Vaccination of Immunocompromised (Focus on HIV+ population)

Benjamin Kagina
bm.kagina@uct.ac.za

Immunodeficiency states

- Primary: Naturally occurring defects of innate or acquired immunity, usually inherited as single-gene disorders

- Secondary: Arise when immunologically intact individuals develop altered immune function as a result of exogenous factors (eg, HIV infection)

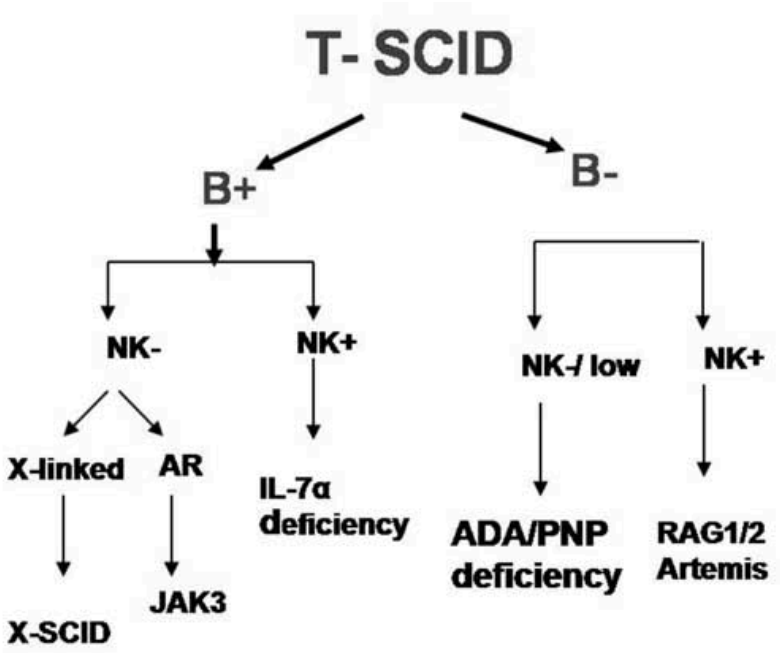
Slide adapted from Brian Eley talk (Vaccinology 2013)

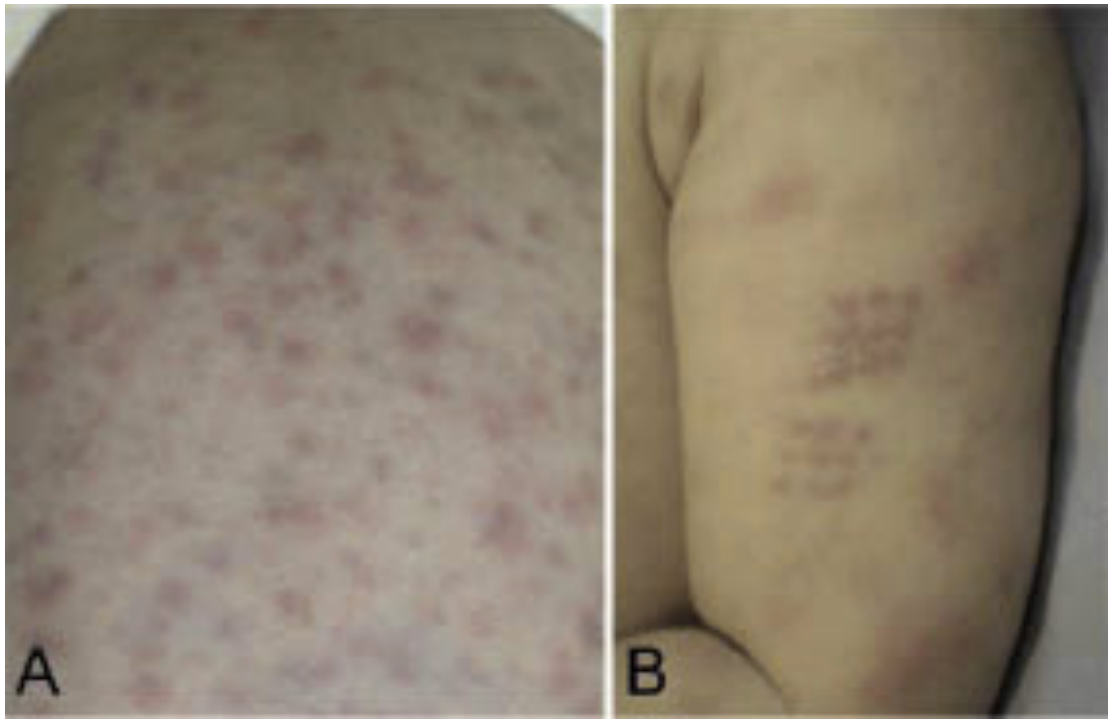
PRIMARY IMMUNODEFICIENCY DISEASES	
Humoral deficiencies	Severe antibody deficiencies e.g. X-linked agammaglobulinaemia, Common variable immunodeficiency
	Less severe antibody deficiencies e.g. IgA deficiency, IgG subclass deficiency
Cell-mediated deficiencies	Complete defects e.g. severe combined immunodeficiency, complete DiGeorge syndrome
	Partial defects e.g. most patients with DiGeorge syndrome, Wiscott-Aldrich syndrome, ataxia telangiectasia
Complement deficiencies	Early components e.g. C1, C4, C2, C3 deficiencies
	Late components e.g. C5-C9, properdin and factor B deficiencies
Phagocytic disorders	Chronic granulomatous disease, leukocyte adhesion defects, myeloperoxide deficiency
Disorders affecting the interferon-gamma pathway	Leucocyte Mycobactericidal defects e.g. IL-12 & IL-23 receptor β1 chain deficiency, IFN-γ receptor 1 & 2 deficiency, STAT1 deficiency
SECONDARY IMMUNODEFICIENCIES	
HIV / AIDS	
Glucocorticosteroids	
Functional hyposplenia / Asplenia	
Immunosuppressive therapy, radiation therapy, solid organ transplant recipients	
Bone marrow transplant recipients	

Adapted from: American Academy of Pediatrics Red Book, 28th edition, 2009

BCG contraindication in SCID

SCID diagnosis approach:





Japanese SCID case of disseminated BCG
No B/ NK cells

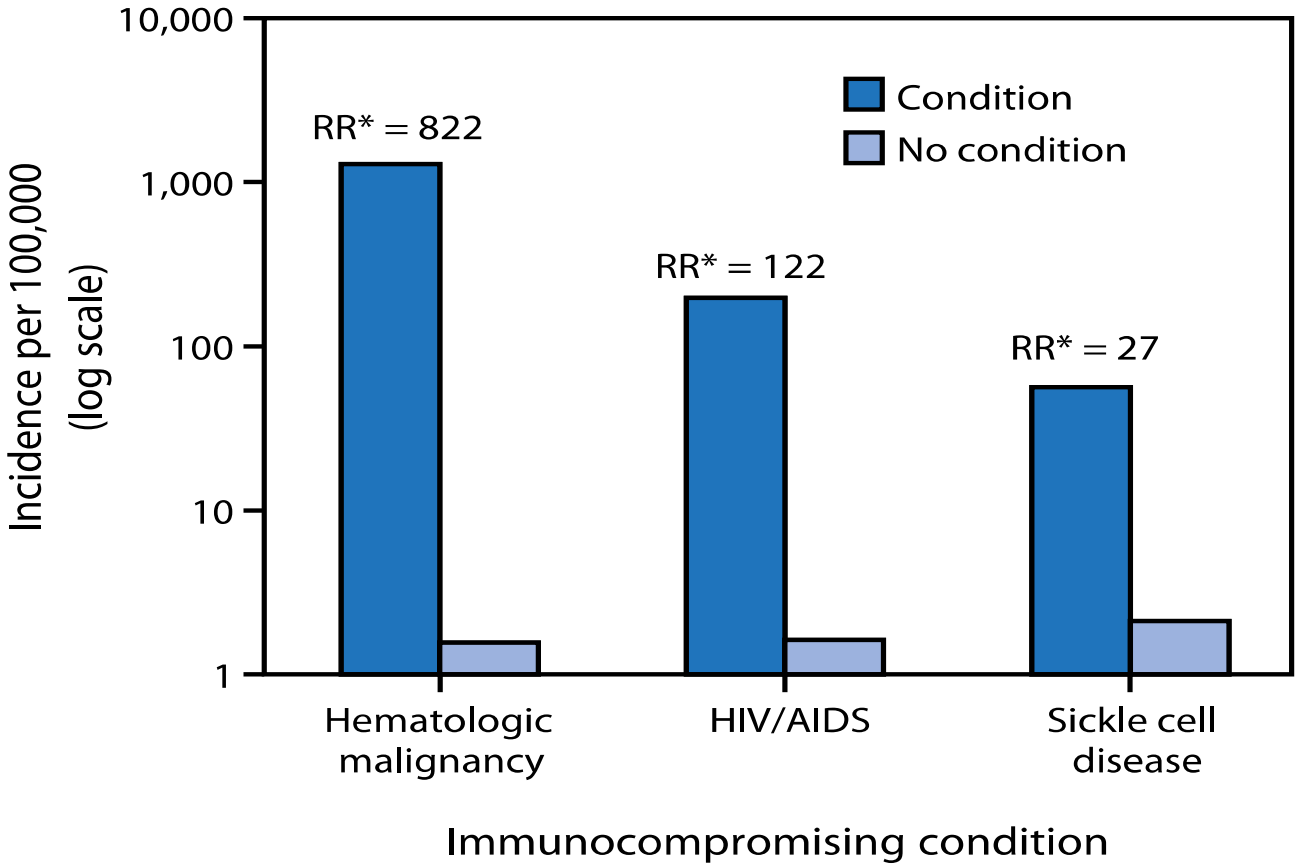
Note:
prevalence @ 1 in 65,000 births

Takahiro Satoh, et al.2012 Acta Derm Venereol 92

Efficacy of 13-Valent Pneumococcal Conjugate Vaccine (PCV-13) against Invasive Pneumococcal Disease (IPD):

Impact of immunocompromising conditions

FIGURE. Annual average incidence of PCV13-type IPD in children aged 6–18 years, with and without selected underlying immunocompromising conditions — United States 2007–2009



Vaccination of HIV^{+} population

Introduction

-HIV-infection negatively affects the immune response to vaccines through:

a) B cell dysfunctions

b) Immune activation/impaired cell-mediated immunity

c) Net state of immunosuppresion

BCG contraindication in immunocompromised children

Not only ineffective, but may also be risky: disseminated BCG disease in HIV+ infants

Box 1. **Four scenarios, outlined by WHO, that affect the balance of risks and benefits of BCG vaccination in settings with high burdens of tuberculosis and HIV infection[14]**

1. Infants born to women of unknown HIV status

The benefits of BCG vaccination outweigh the risks, and infants should be vaccinated.

2. Infants whose HIV infection status is unknown and who demonstrate no sign or symptom of HIV infection, but who are born to women known to be HIV-infected

The benefits of BCG vaccination usually outweigh the risks, and infants should receive the vaccine after consideration of local factors.

3. Infants who are known to be HIV-infected, with or without signs or symptoms of HIV infection

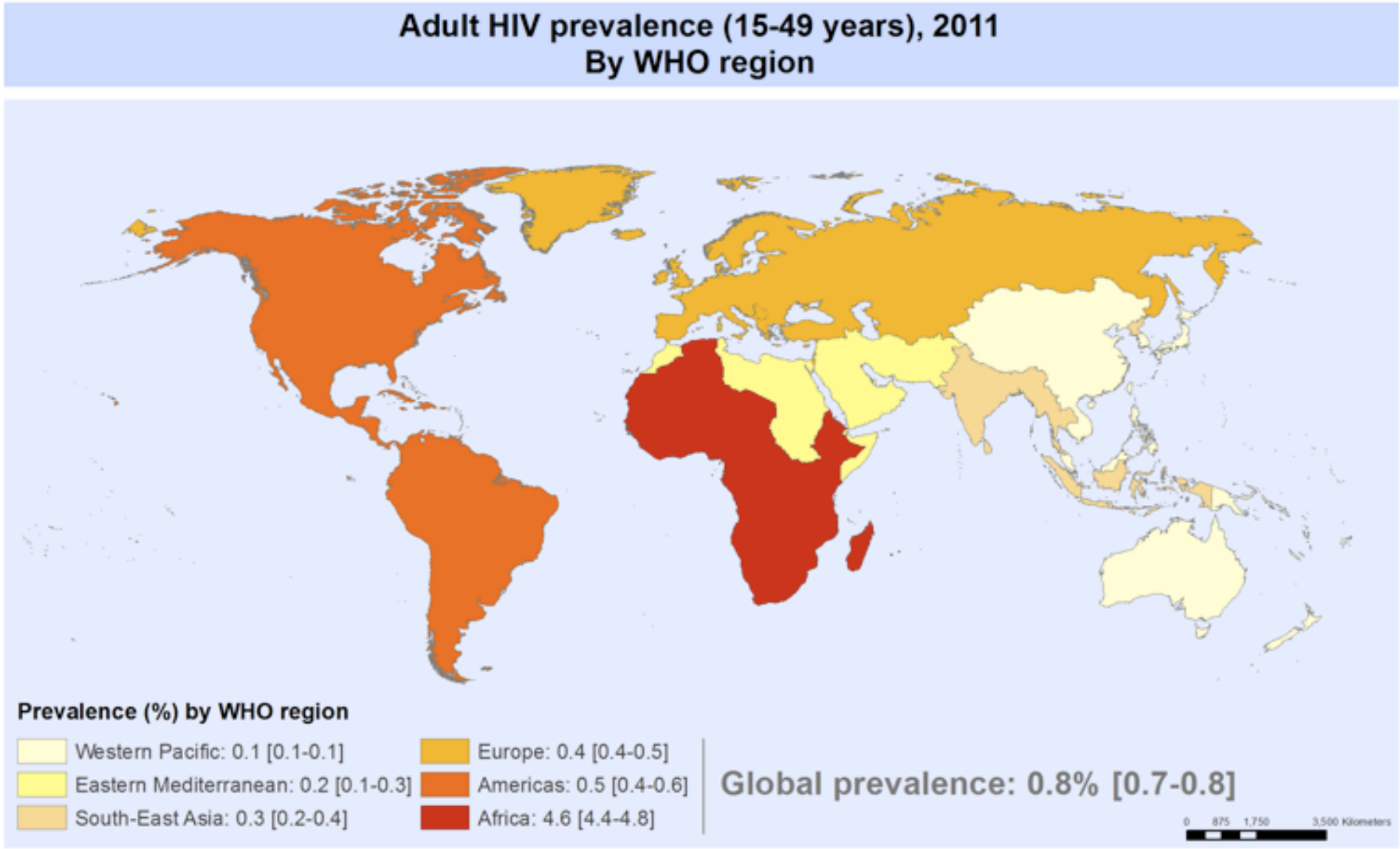
The risks of BCG vaccination outweigh the benefits and infants should not receive the vaccine, but they should receive other routine vaccines.

