Should an Additional Dose of MCV be Recommended for HIV-infected Adolescents and Adults?

SAGE Working Group on Measles and Rubella

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Meeting of the Strategic Advisory Group of Experts on immunization, October 2015 – conclusions and recommendations

The Strategic Advisory Group of Experts on immunization (SAGE)[1] met on 20–22 October 2015. This report summarizes the discussions, conclusions and recommendations.[2] For the malaria session, SAGE was joined by the Malaria Policy Advisory Committee (MPAC) and the conclusions and recommendations concerning malaria vaccine are those of both committees.

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, octobre 2015 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts sur la vaccination (SAGE)[1] s'est réuni du 20 au 22 octobre 2015. Le présent rapport résume les discussions, conclusions et recommandations auxquelles il est parvenu.[2] Le Comité de pilotage de la politique de lutte antipaludique (MPAC) s'est joint au SAGE pour la session consacrée au paludisme: les conclusions et recommandations relatives au vaccin antipaludique émanent donc de ces deux Comités.

SAGE reviewed evidence indicating that an increasingly large number of HIV-infected children will receive antiretroviral therapy and that these children are at increased risk of measles because of poor antibody responses following vaccination prior to initiation of highly active antiretroviral therapy (HAART). While HAART does not restore measles immunity from previously received vaccine doses, it enables higher and more prolonged antibody responses following revaccination.

SAGE recommended that an additional dose of MCV be administered to HIV-infected children receiving HAART following immune reconstitution. If CD4+ T lymphocyte counts are being monitored, an additional dose of MCV should be administered when immune reconstitution has been achieved, e.g. when the CD4+ T lymphocyte count reaches 20%–25%. Where CD4+ T lymphocyte monitoring is not available, children should receive an additional dose of MCV 6–12 months after initiation of HAART. Current evidence is insufficient to recommend an additional dose for children who start HAART prior to the first dose of MCV.

A supplementary dose of MCV should be considered soon after diagnosis of HIV infection in children older than 6 months who are not receiving HAART, and for whom the risk of measles is high, with the aim of providing partial protection until they are revaccinated after immune reconstitution with HAART.

SAGE requested evidence on the need for measles revaccination of HIV-infected adolescents and adults. Further research is needed to monitor the long-term immune responses to measles vaccine in HIV-infected children revaccinated after starting HAART and in HIV-infected children starting HAART prior to receiving their first dose of MCV.

In October 2015, SAGE requested evidence on the need for measles revaccination of HIV-infected adolescents and adults.

SAGE Recommendations for HIV-infected Children Receiving HAART

SAGE recommended that an additional dose of MCV be administered to HIV-infected children receiving HAART following immune reconstitution. Where CD4+ T lymphocyte counts are monitored, an additional dose of MCV should be administered when immune reconstitution has been achieved, e.g. when CD4+ T lymphocytes are ≥ 20 to 25%. Where CD4+ T lymphocyte monitoring is not available, children should receive an additional dose of MCV 9-12 months after initiating HAART.

Evidence for Policy Decision

Current recommendations on measles vaccination of HIV-infected adolescents and adults

Systematic review of measles seroprevalence in HIV-infected adolescents and adults

Systematic review of measles vaccine immunogenicity, effectiveness and safety in HIV-infected adolescents and adults

Proposed recommendations

Current Recommendations on Measles Vaccination of HIV-infected Adolescents and Adults

WHO Position Paper – April 2017

Given the severe course of measles in patients with AIDS, measles vaccination should be routinely administered to **potentially susceptible, asymptomatic HIV-infected children and adults**. Vaccination may even be considered for those with symptomatic HIV infection if they are not severely immunosuppressed according to conventional definitions.

ACIP

Adults with human immunodeficiency virus (HIV) infection and CD4+ T-lymphocyte count ≥200 cells/μl for at least 6 months **who do not have evidence of measles, mumps, or rubella immunity** should receive 2 doses of MMR at least 28 days apart. Adults with HIV infection and CD4+ T-lymphocyte count <200 cells/μl should not receive MMR.

