

Should an Additional Dose of MCV be Recommended for HIV-infected Children Receiving HAART?

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Summary of evidence

Current recommendations

Increasing number of HIV-infected children will receive HAART

Increased measles morbidity and mortality in HIV-infected children

Lower measles seroprevalence in HIV-infected children

Waning antibody levels in HIV-infected children

Limited data on measles vaccine effectiveness in HIV-infected children

HAART does not restore measles immunity

Improved responses to measles vaccine on HAART

Consistent with knowledge of impact of HIV on immune system

Mathematical models suggest accumulation of susceptibles

Measles vaccine is safe in HIV-infected children

Optimal timing of revaccination is not known

Children who received MCV1 after HAART may be protected

Revaccination of HIV-infected children should be feasible

Current recommendations on measles vaccination of HIV-infected children

WHO Position Paper

Measles vaccination should be routinely administered to potentially susceptible, asymptomatic HIV-positive children and adults.

Vaccination may even be considered for those with symptomatic HIV infection if not severely immunosuppressed.

The first dose of MCV may be offered as early as age 6 months.

ACIP

Persons with perinatal HIV infection who were vaccinated with measles-, rubella-, or mumps-containing vaccine before establishment of effective ART **should receive 2 appropriately spaced doses of MMR vaccine (i.e., 1 dose now and another dose at least 28 days later) once effective ART has been established.**

An increasing number of HIV-infected children will receive antiretroviral therapy

An estimated 740,000 HIV-infected children in low and middle-income countries were receiving antiretroviral therapy as of December 2013

630,300 (85%) resided in Africa

These children represent only 23% (21-25%) of the estimated 3.2 million (2.9 to 3.5 million) children younger than 15 years of age living with HIV

New WHO guidelines are to treat all HIV-infected persons

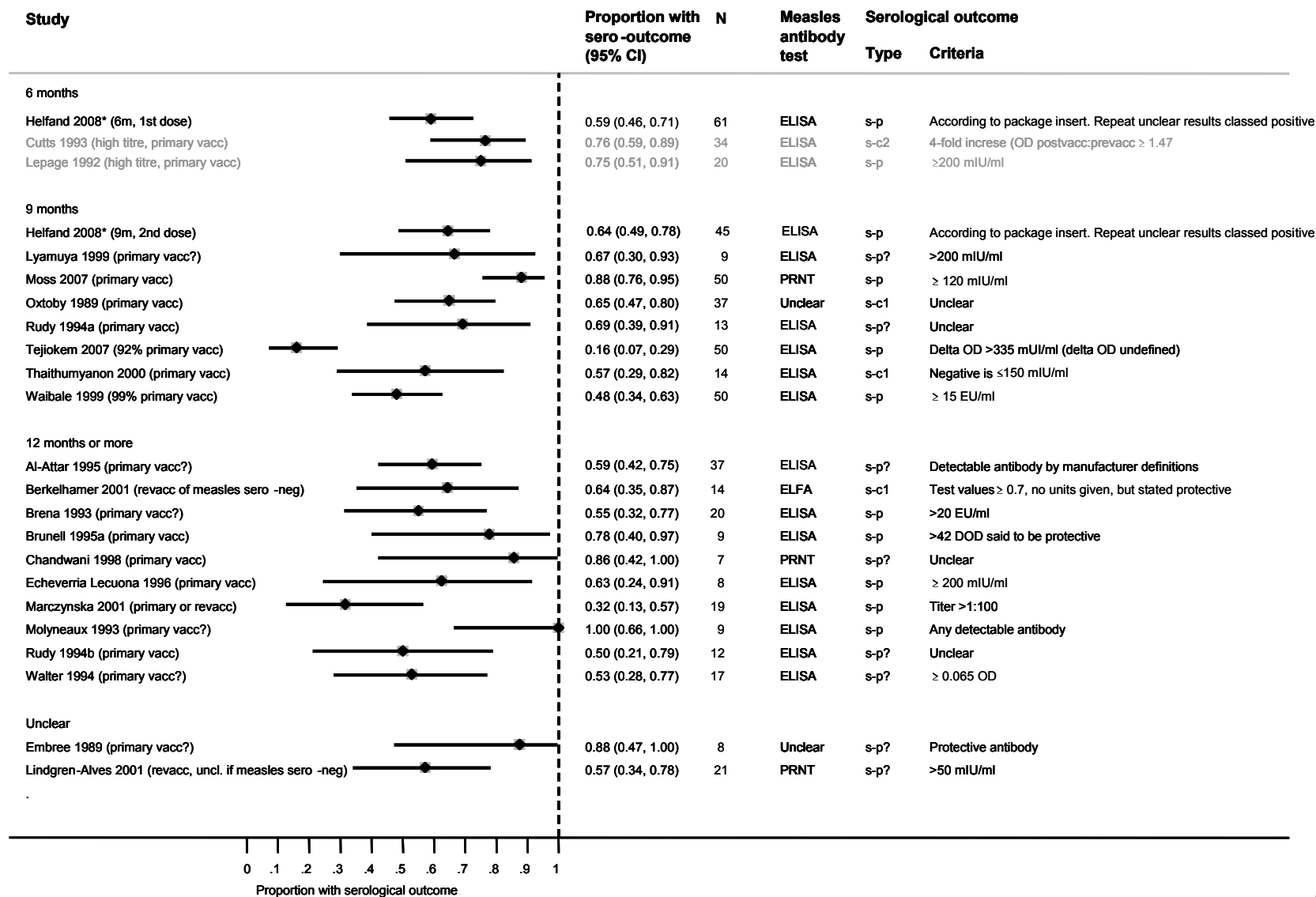
Increased measles morbidity and mortality in HIV-infected children

