PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga

REGIONE VENETO
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VERONA

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Dipartimento delle Dipendenze

Screening and treatment of HIV and drug related diseases among drug users: a scientific update

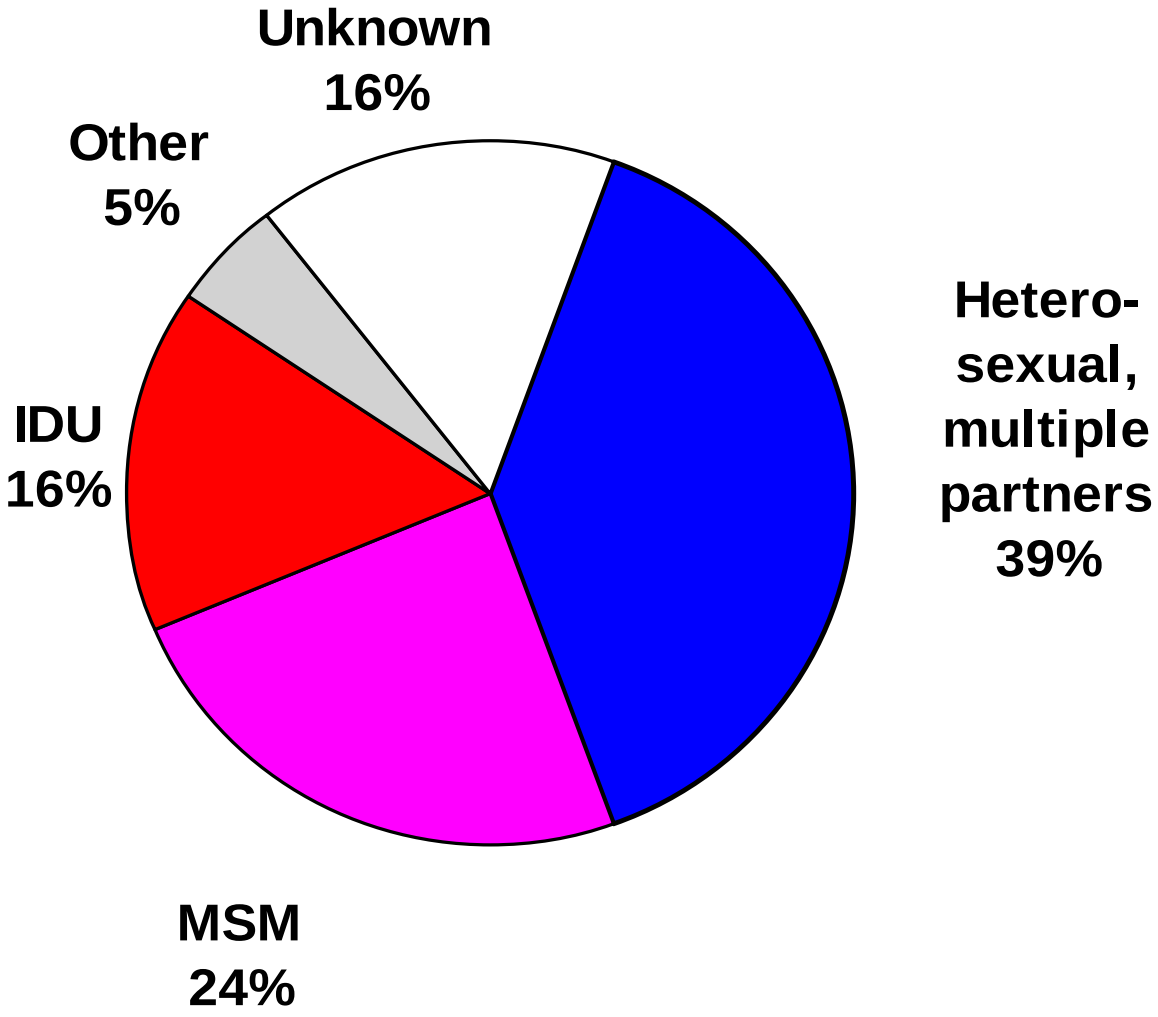
HBV vaccination in HIV infected patients and drug users

