

# Measuring vaccine impact

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ŌTĀKOU WHAKAIHU WAKA



# GLOBAL PUBLIC HEALTH

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## Global Public Health Impact of Vaccines in Children

Peter McIntyre and Tony Walls

<https://doi-org.ezproxy.otago.ac.nz/10.1093/acrefore/9780190632366.013.64>

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# Talk Structure

- Vaccine coverage
- Surveillance data
- Disease burden measures
  - Importance of severity
  - Vaccine/study specific: long term maintenance
- Impact measures
  - Before-after: importance of baseline data
  - Study designs using disease and coverage data
  - Examples

SAGE Working Group on Quality and Use of  
Immunization and Surveillance Data:

# Immunisation Registers – AIR in Australia and NZ

## Australian Immunisation Register (AIR)



- All age (2016) ACIR 1995
- Date of vaccination
- Date of birth
- Indigenous status
- Area of residence
  
- Pregnancy status

AOTEAROA  
IMMUNISATION  
REGISTER

Aotearoa Immunisation Register

## National Health Index

The National Health Index (NHI) is a mechanism for uniquely identifying every health care user.

All age (2023) NIR 2005  
+ ethnicity and deprivation score

# Routine data – notifications, hospitalisations, deaths



## Vaccine preventable diseases in Australia

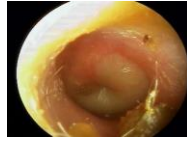
Disease	Notifications <sup>(a)</sup>			Hospitalisations in 2022	Deaths in 2022
	2022	2023	2024		
Covid-19	10,327,843	864,335	342,010	320,053	9,862
Influenza	233,454	289,151	365,485	13,306	306
RSV	-	128,101	175,908	8,274	58
Whooping cough (pertussis)	483	2,454	57,102	28	0
Shingles (herpes zoster)	10,583	13,427	10,131	2,412	65
Pneumococcal disease	1,858	2,269	2,386	2,005	23
Mumps	47	132	188	51	<3
Rotavirus	6,465	8,447	10,084	893	<3
Chickenpox (varicella)	1,837	2,625	2,359	328	7
Meningococcal disease	125	143	136	118	7
Hepatitis A	144	216	238	84	<3
Hepatitis B (acute/newly acquired)	62	97	86	43	4
Measles	7	26	57	<6	0
Hib	11	12	6	36	0
Tetanus	1	4	5	7	0
Polio	0	0	0	0	17
Rubella	3	4	2	<6	0
Diphtheria	31	12	9	<6	0

# Disease burden measures 1

## invasive bacterial diseases – Hib was simple



Haem influenzae



Strep pneumoniae



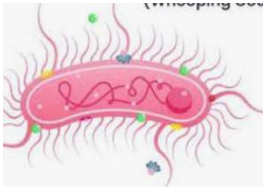
Meningococcus

- Most < 5 years
  - Blood culture routine
  - Most + blood cultures
  - One serotype -b
- All ages
  - Blood culture less common
  - Non bact pneumonia
  - Otitis media
  - Many serotypes
- All ages
  - Cultures often neg
    - PCR
  - Multiple serotypes

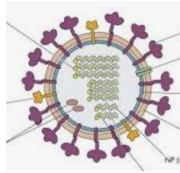
Laboratory networks and reference laboratories needed

## Disease burden measures 2

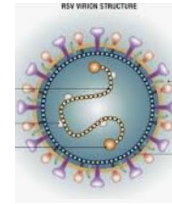
### Respiratory infections



Pertussis



Influenza



RSV

- Culture often neg
  - Infant disease
  - Testing practices
  - PCR
  - Typing not important
- Testing practices
  - PCR
  - Typing important
- Infants
  - PCR
  - Typing not important

High testing + mandatory laboratory notification in Australia

# PCR testing for influenza and pertussis – Australia

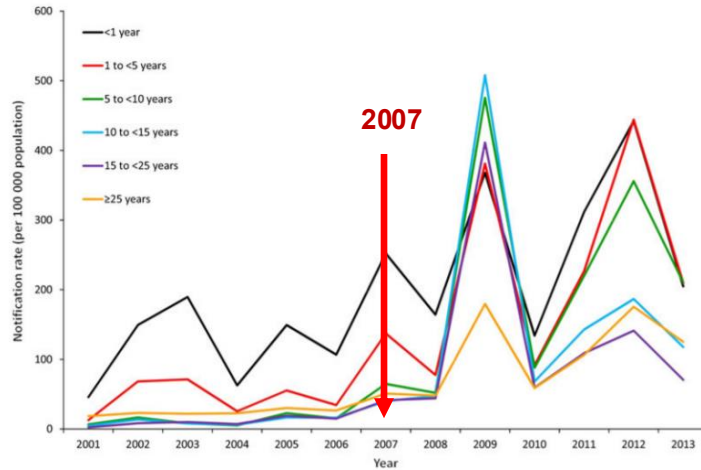
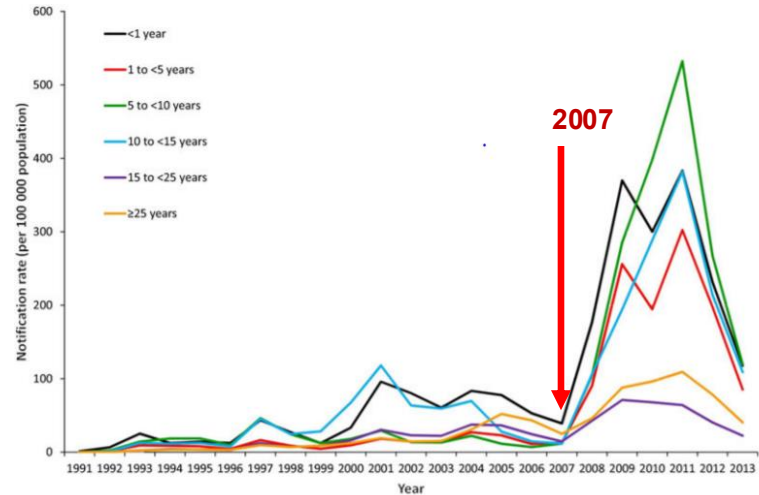


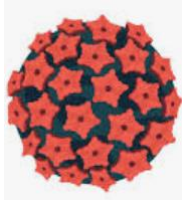
Fig. 1. Annual influenza notification rate per 100 000 age-specific population, 1 January 2001 to 31 December 2013, Australia.



