# Overview On Vaccination

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VACFA vaccines for africa

# Importance of vaccination

- **Vaccines promote health:** help people stay healthy, removing a major obstacle to human development.
- **Vaccines have an expansive reach:** protect individuals, communities, and entire populations (the eradication of smallpox is a case in point).
- **Vaccines save lives and costs:** immunization for children ranked fourth place on a list of 30 cost-effective ways of advancing global welfare (Copenhagen Consensus, 2008)
- **Vaccines have rapid impact**

*Acknowledgement: Greg Hussey*

**“With the exception of safe water, no other modality…has had such a major effect on mortality reduction and population growth”.**

Plotkin and Mortimer in “Vaccines” 1st Ed. 1988

# Presentation outline

1) How does a vaccine work?

2) What are some key determinants of successful vaccination?

3) Effects of HIV infection on vaccination

4) Should HIV be a public health concern in the control, elimination and eradication of VPDs?

5) Conclusions


# 1)How does a vaccine work?

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# What is a vaccine?

-A vaccine is a biological preparation that improves immunity to a particular disease

-Contains an agent that resembles a disease-causing microorganism

-Often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins.

**Ref:** http://www.who.int/topics/vaccines/en/

# How does a vaccine work?

Initiation of a vaccine response following injection:

(1) The pathogen-associated patterns contained in vaccine antigens attract **dendritic cells**, **monocytes**, and **neutrophil**s that patrol the body

(2) Elicitation of sufficient "danger signals" by the vaccine antigens (Ag)/adjuvants (Adj) **activates** monocytes and dendritic cells

# How does a vaccine work?

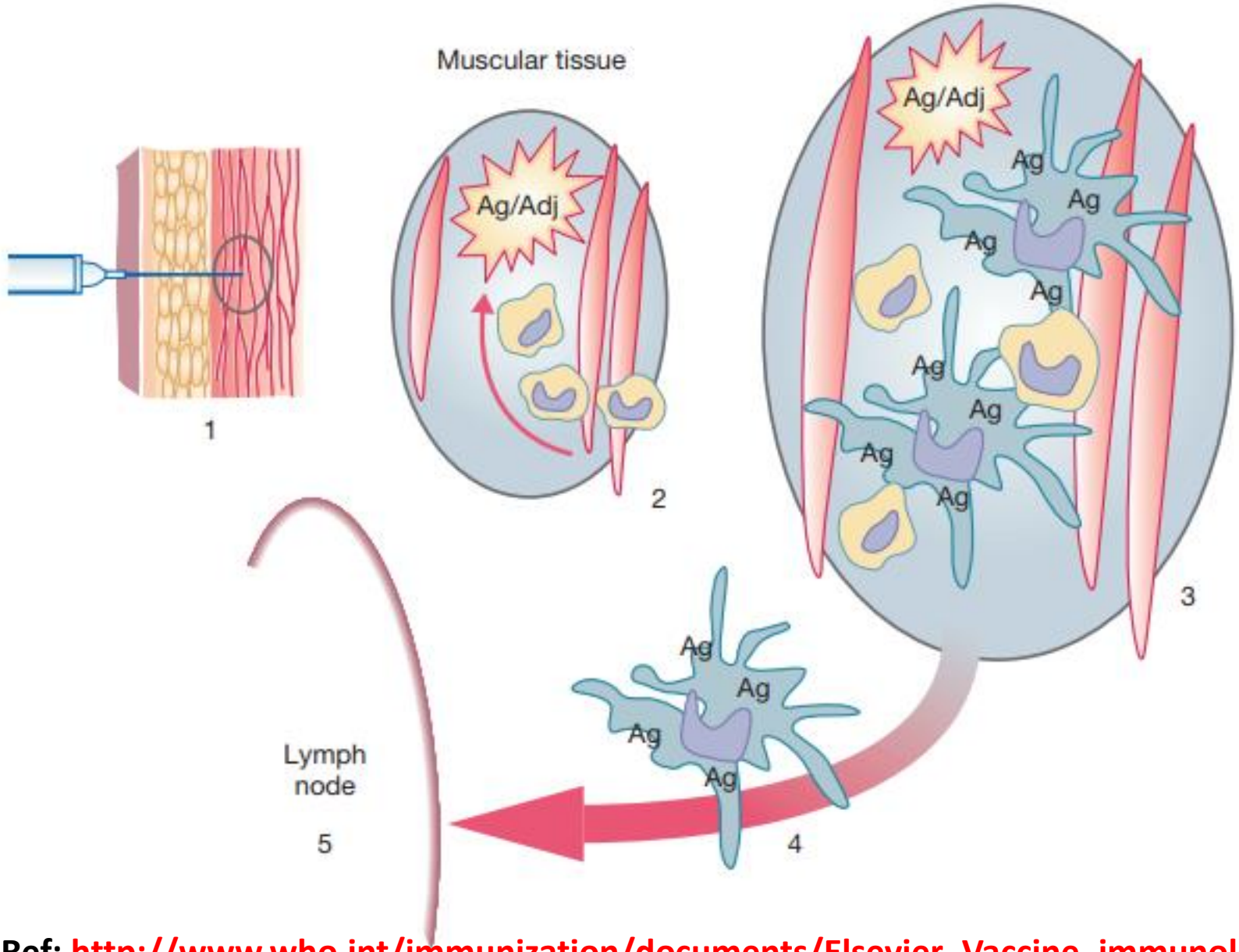
*Initiation of a vaccine response following injection:*

3) The activation changes their **surface receptors** and induces their migration along lymphatic vessels