Mario Cruciani, MD

Verona 3rd April 2014

HBs antigen prevalence in 2000

Risk Factors for Hepatitis B



MMWR 2006;55(RR-16):6-7

Hepatitis B Vaccine in Immunocompetent

- **Composition** — **Recombinant HBsAg**
- **Efficacy** — **95% (Range, 80%-100%)**
- **Duration of Immunity** — **20 years or more**
- **Schedule** — **3 Doses**
- **Booster doses not routinely recommended**

Hepatitis B Vaccine Formulations

- **Recombivax HB (Merck)**
  - **5 mcg/0.5 mL (pediatric)**
  - **10 mcg/1 mL (adult)**
  - **40 mcg/1 mL (dialysis)**

- **Engerix-B (GSK)**
  - **10 mcg/0.5 mL (pediatric)**
  - **20 mcg/1 mL (adult)**

Twinrix

- Combination hepatitis A vaccine (pediatric dose) and hepatitis B (adult dose)
- Schedules
  - 0, 1, 6 months, or
  - 0, 7, 21- 30 days and a booster dose at 12 months
- Approved for persons 18 years of age and older

Prevaccination Serologic Testing

- Not indicated before routine vaccination of infants or children
- Recommended for
  - all persons born in Africa, Asia, the Pacific Islands, and other regions with HBsAg prevalence of 8% or higher
  - household, sex, and needle-sharing contacts of HBsAg-positive persons
  - HIV-infected persons
- Consider for
  - Groups with high risk of HBV infection (MSM, IDU, incarcerated persons)

Postvaccination Serologic Testing

- Not routinely recommended following vaccination of infants, children, adolescents, or most adults
- Recommended for:
  - Infants born to HBsAg+ women
  - Hemodialysis patients
  - Immunodeficient persons
  - Sex partners of persons with chronic HBV infection
  - Certain healthcare personnel

Vaccine 27 (2009) 17–22

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Serologic response to hepatitis B vaccine with high dose and increasing number of injections in HIV infected adult patients

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Study design

- Prospective and open-label trial in HIV-infected subjects being monitored in our center.
- Consecutive subjects tested seronegative for HBs antigen, anti-HBs and anti-HBc, and without a history of previous HBV vaccine were enrolled in the study.
- Patients with < 200 CD4/ul excluded
- 3 intramuscular (in the deltoid site) doses of HBVAXPRO^{TM} 40 ug/ml (Aventis Pasteur MSD Spa, Rome) with 1 month intervals.
- Initial non-responders (anti-HBs <10 IU/L) to the first 3 doses were given 1–3 additional monthly doses of vaccine.
- Anti-HBs titers measured 4 weeks after the 3rd dose, after each additional dose in non-responders, and at FU 12 and 24 months after the last vaccine dose.

Table 1
Baseline characteristics and demographics of the 92 enrolled patients.

Mean age, years ± SD (range)	41 ± 8 (27–75)
Male/female	61/31
Risk factors for HIV: number (%)	
MSM	38 (41)
Heterosexual	34 (37)
Drug addiction	13 (14)
Other/unknown	7 (8)
Median CD4 count at time of vaccination, cells/μL (range)	533 (219 –1298)
Nadir of CD4, median cells/μL (range)	286 (2–730)
Median RNA viral load at time of vaccination, copies/mL (range)	<100 (<100–814,560)
Stage of HIV disease according to the CDC classification system, number (%)	
A1	31 (33.6)
A2	25 (27.1)
A3	2 (2.1)
B1	7 (7.6)
B2	21 (22.8)
B3	1 (1.0)
C1	2 (2.1)
C2	1 (1.0)
C3	1 (1.0)
Number of patients (%) on HAART	74 (80)