Measles vaccines: WHO position paper – April 2017. Wkly Epi Rev 2017;92:205-28.
Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013. MMWR 2013;62:1-34.

Burden of Measles in HIV-infected Adolescents and Adults

Limited data on burden of measles in HIV-infected adolescents and adults despite large outbreaks in regions of high HIV prevalence (e.g. South Africa and Malawi)

Several published case reports and case series

Eight cases of measles inclusion body encephalitis in immunocompromised HIV-infected adults in South Africa

No data on measles incidence or severity in HIV-infected compared to uninfected adults

Systematic Review of Measles Vaccination of HIV-infected Adults

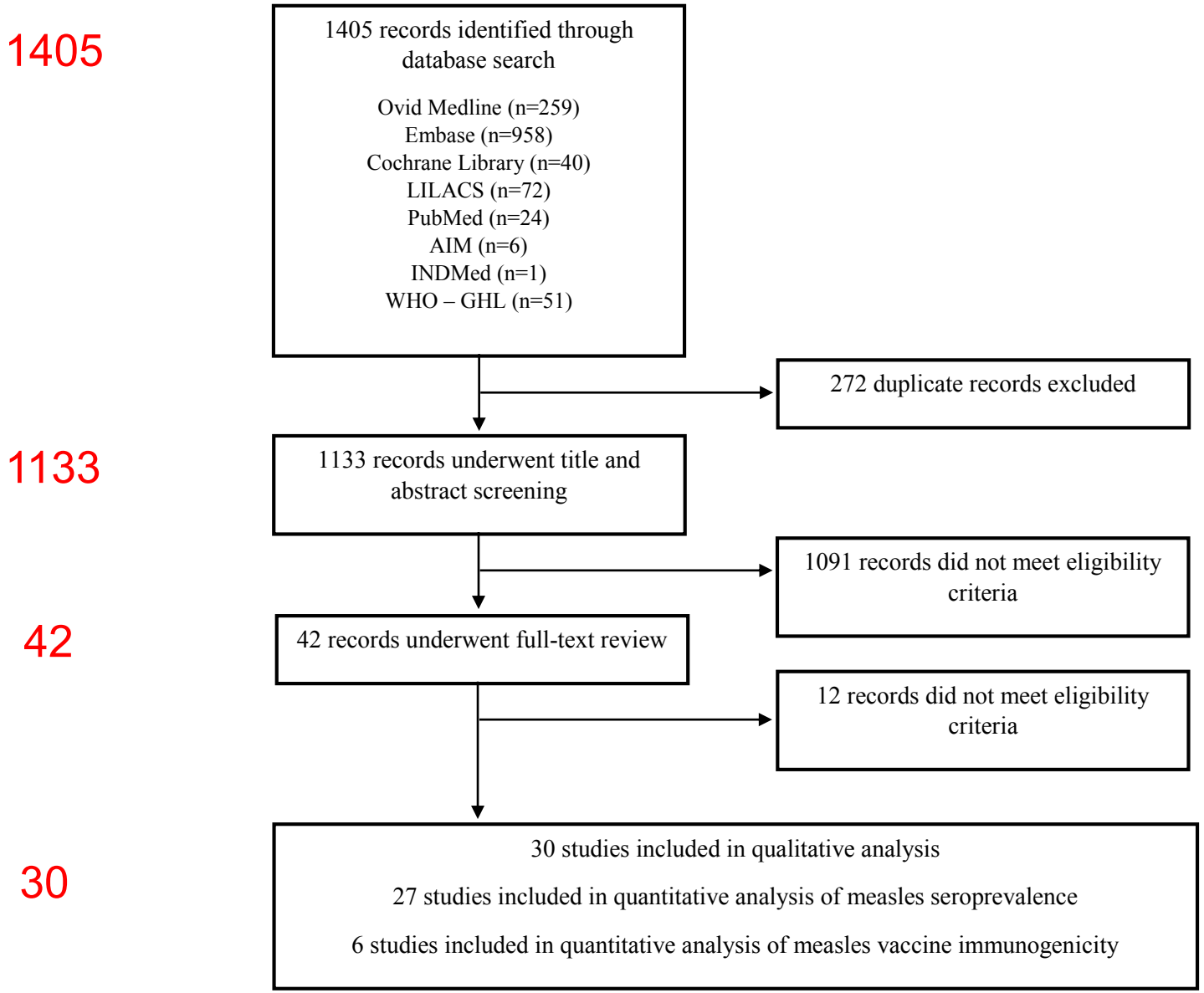
Searched Medline (Ovid), Embase, Cohrane Library, PubMed, LILACS, INDMED and WHO GHL databases