4) Migration to the draining lymph nodes

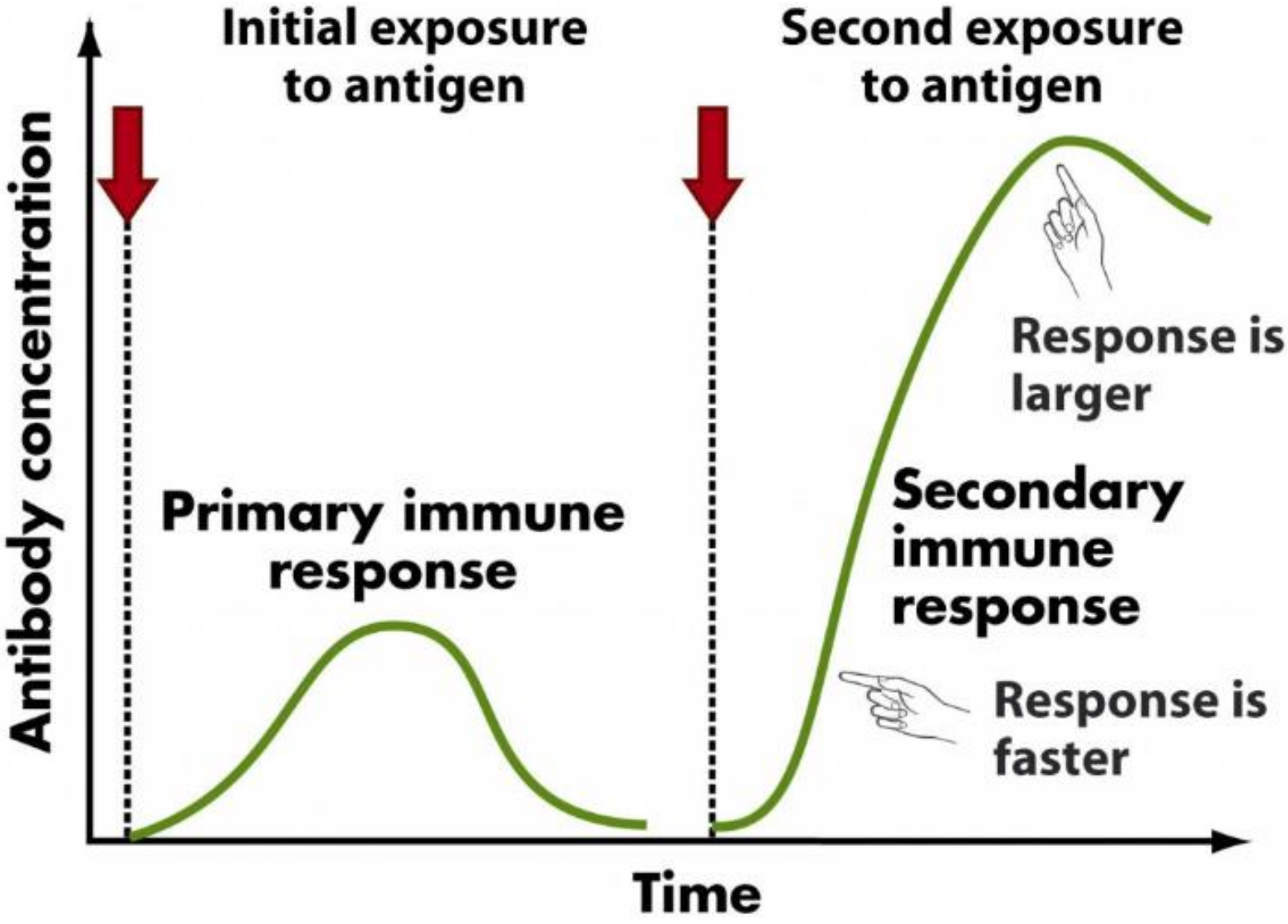
5) In the lymph nodes, the **activation of T** and **B lymphocytes** will take place