4. Infants with unknown HIV infection status but who have signs or symptoms of HIV infection and were born to HIV-infected mothers

The risks of BCG vaccination usually outweigh the benefits, and children should not be vaccinated during the first few weeks of life, since clinical symptoms of HIV infection typically occur after 3 months of age. However, the vaccine can be given if HIV infection is ruled out by early virological testing.

BCG, bacille Calmette-Guérin.

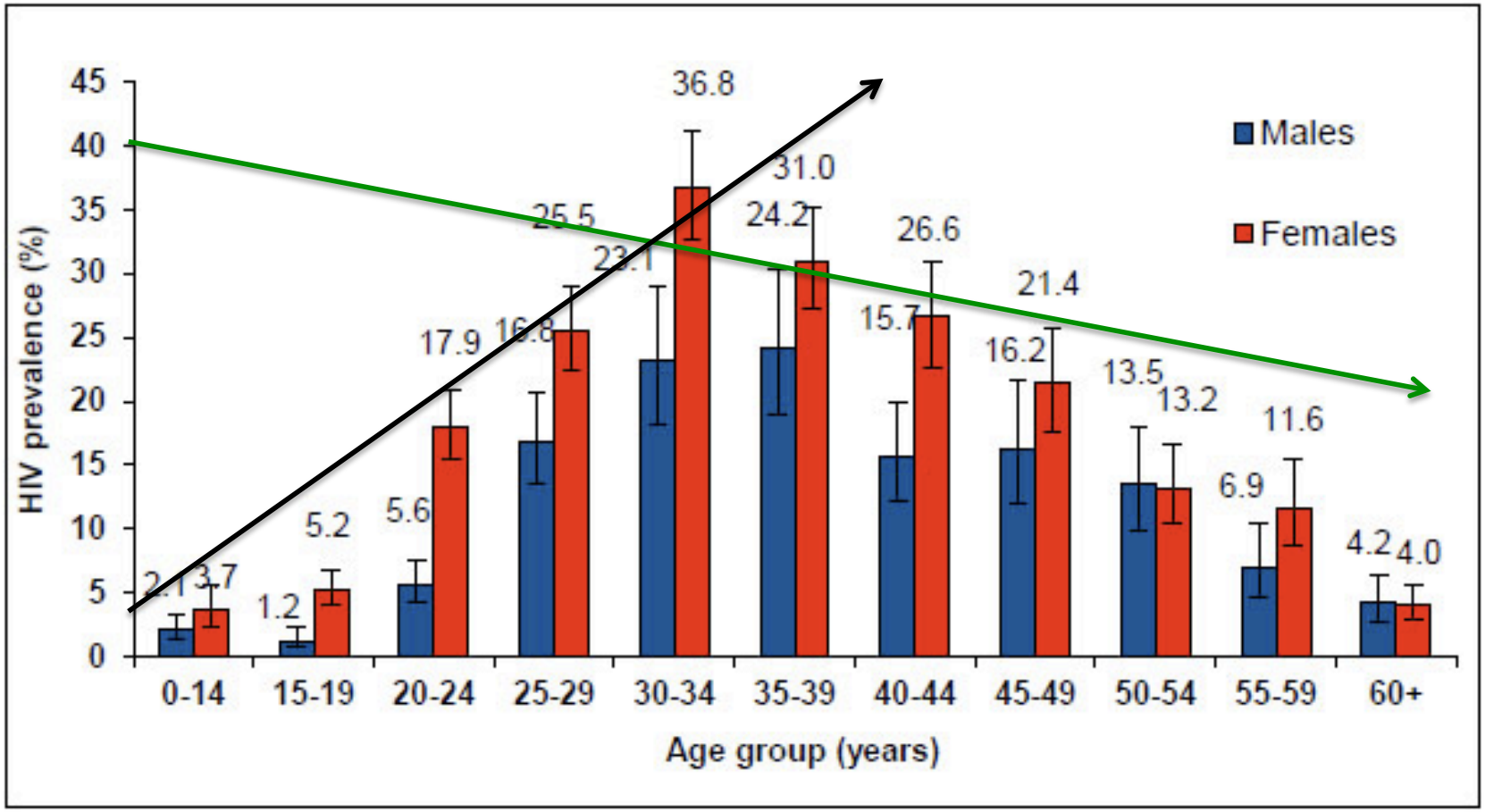
Hesseling, et al. Bull World Health Organ vol.87 n.7 Genebra Jul. 2009



http://gamapserver.who.int/mapLibrary/app/searchResults.aspx

HIV+ prevalence peaks later in life

Figure 1: HIV prevalence by age and sex, South Africa, 2012



Increasing HIV prevalence

Decreasing vaccine-induced immunity

Figure adapted from the SA national academy of sciences

HIV/AIDS INVITED ARTICLE

Kenneth H. Mayer, Section Editor

Long-term Immune Responses to Vaccination in HIV-Infected Patients: A Systematic Review and Meta-Analysis