Largest prospective study of measles in HIV-infected children

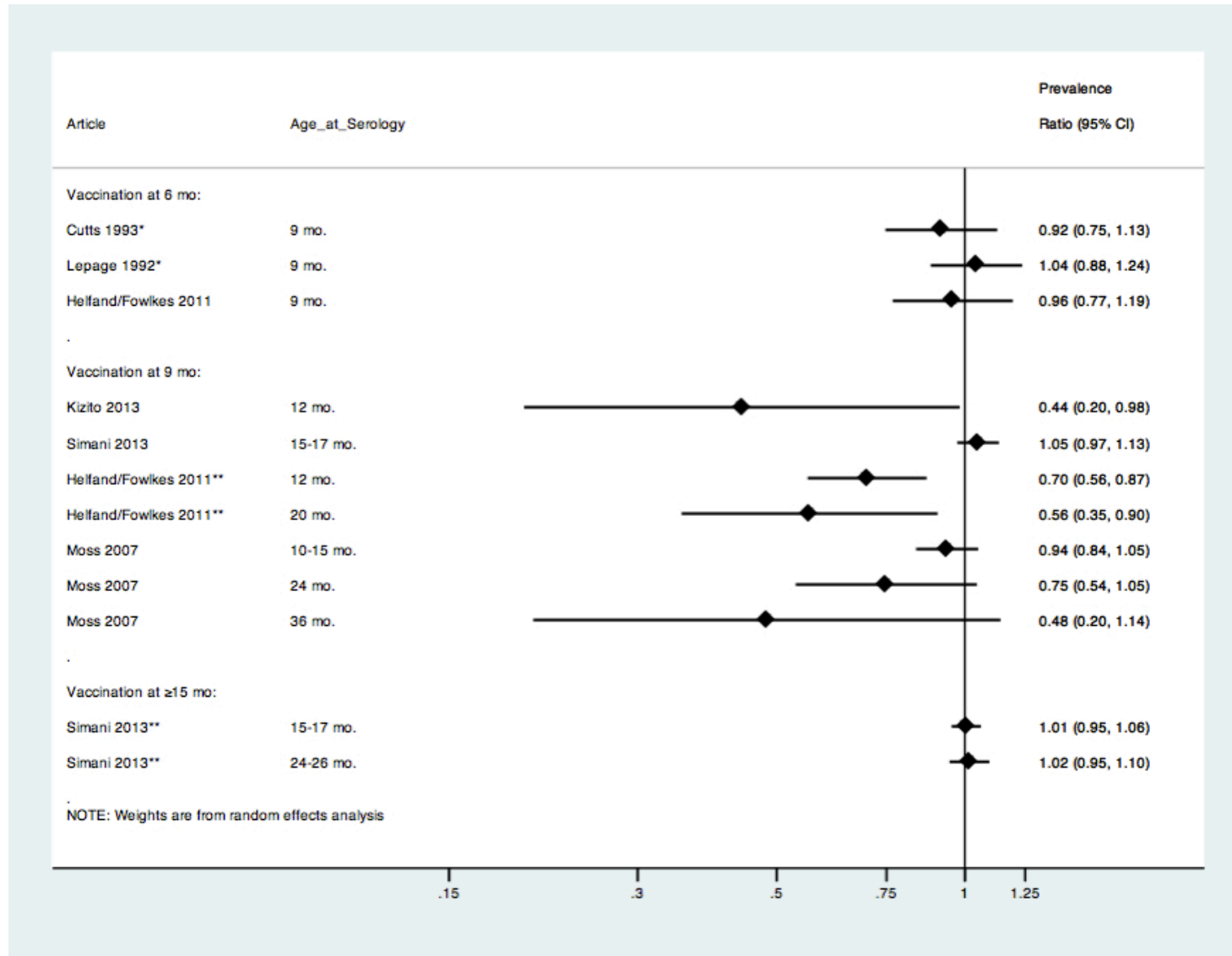
1035 children with confirmed measles, 62 of whom died