# How does a vaccine work?



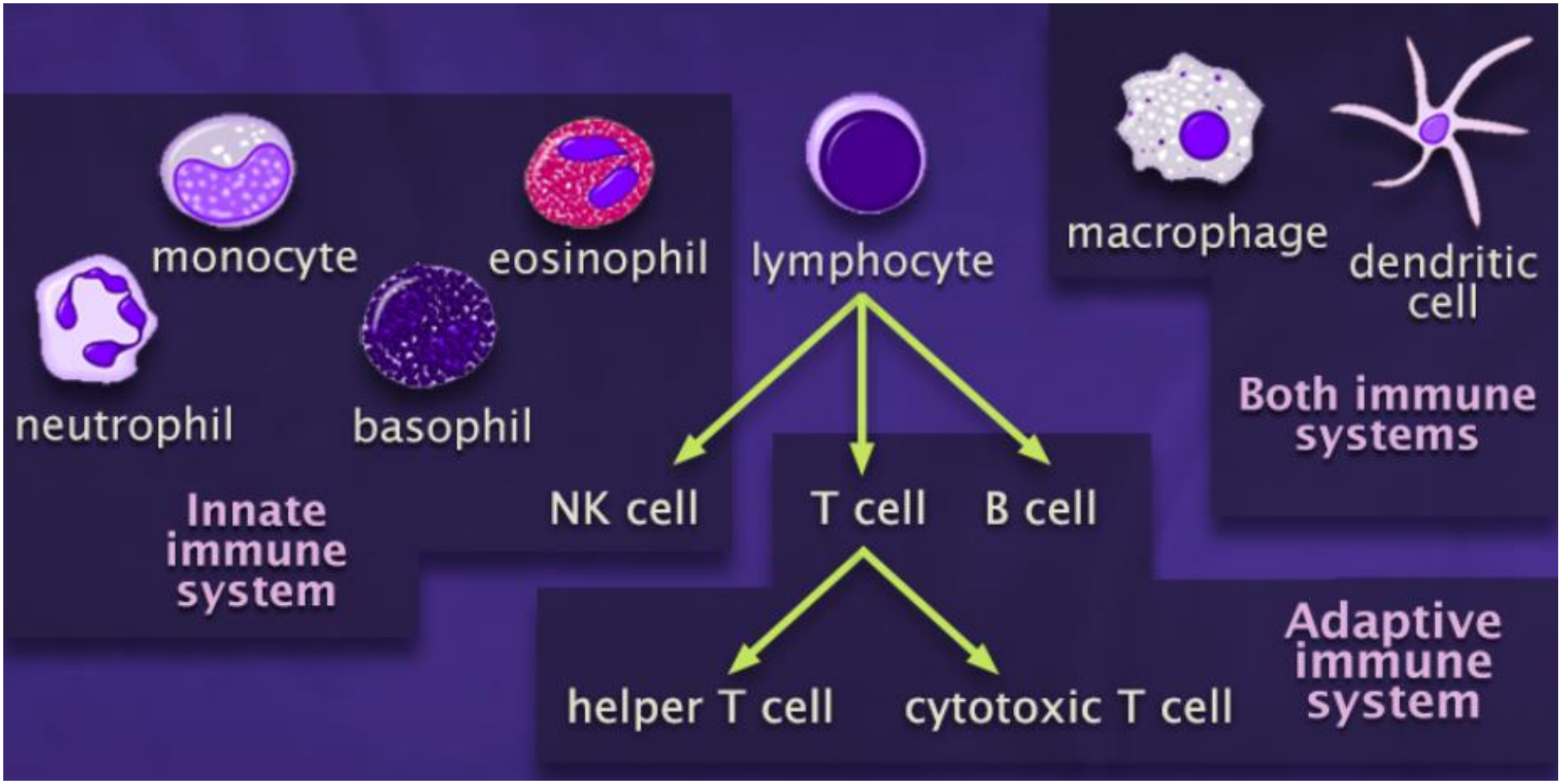

**Ref:** http://www.who.int/immunization/documents/Elsevier_Vaccine_immunology.pdf

# Immune response after vaccination




Ref: https://nrvs.info/how-do-vaccines-work/

# Different types of immune cells are involved



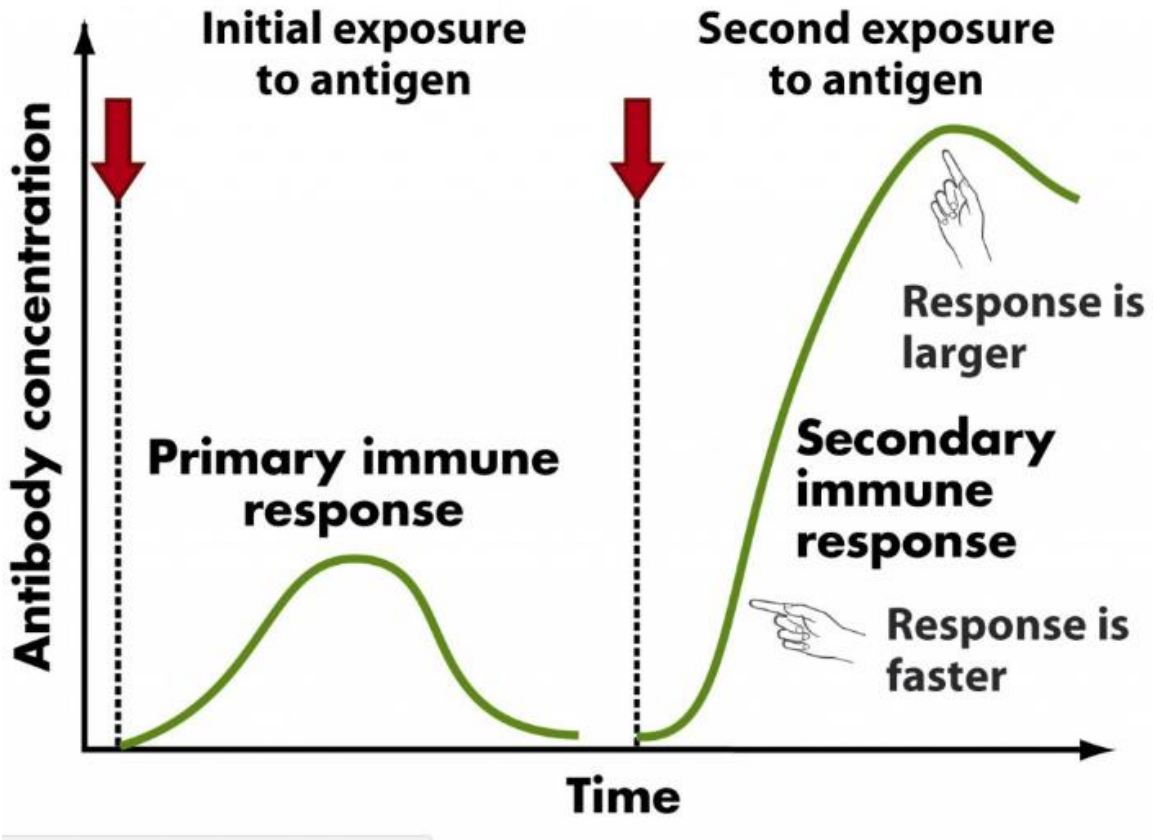

**Broadly falls into: innate or adaptive immune system**

**Ref:** https://www.hhmi.org/biointeractive/cells-of-the-immune-system

# Hallmarks of vaccination

1) Specificity

2) Memory



# Smallpox eradication and creation of EPI

- Smallpox eradication launched in Jan 1967. Last case reported in Somalia in 1977.
- Smallpox eradication certified in Dec 1979 -- proof of the power of vaccines.
- EPI set up in 1974 at a time of great optimism for public health.

*When EPI was established in **1974**, only about **5%** of the world's children were protected from the 6 diseases: **DTP**, Polio, Measles and TB*

# Examples of successful vaccination

## about 50 licensed human vaccines..

| Disease | 20th Century Annual Morbidity | 2005 Total | % Decrease |
|---|---|---|---|
| Smallpox | 48,164 | 0 | 100 |
| Diphtheria | 175,885 | 0 | 100 |
| Pertussis | 147,271 | 25,616 | 83 |
| Tetanus | 1,314 | 27 | 98 |
| Polio (paralytic) | 16,316 | 1* | >99.9 |
| Measles | 503,282 | 66 | >99.9 |
| Mumps | 152,209 | 314 | >99 |
| Rubella | 47,745 | 11 | >99.9 |
| Congenital rubella | 823 | 1 | 99.8 |
| *Haemophilus influenzae* (<5 years) | 20,000 (est) | 226 (serotype B or unknown serotype) | 99 |

Atkinson, W., Wolfe, S., Hamborsky, J., & McIntyre, L. (Eds.). (2009). Impact of vaccines in the 20th & 21st Centuries. In *Centers for disease control and prevention: Epidemiology and prevention of vaccine-preventable diseases* (Appendix G: Data and statistics) (11th ed.). Washington, D.C.: Public Health Foundation.
Retrieved from http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/impact-of-vaccines.pdf

# Evolution of vaccination

However, no major success has been recorded in the development of effective **HIV**, TB, Malaria vaccines as examples…..