From establishment of each database to March 16, 2017

Search terms were adapted for each database and included HIV-related keywords in conjunction with measles vaccine-related keywords

References of included studies and relevant reviews were examined to identify publications not identified in the database search

Systematic Review Flow Chart



Measles Seroprevalence in HIV-infected Adults

27 studies involving 9,607 HIV-infected adolescents and adults estimated measles seroprevalence

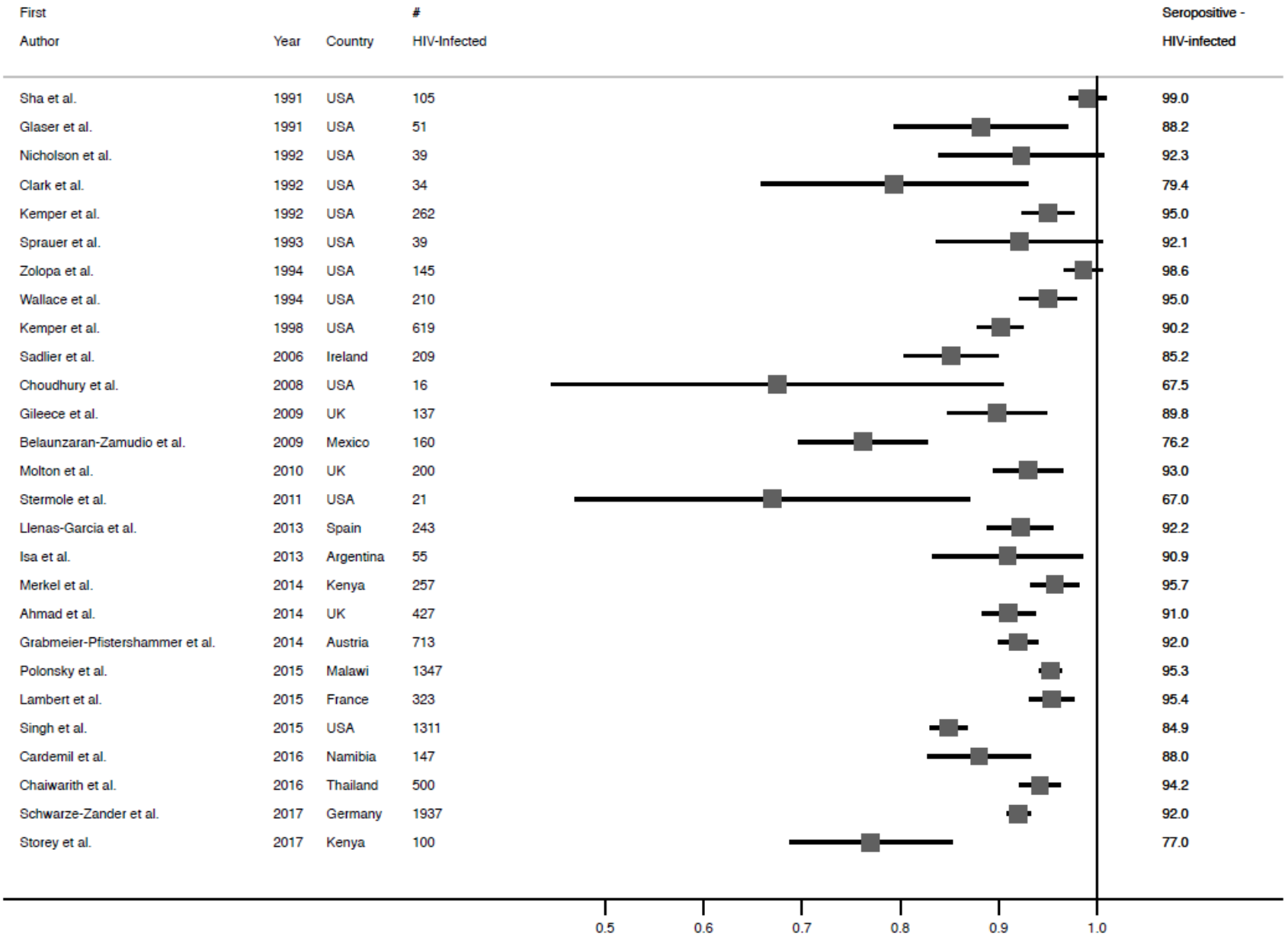
Median seroprevalence was 92% (IQR: 85.2% - 95.0%)