Annual pertussis notification rate per 100 000 age-specific population, 1 January 2001 to 31 December 2013,

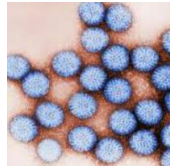
## Disease burden measures 3

### New surveillance measures needed



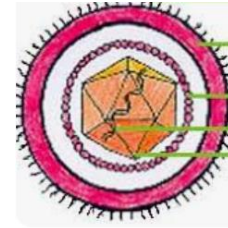
HPV

- No culture
- Cervical smears
- PCR
- Typing important



Rotavirus

- No culture
- Ag → PCR
- Hospitalised cases
- Typing not important



Varicella

- Seldom tested
- Not reported
- Hospitalised cases
- Zoster

Limited role for disease notification data

## Disease burden measures 3

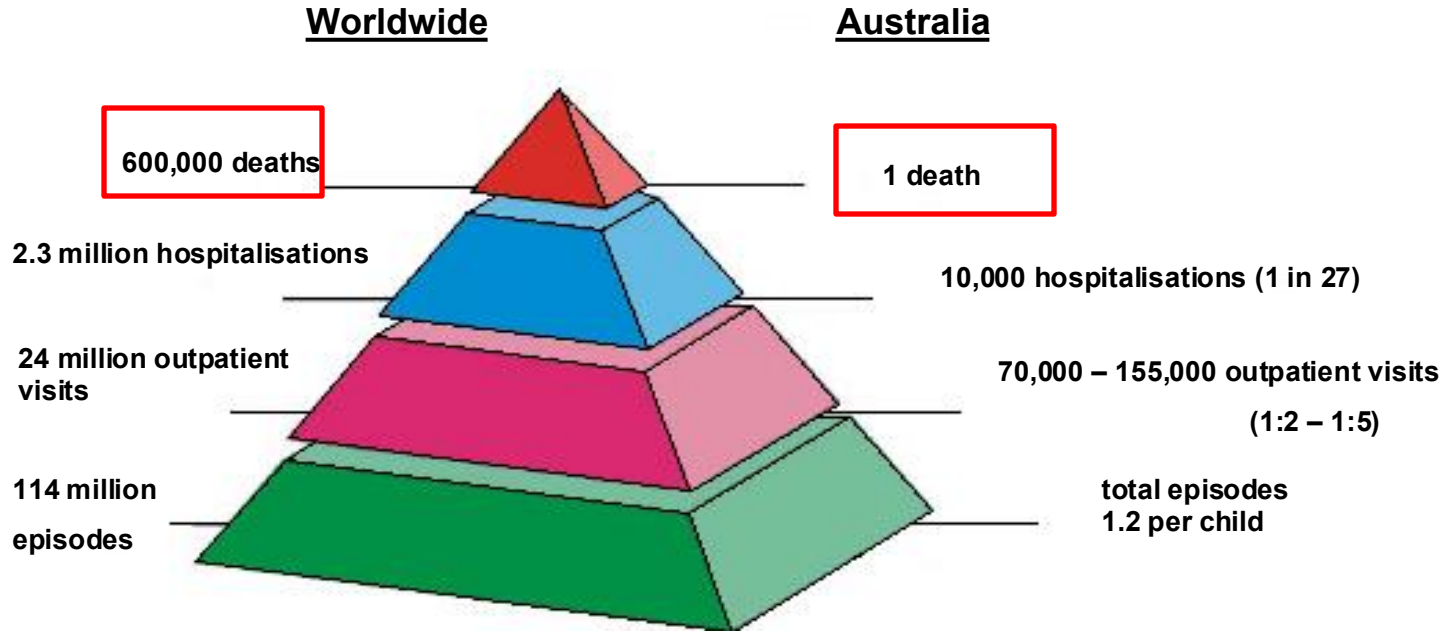
### New surveillance measures needed



# Severity and Vaccine Probe studies



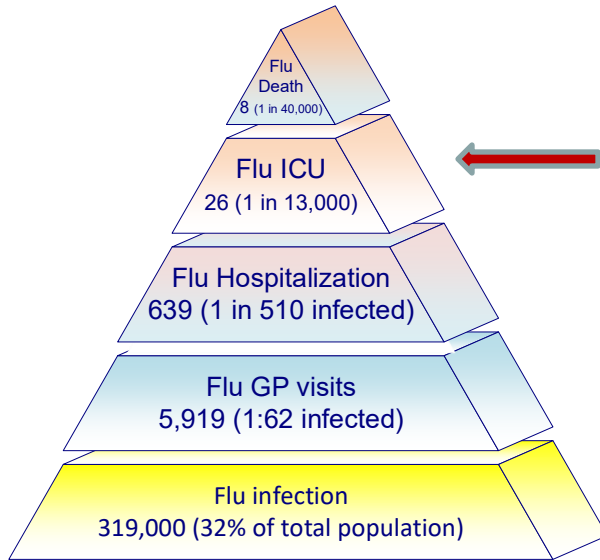
# Rotavirus disease pyramid



## Influenza burden pyramid – NZ

SHIVERS  
project

1,000,000 people over one season



ICU cases best ascertained

- criteria for ICU care uniform
- almost all tested

- Serosurvey: 32% influenza seroC
- Of infected:
  - 24% influenza-like illness (ILI)
- Of infected with PCR confirmed influenza:
  - 26% visited a GP