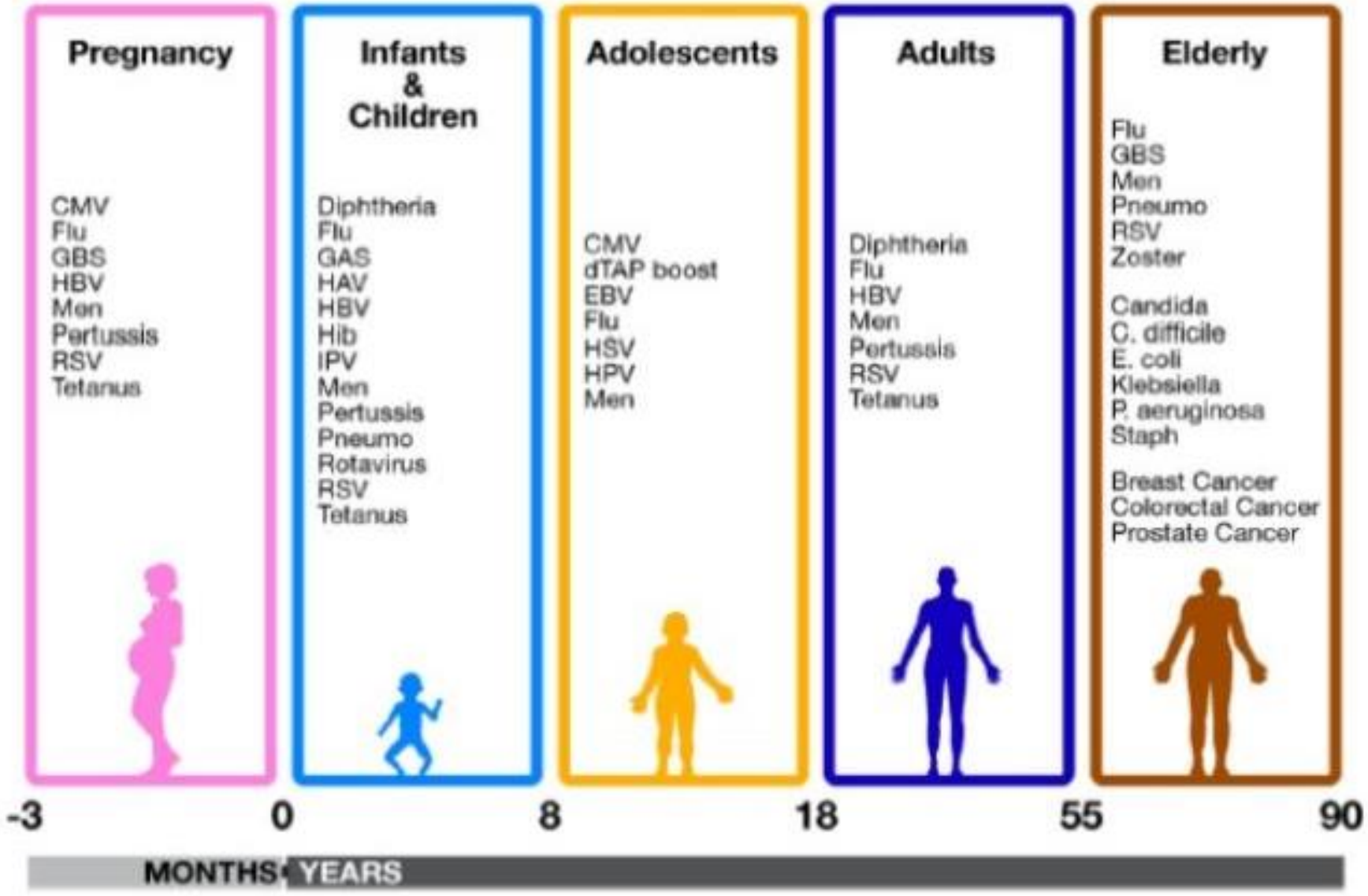
*Led to establishment of Human Vaccine Project in 2015 aimed at detailed understanding of:*

-Human immunome program (B & T cell receptors)

**-The rule of immunogenicity program**

-Universal influenza vaccine initiative

# Expand vaccination beyond infancy



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**2)What are some key determinants of successful vaccination?**

