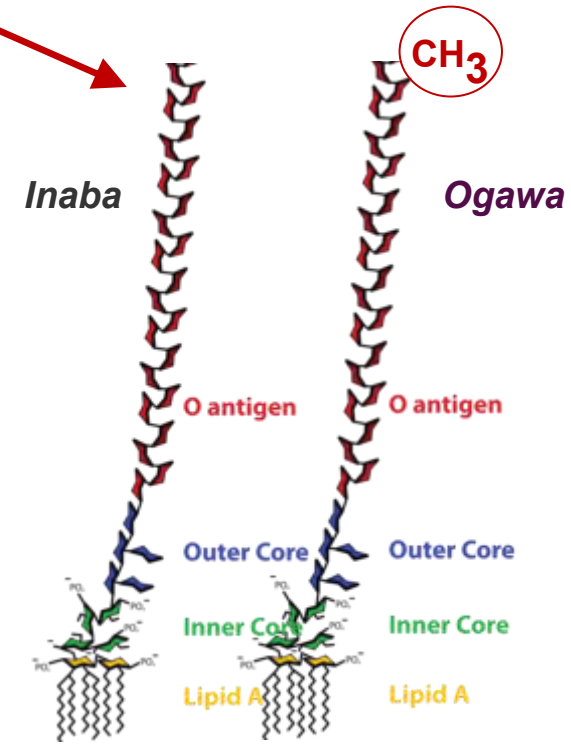
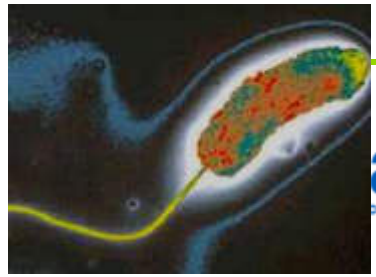
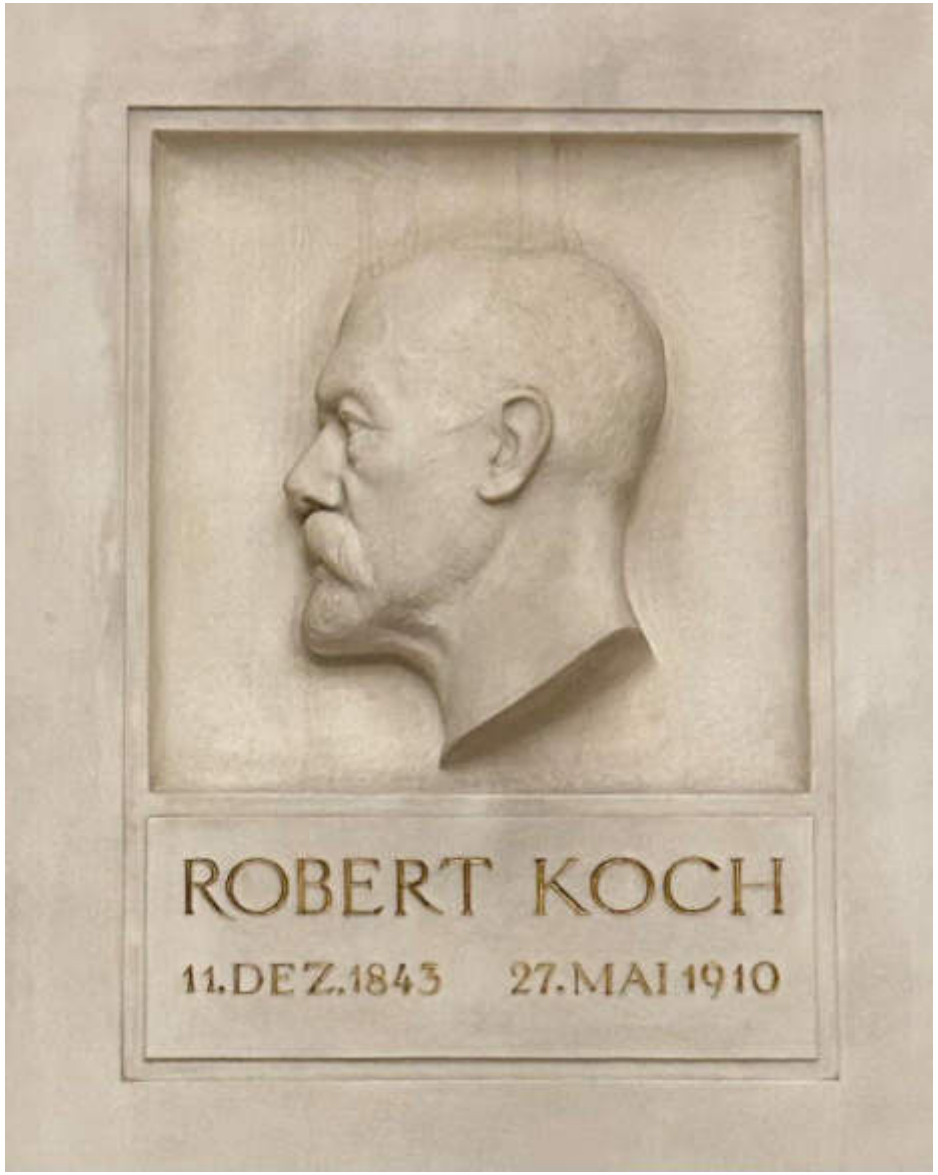


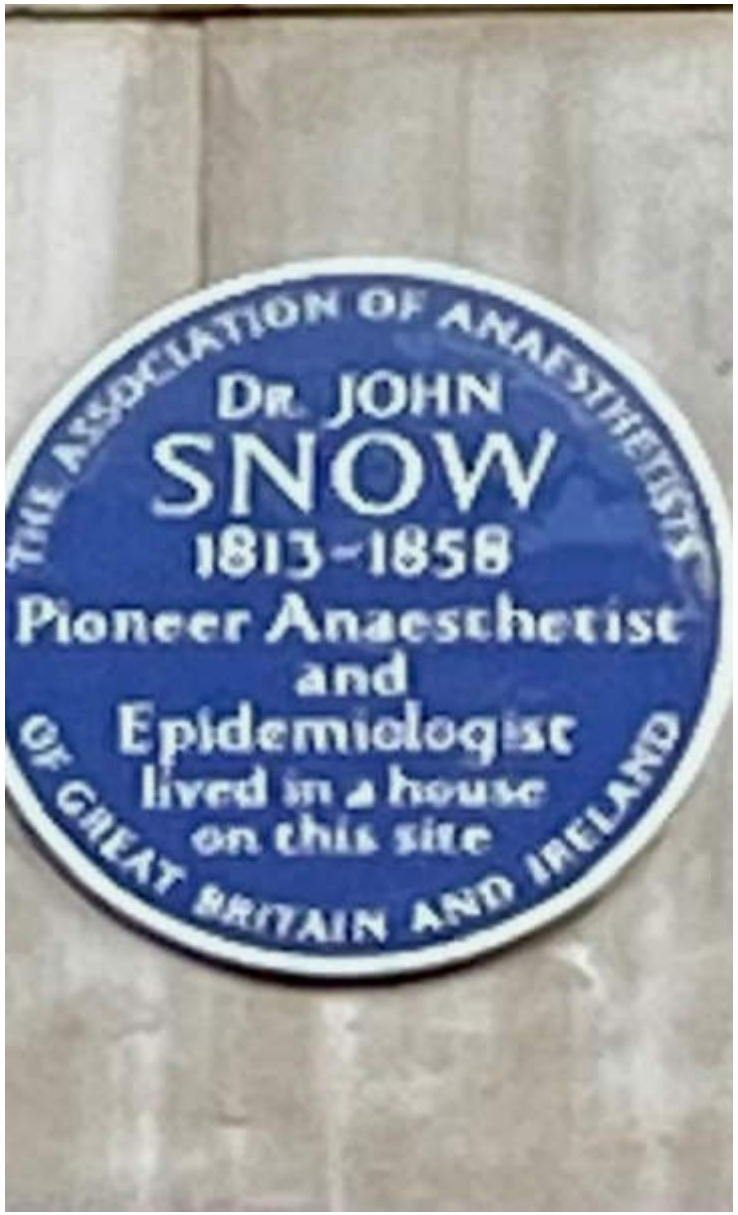
Fig. 1 Classification of *Vibrio cholera*. *V. cholerae* is classified firstly by serotype. O1 is subdivided into two biotypes, classic and El Tor on the basis of phenotypic characteristics (although genetic hybrids between the *V. cholerae* O1 classic and El Tor biotypes have been reported). Organisms in both biotypes are further classified according to the presence of somatic antigens into two major serotypes (Inaba and Ogawa) and an unstable intermediate type (Hikojima)

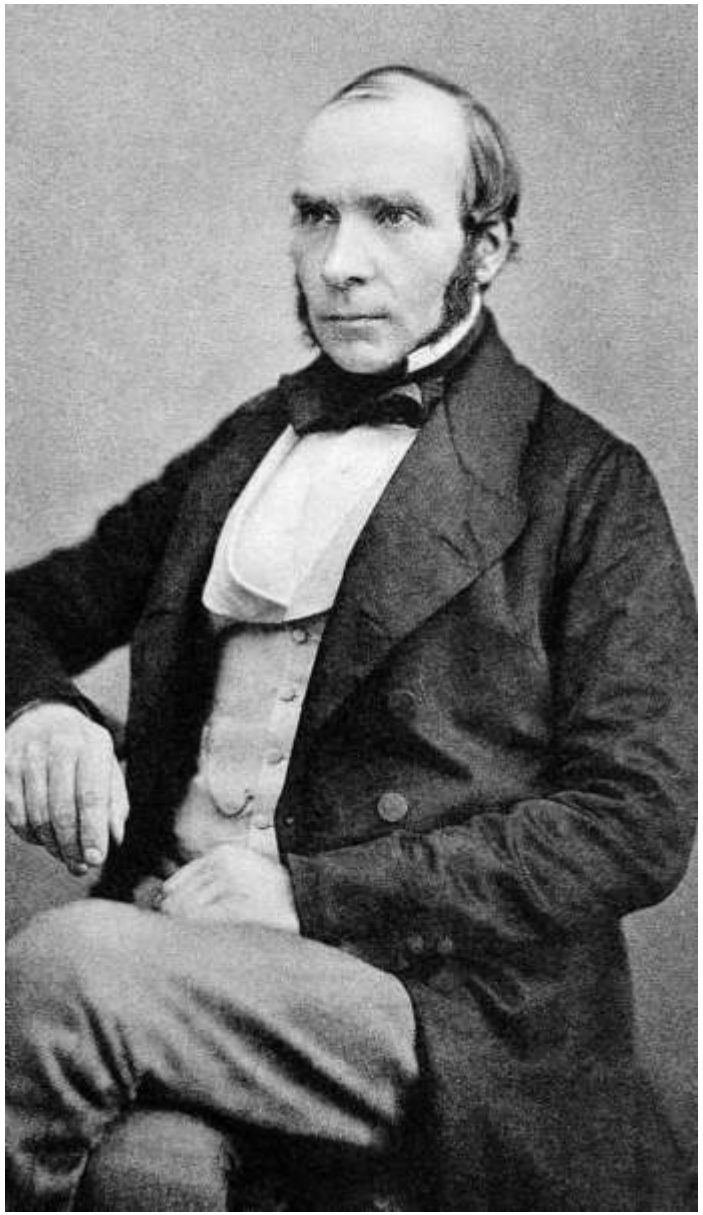
Figure modified from Chowdhury *et al.* Ann Clin Microbiol Antimicrob (2017) 16:100



