Correlates of Immunity in Vaccinology

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1) Vaccine development

2) Vaccine evaluation

Vaccine evaluation

Pre-licensing (phase I-III)

Vaccine efficacy:
-% reduction in disease incidence (vaccinated Vs unvaccinated) groups

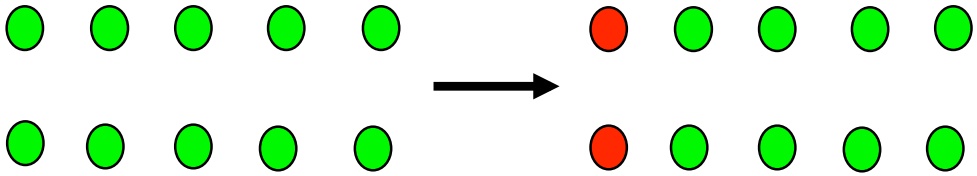
-under optimal conditions (eg RCT)

Post-licensing (phase IV)

Vaccine effectiveness:
-Protective ability of a vaccine towards the target disease/outcomes of interest in real life situations

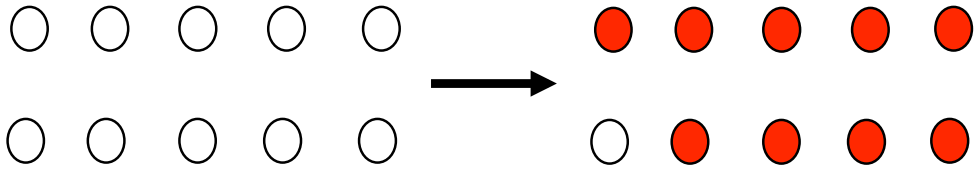
Vaccine efficaccy = ARU-ARV/ARU x 100

Vaccinated



***ARV*= 2/10 = 0.2**

Unvaccinated



***ARU* = 9/10 = 0.9**

$$\textbf{Efficacy} = \frac{0.9 - 0.2}{0.9} = 78\%$$

Vaccine effectiveness

-Many study designs can be used to calculate this measure:

-Case-control study

-Screening method

-Cohort study

-Household contact study

-If:

PCV= vaccination coverage in cases

PPV= Population vaccination coverage

$$\text{Effectiveness} = 1 - \frac{\text{PCV} \times (1-\text{PPV})}{(1-\text{PCV}) \times \text{PPV}} = (1-\text{OR}) \times 100$$

Correlates of Immunity in Vaccinology

1) How well does a candidate vaccine prevent the targeted disease?

2) Is there a threshold in vaccine prevention to the target disease that constitutes a public health benefit?

Seroconversion

- Seroconversion is the development of detectable and specific antibodies to a pathogen in the blood serum
- Seroconversion can result due to infection or immunization
- Serology (the testing for antibodies) is used to determine antibody positivity.

Seroconversion

- Prior to seroconversion, the blood test is seronegative for the antibodies; after seroconversion, the blood test is seropositive for the antibody

- Seroconversion - you may have developed immunity to the specific infection

- Seroconversion- may indicate current infection–eg, HIV seroconversion to p24 and/or p41 antibody production or HBV–seroconversion to surface antibody-HBsAb.

Seroprotection

- The level of antibody titers equal or above which you are regarded as being protected from disease.

- Seroprotection rates refer to the % of host with antibody titers equal or above the assay cut-off were set such that subjects who had titers above the cut off could be considered protected from disease.

Factors that may influence seroprotection rates following vaccination

- Age – elderly and very young / premature infants
- Immune deficiency
- Genetic factors
- Dose of vaccine
- Nutritional status – malnourished / vitamin A deficient
- Route of administration – id vs im

Serosurveillance

- Useful to measure immunity in a population, complements traditional disease surveillance methods
- Immunity to antigens such as: measles, mumps, rubella, varicella, hepatitis A, hepatitis B, hepatitis C, diphtheria, tetanus, polio and pertussis, rubella, etc
- Bloods from biobanks can be used for the serosurveillance

Correlate/s (Surrogate) of protection

- A *measurable* sign/s that a person is immune, i.e protected against becoming infected and/or developing disease.