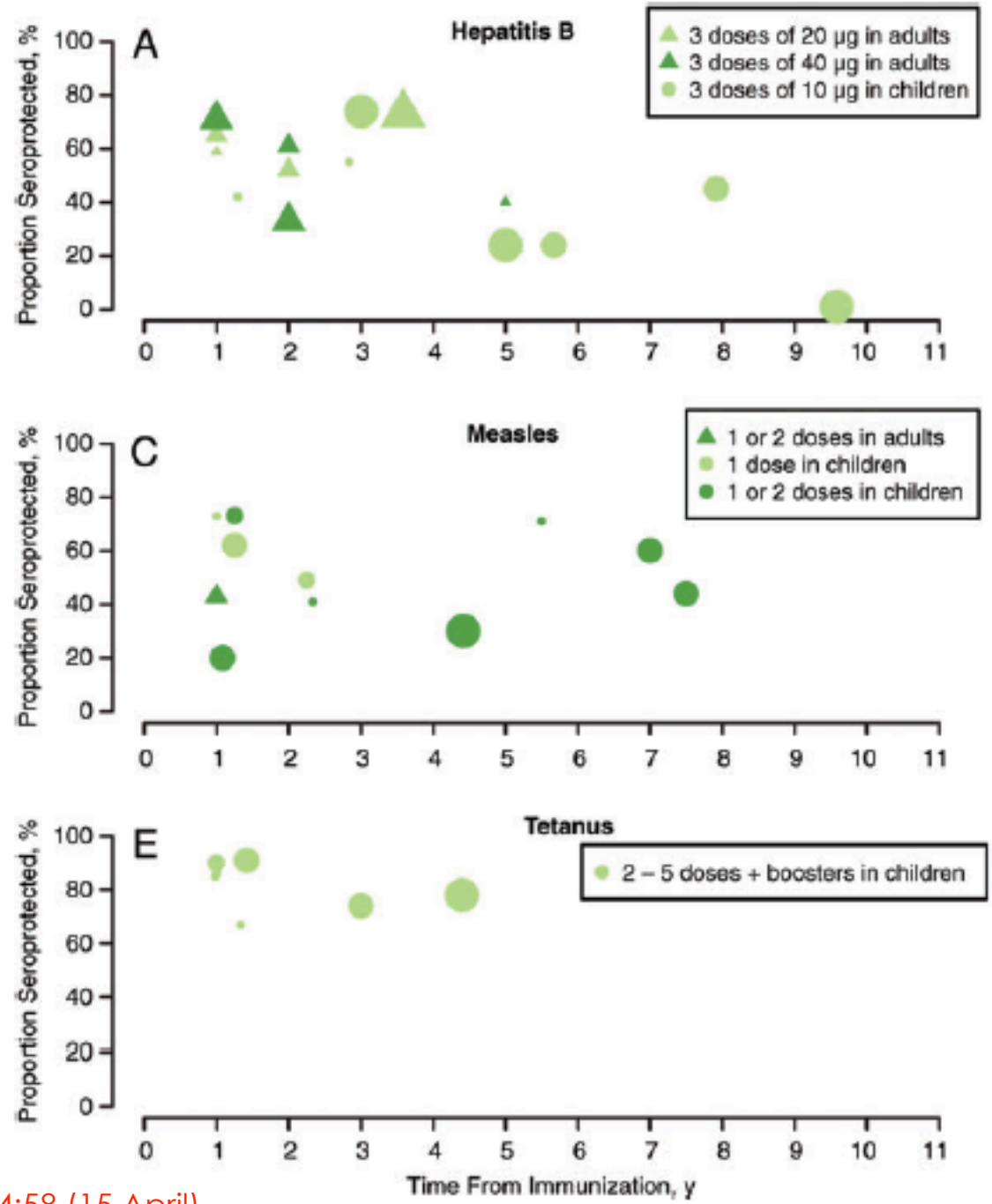
Solen Kernéis,[1,2,3,4,5] Odile Launay,[1,2,4] Clément Turbelin,[3,5] Frédéric Batteux,[1,6] Thomas Hanslik,[7,8] and Pierre-Yves Boëlle[3,5]

[1]Paris Descartes University, [2]Centre d'Investigation Clinique (CIC) BT505 and [3]Unité Mixte de Recherche en Santé (UMR S) 707, Inserm, [4]CIC BT505, Assistance Publique-Hôpitaux de Paris, [5]UMR S 707, Pierre et Marie Curie University, [6]Laboratoire d'Immunologie Biologique, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Paris; [7]Department of Internal Medecine, Ambroise Paré Hospital, Assistance Publique-Hôpitaux de Paris, Boulogne Billancourt; and [8]Versailles Saint-Quentin-en-Yvelines University, Versailles, France

Vaccine-induced antibodies may wane more quickly in persons living with human immunodeficiency virus (HIV) than in healthy individuals. We reviewed the literature on vaccines routinely recommended in HIV-infected patients to estimate how seroprotection decreases over time in those who initially responded to immunization. For each study retrieved from the literature, the decrease of seroprotection was modeled with a log binomial generalized linear model, and data were pooled in a meta-analysis to provide estimates of seroprotection 2 and 5 years after the last vaccine administration. Our analyses confirmed that the duration of seroprotection was shorter in HIV-infected patients and that with current guidelines, a substantial proportion of patients would have lost protective antibodies before a booster was proposed. We therefore discuss the implications for the monitoring of antibody levels and timing of revaccination in these patients.

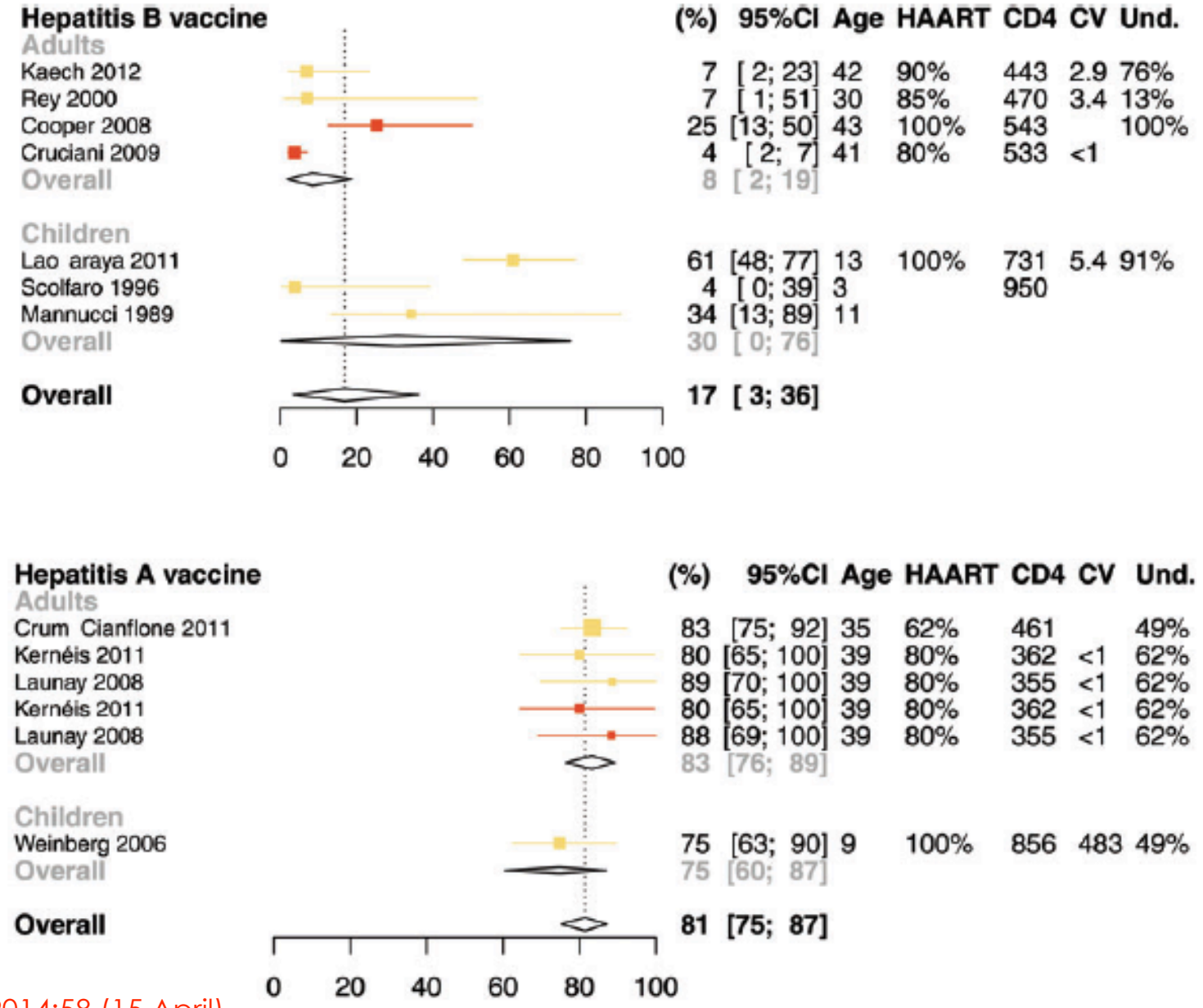
Keywords. vaccination; HIV; meta-analysis.