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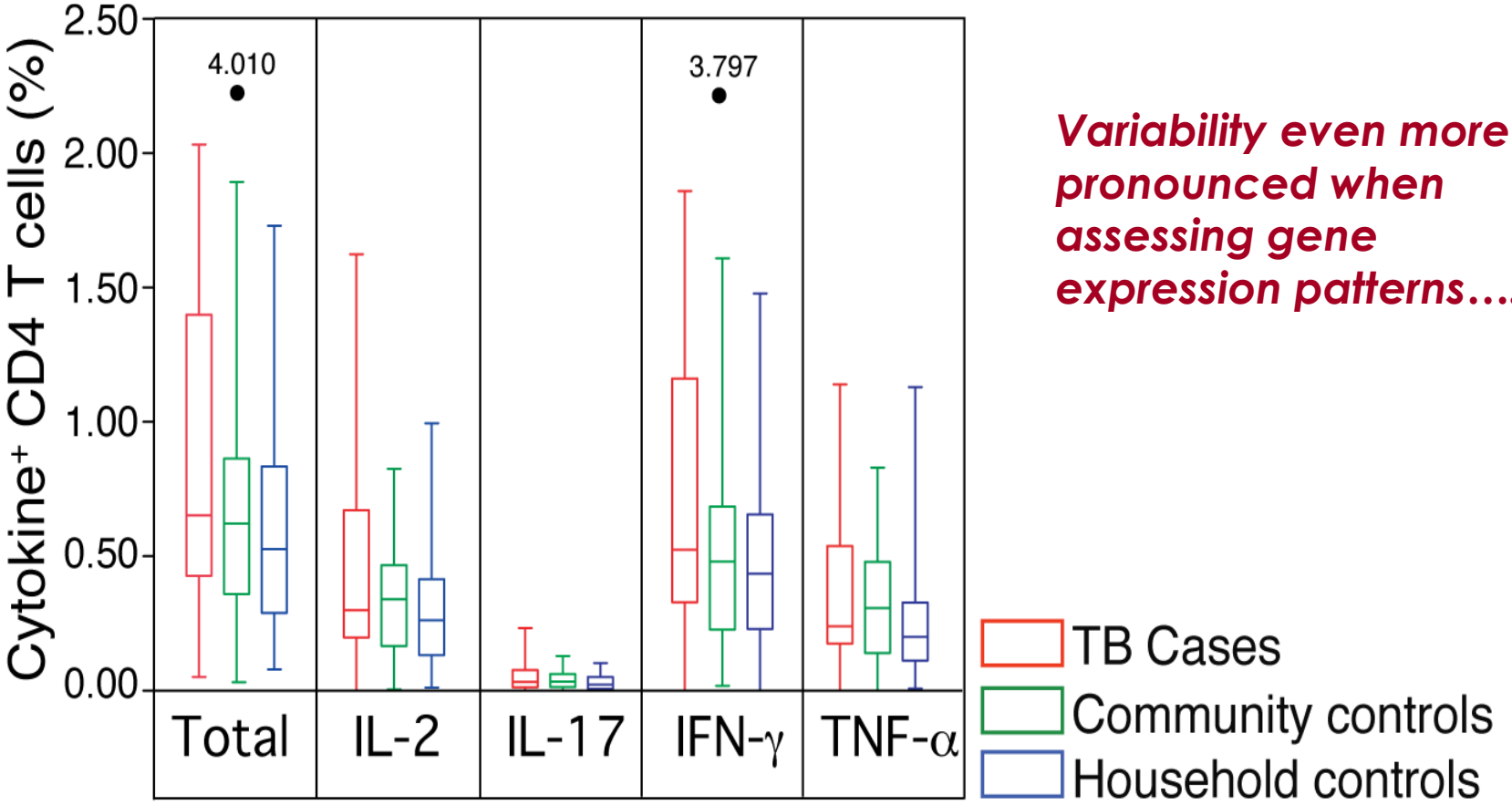
# BCG vaccine


10 Doses
BCG VACCINE
(FREEZE-DRIED)
Active Immunizing Agent
For Intracutaneous Injection Only.
DIN 00075124
DIN 00075442
PASTEUR MÉRIEUX CONNAUGHT

# Specific T Cell Frequency and Cytokine Expression Profile Do Not Correlate with Protection against Tuberculosis after Bacillus Calmette-Guérin Vaccination of Newborns

Benjamin M. N. Kagina[1], Brian Abel[1], Thomas J. Scriba[1], Elizabeth J. Hughes[1], Alana Keyser[1], Andreia Soares[1], Hoyam Gamieldien[1], Mzwandile Sidibana[1], Mark Hatherill[1], Sebastian Gelderbloem[2], Hassan Mahomed[1], Anthony Hawkridge[2], Gregory Hussey[1], Gilla Kaplan[3], Willem A. Hanekom[1], and other members of the South African Tuberculosis Vaccine Initiative[1]