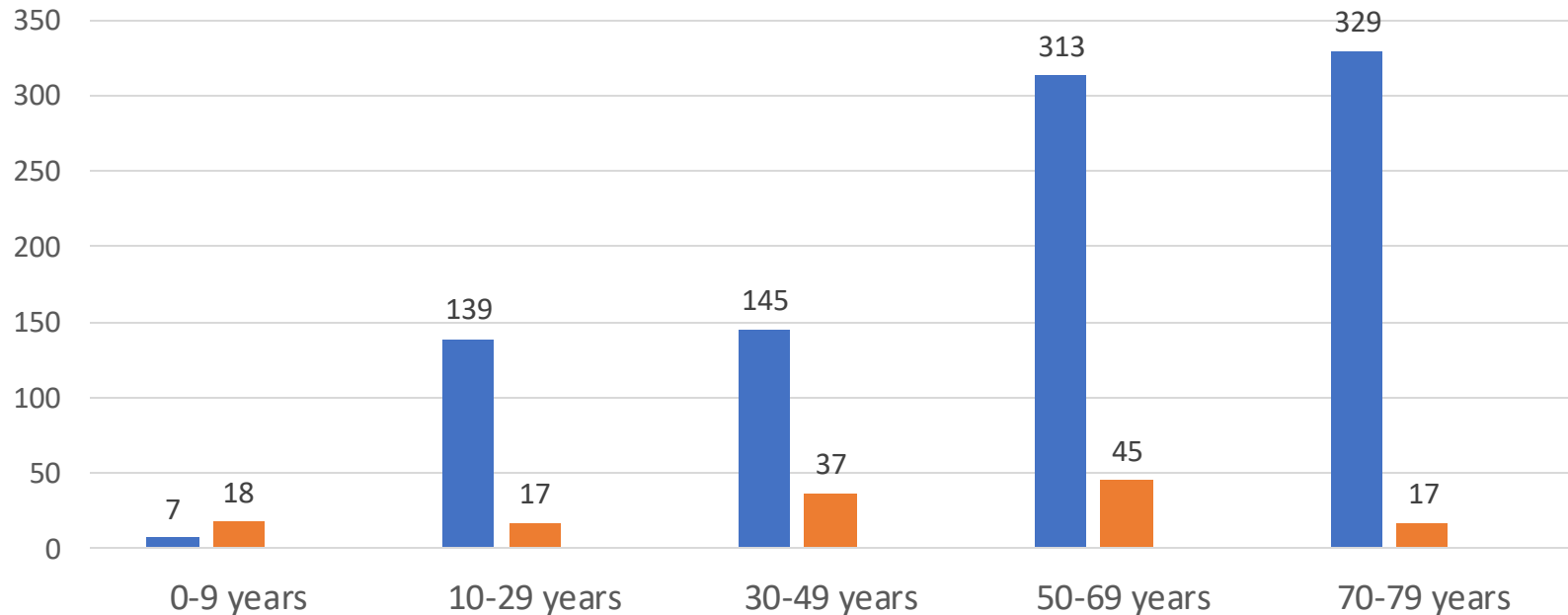
# SHIVERS

Influenza vaccine effectiveness in preventing influenza-associated intensive care admissions and attenuating severe disease among adults in New Zealand 2012–2015

	<b>% vacc (+ Flu PCR)</b>	<b>% vacc (- Flu PCR)</b>	<b>VE (95% CI)</b>
Hospitalised, no ICU	45%	60%	37% (23-48)
ICU admission	22%	53%	82% (45-94)

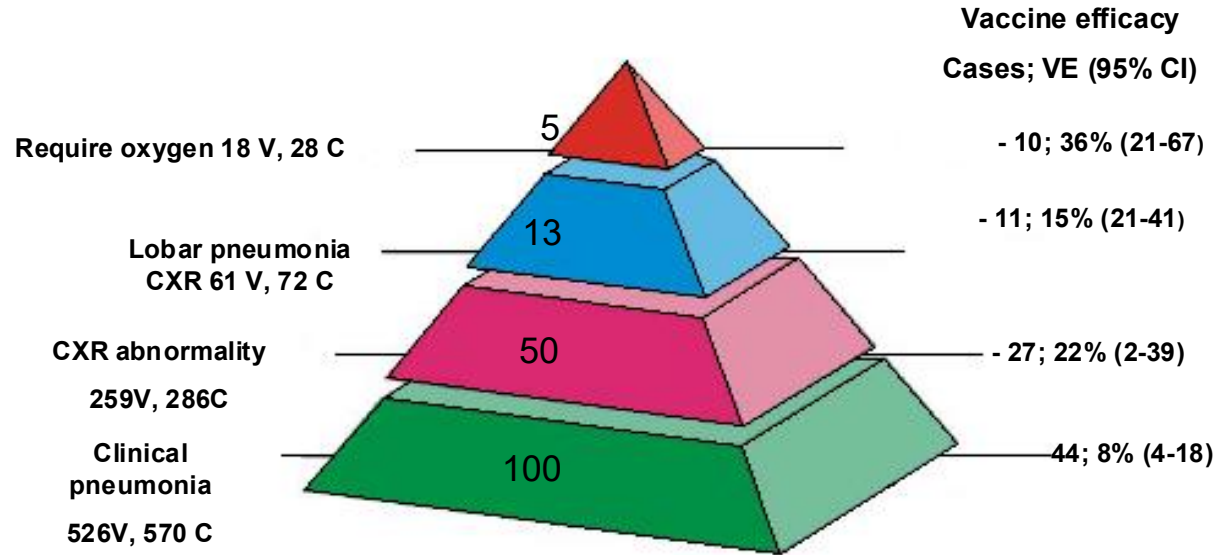
# Incidence per million of ICU admission

NSW COVID-19 2021 (1) vs Pandemic Flu H1N1 2009 (2)



1. NSW COVID-19 surveillance Jun-Oct 2021
2. H1N1 influenza NEJM 2009; 361: 1925-1934

# Pneumonia severity and vaccine efficacy - Hib Gambia RCT



# When high quality lab facilities are not available: The vaccine probe approach

Incidences of vaccine-preventable *Haemophilus influenzae* type b pneumonia and meningitis in Indonesian children: hamlet-randomised vaccine-probe trial

Bradford D Gessner, Agustinus Sutanto, Mary Linehan, I Gusti Gede Djelantik, Tracy Fletcher, I Komang Gerudug, Ingerani, David Mercer, Vanda Moniaga, Lawrence H Moulton, Kim Mulholland, Carib Nelson, Soewignjo Soemohardjo, Mark Steinhoff, Anton Widjaya, Philippe Stoeckel, James Maynard, Soemarjati Arjoso

Lancet 2005; 365: 43-52  
See Comment page 5  
Association Pour l'Aide à la  
Recherche Médicale