Solen *et al.* CID 2014:58 (15 April)



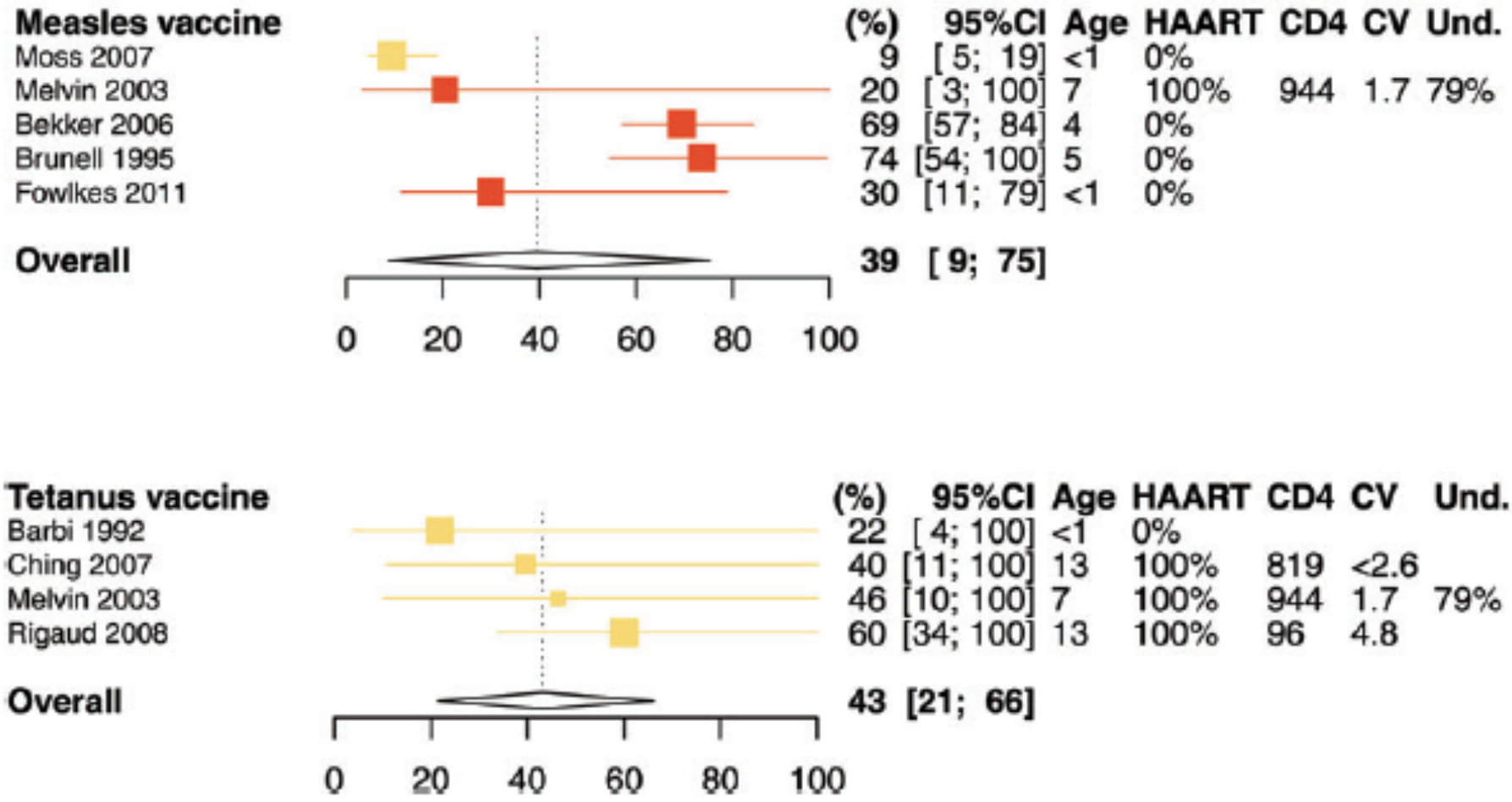
Solen *et al.* CID 2014:58 (15 April)

Meta-analysis of the percentages of seroprotection 5 years after the last vaccine dose



Solen *et al.* CID 2014:58 (15 April)

Meta-analysis of the percentages of seroprotection 5 years after the last vaccine dose



Solen *et al.* CID 2014:58 (15 April)

Long-term Immune Responses to Vaccination in HIV-Infected Patients:

Summary of key findings:

1) Anti–HBs virus antibodies should be measured yearly in adults and every 2–5 years in children

2) Anti–hepatitis A virus antibodies should be monitored every 5 years

3) For tetanus, the interval of 10 years between boosters seems reasonable.

4) For measles, the initial vaccination should include 2 doses, ideally administered after the start of HAART.

A third dose could be proposed 2–5 years after primary vaccination.

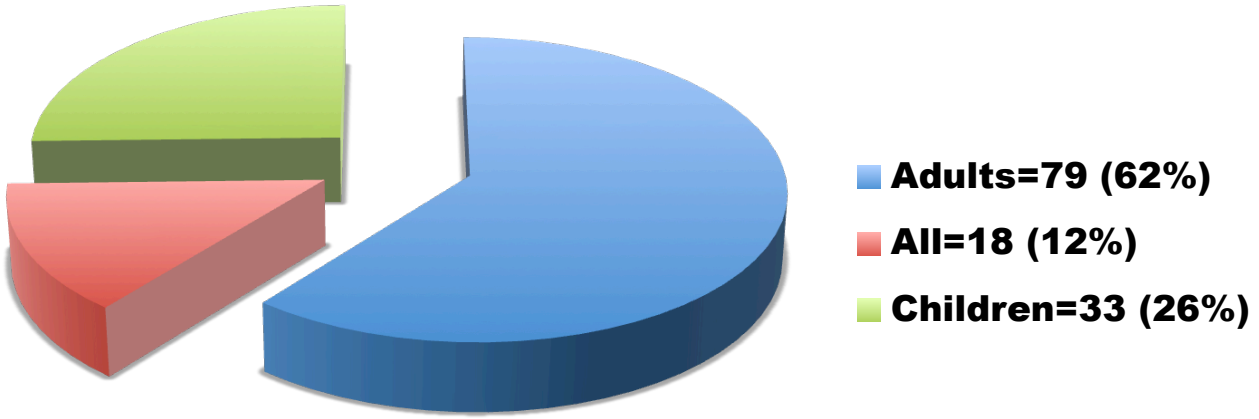
Solen *et al.* CID 2014:58 (15 April)