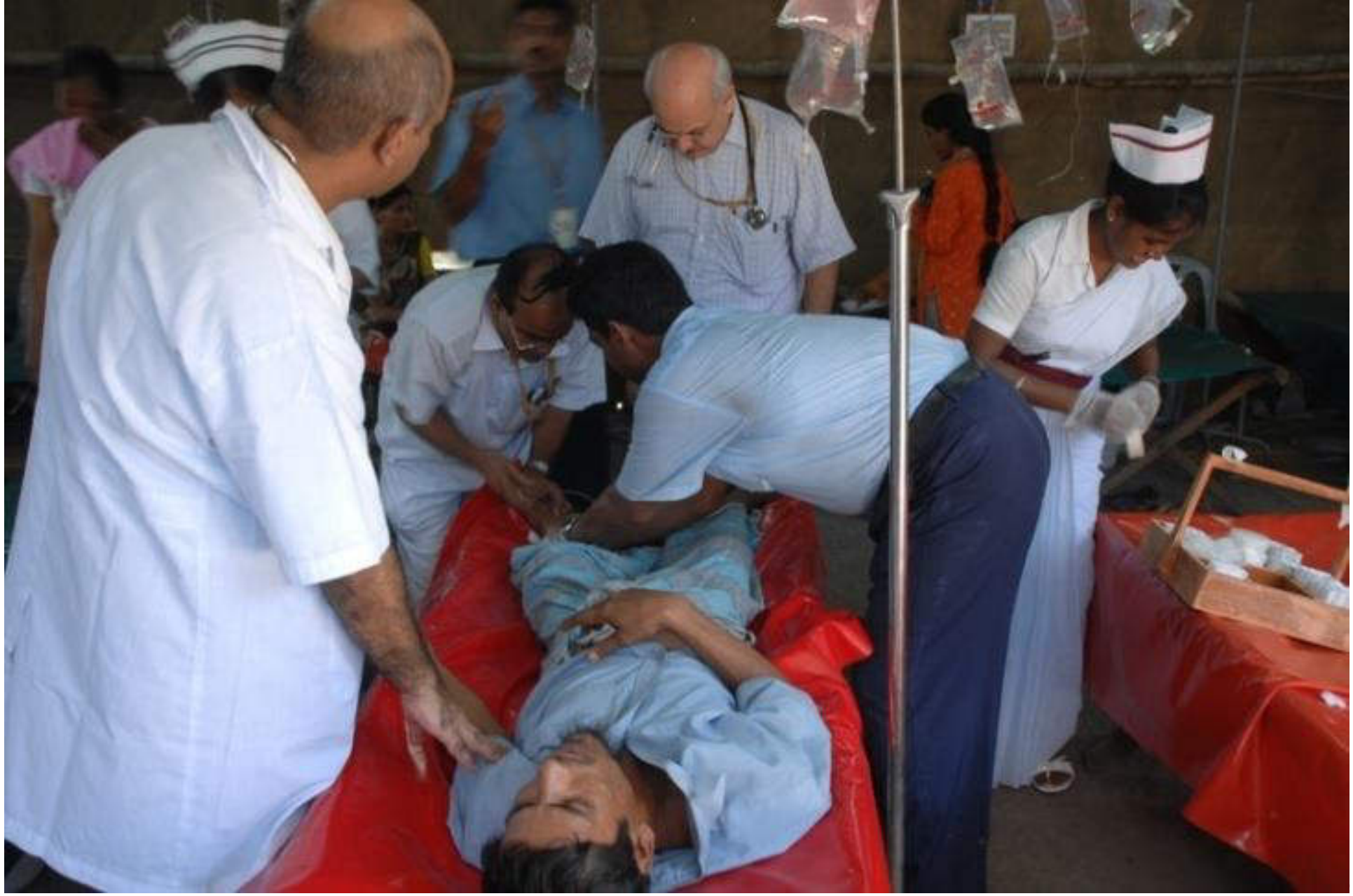



ROBERT KOCH
11.DEZ.1843 27.MAI 1910


THE ASSOCIATION OF ANAESTHETISTS
DR. JOHN
SNOW
1813–1858
Pioneer Anaesthetist
and
Epidemiologist
lived in a house
on this site
OF GREAT BRITAIN AND IRELAND




SOURCE
OF THE
SOUTHWARK
WATER WORKS



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FRESH

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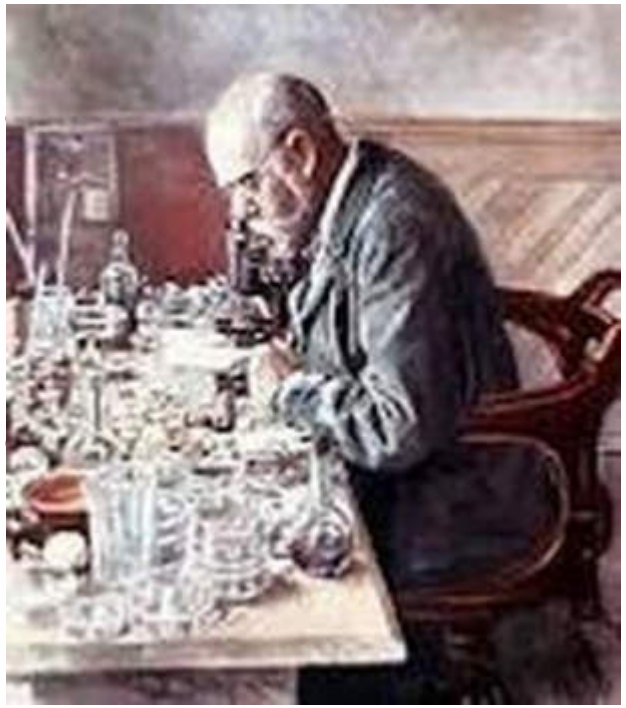
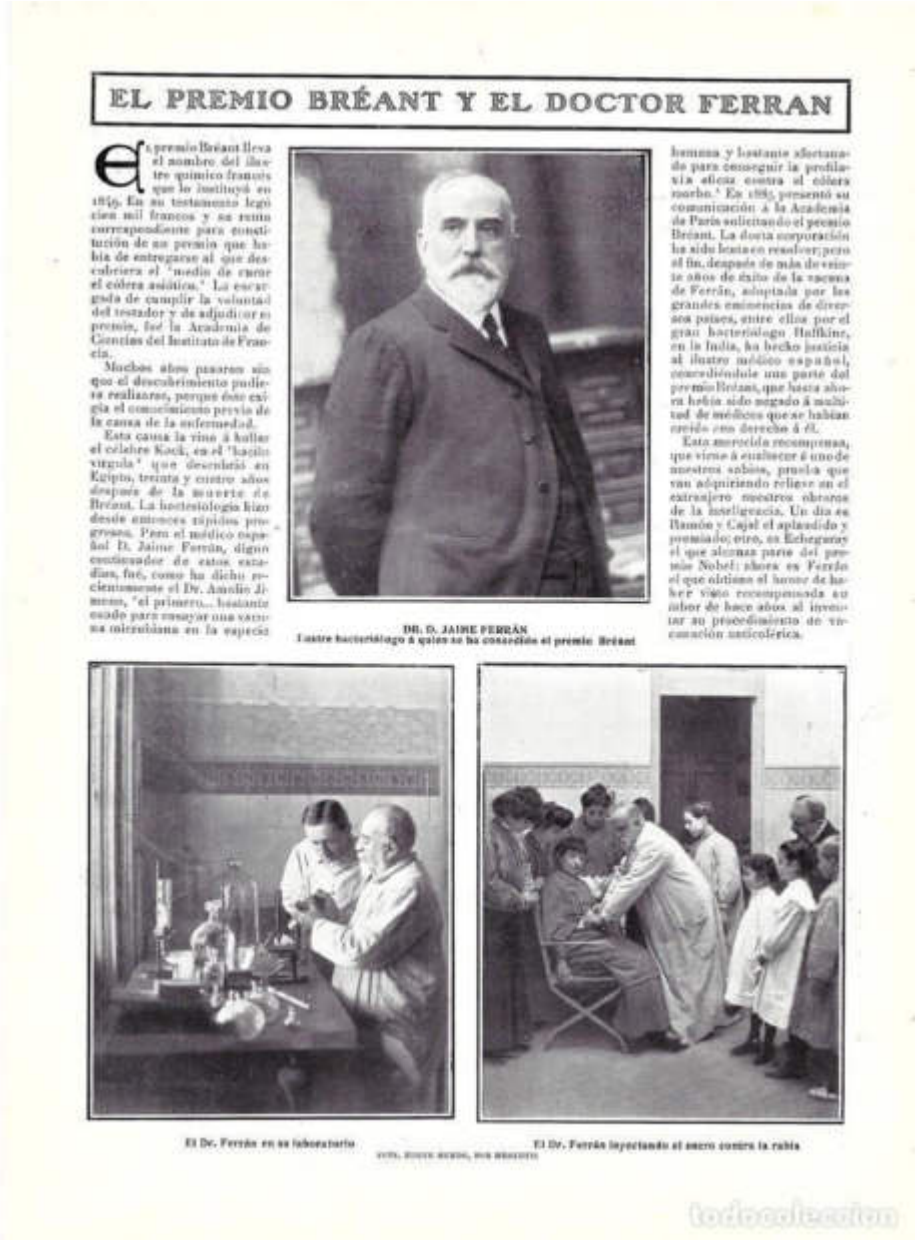
PIONEER WORK



Robert Koch
(1843 –1910)



EL PREMIO BRÉANT Y EL DOCTOR FERRAN

El premio Bréant lleva el nombre del ilustre químico francés que lo instituyó en 1859. En su testamento legó cien mil francos y su renta correspondiente para constitución de un premio que había de entregarse al que descubriera el 'medio de curar el cólera asiático.' La encargada de cumplir la voluntad del testador y de adjudicar el premio, fué la Academia de Ciencias del Instituto de Francia.

Muchos años pasaron sin que el descubrimiento pudiera realizarse, porque éste exigía el conocimiento previo de la causa de la enfermedad.

Esta causa la vino á hallar el célebre Koch, en el 'bacilo virgula' que descubrió en Egipto, treinta y cuatro años después de la muerte de Bréant. La bacteriología hizo desde entonces rápidos progresos. Pero el médico español D. Jaime Ferrán, digno continuador de estos estudios, fué, como ha dicho recientemente el Dr. Amalio Jimeno, 'el primero... bastante osado para ensayar una vacuna microbiana en la especie humana y bastante afortunado para conseguir la profilaxis eficaz contra el cólera morbo.' En 1885 presentó su comunicación á la Academia de París solicitando el premio Bréant. La docta corporación ha sido lenta en resolver; pero al fin, después de más de veinte años de éxito de la vacuna de Ferrán, adoptada por las grandes eminencias de diversos países, entre ellos por el gran bacteriólogo Haffkine, en la India, ha hecho justicia al ilustre médico español, concediéndole una parte del premio Bréant, que hasta ahora había sido negado á multitud de médicos que se habían creído con derecho á él.