No statistically significant differences were reported in 10 studies of measles seroprevalence in HIV-infected and HIV-uninfected adults

Three of seven studies reported lower antibody levels in HIV-infected compared to HIV-uninfected adults

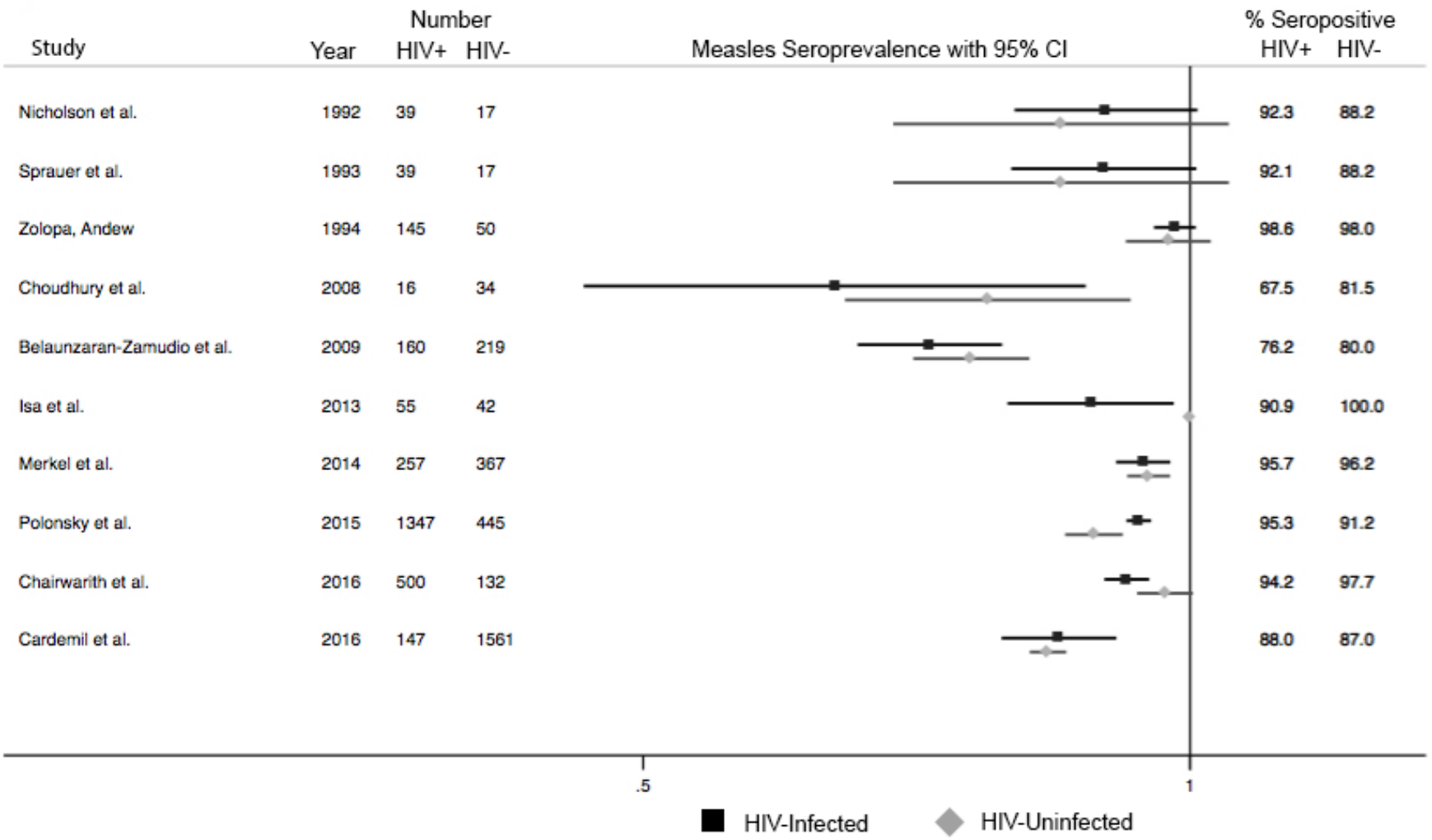
Eleven studies reported older age or earlier birth cohort was a risk factor for measles seropositivity (wild-type infection)