Flow diagram of the study in HIV

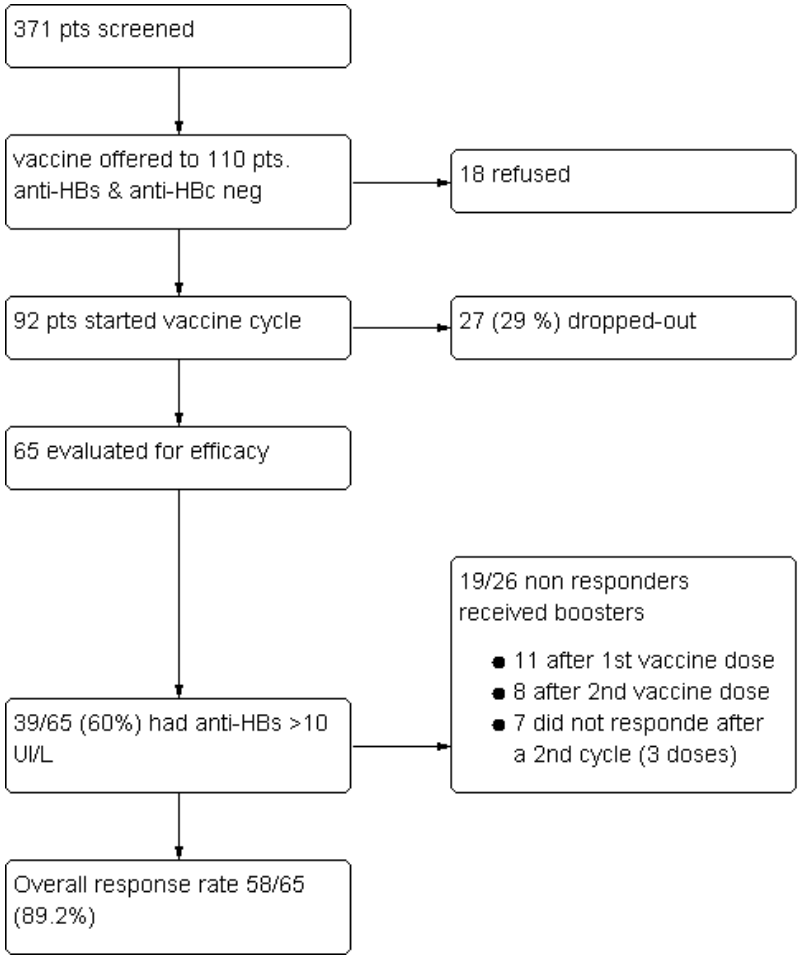


Table 2
Multivariate analysis of factors related to outcome of HBV vaccination. The overall significance of the model is confirmed by likelihood ratio χ^2 (3 d.o.f.) = 15.93, p-value = 0.0012.

	OR	Standard error	z	p-value	(95% confidence interval)
Gender (male)	0.198	0.147	−2.18	0.03	0.046–0.851
CD4 count	1.485	0.260	2.26	0.024	1.053–2.093
Viral load	0.264	0.166	−2.11	0.035	0.077–0.910