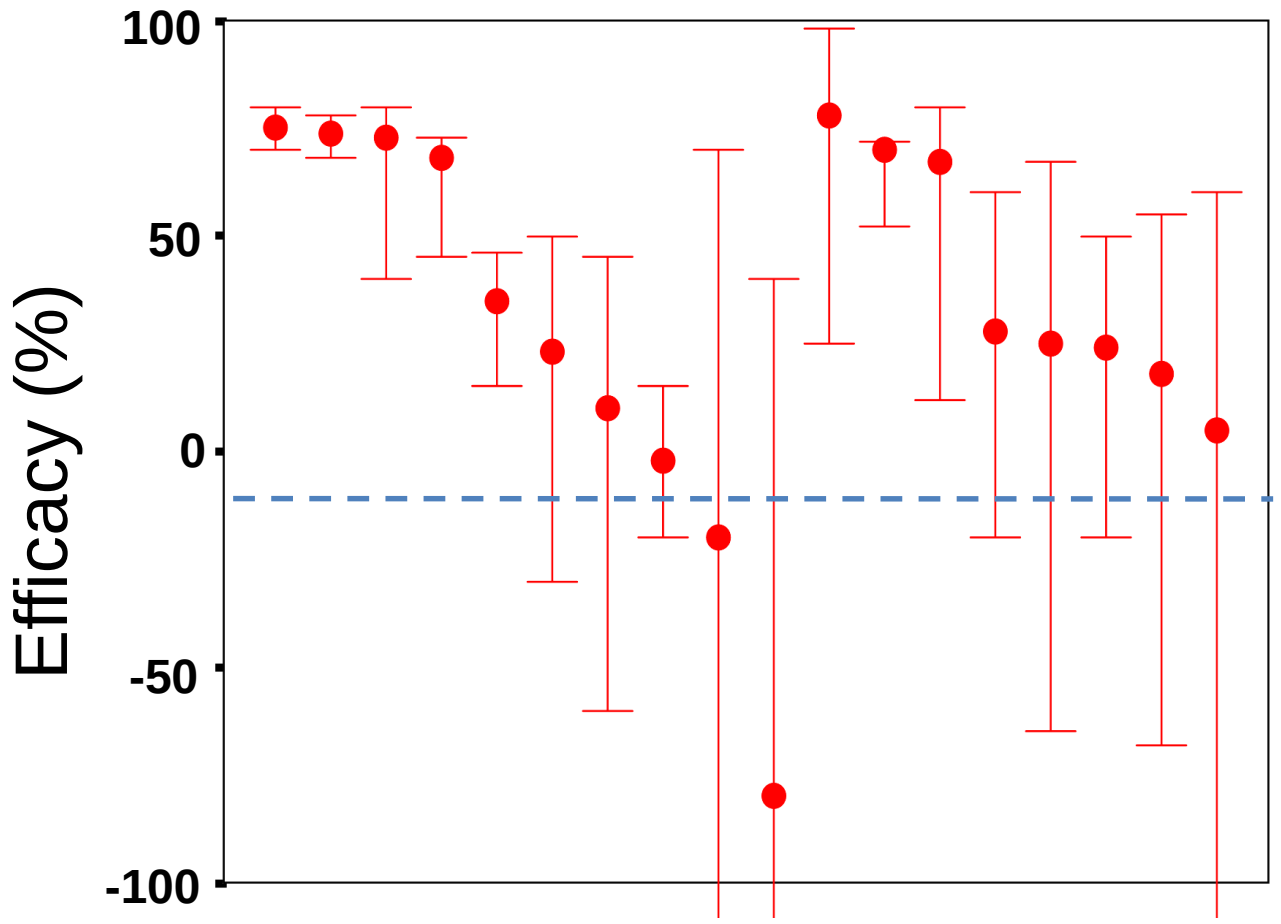

***Variability even more pronounced when assessing gene expression patterns….***

*Kagina B. et al. AJRCCM 2010;182:1073.*

*BCG given at birth. Infants followed for 2 years to assess protection; Whole blood incubation with BCG at 10 weeks of age for 12 hours.

satvi

# BCG-induced protection against pulmonary TB is variable




*P. Fine. 2000. BCG Vaccines and Vaccination. In: L. B. Reichman and E. S. Hershfield. Tuberculosis. A comprehensive International Approach. 2nd Edition.

# Determinants of vaccination success

**Demographic and Patient Characteristics**
Age, Gender, Geographic location, Smoking, Body mass index, Nutritional status

**Genetic Factors**
HLA type
Other immune response genes

**Comorbid diseases**
Autoimmune conditions, Renal failure, Liver failure
Parasitic infections, **Immunocompromised/HIV**

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# Effects of HIV infection on the immune cells

**Innate system:** mucosal DCs and tissue macrophages are among the first cells to be infected.

**Dendritic cells-**infected, migrate to lymph node and interact with CD4 T cells (systemic spread of the HIV infection)

**Eosinophils**, **γδ T cells**, **monocytes** and **neutrophils** may be directly infected by HIV.

HIV may even reach the bone marrow and infect **progenitor cells** and establish reservoirs

# Effects of HIV infection on the immune cells

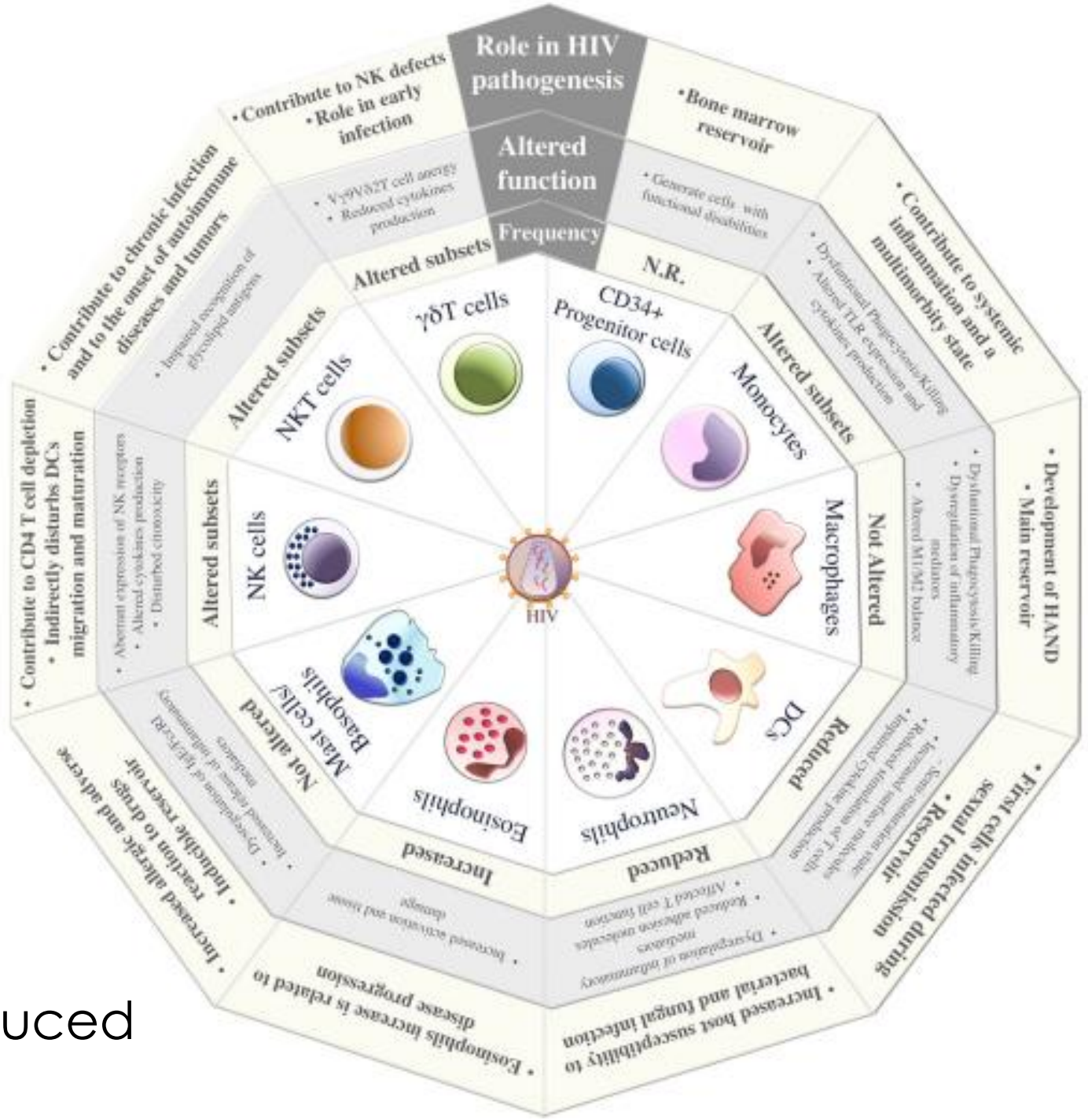
-Alteration of **phenotypic characteristics** of innate immune cells

-Alteration of **functional characteristics** of innate immune cells

-Results to **immune dysregulation**

-An obvious consequence is depletion of **CD4 T cells**

Suboptimal vaccine-induced response?