Measles Seroprevalence in HIV-infected Adults



Measles Seroprevalence is Similar in HIV-infected and Uninfected Adults

Summary of studies with a comparison group



Measles Vaccine Immunogenicity in HIV-infected Adults

Six studies examined the immunogenicity of MCV in 109 seronegative HIV-infected adults

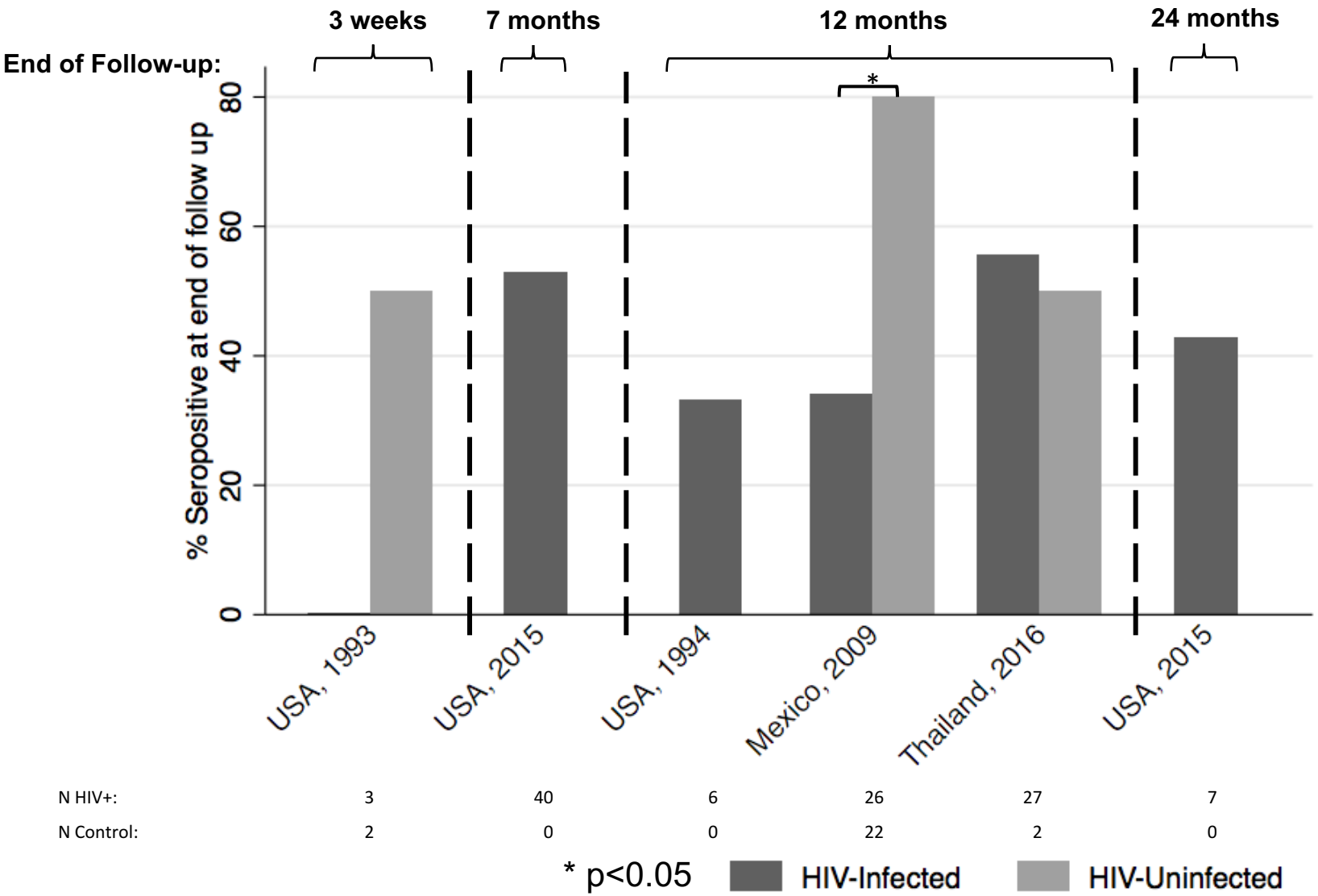
Heterogeneity among studies:

- Dates of publication: 1993 to 2016
- Follow-up: 3 weeks to 24 months post-vaccination

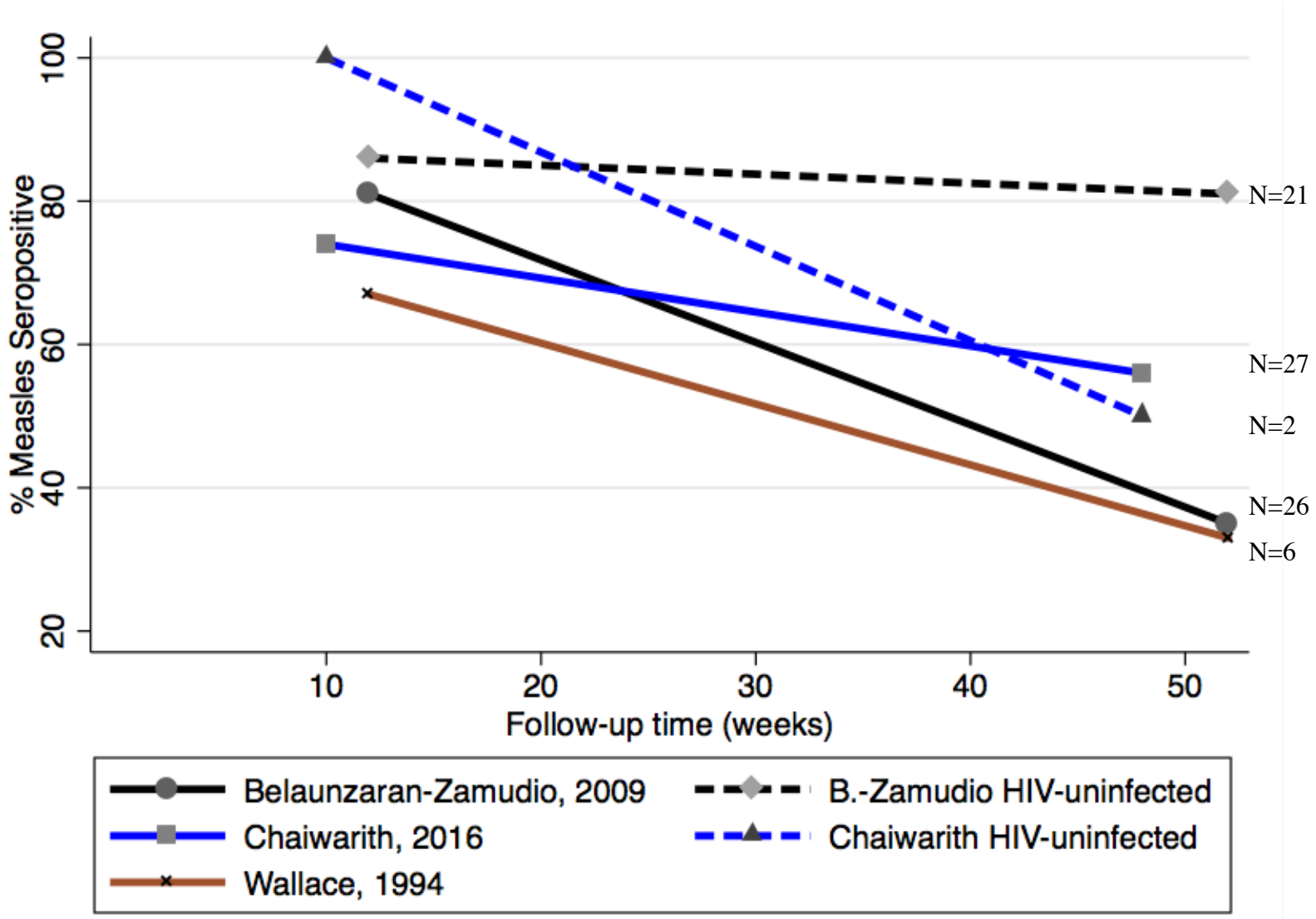
Seropositivity at end of follow-up ranged from 0% to 56% (median 39%)