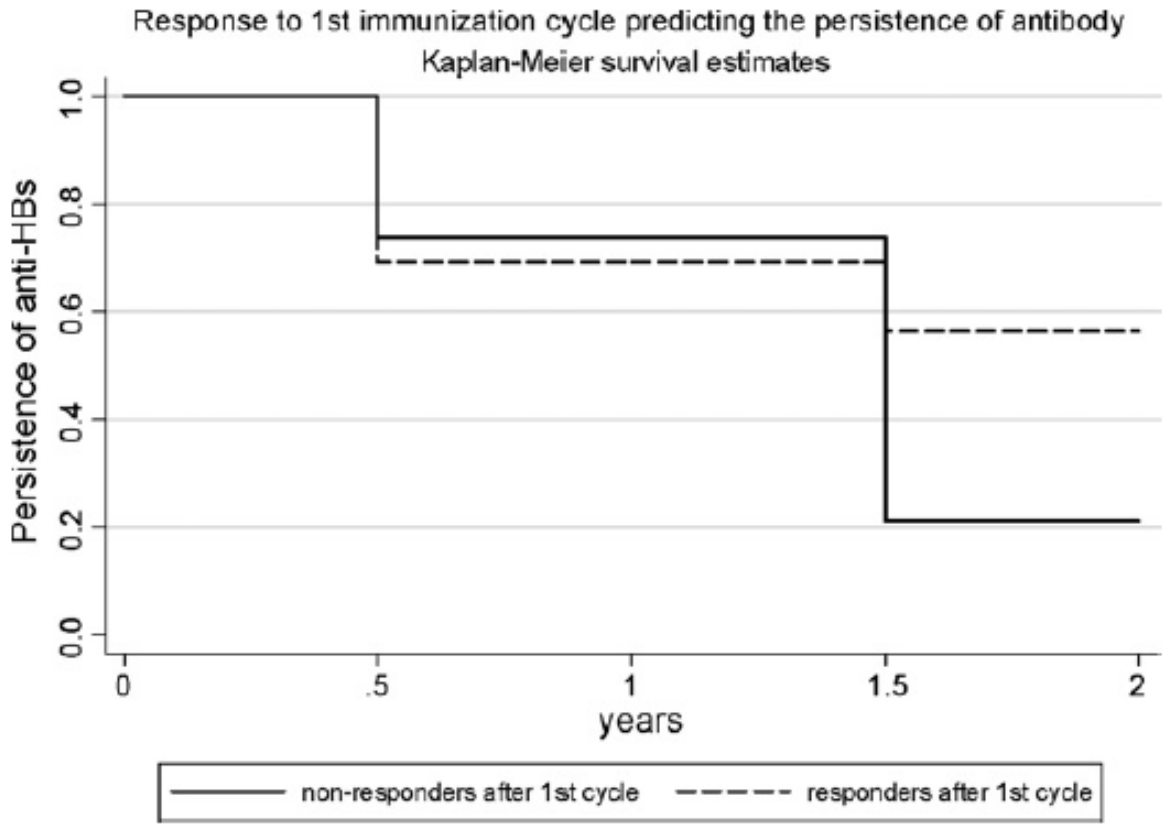


Fig. 1. Time to loss of seroprotective HBs antibody titers by Kaplan-Meier survival analysis between responders after the 1st cycle of vaccination and non-responders after the 1st cycle receiving boosts. $p = 0.05$ by log-rank test for equality of survivor functions.