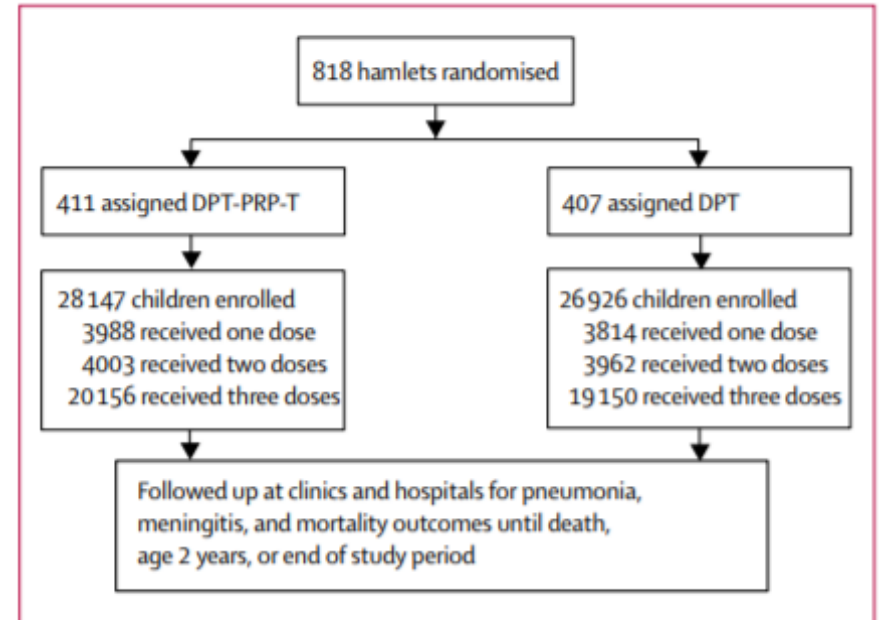


Figure 1: Trial profile

## Lombok - 2

Meningitis outcome	At least one vaccine dose			Vaccine-preventable Hib incidence (95% CI), per 10 <sup>5</sup> child-years
	Prevented proportion, %*	Incidence per 10 <sup>5</sup> child-years		
		Control group	Intervention group	
Microbiologically confirmed Hib	86	19	2.6	16 (1.4 to 31)
Probable bacterial or confirmed Hib	55	86	39	47 (13 to 81)
Possible or probable bacterial or confirmed Hib	50	134	67	67 (22 to 112)
Lumbar puncture	26	346	258	89 (10 to 167)
Meningitis admission	16	538	451	87 (-15 to 189)
Meningitis admission or clinic assessment for seizures	22	701	543	158 (42 to 273)

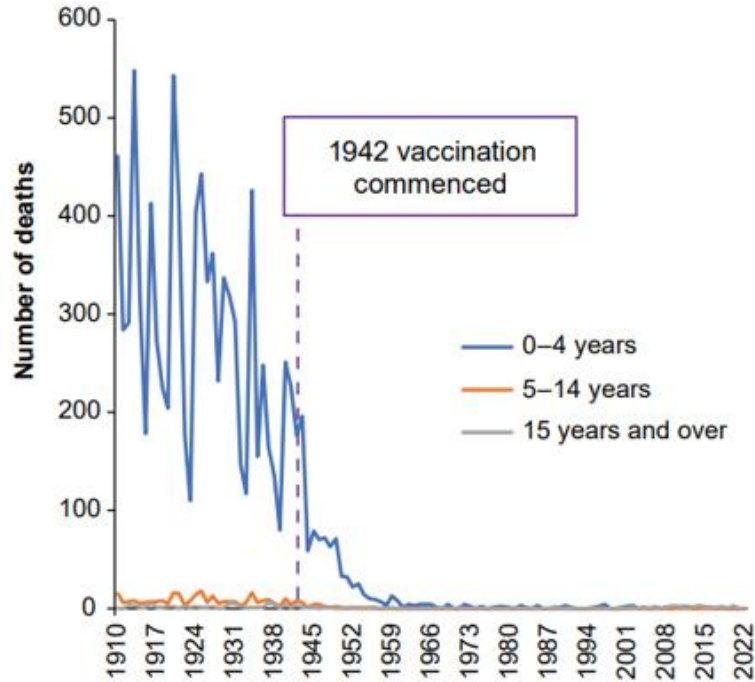
**Table 3: Incidences of vaccine-preventable Hib meningitis**

# Efficacy, effectiveness, herd immunity and impact

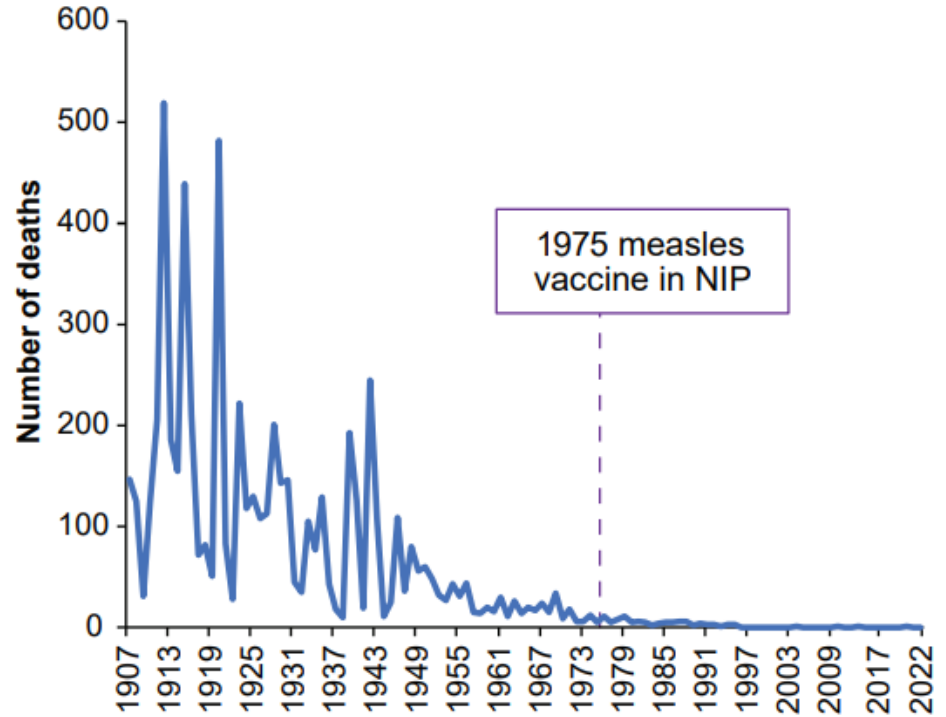
- **Efficacy** = *direct* protection to an individual - from a clinical trial
- **Effectiveness** = *direct* protection in the field - post vaccine introduction
- **Herd immunity** = *indirect* effect due to reduced disease transmission
- **Impact** = population level effect of a vaccination programme
  - disease trends
  - disease + vaccine coverage

# Measuring vaccine impact

## Pertussis deaths – Australia 1910 -2022



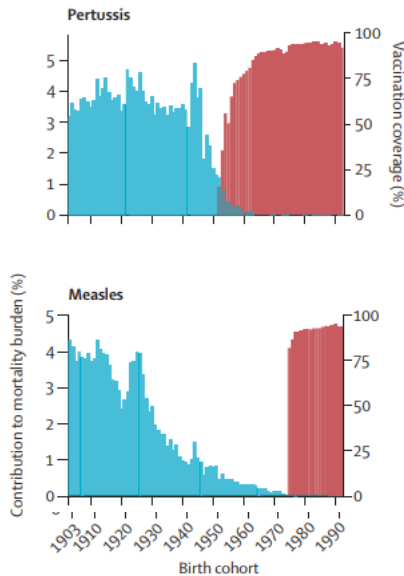
## Measles deaths Australia 1910 -2022



Source: AIHW analysis of National Mortality database; AIHW 2010 GRIM books.