Trend for higher immunogenicity in more recent studies after introduction of HAART

Measles Vaccine Immunogenicity in HIV-infected Adults



Duration of Measles Seropositivity following Vaccination of HIV-infected Adults



Measles Vaccine Efficacy and Effectiveness

No study reported measles vaccine efficacy or effectiveness in HIV-infected adolescents and adults, with or without a comparison group of uninfected adults.

Measles Vaccine Safety

Only four studies of the immunogenicity of measles vaccine in HIV-infected adolescents and adults reported adverse events

These studies included 109 HIV-infected and 6 uninfected adults followed for a maximum of 24 months

Only two studies reported use of antiretroviral therapy

No severe adverse events were reported

Case Report of Serious Adverse Event

21-year-old man with AIDS who received 2nd MMR, developed fatal pneumonia and had measles vaccine virus RNA identified in lung tissue.

- Presented 11 months after vaccination
- Previously vaccinated against measles
- Thorascopic lung biopsy
- RT-PCR and genome sequencing

Angel JB, et al. Ann Int Med 1998;129:104-6.

Evidence to Inform SAGE Recommendations

1. The quality of evidence is low that measles seroprevalence does not differ between HIV-infected and uninfected adolescents and adults as it is based on ten cross-sectional, observational studies.

2. The quality of evidence is very low on the immunogenicity and safety of measles vaccine in HIV-infected adolescents and adults.

3. No evidence on the efficacy or effectiveness of MCV in HIV-infected adolescents and adults was identified.

Draft Recommendations

Current WHO recommendations are that measles vaccination should be routinely administered to potentially susceptible, asymptomatic HIV positive children and adults. Vaccination may be considered for those with symptomatic HIV infection if they are not severely immunosuppressed according to conventional definitions.

1.Studies of measles seroprevalence and measles vaccine immunogenicity among HIV-infected adults do not support the need for an additional dose of measles vaccine following immune reconstitution with HAART.

2.Measles susceptible adults, whether HIV infected or not, may require targeted vaccination efforts to achieve regional measles elimination goals.