Ref: Milena SE et al., Immunol Res (2016) 64:1118–1132

# Using live BCG in HIV+ babies

- Vaccine efficacy not known
- Serious adverse events – *BCGosis*
  - (up to 110-417 per 100,000 vaccinations in RSA)
  - (Hesseling et al., Vaccine, 2007)
- Benefit/risk ratio not known

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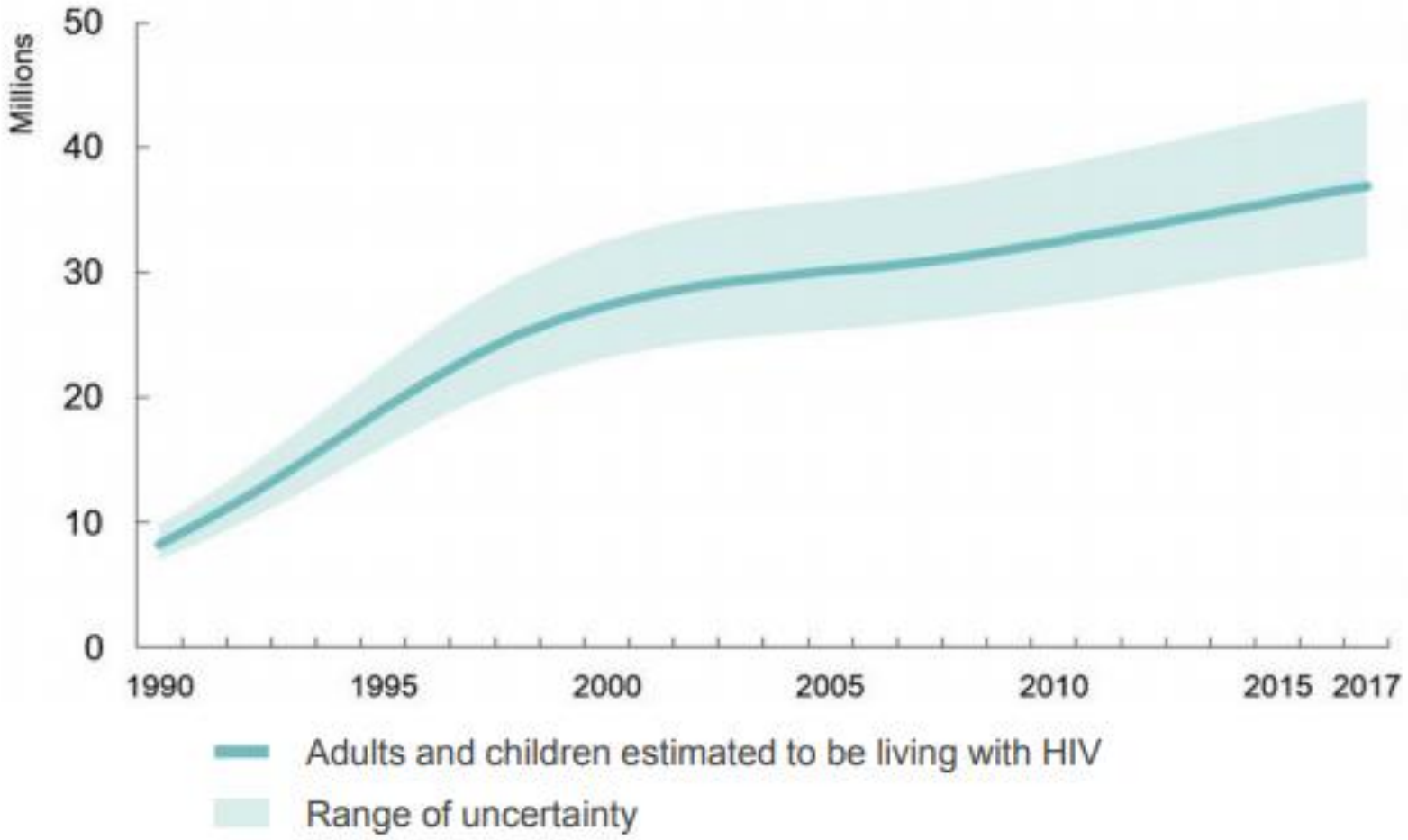
## Adults and children estimated to be living with HIV | 1990–2017




Ref: **http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf**

# Effects of in utero HIV on the innate immune cells

-Commonly referred to as HIV exposed uninfected (HEU)