	No.	Deaths (%)	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
HIV-1 infection						
No	992	45 (4.5)	1.0		1.0	
Yes	172	23 (13.4)	3.2 (1.9 – 5.5)	<0.001	2.5 (1.4 – 4.6)	0.003
Maternal education						
≤ 8 years	770	53 (6.9)	2.2 (1.1 – 4.4)	0.02	2.4 (1.2 – 4.8)	0.02
> 8 years	312	10 (3.2)	1.0		1.0	
Desquamating rash						
No	725	32 (4.4)	1.0		1.0	
Yes	437	36 (8.2)	1.9 (1.2 – 3.2)	0.008	2.2 (1.3 – 3.6)	0.004

Measles seroprevalence is lower in HIV-infected than uninfected children after vaccination



Measles seroprevalence is lower in HIV-infected than uninfected children after vaccination

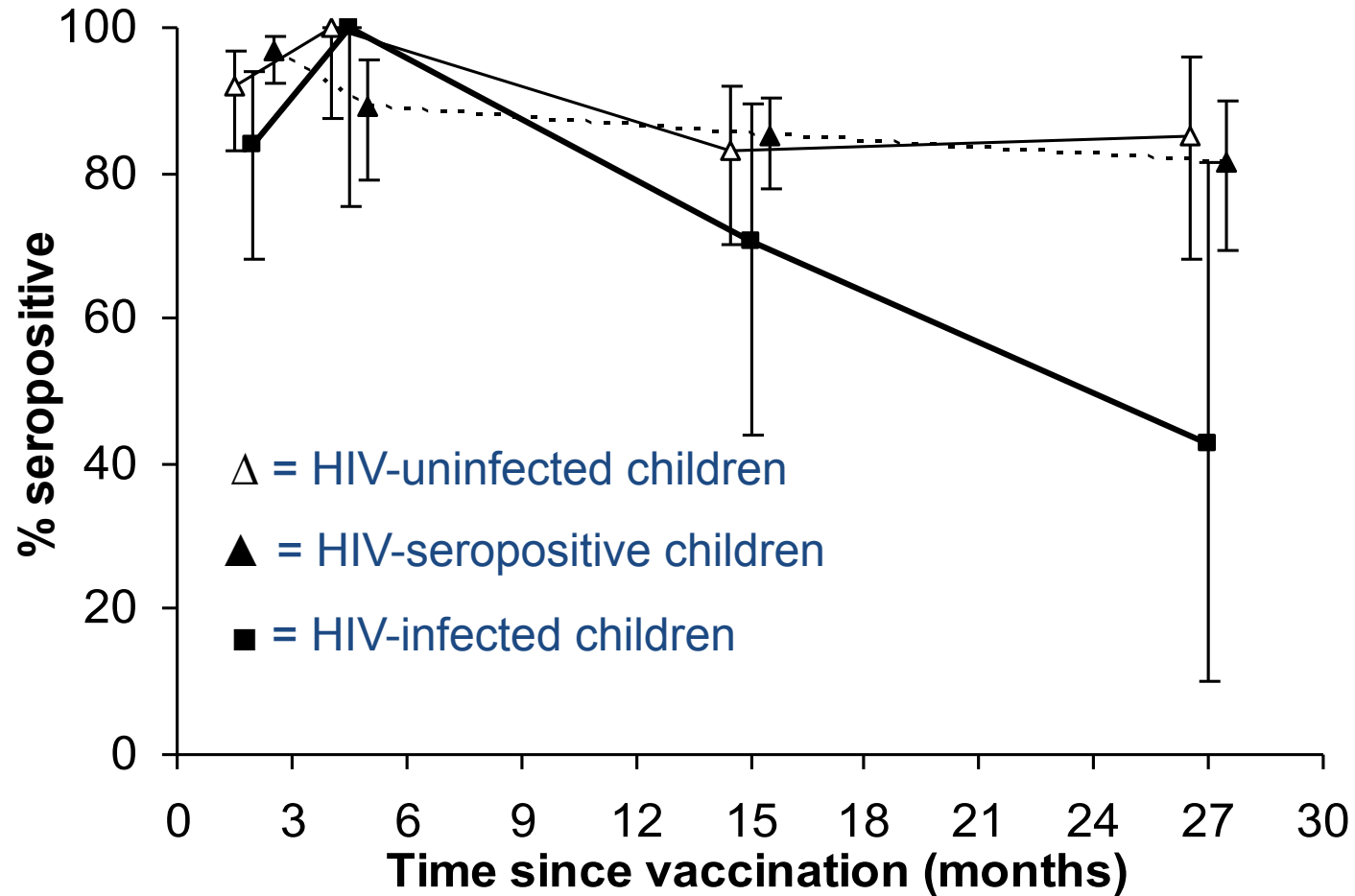


Measles seroprevalence is lower in HIV-infected than uninfected children after vaccination

Studies without comparison groups

Reference	Country	No. of children	HAART	Response to primary immunization
Oxotby 1989	Zaire	37	No	36% of 11 symptomatic 77% of 26 asymptomatic
Krazinski 1989	United States	8	No	25%
Palumbo 1992	United States	35	No	37%
Thaithumyanon 2000	Thailand	16	No	57%
Helfand 2008	Malawi	45	No	59%
Chandwani 2011	United States	15	No	67%
Abzug 2012	United States	193	Yes	52%
Rainwater 2013	Zambia	169	Yes	23%

Protective antibody levels wane in HIV-infected children not receiving HAART



Antiretroviral therapy improves responses to measles revaccination

Reference	Country	No. of children	Age	Response to repeat immunization
Berkelhamer 2001	United States	14	2-11 y	64%
Melvin 2003	United States	18	3-14 y	83%
Farquhar 2009	Kenya	18	NA	78%
Aurpibul 2007, 2010	Thailand	51	Mean, 10.2 y	90% after 1 mos 85% after 3 yrs
Abzug 2012	United States	193	2-19 yrs	89% at 8 weeks 80% at 80 weeks
Rainwater 2013	Zambia	19	9-60 mos	95% of children receiving HAART

Measles vaccine is safe in HIV-infected children

The evidence does not demonstrate a serious risk in using measles vaccine in HIV-positive children. Although millions of doses of measles vaccine have been administered to HIV-positive children, only 1 case report was identified that suggested possible severe adverse events following immunization. However, ascertainment of such events may be incomplete.

Global Advisory Committee on Vaccine Safety, report of meeting held 17-18 June 2009. *Weekly Epidemiological Record* 2009;84:325-32.

J Infect Dis 2011; 204 Suppl 1:S164-78.