Nomenclature for Immune Correlates of Protection After Vaccination

Stanley A. Plotkin[1] and Peter B. Gilbert[2,3]

[1]University of Pennsylvania and Vaxconsult, Doylestown; [2]University of Washington, and [3]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle

Term	Synonyms	Definition
CoP (correlate of protection)	Predictor of protection	An immune marker statistically correlated with vaccine efficacy (equivalently predictive of vaccine efficacy) that may or may not be a mechanistic causal agent of protection[a]
mCoP (mechanistic correlate of protection)	Causal agent of protection; protective immune function	A CoP that is mechanistically and causally responsible for protection
nCoP (nonmechanistic correlate of protection)	Correlate of protection not causal; predictor of protection not causal	A CoP that is not a mechanistic causal agent of protection

[a] A correlate of protection can be used to accurately predict the level of vaccine efficacy conferred to vaccine recipients (individuals or subgroups defined by the immune marker level).

Clinical Infectious Diseases 2012;54(11):1615–7

VIEWPOINTS

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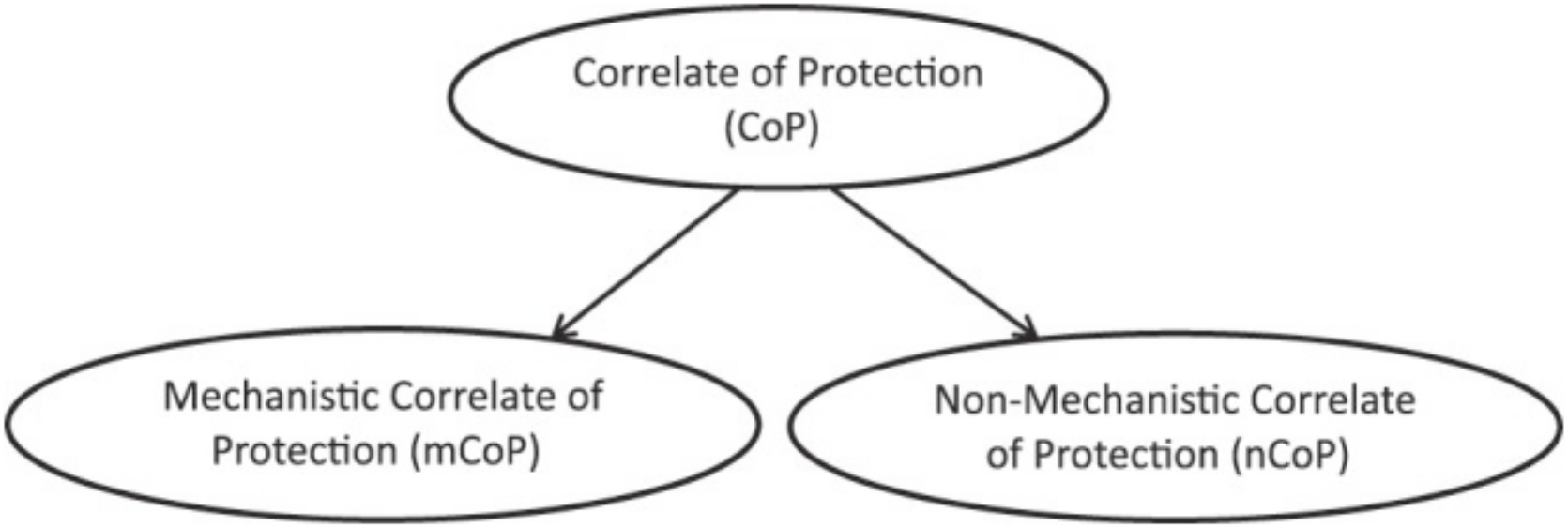