Interventions to improve immunity in HIV-infected persons: Systematic review

-278 studies were selected based on titles and abstracts

-After screening for duplicates, 130 studies were included

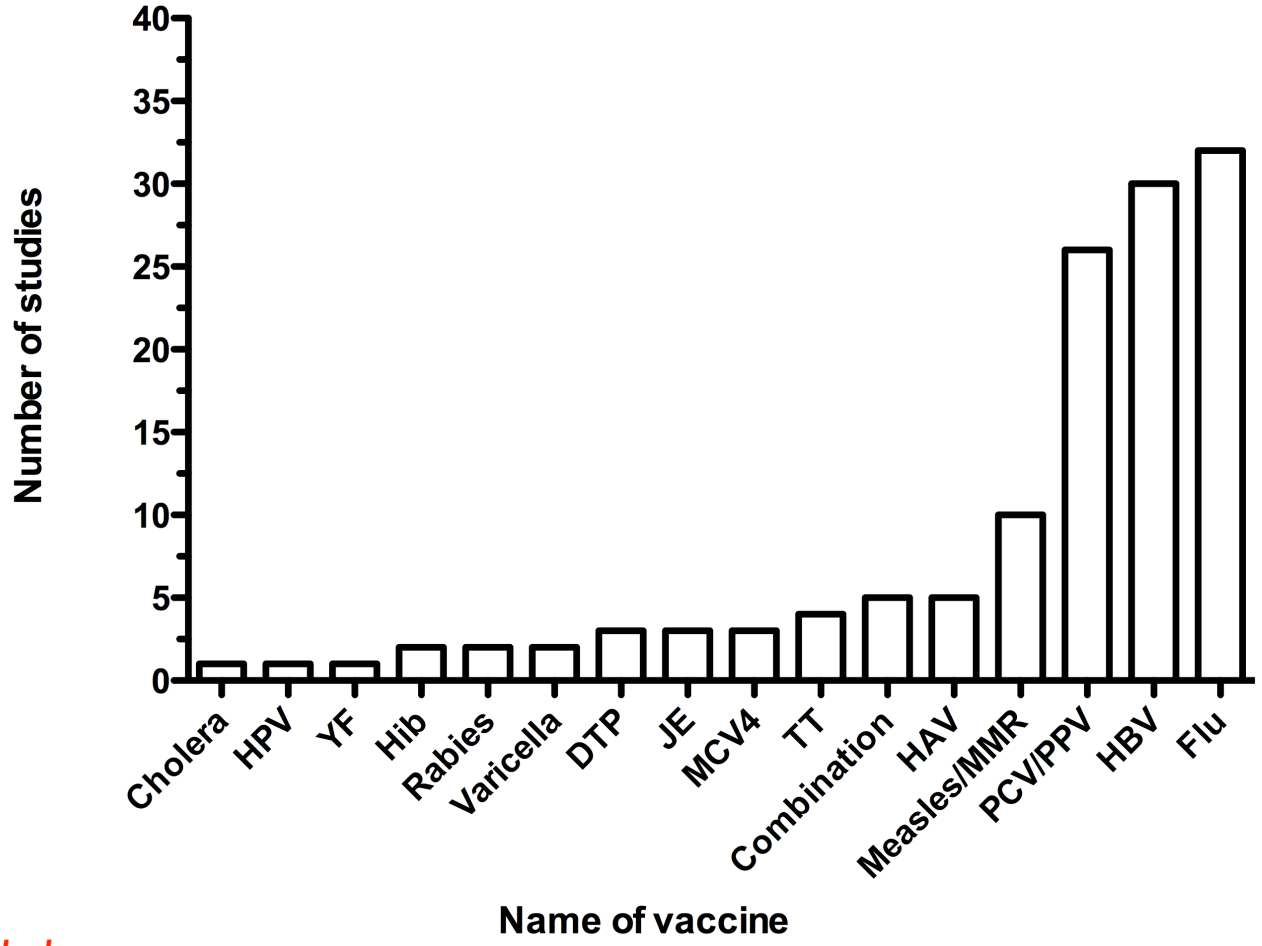
Children, adolescents and adults studies



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review.