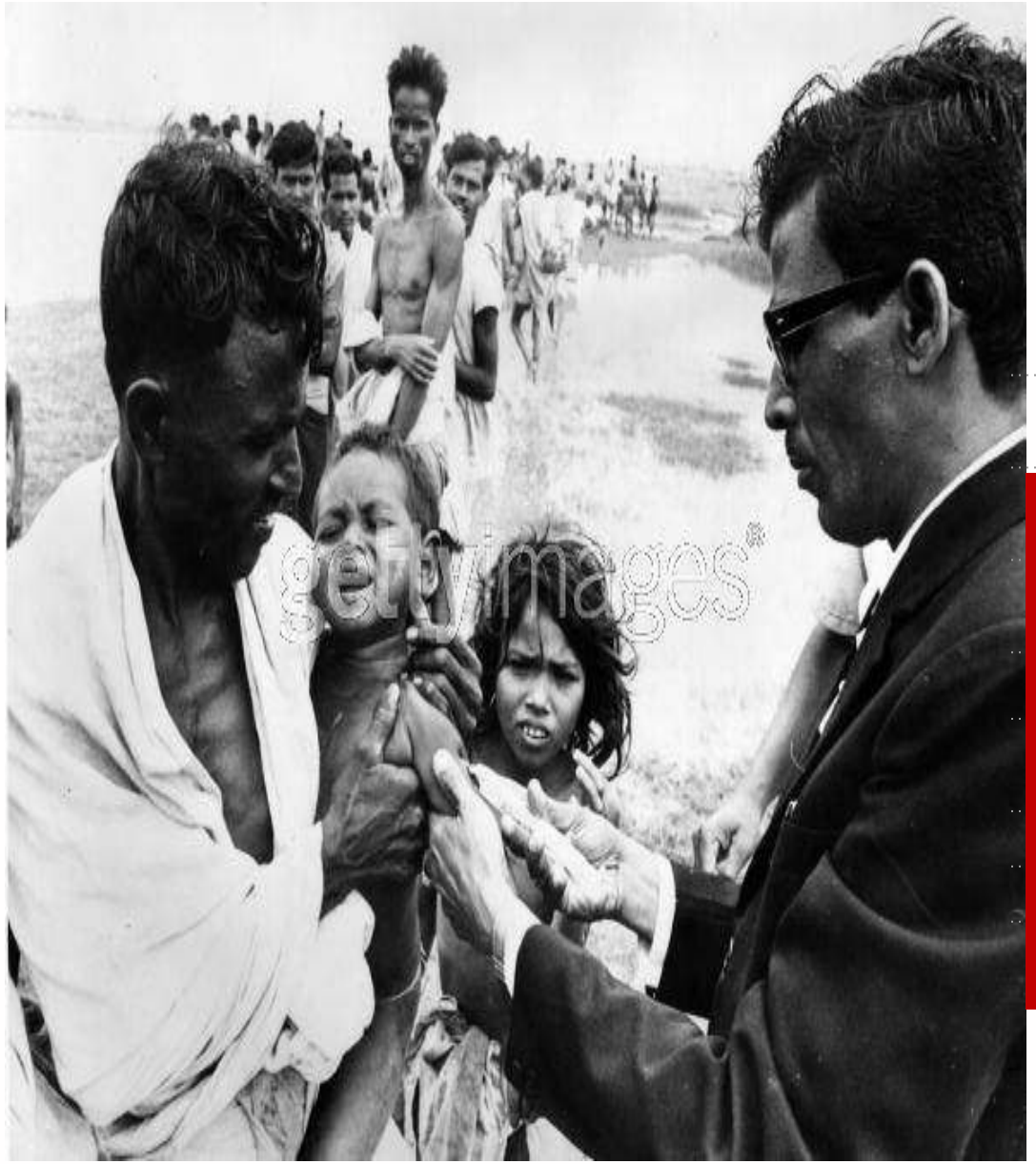
Esta merecida recompensa, que viene á enaltecer á uno de nuestros sabios, prueba que van adquiriendo relieve en el extranjero nuestros obreros de la inteligencia. Un día es Ramón y Cajal el aplaudido y premiado; otro, es Echegaray el que alcanza parte del premio Nobel; ahora es Ferrán el que obtiene el honor de haber visto recompensada su labor de hace años al investigar un procedimiento de vacunación anticolérica.

DR. D. JAIME FERRÁN
Ilustre bacteriólogo á quien se ha concedido el premio Bréant

El Dr. Ferrán en su laboratorio

El Dr. Ferrán inyectando el suero contra la rabia

Jaime Ferrán
(1851-1929)



11th November 1971: A doctor administering a cholera vaccination to a child at the Indian village of Tarapada, after a cyclone caused havoc in the region. (Photo by Central Press/Getty Images)

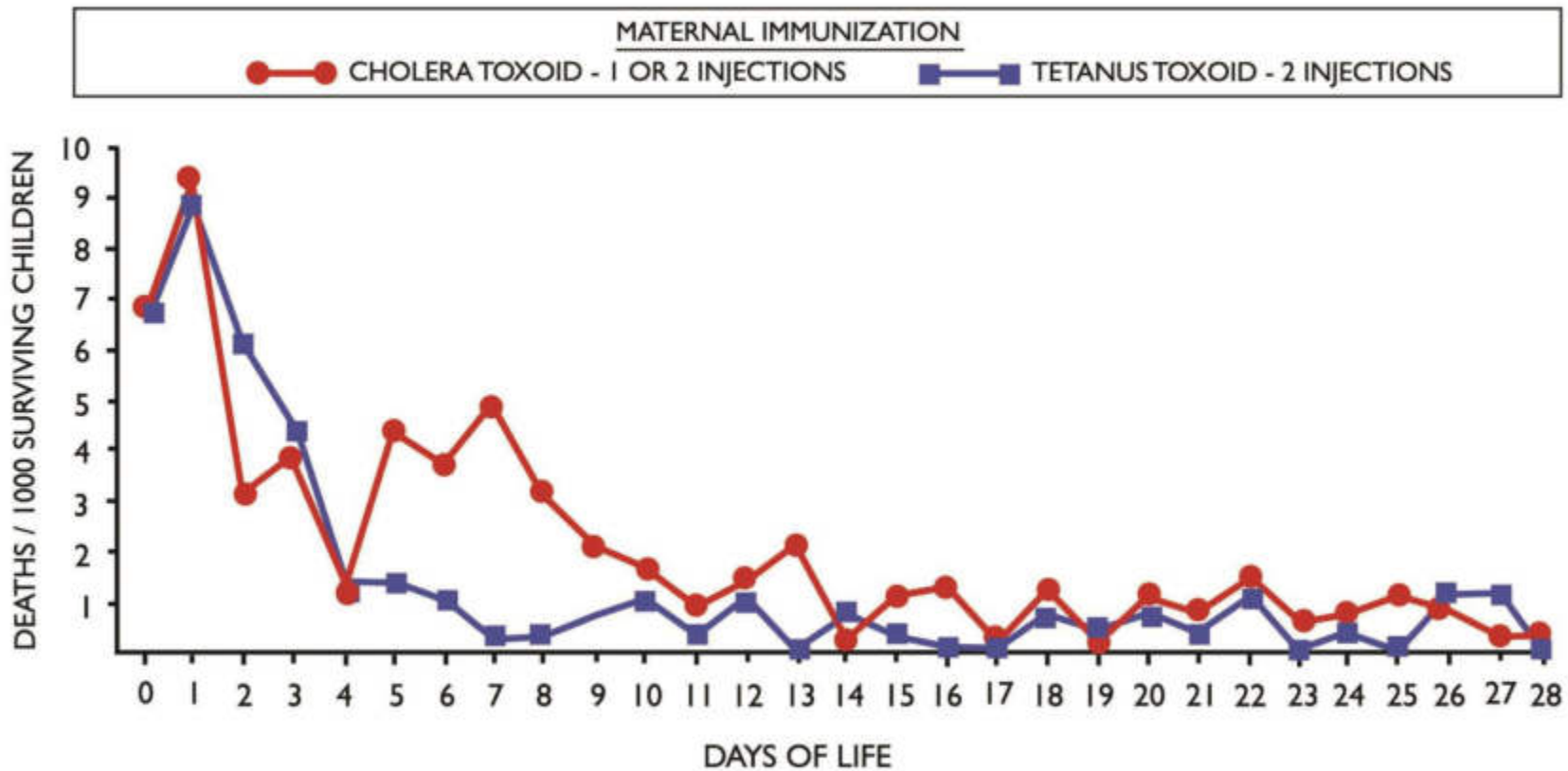
Cholera prevention by vaccination was carried out routinely as well as to control epidemics until the early 1970's

Concept of mass cholera vaccination is not new in our countries

Serendipity at play…

…the “Placebo” effect

NEONATAL DEATH RATES BY AGE OF DEATH FOLLOWING MATERNAL IMMUNIZATION WITH ONE OR TWO DOSES OF CHOLERA OR TWO DOSES OF TETANUS / DIPTHERIA TOXOIDS



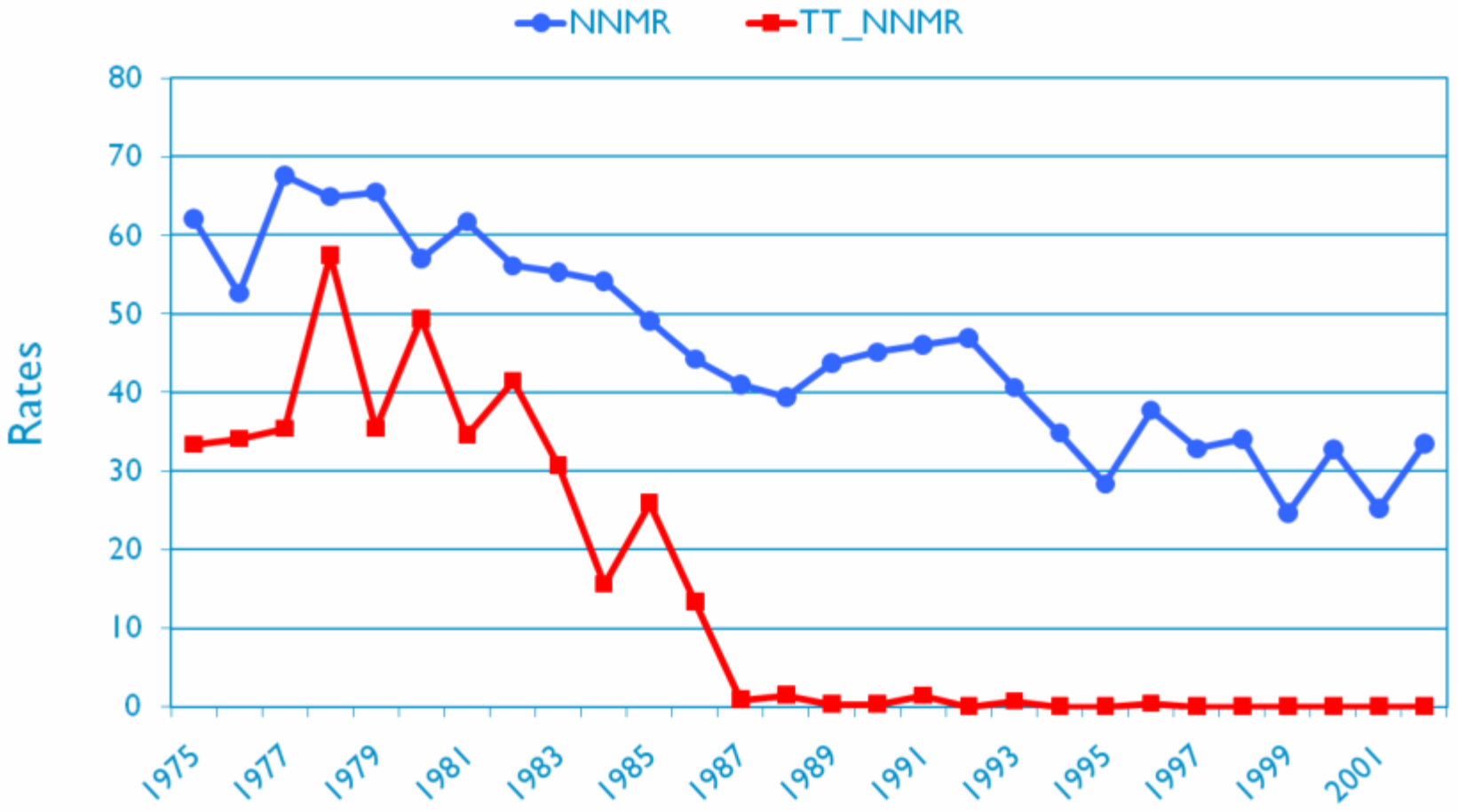
Reduction of neonatal tetanus by mass immunization of non-pregnant women: duration of protection provided by one or two doses of aluminium-adsorbed tetanus toxoid*

R.E. Black, D.H. Huber, & G.T. Curlin

Bulletin of the World Health Organization, 58(6) 927-930 (1980)

*From the International Centre for Diarrhoeal Diseases Research, Dacca, Bangladesh.