Measles vaccine is safe in HIV-infected children

Measles vaccine is safe in HIV-infected children

Updated systematic review

11 of 14 cohort studies included reported on safety
9 distinct cohorts

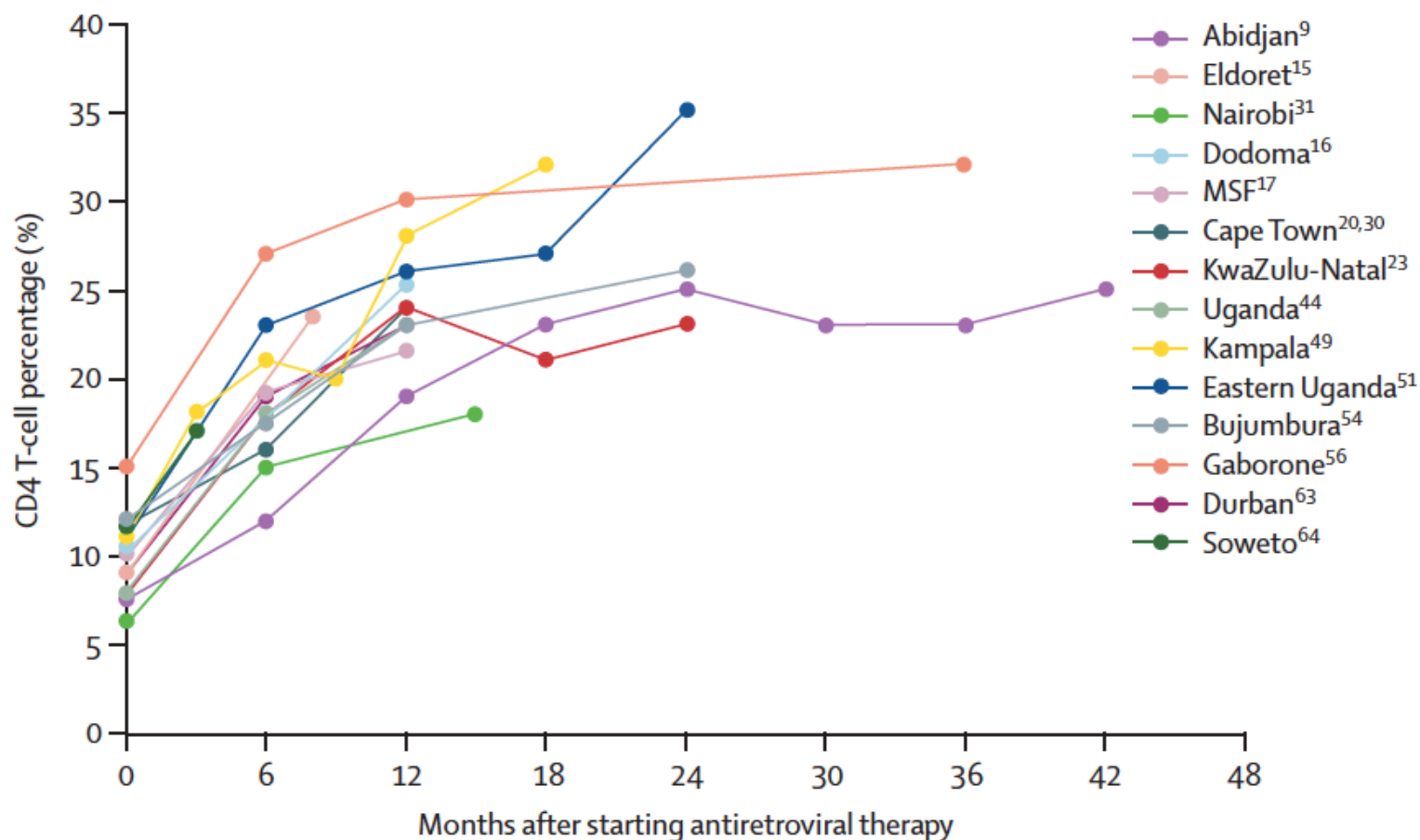
350 HIV-infected children vaccinated against measles

Deaths post-vaccination reported in 6 studies

58 deaths among 309 vaccinated HIV-infected children (18.8%)

no deaths were reported to be related to vaccination

Optimal timing of measles revaccination in relation to antiretroviral therapy



Revaccination of HIV-infected children should be programmatically feasible

HIV-infected children on ART receive intensive follow-up and care.

The care of HIV-infected children is typically delivered at specialized clinics and not at maternal and child health clinics.

Some HIV-infected children will be revaccinated against measles after immune reconstitution with antiretroviral therapy through SIAs and MCV2.

With increasing emphasis on early diagnosis and treatment of HIV-infected children, some children may start antiretroviral therapy prior to measles vaccination. These children may not require revaccination.

Key proposed recommendations

An additional dose of MCV should 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.

HIV-infected children who start HAART prior to the first dose of MCV may develop protective immunity to measles virus. Current evidence is insufficient to recommend revaccination of these children.

Key proposed recommendations

A supplementary dose of MCV should be considered shortly after diagnosis of HIV infection in children older than 6 months of age who are not receiving HAART, and for whom the risk of measles is high, to provide protection until they are revaccinated after immune reconstitution with HAART. This additional dose should be administered at least one month after a prior dose of MCV.

Long-term immune responses to measles vaccine should be monitored in HIV-infected children revaccinated after starting HAART and in HIV-infected children who start HAART prior to receiving their first dose of MCV.