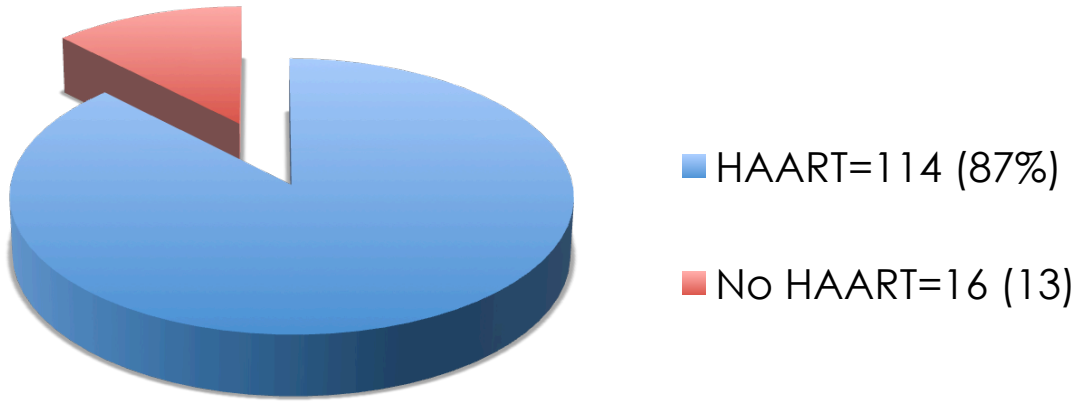
Vaccines studied



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review

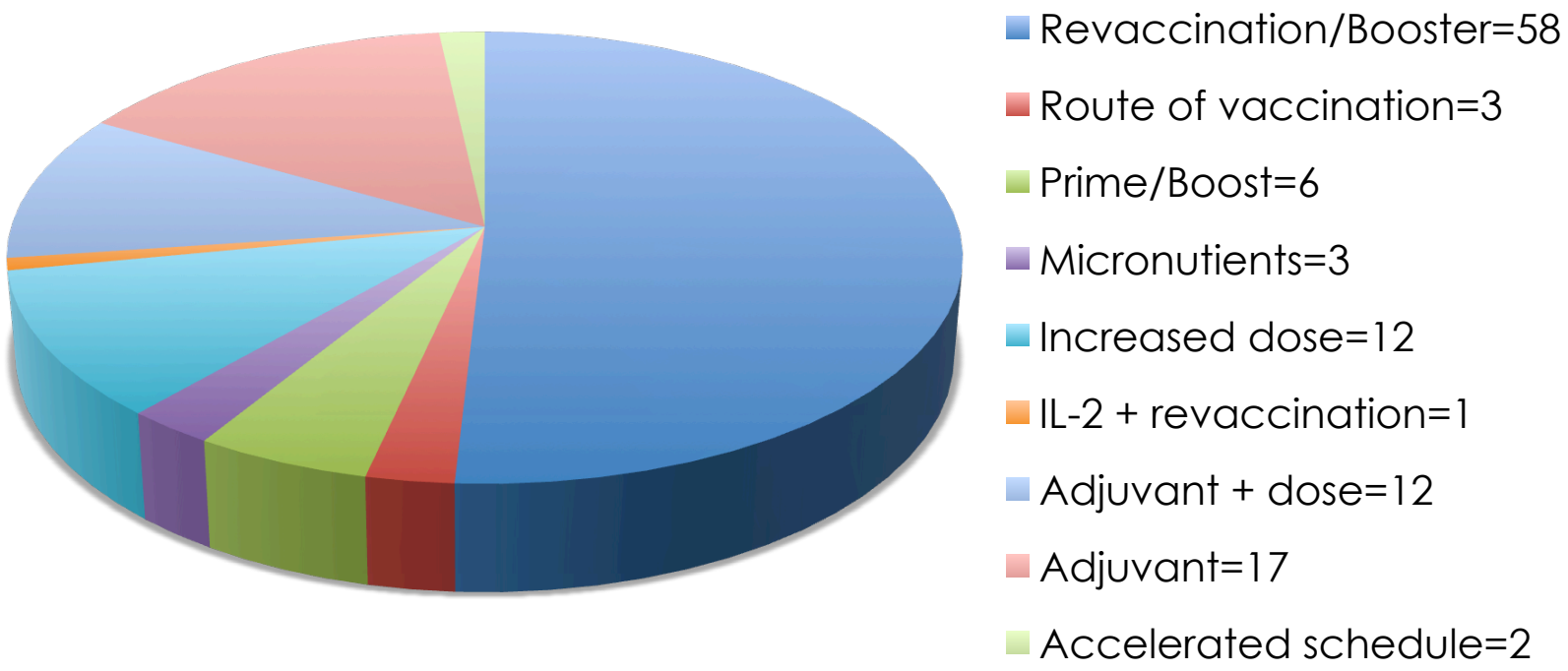
Main intervention is HAART



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review

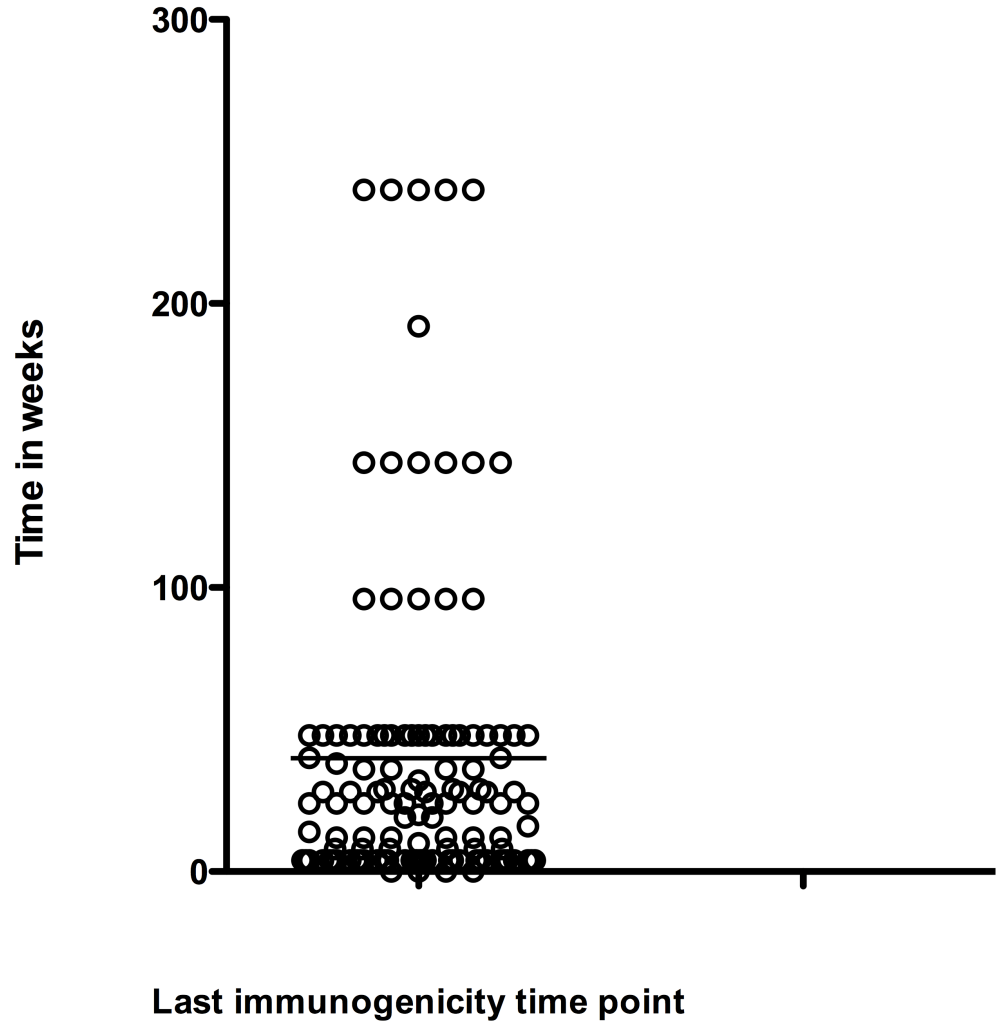
Together with HAART (n=114), interventions evaluated are:



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review:

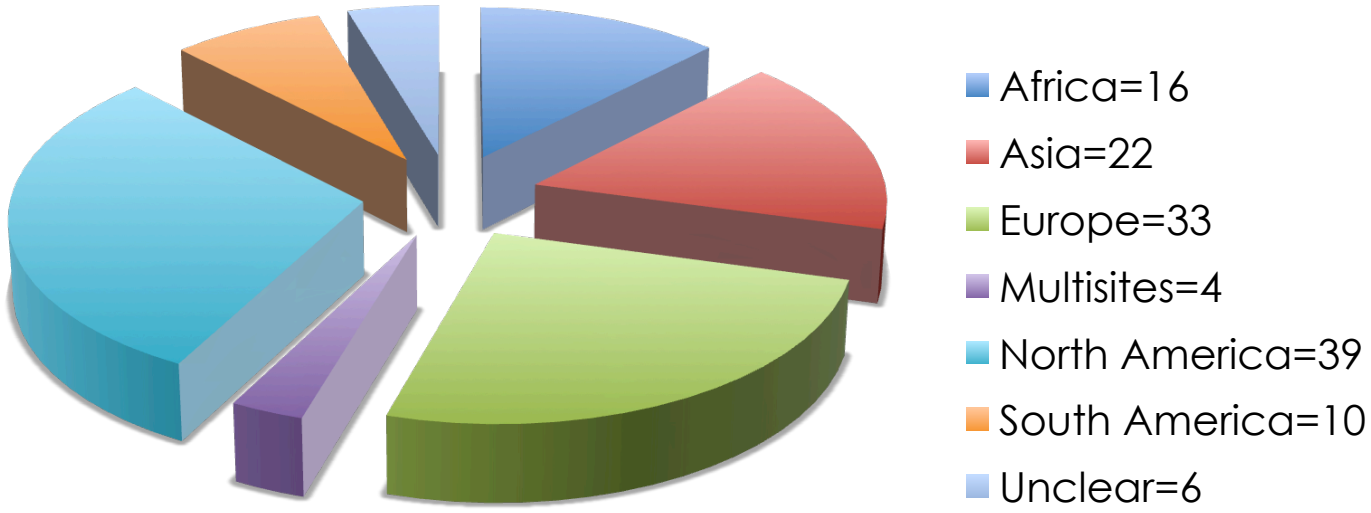
Duration of immunogenicity evaluations



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review

Studies by continent



Ongoing study

Interventions to improve immunity in HIV-infected persons: Systematic review

Preliminary conclusions

1) More studies done in adults than young children

2) Majority of the studies have assessed influenza and HBV

3) HAART and revaccination/booster strategy most assessed

4) Majority of studies have not evaluated immune responses beyond 1year after the intervention