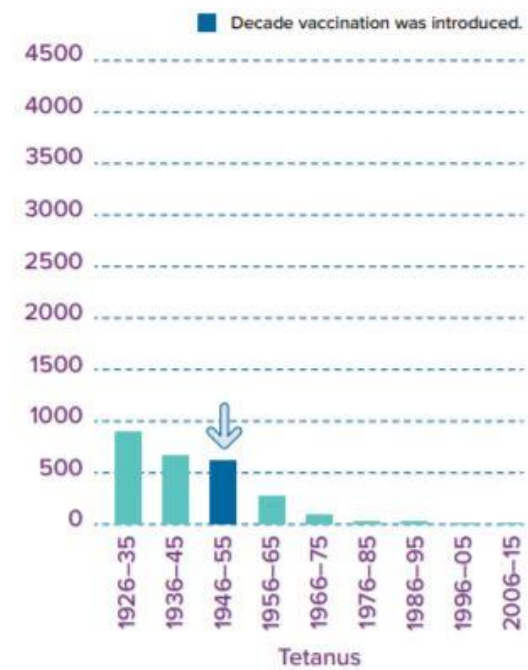
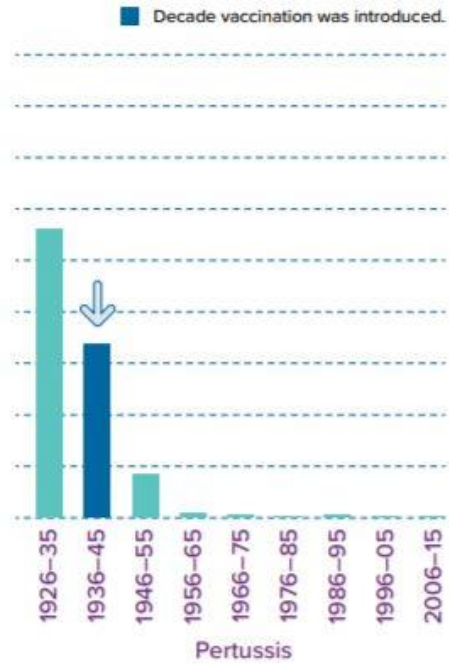
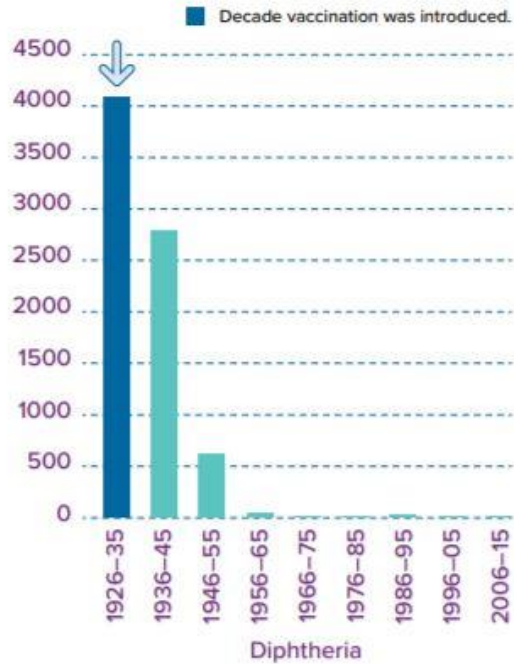
# Effect of vaccination programmes on mortality burden among children and young adults in the Netherlands during the 20th century: a historical analysis

Maarten van Wijhe, Scott A McDonald, Hester E de Melker, Maarten J Postma, Jacco Wallinga