Neonatal mortality rate due to all causes and tetanus in ICDDR,B service area, 1975-2002



Duration of Protective Immunity Conferred by Maternal Tetanus Toxoid Immunization: Further Evidence from Matlab, Bangladesh

Michael A. Koening, PhD, Nikhil chandra Roy, MA, Thomas McElrath, PhD, Md. Shahidullah, PhD, and Bogdan Wojtyniak, ScD

Am J Public Health. 1998; 88:903-907

From injected vaccine to oral

- **Injected killed whole-cell cholera vaccines** had been in wide-spread use for more than 70 years
  - modest efficacy ~50%, short duration of protection (~3–6 months), high reactogenicity
  - WHO discontinued the recommendation for use in the 1970s
  - Swedish Bacteriological Laboratory (SBL)
    - Heat inactivated-classical O1 Inaba (Cairo 48)
    - Heat inactivated- classical O1 Ogawa (Cairo 50)
- **Inactivated Oral Cholera Vaccines**
  - **Whole Cell (WC)**
    - Heat inactivated-classical O1 Inaba (Cairo 48)
    - Heat inactivated- classical O1 Ogawa (Cairo 50)
    - Formalin inactivated classical Ogawa (Cairo 50)
    - Formalin inactivated El Tor Inaba (Phil 6973)
  - **WC + rCholera Toxin B (WC + rCTB)**

The oral cholera cold chain team for the Phase III trial in Matlab, 1985 with John Clemens* and Mr Bodrul Ahsan Prodhan** from ICDDR,B

From injected vaccine to oral

Inactivated OCV

Field Trial Bangladesh 1985

- Phase 3 placebo-controlled RCT comparing WC + rCTB, WC and Escherichia coli K12 placebo
- Safe with moderate efficacy

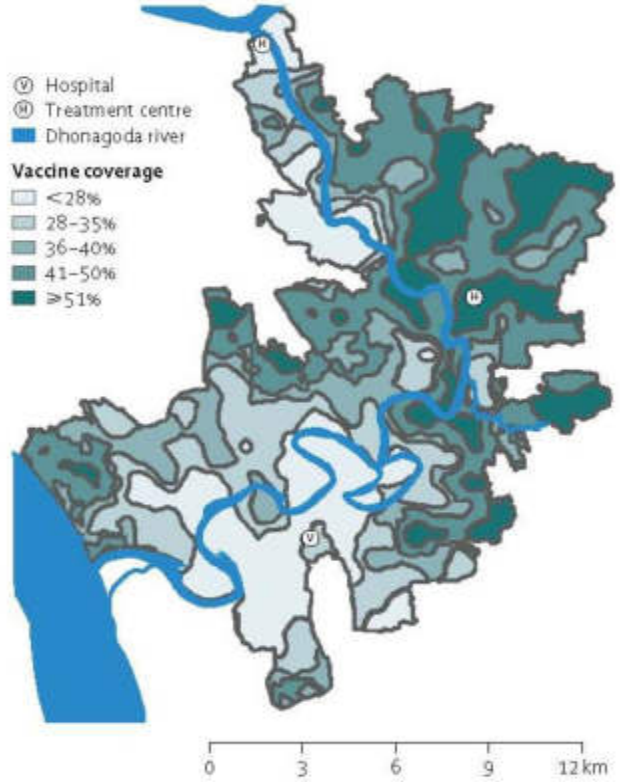
	VE 6 months	VE 3 years
• **WC + rCTB**	**85%** (all ages)	**50%** (lower VE in children under 5y)
• **WC**	**58%**	**52%** (lower VE in children under 5y)

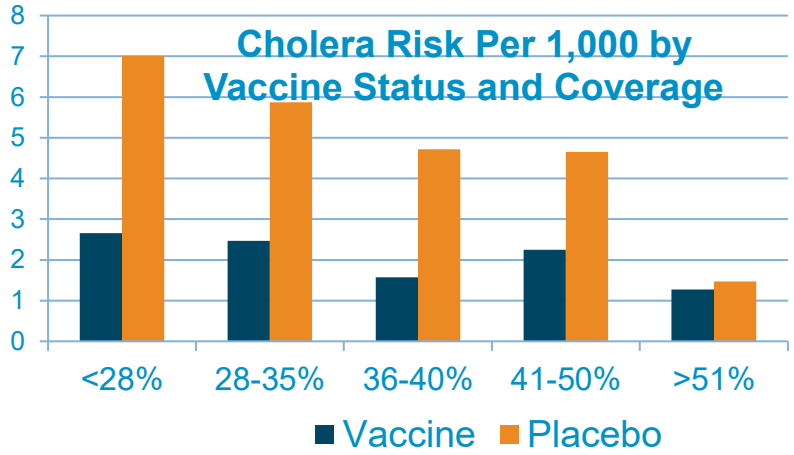
Clemens JD, Sack DA, Harris JR, Van Loon F, Chakraborty J, Ahmed F, et al. Field trial of oral cholera vaccines in Bangladesh: results from three-year follow-up. Lancet. 1990;335:270-3.

Herd Immunity conferred by killed Cholera Vaccine

- A Matlab trial of killed oral cholera vaccines showed moderate levels of direct protection.
- Reanalysis of cholera incidence rates after cholera vaccination showed significant herd immunity conferred by the vaccine, depending on the coverage rates at *bari* (household compound) level.

Ali, M. et al., Lancet, 2005





Inactivated Oral Cholera Vaccines

WC + rCTB → **D** (*Valneva*)

OraVacs –Enteric coated capsule (China and Philippines) *(Shanghai United Cell Biotechnology, China)*

-WHO Prequalified
-Complex to deliver and administer
-Expensive
-Successful travelers' vaccine
-Short term protection against ETEC

Heat inactivated Inaba (Cairo 48)
Heat inactivated Ogawa (Cairo 50)
Formalin inactivated (Cairo 50)
Formalin Inactivated El Tor Inaba (Phil 6973)

mORC-Vax™ *(VaBiotech, VietNam)*
Cholvax *(Incepta, Bangladesh)*

WC → **Shanchol** *(Shantha, India)*
+ O139

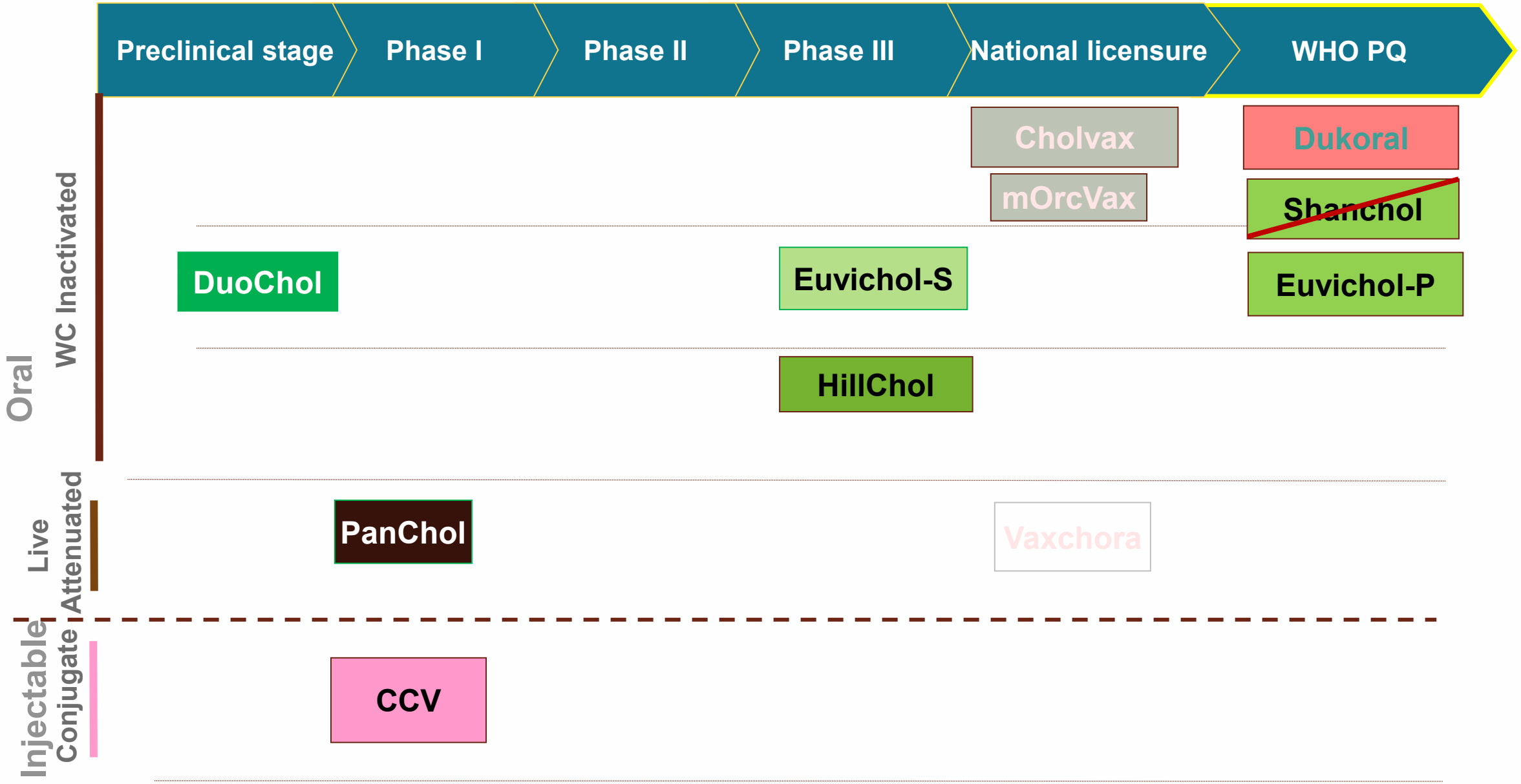
Euvichol-Plus *(EuBiologics, Korea)*

-WHO Prequalified
-Simple to deliver and administer
- <$2/dose
- **Stockpiled OCV**