-Neutrophils found to have an **impaired production of**

**reactive oxygen species (ROS)**: data obtained from

Maternal venous blood and CB specimens

# Effects of in utero HIV on CD4+ T cells

-Exposure to high levels of HIV-1 viremia *in utero*,

**even in the absence of perinatal transmission, may**

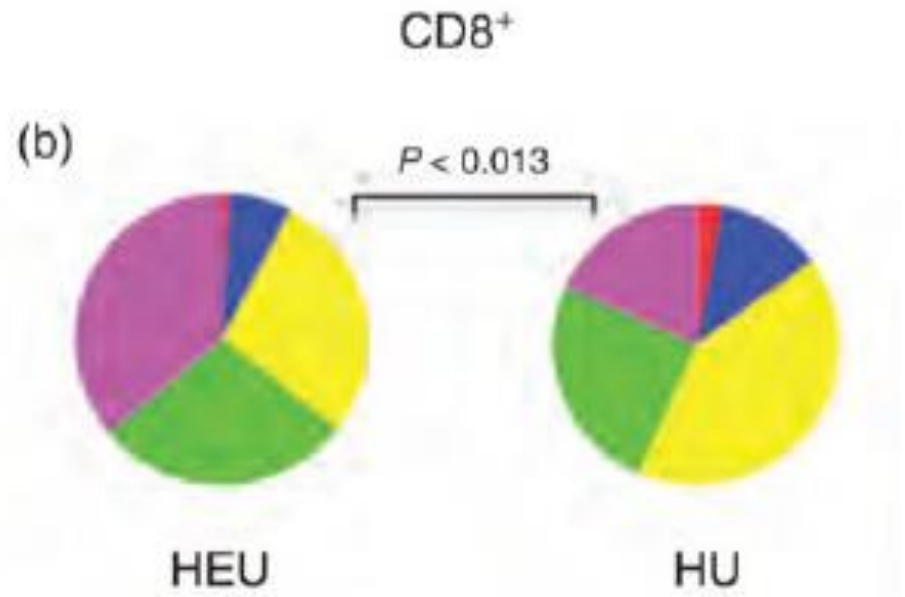
**affect the infant's developing immune system:**

reduced CD4 T cell counts with high maternal

viremia

**Ref:** **Fatima Kakka *et al.*, 2014 BMC Infec Diseases**

# Pertussis vaccine-induced T cell response: HEU; HU (HIV Unexposed)

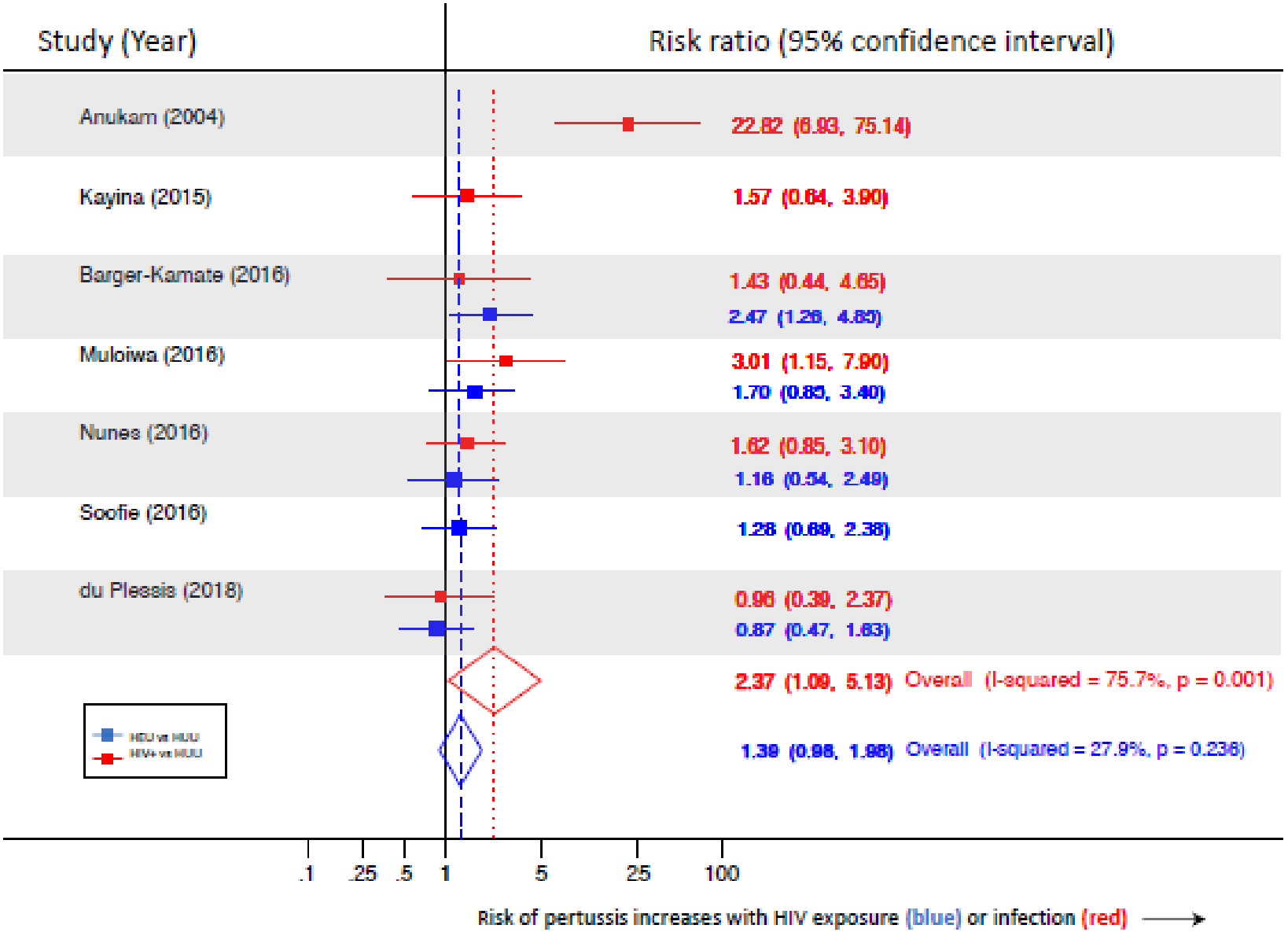



Pertussis vaccination at 8 weeks
Blood taken at 14 weeks

Cytokines:
IL-2, IL-17, IL-13 and IFN-g


**Ref:** Elvis BK *et al.*, 2014, AIDS

# Risk for pertussis: HEU; HIV+




**Ref:** Muloiwa R *et al.*, 2018 (Manuscript submitted)

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# 5)Conclusions

University of Cape Town • iYunivesithi yaseKapa • Universiteit van Kaapstad

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# Conclusions

-Vaccination is a key global public health intervention

-There are ongoing research initiatives to guide the design of rational new vaccines

-HIV infection may cause a dysregulation of an immune response to vaccination

# Conclusions

-Vaccine-induced immune response in the presence of HIV infection may be suboptimal

-HIV infection is a critical aspect of vaccination programs in the control of VPDs

-Vaccination of HIV infected persons considered as a continuum of care

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