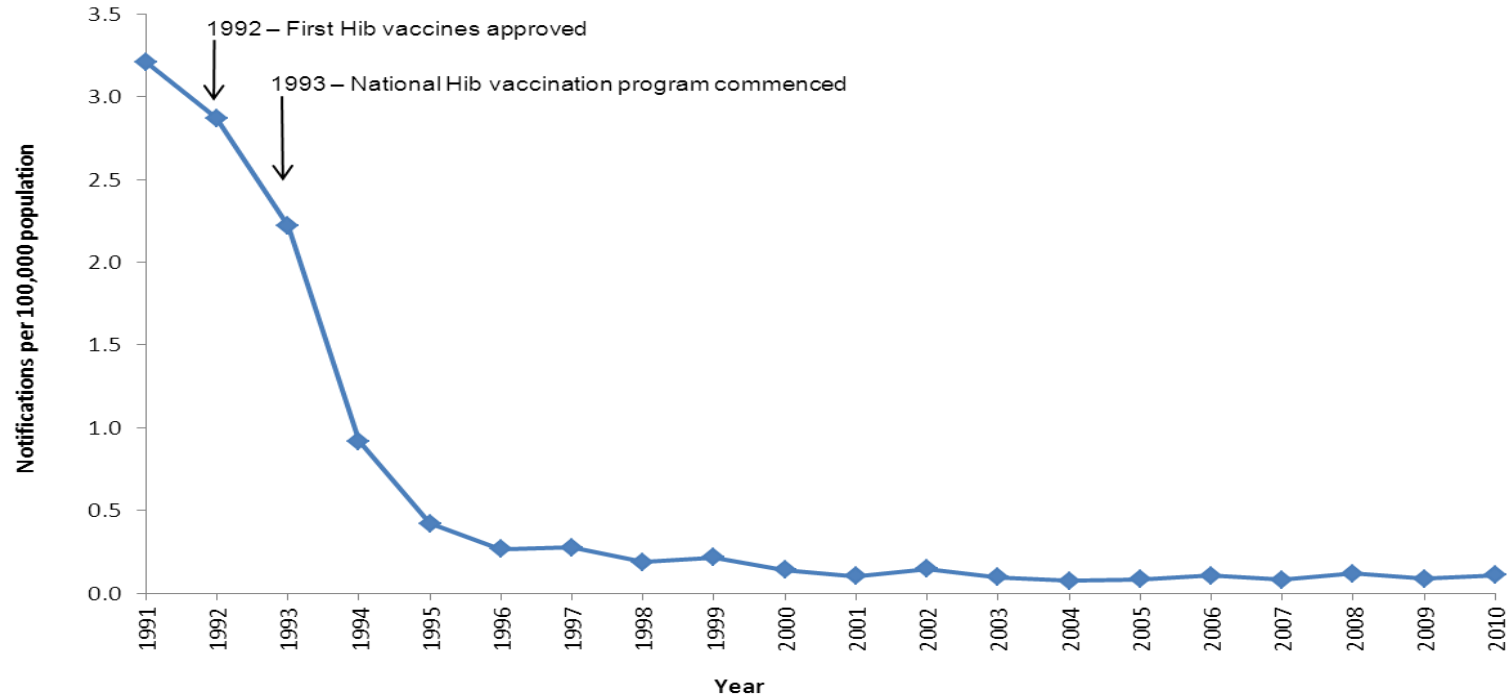


	Year of introduction of vaccination	Average contribution to all-cause mortality burden		Reduction in mortality burden due to mass vaccinations (95% prediction interval)	
		Before introduction	After introduction	YLL20 in thousands	Deaths in thousands
Diphtheria	1953	1.36%	0.004%	38 (28-52)	3 (2-4)
Pertussis	1954	3.75%	0.024%	103 (79-134)	6 (4-7)
Tetanus	1954	0.13%	0.003%	3 (1-6)	0.2 (0.1-0.4)
Poliomyelitis	1957	0.15%	0.005%	3 (1-8)	0.3 (0.1-0.6)
Measles*	1976	..	..	0.3 (0.2-0.5)	0.02 (0.01-0.03)
Mumps†	1987	0.01%	..	..	..
Rubella‡	1987	0.02%	..	..	..

# Bacterial VPDs – high case fatality – Australia



# “Disappear-o-gram” – Hib disease



# Care with interpreting trends

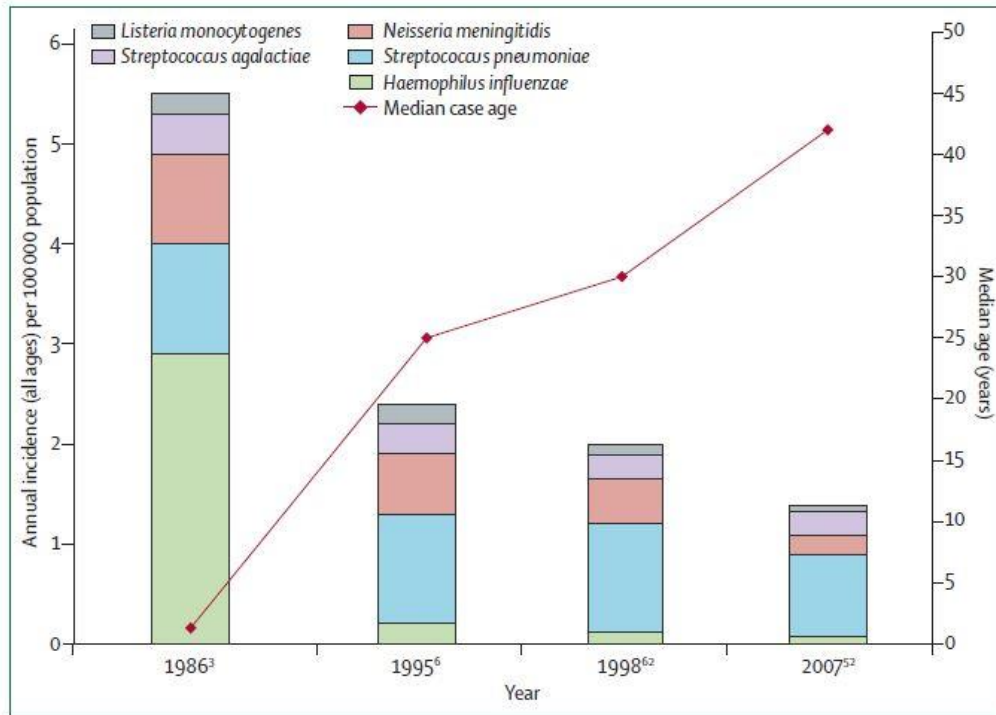


Figure 2: Prevalence of bacterial meningitis in the USA attributable to *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Streptococcus agalactiae*, and *Listeria monocytogenes*, 1986–2007<sup>3,6,5,2</sup>