New Products in the Pipeline

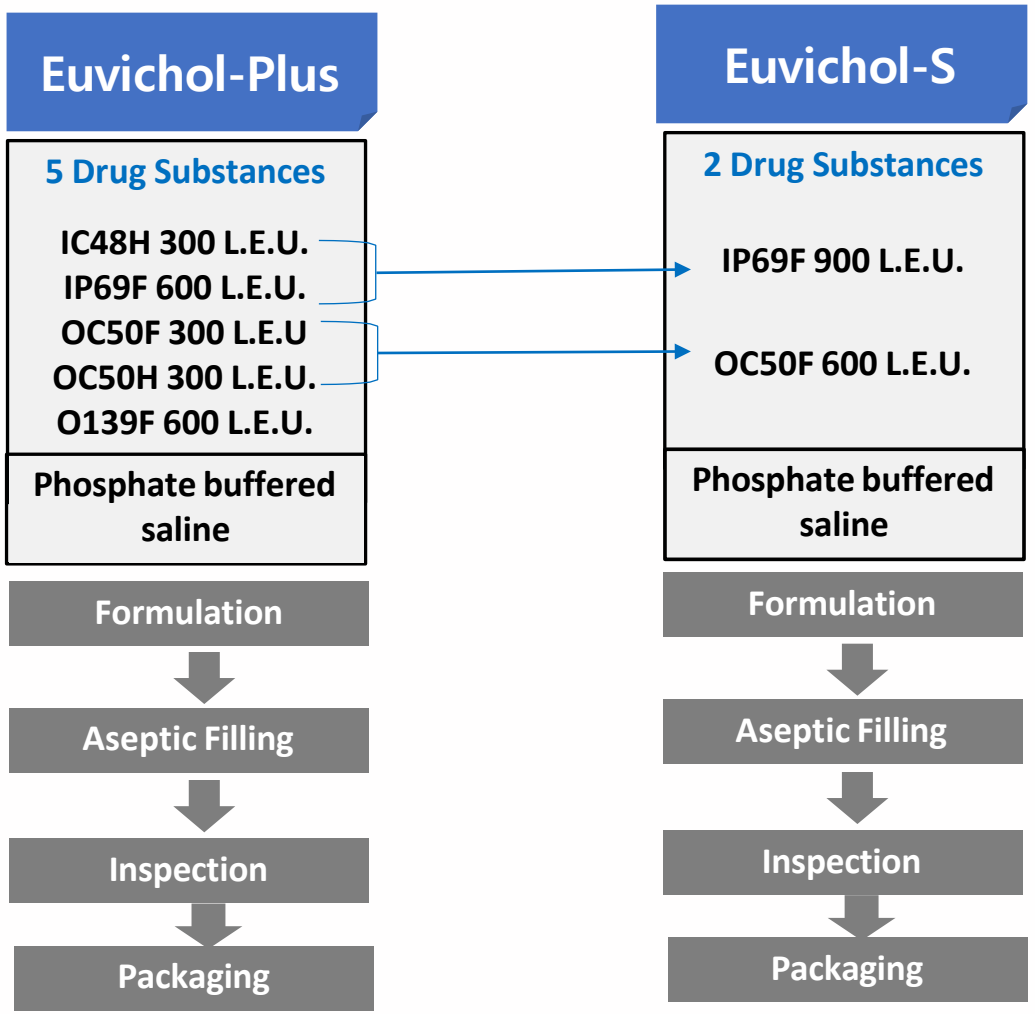
International Vaccine Institute

Landscape : Cholera Vaccines Pipeline



OCV_Euvichol-S

- Supply is expected to increase by 38% by switching from Euvichol-Plus to Euvichol-S.
- Pricing reduction is expected.
- We expect to submit our dossier to KMFDS in March 2023, anticipating an approval by year-end.
- PQ timeline will be subject to the feasibility of expedited review by PQ team.
- Expect to achieve the Controlled Temperature Chain (CTC) with Euvichol-S.



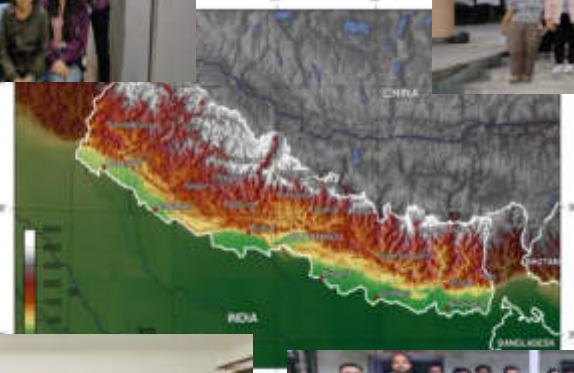
Reformulation of OCV

Lower cost
Increased supply

- A Phase III, Multicenter, Observer-Blinded, Randomized, Active Controlled Trial to Evaluate Immune Non-Inferiority, Safety and Lot-to-Lot Consistency of Euvichol-Simplified (**Euvichol-S**) Compared to Shanchol in 1 to 40 years old Healthy Nepalese Participants
  - To demonstrate non-inferiority of Euvichol-S compared to Shanchol™ as measured by seroconversion rates of anti-*V. cholerae* O1 Inaba and anti-*V. cholerae* O1 Ogawa vibriocidal titer 2 weeks after second dose for all ages
  - 4 Sites in Nepal
  - N=2,530 subjects (age 1-40 y)
  - Enrollment began 4 October
- Results expected 1Q 2023
- Registration late 2023

Dhulikhel Hospital, Kavre

Kanti Children's Hospital, Kathmandu



Nepalgunj Medical College

BPKIHS: Dharan

Funded by BMGF
Conducted by IVI in collaboration with EuBiologics

DuoChol

Increased supply *Improved short-term efficacy*

Improved thermostability *Reduced delivery cost*

- Lyophilized mixture of formalin inactivated whole-cells of serotype O1 *V. cholerae* Inaba and Ogawa with cholera toxin B-subunit (rCTB) contained in an enterocoated capsule to be taken in two doses 2 to 6 weeks apart

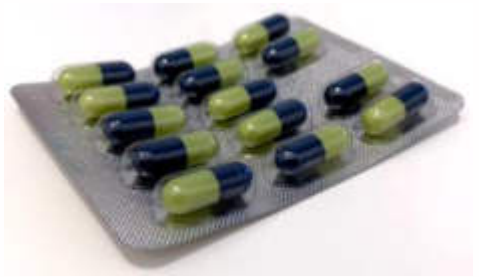
➢ Dukoral in a capsule

Advantages

- 85% efficacy against cholera for 9 months in under 6y
- Protection against ETEC diarrhea for 6-9 months for all ages
- Cost similar to current OCV
- Thermostability demonstrated at 40 C for 6 months
- Weight/volume of product substantially reduced
  - Significantly lower product delivery costs
  - Significantly less waste

Disadvantage

- Children under 4y may not reliably swallow capsule
  - Will require dissolution in liquid



Funded by Wellcome Trust, Govt of Sweden
Jan Holmgren, University of Gothenburg and IVI

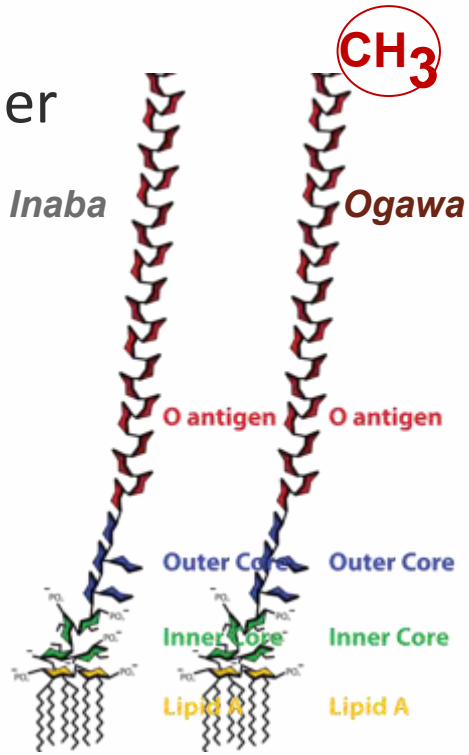
Comparison of Dukoral, DuoChol and Euvichol-P

		Dukoral		Duochol		Euvichol-P	
	Antigens	1.25 X 10 11 bacteria	Ratio		Ratio		Ratio
		O1 **Inaba** classical Cairo 48 [Heat]	1	O1 El Tor **Inaba** MS1955 (created from Phil6973 by deletion of its wbeT and ctxAB genes) [Formalin]	1	O1 **Inaba** classical Cairo 48 [Heat]	1.5
		O1 El Tor **Inaba** Phil 6973 [Formalin]	1			O1 El Tor **Inaba** Phil 6973 [Formalin]	
		O1 **Ogawa** classical Cairo 50 [Heat]	1	O1 El Tor **Ogawa** (created from MS1955 by reinsertion of wbeT) [Formalin]	1	O1 **Ogawa** classical Cairo 50 [Heat]	1
		O1 **Ogawa** classical Cairo 50 [Heat]	1			O1 **Ogawa** classical Cairo 50 [Formalin]	
						V. cholerae O139 4260B[Formalin]	
		1 mg rCholera Toxin B		1 mg rCholera Toxin B			
	Exicpient	Sodium dihydrogen phosphate dihydrate 2.0 mg, disodium hydrogen phosphate dihydrate 9.4 mg, sodium chloride 26 mg, sodium hydrogen carbonate 3600 mg, sodium carbonate anhydrous 400 mg, saccharin sodium 30 mg, sodium citrate 6 mg.		sucrose		Sodium phosphate dibasic dihydrate 4.68 mg, Sodium phosphate monobasic dihydrate, 0.97 mg, Sodium chloride 12.75 mg	
	Indication	Protection against cholera and ETEC diarrhoea for adults and children from 2 years of age who will be visiting areas with an ongoing or anticipated epidemic or spending an extended period of time in areas in which cholera infection is a risk		Desired: Indicated for protection against cholera and ETEC diarrhoea for children 1 year or older		Prevention of Cholera caused by Vibrio cholerae	
Dosing	6 year and older	2 doses 1-6 week apart (booster recommended after 2 years)		2 doses at two or more week interval		2 doses at two week interval	
	2-5 years	3 doses 1-6 week apart (booster recommended after 6 months)		(Dissolved capsule) 2 doses at two or more week interval			
	> 1 year			(Dissolved capsule) 2 doses at two or more week interval			
Estimated efficacy against cholera diarrhea in first 6-9 month	All ages	85% (no difference by age strata)		Expected to match Dukoral		58% (no difference by age strata)	
Estimated efficacy against ETEC diarrhea over 3 months	All ages	67% against any and 86% protection against severe		Expected to match Dukoral		None	

HillChol

Lower cost
Increased supply

- Hillchol® consists of formalin-inactivated *Vibrio cholerae* O1 El Tor Hikojima strain expressing approximately 50% each of Ogawa and Inaba O1 LPS antigens.
- Phase I/II, safety and immunogenicity study conducted in adults, older children, and younger children in Bangladesh.
  - HillChol™ was non-inferior to Shanchol™, in terms of seroconversion and Geometric Mean Titer for both the Ogawa and Inaba serotypes
- Phase 3 trial in 2022
- Possible national registration in 2023
- 15M doses/yr



Bharat Biotech and Hilleman Labs

Chowdhury F, Ali Syed K, Akter A, Rahman Bhuiyan T, Tauheed I, Khaton F, Biswas R, Ferdous J, Al Banna H, Ross AG, Mc Millan N, Sharma T, Kanchan V, Pal Singh A, Gill D, Lebens M, Nordqvist S, Holmgren J, Clemens JD, Qadri F. A phase I/II study to evaluate safety, tolerability and immunogenicity of Hillchol®, an inactivated single Hikojima strain based oral cholera vaccine, in a sequentially age descending population in Bangladesh. Vaccine. 2021 Jul 22;39(32):4450-4457. doi: 10.1016/j.vaccine.2021.06.069. Epub 2021 Jul 1. PMID: 34218960.