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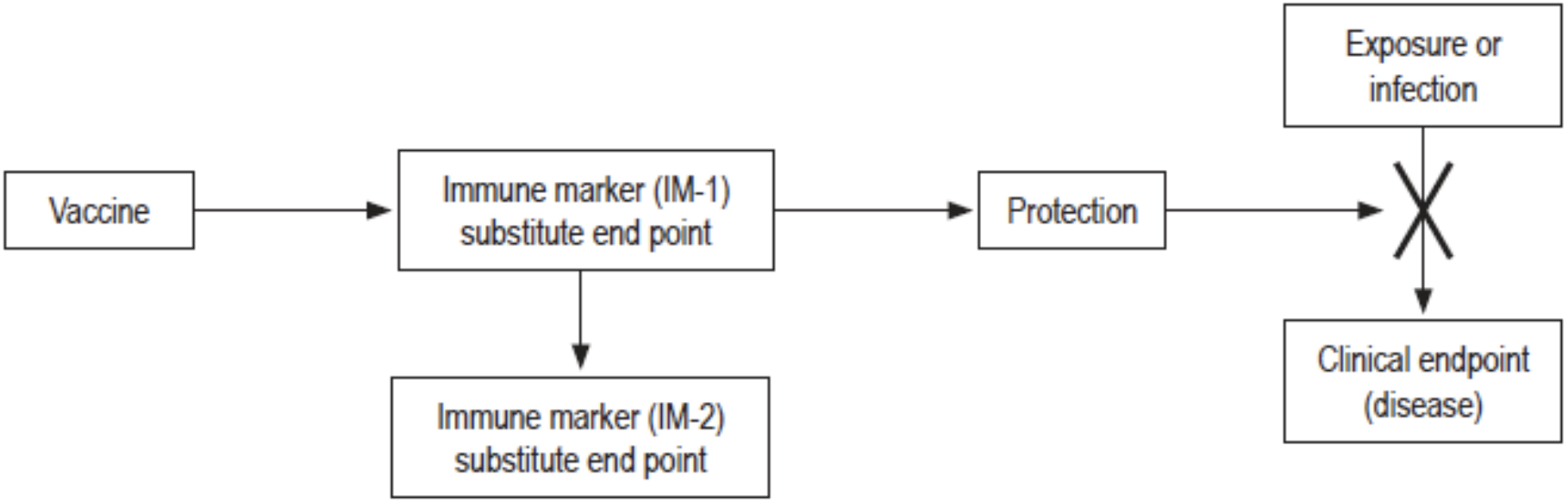
Correlate/s (Surrogates) of protection