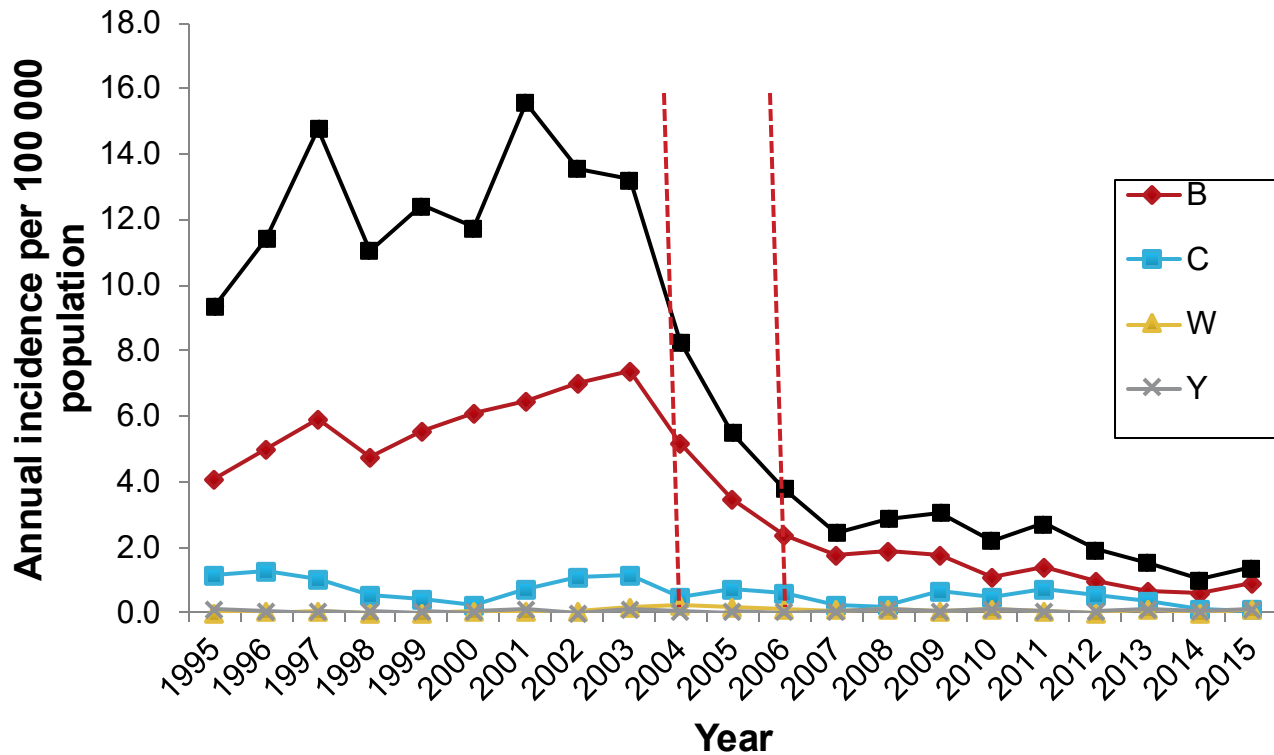
# Meningitis B epidemic NZ 1997 - 2004



Charlotte Cleverley-Bisman, pictured with father Perry Bisman, became the face of the vaccination campaign. Picture / Chris Skelton



# Notified meningococcal disease by serogroup 1995-2015 - NZ



# A Prospective Study of the Effectiveness of the New Zealand Meningococcal B Vaccine



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Vol. 166, No. 7  
 DOI: 10.1093/aje/kwm147  
 Advance Access publication July 5, 2007

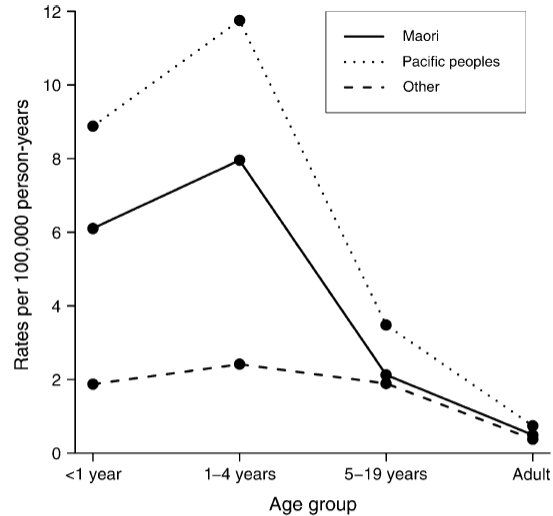


FIGURE 1. Estimated meningococcal rates in New Zealand (cases per 100,000 person-years) for each age and ethnic group of the reference group (unvaccinated persons in the lowest deprivation quintile in the fourth quarter of 2006).

TABLE 1. Significant factors in modeling meningococcal disease rates (score statistics) in New Zealand, 2001–2006

Factor	df	Chi-square	p value
Region	3	13.68	<0.005
Age	3	30.96	<0.0001
Ethnicity	2	44.76	<0.0001
Deprivation	1	27.22	<0.0001
Year	5	43.01	<0.0001
Quarter	3	59.51	<0.0001
Vaccinated	1	25.67	<0.0001
Deprivation by age	3	9.02	0.03
Age by ethnicity	6	33.49	<0.0001
Region by deprivation	3	10.37	0.02

3.7 x higher incidence in unvaccinated  
 Estimated VE = 73%

# Divergent findings about waning pertussis VE 1 – 3 yrs of age

Age (y)	Doses	Cases (%), N = 3123	Controls (%), N = 61 636	OR (95% CI)	Estimated VE (95% CI)
1		N = 870	N = 15 170		
	0	162 (18.6)	774 (4.5)	Reference	Reference
	3	662 (76.1)	15 170 (87.6)	0.21 (0.17–0.25)	79.2 (75.0–82.8)
2		N = 927	N = 18 438		
	0	140 (15.1)	887 (4.8)	Reference	Reference
	3	754 (81.3)	16 354 (88.7)	0.29 (0.24–0.36)	70.7 (64.5–75.8)
3		N = 1326	N = 25 878		
	0	150 (11.3)	1186 (4.6)	Reference	Reference
	3	1141 (86.1)	23 031 (89.0)	0.41 (0.34–0.49)	59.2 (51.0–66.0)

Duration of Protection After First Dose of Acellular Pertussis Vaccine in Infants

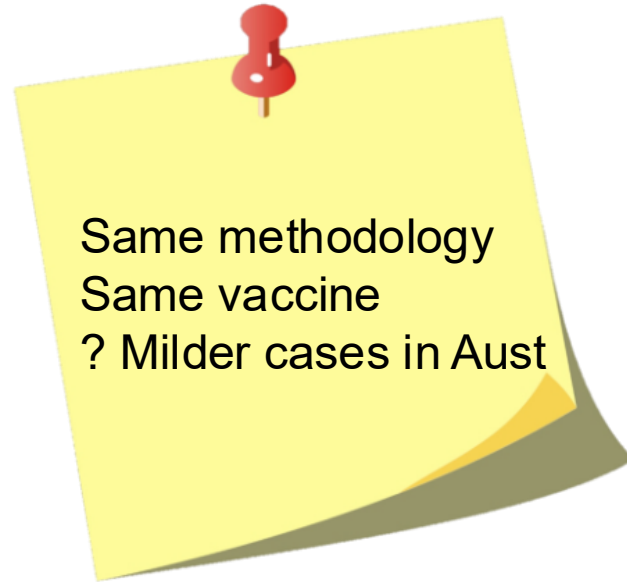
**AUTHORS:** Helen E. Quinn, PhD, MAE,<sup>a,b</sup> Thomas L. Snelling, BMBS (Hons), Grad Dip Clin Epid,<sup>c</sup> Kristine K. Macartney, MBBS, BMedSci, MD,<sup>a,b</sup> and Peter B. McIntyre, MBBS, PhD<sup>a,b</sup>