PanChol LAV

Single Dose *Improved efficacy under 5y*

- Live attenuated OCV candidate derived from a variant El Tor O1 Ogawa *V. Cholerae* clinical isolate from the 2010 Haiti outbreak
- Genetically altered for deletion of diarrheagenic factors and incorporation of safeguards against vac cine reversion
  - Bivalent expressing Ogawa and Inaba serotypes
  - Produces CtxB only
  - Non-motile/non-reactogenic
  - Incapable of genetic exchange
  - Active CRISPR-mediated resistance against toxigenic reversion
  - ➢ Induces rapid protection kinetics in infant rabbits through a probiotic-like effect (inhibiting coloniz ation of pathogenic cholera)
  - ➢ Induces adaptive protective immune response in adult germ-free mice
- ➢ Phase 1 Trial to start in Oct 2022

Matthew Waldor, Harvard
Funded by Wellcome Trust

Sit B, Zhang T, Fakoya B, Akter A, Biswas R, Ryan ET, Waldor MK. Oral immunization with a probiotic cholera vaccine induces broad protective immunity against Vibrio cholerae colonization and disease in mice. PLoS Negl Trop Dis. 2019 May 31;13(5):e0007417. doi: 10.1371/journal.pntd.0007417. PMID: 31150386; PMCID: PMC6561597.

Cholera Conjugate Vaccine

Increased supply

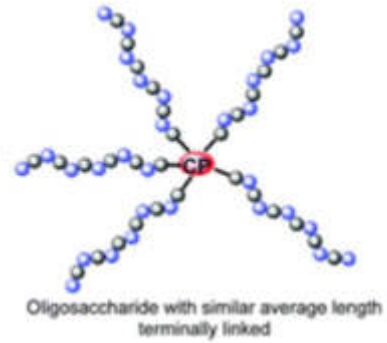
Improved long-term efficacy

Reduced delivery cost

- Approximately half of the cholera cases and deaths are estimated to occur in children under five years
- Current OCV has reduced efficacy in children under 5 yrs; and a single dose has no efficacy
  - Not ideally suitable for delivery through EPI
- Conjugate vaccines elicit long lasting T-cell dependent immune responses in young children, often with a single dose
- An injected vaccine with a long duration of protection can be cost effectively incorporated into EPI, reducing the burden of repeated vaccination campaigns, and building population immunity from infancy up
- A COG analysis suggested a cost of 0.42 USD per dose

Single point sugar-carrier protein (CP) attachment

Can load various Sugar to Protein Carrier Ratios



Funded by RIGHT Fund, Wellcome Trust, Open Philanthropy
Conducted by IVI in collaboration with MGH, NIH and EuBiologics

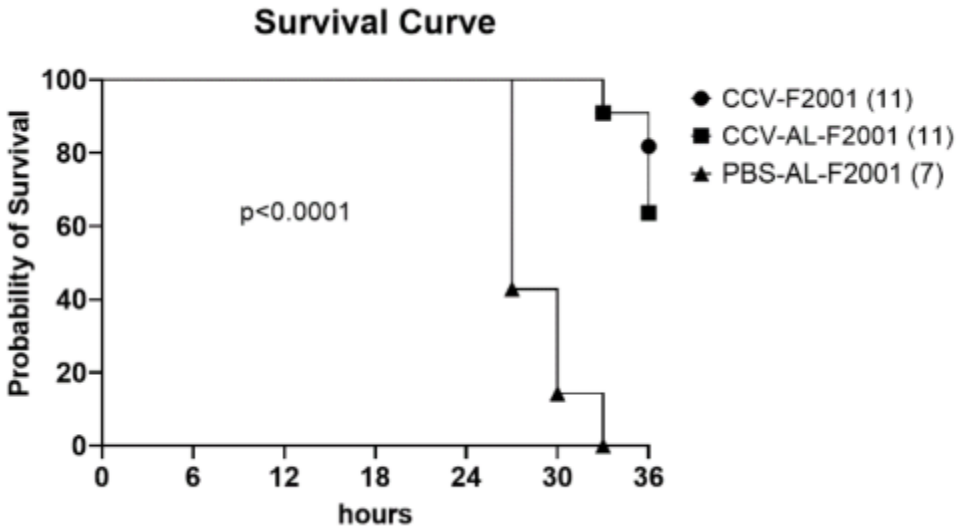
Cholera Conjugate Vaccine

Increased supply

Improved long-term efficacy

Reduced delivery cost

- Pre-clinical development is complete including toxicology studies



immunogenic and protective in suckling mice against virulent strain *V. cholerae* O1 NI16961; ATCC 39315

- Phase 1 trial in preparation with Oct 2022 start

A Phase I, multicenter, observer-blinded, randomized, placebo-controlled, dose escalation trial to evaluate the safety and immunogenicity of the OSP:rTTHc cholera conjugate vaccine in 19 to 45 years old healthy Korean participants

Funded by RIGHT Fund, Wellcome Trust, Open Philanthropy
Conducted by IVI in collaboration with MGH, NIH and EuBiologics

OCV_Current Unmet Needs

- **Shortage of oral cholera vaccine**
  - Global trend is moving towards more numerous, widespread and severe outbreaks due to floods, droughts, conflict, population movements etc.
  - Current supply is not sufficient to serve demand for reactive campaigns to outbreaks

Development of Euvichol-S and expansion ongoing

- **Lower efficacy for children under 5 years of age**
  - OCV are limited to induce high level durable protective immunity in young children

Cholera Conjugate Vaccine (injectable) under development in collaboration with IVI and Massachusetts General Hospital

International Coordinating Group (ICG) on Vaccine Provision

- **The International Coordinating Group (ICG) on Vaccine Provision was established in 1997 as a mechanism to manage and coordinate the provision of emergency vaccine supplies and antibiotics to countries during major outbreaks.**
- **Since 2013, the ICG for cholera vaccine manages the global stockpile of OCV which was created as an additional tool to help control cholera epidemics. Since its establishment until October 2022, almost 73 million doses of OCV were shipped to 23 countries for emergency response.**

A **timely** response is **essential**...

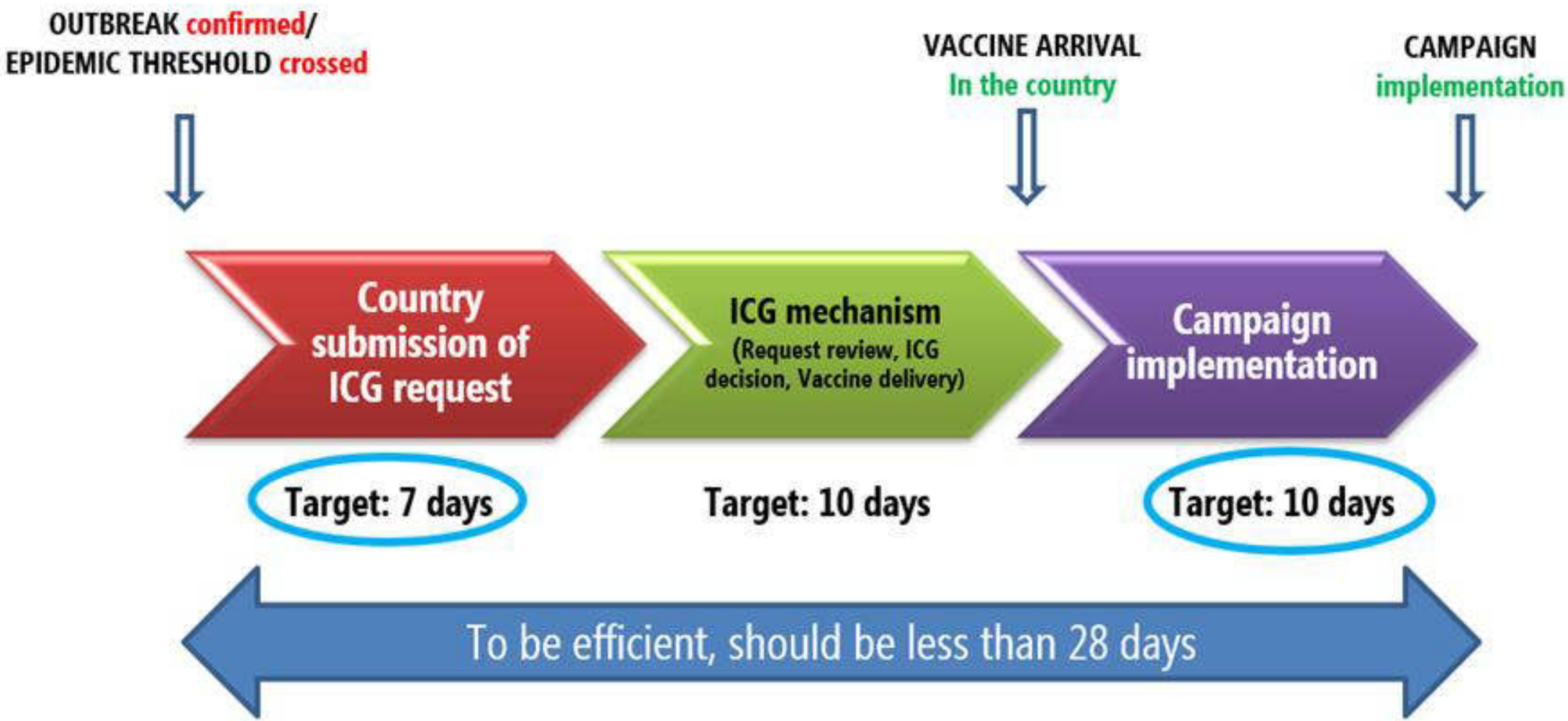
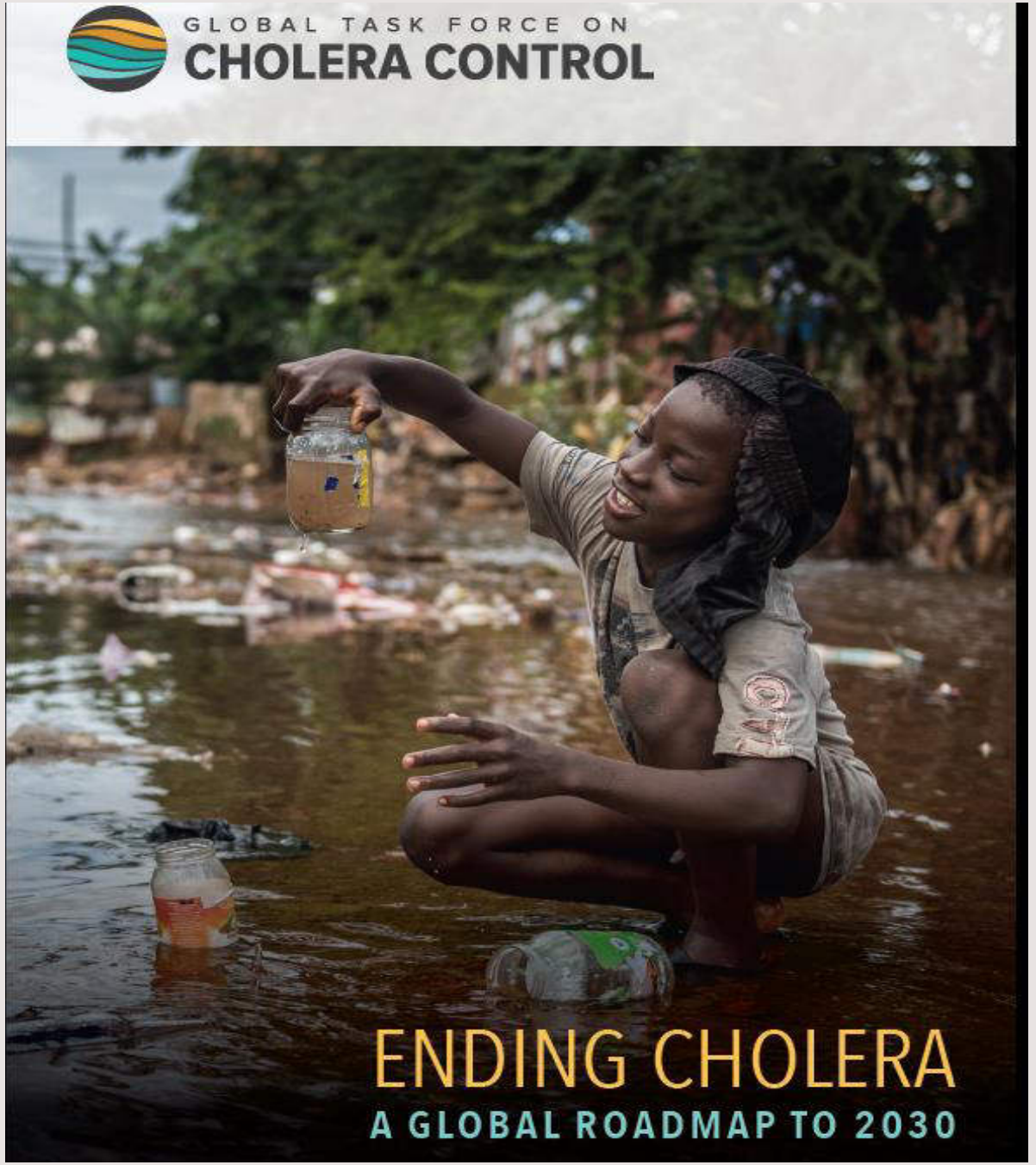