5) Number of studies done in African countries do not match the scale of the HIV epidemic on the continent

Ongoing study

Safety of vaccines in HIV-infected population: Measles

Measles Vaccination in HIV-Infected Children: Systematic Review and Meta-Analysis of Safety and Immunogenicity

Pippa Scott,[1] William J. Moss,[2] Zunera Gilani,[2] and Nicola Low[1]

[1]Division of Clinical Epidemiology and Biostatistics, Institute of Social and Preventive Medicine, University of Bern, Switzerland; and [2]Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland

Background. Measles control may be more challenging in regions with a high prevalence of HIV infection. HIV-infected children are likely to derive particular benefit from measles vaccines because of an increased risk of severe illness. However, HIV infection can impair vaccine effectiveness and may increase the risk of serious adverse events after receipt of live vaccines. We conducted a systematic review to assess the safety and immunogenicity of measles vaccine in HIV-infected children.

Methods. The authors searched 8 databases through 12 February 2009 and reference lists. Study selection and data extraction were conducted in duplicate. Meta-analysis was conducted when appropriate.

Results. Thirty-nine studies published from 1987 through 2008 were included. In 19 studies with information about measles vaccine safety, more than half reported no serious adverse events. Among HIV-infected children, 59% (95% confidence intervals [CI], 46–71%) were seropositive after receiving standard-titer measles vaccine at 6 months (1 study), comparable to the proportion of seropositive HIV-infected children vaccinated at 9 (8 studies) and 12 months (10 studies). Among HIV-exposed but uninfected and HIV-unexposed children, the proportion of seropositive children increased with increasing age at vaccination. Fewer HIV-infected children were protected after vaccination at 12 months than HIV-exposed but uninfected children (relative risk, 0.61; 95% CI, .50–.73).

Conclusions. Measles vaccines appear to be safe in HIV-infected children, but the evidence is limited. When the burden of measles is high, measles vaccination at 6 months of age is likely to benefit children of HIV-infected women, regardless of the child's HIV infection status.

Safety of vaccines in HIV-infected population: PCV

Safety profile of pneumococcal conjugate vaccines: systematic review of pre- and post-licensure data

Frank DeStefano,[a] Dina Pfeifer[b] & Hanna Nohynek[c]

Abstract A 7-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV7) was licensed in the United States of America in 2000, but no comprehensive postmarketing review of safety has been carried out. We conducted a systematic review of the safety of PCV7 and other pneumococcal conjugate vaccines. A total of 42 studies were included in the review. Reactogenicity data from some randomized trials suggest that PCV7 may result in more local reactions and fever than certain comparison vaccines. However, the reactions were mild and self-limited, and PCV7 did not carry an increased risk of severe injection-site reactions or high fever. Some, although not all, of the randomized trials in children found that mild local and systemic reactions associated with PCV7 may increase with the number of doses, at least over the three-dose primary series. In addition, PCV7 and other pneumococcal conjugate vaccines were found to have tolerable reactogenicity in Native American and African populations and in medically high-risk groups for which pneumococcal vaccination is recommended. Two of the largest studies of PCVs, one involving PCV7 and the other, PCV9, found a statistically significant increased risk of hospitalization for reactive airway disease, including asthma. Another large trial of PCV9, however, did not find an increased risk of asthma. In conclusion, this review of the evidence did not identify any major safety problems with PCV7 or any other pneumococcal conjugate vaccine, with the possible exception of reactive airway disease, which may bear further scrutiny as additional data become available.

Bulletin of the World Health Organization 2008;86:373–380.

Safety of vaccines in HIV-infected population: YF

Am. J. Trop. Med. Hyg., 86(2), 2012, pp. 359–372
doi:10.4269/ajtmh.2012.11-0525

The Safety of Yellow Fever Vaccine 17D or 17DD in Children, Pregnant Women, HIV+ Individuals, and Older Persons: Systematic Review

Roger E. Thomas,* Diane L. Lorenzetti, Wendy Spragins, Dave Jackson, and Tyler Williamson

Department of Family Medicine, Faculty of Medicine, University of Calgary, Alberta, Canada; Department of Community Health Sciences, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada; Independent Research Consultant, Calgary, Alberta, Canada

Abstract. Yellow fever vaccine provides long-lasting immunity. Rare serious adverse events after vaccination include neurologic or viscerotropic syndromes or anaphylaxis. We conducted a systematic review of adverse events associated with yellow fever vaccination in vulnerable populations. Nine electronic bibliographic databases and reference lists of included articles were searched. Electronic databases identified 2,415 abstracts for review, and 32 abstracts were included in this review. We identified nine studies of adverse events in infants and children, eight studies of adverse events in pregnant women, nine studies of adverse events in human immunodeficiency virus-positive patients, five studies of adverse events in persons 60 years and older, and one study of adverse events in individuals taking immunosuppressive medications. Two case studies of maternal–neonate transmission resulted in serious adverse events, and the five passive surveillance databases identified very small numbers of cases of yellow fever vaccine-associated viscerotropic disease, yellow fever vaccine-associated neurotropic disease, and anaphylaxis in persons $\geq$ 60 years. No other serious adverse events were identified in the other studies of vulnerable groups.

Safety of vaccines in HIV-infected population: Routine vaccines

Kagina *et al. Systematic Reviews* 2014, **3**:101
http://www.systematicreviewsjournal.com/content/3/1/101

PROTOCOL Open Access

Safety of licensed vaccines in HIV-infected persons: a systematic review protocol

Benjamin M Kagina[1*], Charles S Wiysonge[2], Maia Lesosky[3], Shabir A Madhi[4,5,6] and Gregory D Hussey[1]

Ongoing study

DOI: 10.1111/j.1468-1293.2008.00637.x
HIV Medicine (2008), 9, 795–848

BRITISH HIV ASSOCIATION GUIDELINES

British HIV Association guidelines for immunization of HIV-infected adults 2008

AM Geretti on behalf of the BHIVA Immunization Writing Committee*

Department of Virology, Royal Free Hospital, Royal Free and University College Medical School, Pond Street, London NW3 2QG, UK

Vaccination of HIV^{+} population

Future outlook in the context of South Africa/LMICs

-Burden of VPD in HIV infected and adults: incomplete data?

-Evaluation of vaccination programs: Can this be extended to adolescents and adults?

-Interventions to improve vaccine uptake among HIV-infected adolescents and adults?

-Formal policy of vaccinating HIV-infected persons?

Acknowledgements

-Greg Hussey (UCT, SA)

-Shabir Madhi (NICD, SA)

-Charles Wiysonge (SUN, SA)

-Lesosky Maia (UCT, SA)

-Leila Abdullahi (UCT, SA)

-Violette Dirix (ULB, Belgium)

-Sara Suliman (UCT)

Thank you!