Arrows imply direct causal relationships

http://apps.who.int/iris/bitstream/10665/84288/1/WHO_IVB_13.01_eng.pdf

Correlate/s of protection

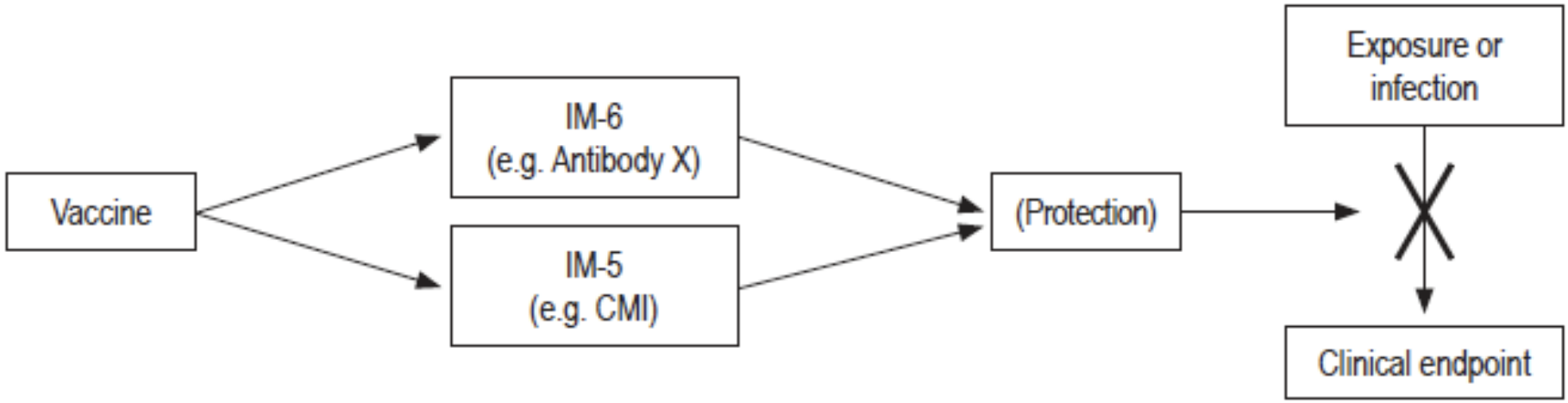


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Table 4. Some quantitative correlates of protection after vaccination.

Vaccine	Test	Correlate of protection	Reference(s)
Diphtheria	Toxin neutralization	0.01–0.1 IU/mL	[14]
Hepatitis A	ELISA	10 mIU/mL	[15]
Hepatitis B	ELISA	10 mIU/mL	[16]
Hib polysaccharides	ELISA	1 mcg/mL	[17]
Hib conjugate	ELISA	0.15 mcg/mL	[18]
Influenza	HAI	1/40 dilution	[19]
Lyme	ELISA	1100 EIA U/mL	[20]
Measles	Microneutralization	120 mIU/mL	[7]
Pneumococcus	ELISA; opsonophagocytosis	0.20–0.35 mcg/mL (for children); 1/8 dilution	[21, 22]
Polio	SN	1/4–1/8 dilution	[23]
Rabies	SN	0.5 IU/mL	[24]
Rubella	Immunoprecipitation	10–15 mIU/mL	[25, 26]
Tetanus	Toxin neutralization	0.1 IU/mL	[27]
Varicella	SN; gpELISA	⩾1/64 dilution; ⩾5 IU/mL	[28, 29]

NOTE. gp, glycoprotein; HAI, hemagglutination inhibition; Hib, *Haemophilus influenzae* type b; SN, serum neutralization.

Programmatic application of correlate of protection

2013 vaccine schedules for South Africa

Compiled by Amayeza Info Services' Vaccine Helpline: 0860 160 160

Age of child	EPI schedule	Age of child	Private practice: Option 1	Private practice: Option 2	Age of child	Private practice: Option 3
At birth	OPV (0) BCG	**At birth**	OPV (0) BCG	OPV (0) BCG HBV[1]	**At birth**	OPV (0) BCG
6 weeks	OPV (1) RV (1) DTaP-IPV//Hib (1) HBV (1) PCV (1)	**6 weeks**	OPV (1) RV (1) DTaP-IPV//Hib (1) HBV (1) PCV (1)	OPV (1) RV (1) DTaP-IPV//Hib/HBV (1) PCV (1)	**2 months**	OPV (1) RV (1) DTaP-IPV//Hib/HBV (1) PCV (1)
10 weeks	DTaP-IPV//Hib (2) HBV (2)	**10 weeks**	RV (2)[2] DTaP-IPV//Hib (2) HBV (2) PCV (2)	RV (2)[2] DTaP-IPV//Hib/HBV (2) PCV (2)	**3 or 4 months**	RV (2)[2] DTaP-IPV//Hib/HBV (2) PCV (2)
14 weeks	RV (2) DTaP-IPV//Hib (3) HBV (3) PCV (2)	**14 weeks**	RV (2 or 3)[2] DTaP-IPV//Hib (3) HBV (3) PCV (3)	RV (2 or 3)[2] DTaP-IPV//Hib/HBV (3) PCV (3)	**4 or 6 months**	RV (2 or 3)[2] DTaP-IPV//Hib/HBV (3) PCV (3)
9 months	Measles vaccine (1) PCV (3)	**9 months**	Measles vaccine	Measles vaccine	**9 months**	Measles vaccine

How about correlate of risk (CoR)?