1 y		N = 454		N = 9027			
	0	124	(27.3)	372	(4.1)	Ref	Ref
	3	315	(69.4)	8204	(90.9)	89 (86, 91)	89 (86, 91)
2 y		N = 491		N = 9790			
	0	110	(22.4)	364	(3.7)	Ref	Ref
	3	373	(76.0)	8980	(91.7)	86 (83, 89)	86 (83, 89)
3 y		N = 567		N = 11,224			
	0	118	(20.8)	431	(3.8)	Ref	Ref
	3	118	(75.5)	10,267	(91.5)	85 (82, 88)	84 (80, 88)

Age-specific effectiveness following each dose of acellular pertussis vaccine among infants and children in New Zealand



# Divergent findings about waning pertussis VE 1 – 3 yrs of age



# **Vaccine-Preventable Disease Incidence vs Vaccine Effectiveness**

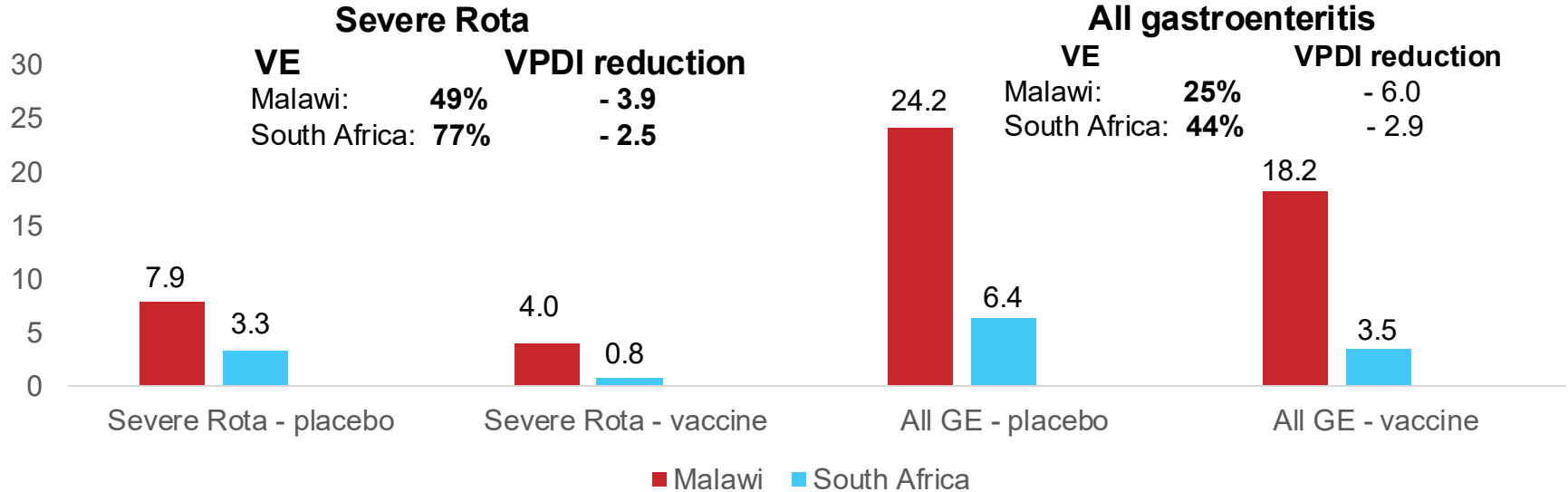


# Effect of Human Rotavirus Vaccine on Severe Diarrhea in African Infants

Shabir A. Madhi, M.D., Nigel A. Cunliffe, M.B., Ch.B., Ph.D., Duncan Steele, Ph.D., Desirée Witte, M.D., Mari Kirsten, M.D., Cheryl Louw, M.D., Bagrey Ngwira, M.D., John C. Victor, Ph.D., M.P.H., Paul H. Gillard, M.D., Brigitte B. Chevart, Ph.D., Htay H. Han, M.B., B.S., and Kathleen M. Neuzil, M.D., M.P.H.

Madhi et al Severe NEJM 2010

## Rotavirus vaccine impact: Malawi and South Africa



# Broader Frameworks

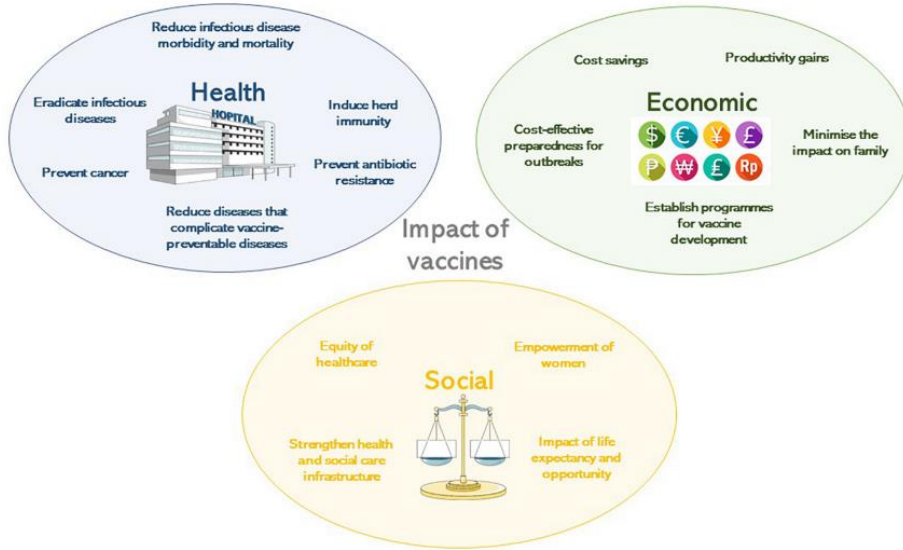


Table 1. Framework of vaccination benefits

Perspective		Benefit categories
Broad	Narrow	Health care cost savings
		Care-related productivity gains
		Outcome-related productivity gains
		Behavior-related productivity gains
		Community health externalities
		Community economic externalities
		Risk reduction gains
		Health gains

## Product & Delivery Research

IVB's Product and Delivery Research (PDR) unit aims to accelerate development and evidence-based use of vaccines against pathogens with significant disease and economic burden in low- and middle-income countries (LMICs).

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Full Value of Vaccine Assessments (FVVA)