Table 1. Cholera cases and deaths reported to WHO from WHO regions, as of 20 March 2023**

Country, area, territory	Suspected/confirmed cases[1]	Total deaths	Cases per 100 000	CFR (%)	Reporting period (DD/MM/YYYY)
Burundi	193	1	2	<1%	08/12/2022 – 19/03/2023
Cameroon	15 309	311	55	2.0	01/10/2021 – 12/03/2023
Democratic Republic of the Congo	24 657	334	26	1.4	01/01/2022 – 2003/2023
Ethiopia	2095	44	2	2.1	01/08/2022 – 20/03/2023
Kenya	7235	116	14	1.6	08/10/2022 – 20/03/2023
Malawi	54 841	1684	272	3.1	01/03/2022 – 20/03/2023
Mozambique	10 854	75	34	<1%	01/09/2022 – 20/03/2023
Nigeria	922	32	<1	3.5	01/01/2023 – 05/03/2023
South Africa	6	1	<1	16.7	01/02/2023 – 04/03/2023
South Sudan	307	1	2	<1%	22/02/2023 – 16/03/2023
United Republic of Tanzania	72	3	<1	4.216	01/02/2023 – 13/03/2023
Zambia	268	7	1	2.6	21/01/2023 – 20/03/2023
Zimbabwe	121	1	1	<1%	12/02/2023 - 19/03/2023
Afghanistan*	22 848	7	57	<1%	01/01/2023 – 20/03/2023
Lebanon	1060	0	19	0	01/1/2023 - 20/03/2023
Somalia	2573	7	101	<1%	01/01/2023 – 12/03/2023
Syrian Arab Republic	21 427	5	101	<1%	01/01/2023 – 11/03/2023
North-west Syria	57 947	23	1252	<1%	16/09/2023 – 18/03/2023
Yemen	1724	3	6	<1%	01/01/2023 – 12/03/2023
Pakistan***	77 714	0	34	0	01/01/2023 – 12/03/2023
Dominican Republic	96	0	<1	0	17/10/2022 – 19/03/2023
Haiti	36 544	632	317	1.7	02/10/2022 – 16/03/2023
Bangladesh (Cox's Bazar)	19	0	-	0	01/01/2023 – 15/03/2023

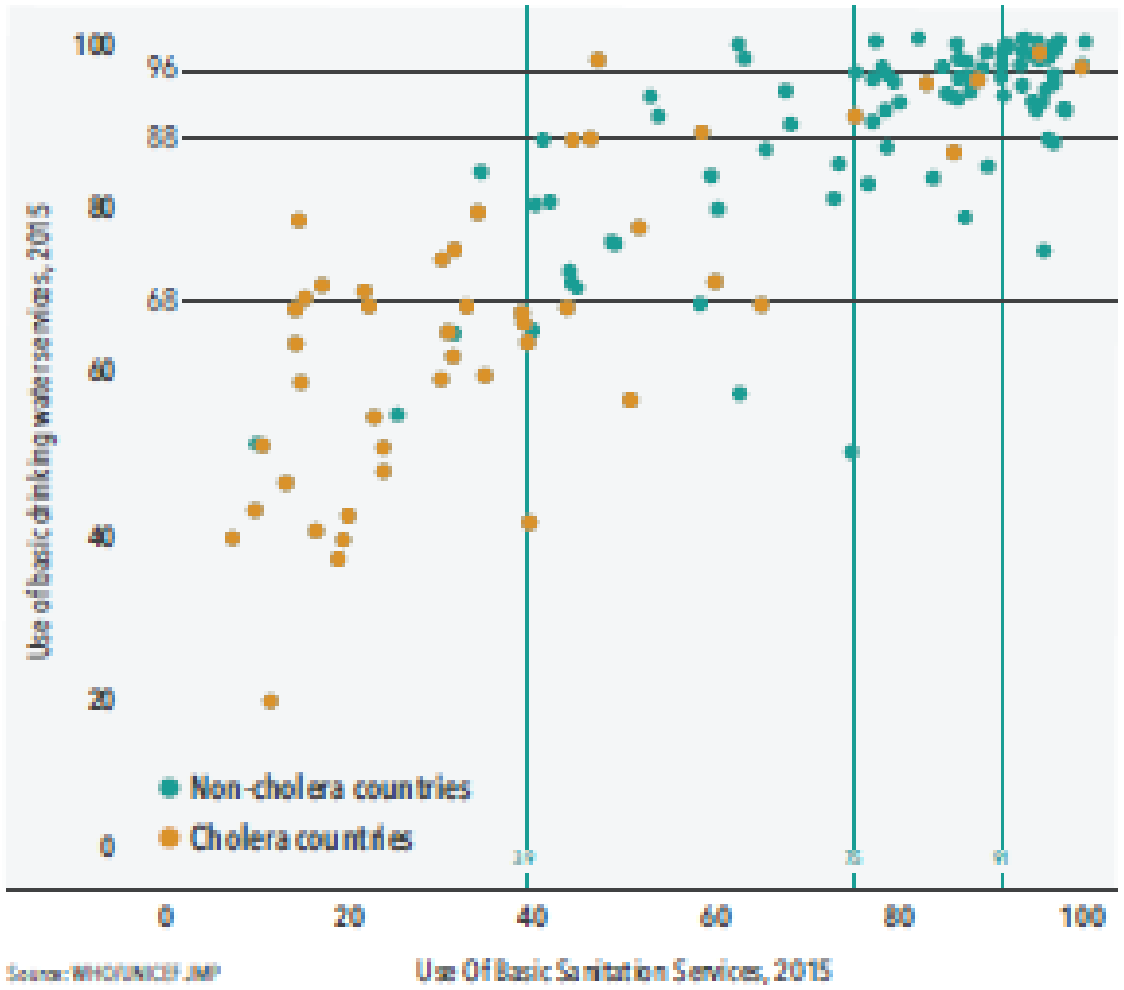

GLOBAL TASK FORCE ON
CHOLERA CONTROL
ENDING CHOLERA
A GLOBAL ROADMAP TO 2030

Ending Cholera—A Global Roadmap to 2030

- Early detection and quick response to contain outbreaks
- A targeted multi-sectoral approach to prevent cholera recurrence
- An effective mechanism of coordination for technical support, advocacy, resource mobilization, and partnership at local and global levels

Cholera "hotspots" are specific and relatively small areas where the cholera burden is most concentrated and that play a central role in the spread of cholera.

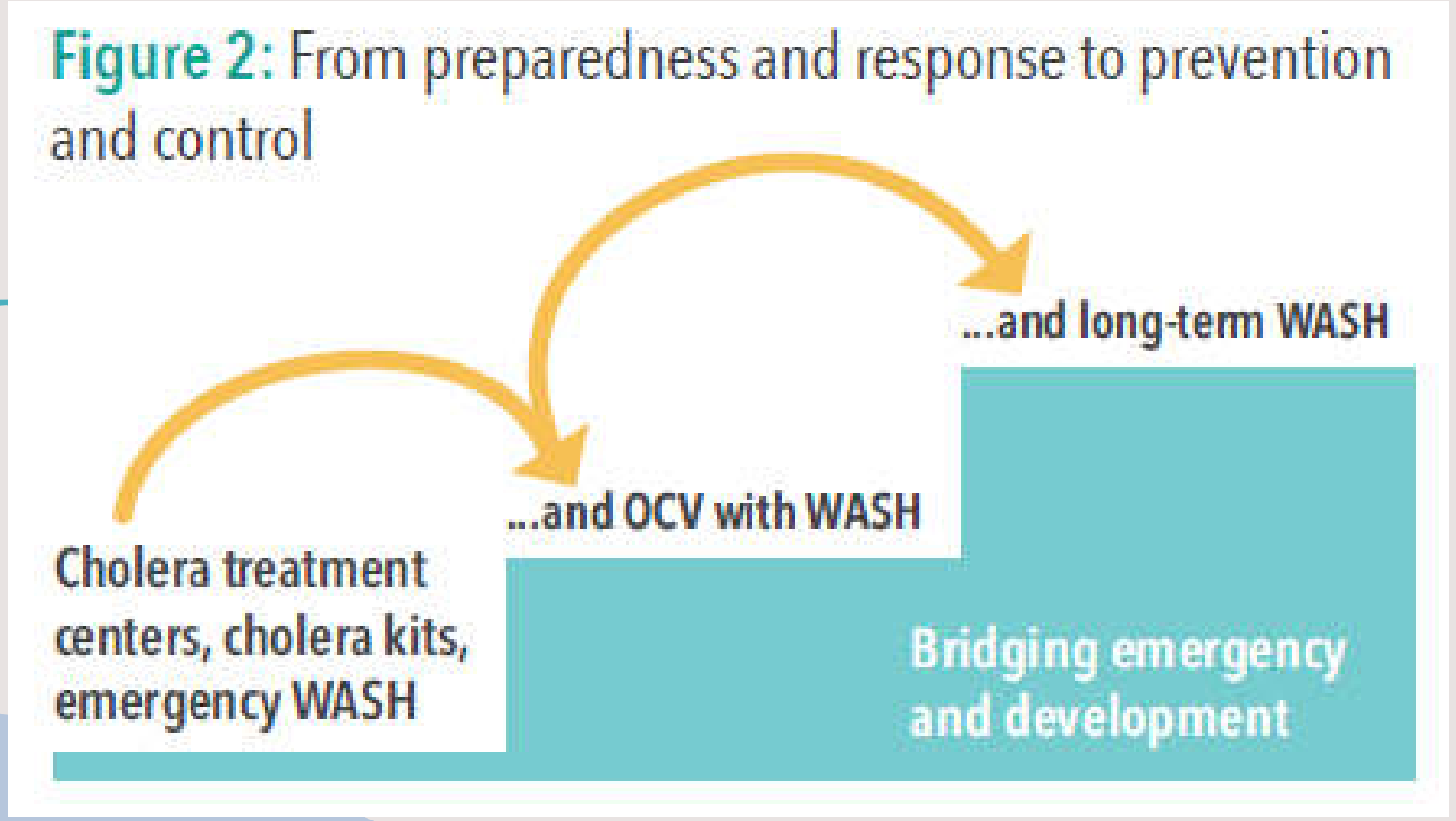
Figure 1: 138 low- and middle-income countries (World Bank definitions) with reported access to water and sanitation



Basic WASH package

- Basic water supply: access to safe drinking water sources (either household connection, public standpipe, borehole, protected dug well, protected spring, or rainwater collection)within a 30-minute round-trip plus household or other disinfection12
- Basic sanitation: access to improved sanitation facilities (connection to a public sewer, connection to a septic system, pour-flush latrine, simple pit latrine, ventilated improved pit latrine)
- Basic hygiene: access to a hand-washing station with soap and water for every household
- Community engagement to manage WASH resources and to promote safe hygiene practice

Basic WASH package




1 NO POVERTY
2 ZERO HUNGER
3 GOOD HEALTH AND WELL-BEING
4 QUALITY EDUCATION
5 GENDER EQUALITY
6 CLEAN WATER AND SANITATION
7 AFFORDABLE AND CLEAN ENERGY
8 DECENT WORK AND ECONOMIC GROWTH
9 INDUSTRY, INNOVATION AND INFRASTRUCTURE
10 REDUCED INEQUALITIES
11 SUSTAINABLE CITIES AND COMMUNITIES
12 RESPONSIBLE CONSUMPTION AND PRODUCTION
13 CLIMATE ACTION
14 LIFE BELOW WATER
15 LIFE ON LAND
16 PEACE, JUSTICE AND STRONG INSTITUTIONS
17 PARTNERSHIPS FOR THE GOALS
SUSTAINABLE DEVELOPMENT GOALS

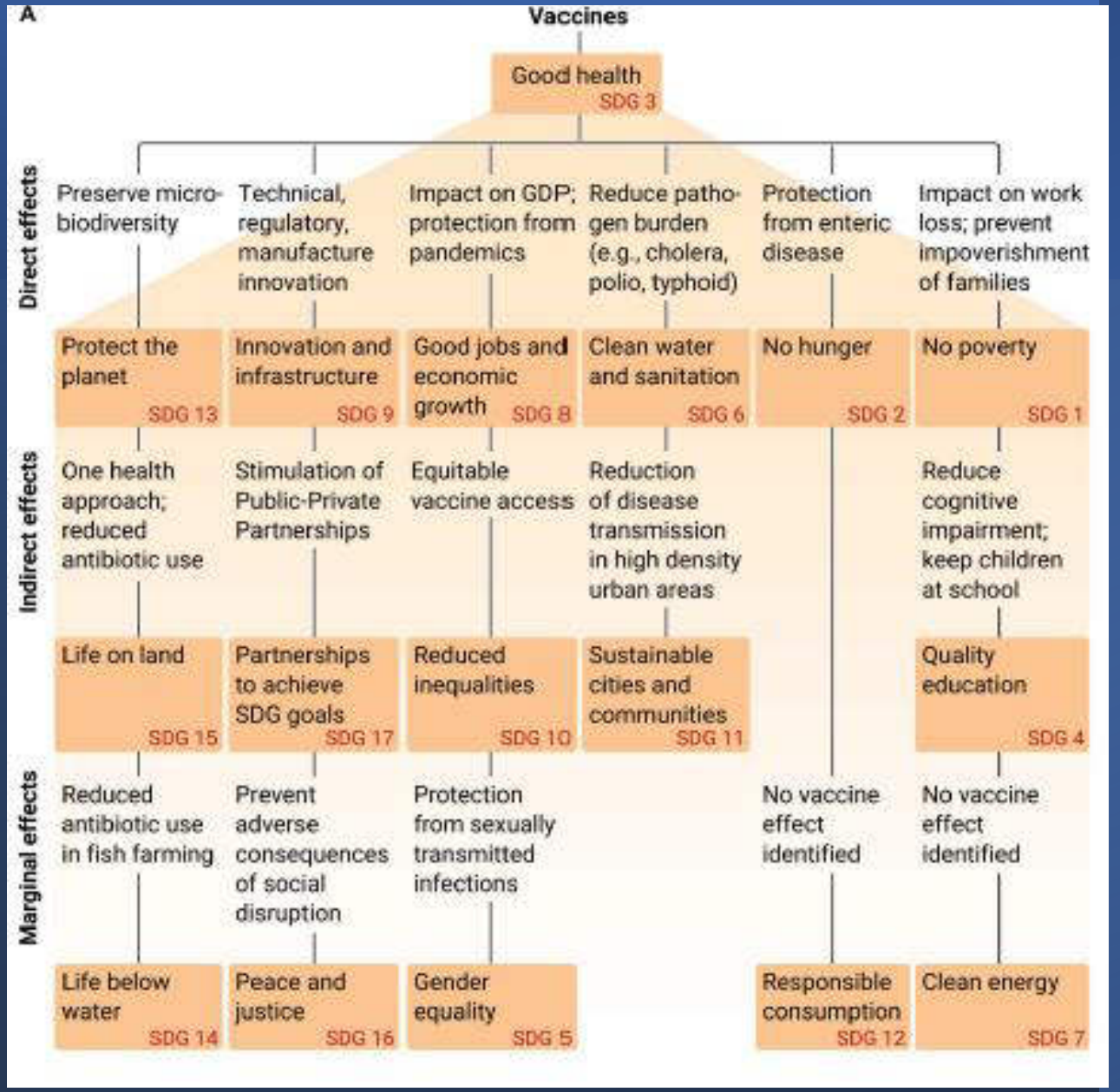
SCIENCE TRANSLATIONAL MEDICINE | VIEWPOINT

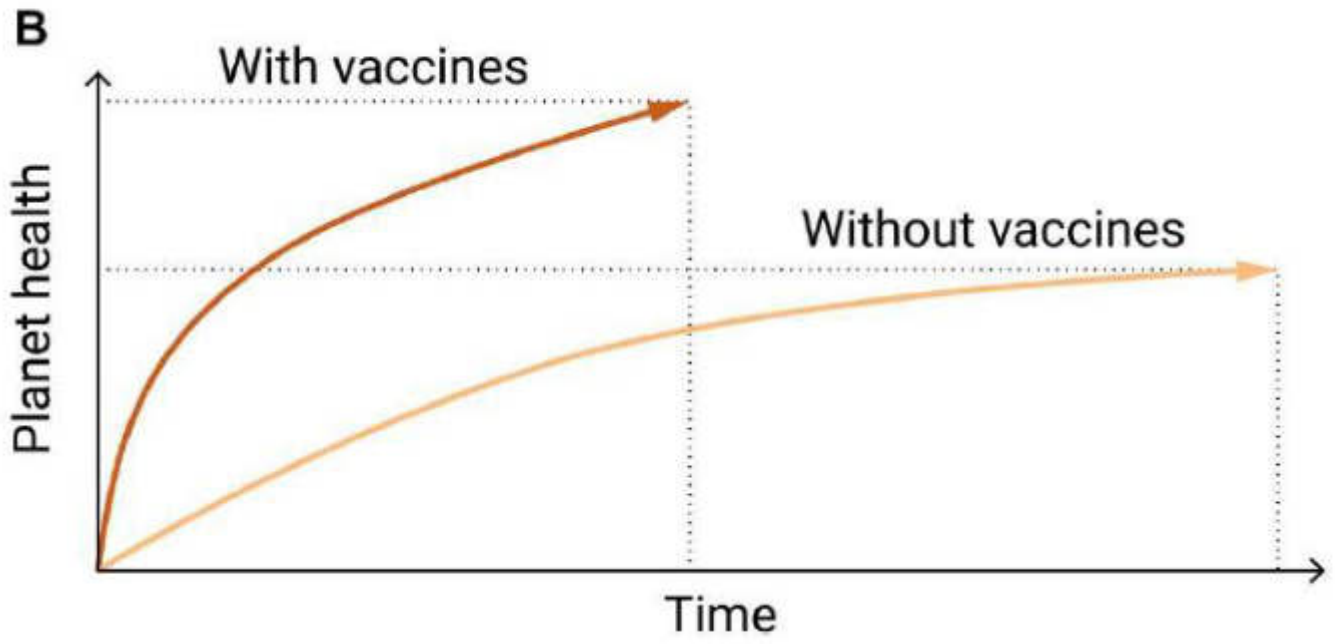
VACCINES

Vaccines for a sustainable planet

Simone Pecetta[1†], Arindam Nandi[2,3], Charlie Weller[4], Vanessa Harris[5,6], Helen Fletcher[7,8], Francesco Berlanda Scorza[9], Mariagrazia Pizza[10‡], David Salisbury[11], Richard Moxon[12], Steve Black[13], David E. Bloom[14], Rino Rappuoli[1*§]

Pecetta *et al.*, *Sci. Transl. Med.* **15**, eadf1093 (2023) 1 March 2023


A
Vaccines
Good health
SDG 3
Direct effects
Preserve micro-biodiversity
Technical, regulatory, manufacture innovation
Impact on GDP; protection from pandemics
Reduce patho-gen burden (e.g., cholera, polio, typhoid)
Protection from enteric disease
Impact on work loss; prevent impoverishment of families
Protect the planet
SDG 13
Innovation and infrastructure
SDG 9
Good jobs and economic growth
SDG 8
Clean water and sanitation
SDG 6
No hunger
SDG 2
No poverty
SDG 1
Indirect effects
One health approach; reduced antibiotic use
Stimulation of Public-Private Partnerships
Equitable vaccine access
Reduction of disease transmission in high density urban areas
Reduce cognitive impairment; keep children at school
Life on land
SDG 15
Partnerships to achieve SDG goals
SDG 17
Reduced inequalities
SDG 10
Sustainable cities and communities
SDG 11
Quality education
SDG 4
Marginal effects
Reduced antibiotic use in fish farming
Prevent adverse consequences of social disruption
Protection from sexually transmitted infections
No vaccine effect identified
No vaccine effect identified
Life below water
SDG 14
Peace and justice
SDG 16
Gender equality
SDG 5
Responsible consumption
SDG 12
Clean energy
SDG 7



Earlier and greater accomplishment envisioned if vaccines are incorporated in the SDG agenda

Current SDG agenda

Thanks to helpful friends

- Jan Holgren and Ann Mari Svennerholm – Göteborg University, Göteborg, Sweden
- Julia Lynch, IVI, Seoul, ROK
- Francisco Luquero and Marta Tufet, Gavi Alliance, Geneva, Switzerland.
- Firdausi Qadri, icddr,b, Dhaka, Bangladesh
- Ed Ryan, Mass General, Harvard Medical School, Boston, MA, USA
- Joachim Hombach, SAGE, WHO, Geneva, Switzerland