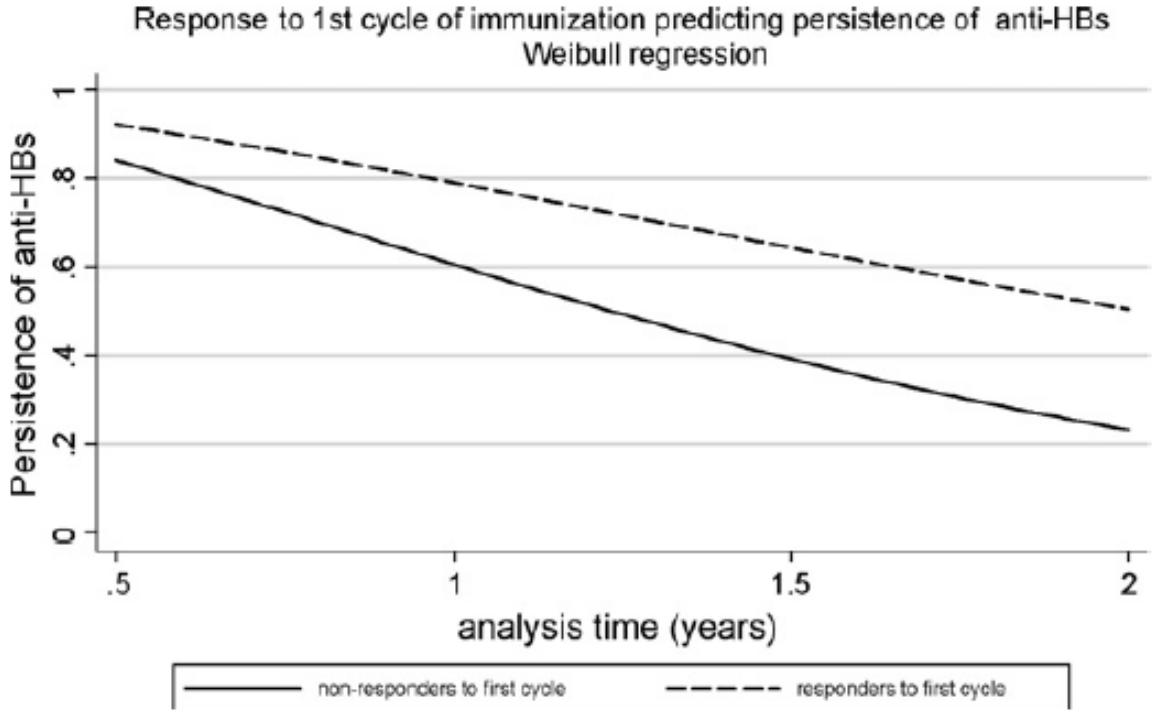


Fig. 2. Weibull regression showing persistence of the anti-HBs antibodies during the follow-up after a succesful HBV vaccination. Antibody titre is expressed as UI/L. In this regression analysis, the dependent variable was the time from seropositive status to seronegative reversion, whereas the explanatory variable was the response to the first cycle of the immunization process. This response was categorical (1 or 0). The group of non-responders to first vaccination cycle loses the antibodies in an accelerated way compared to the group of responders to the first vaccination cycle, and this difference was statistically significant ($p = 0.037$).

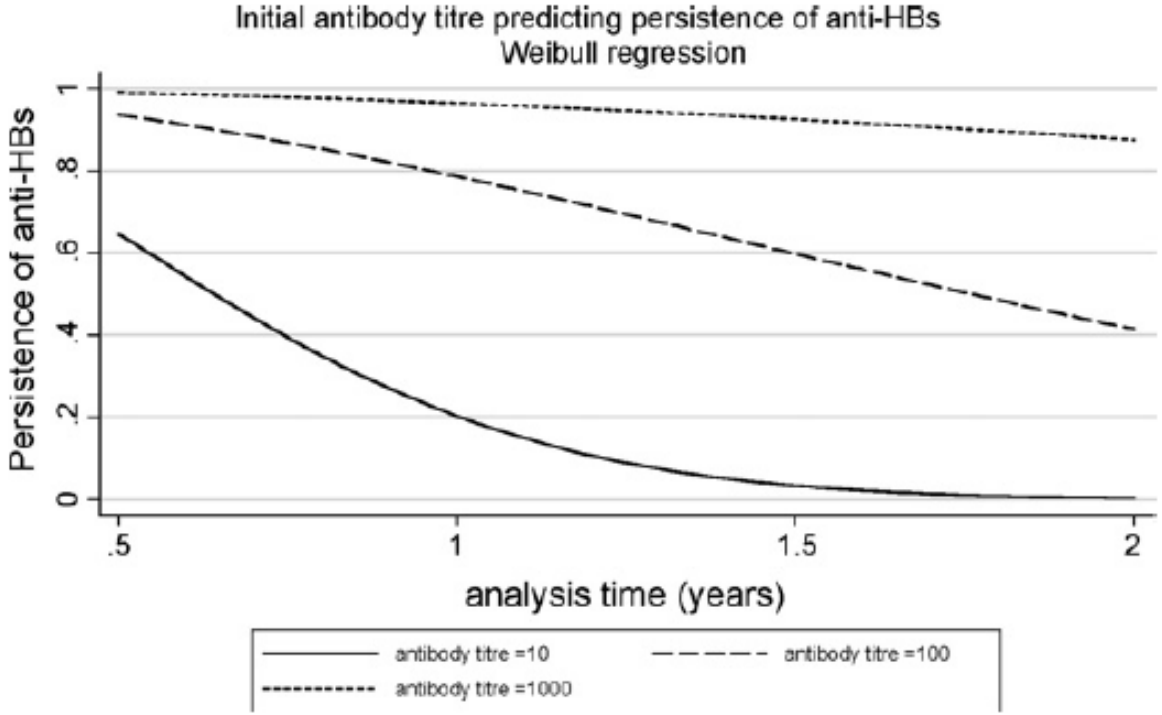
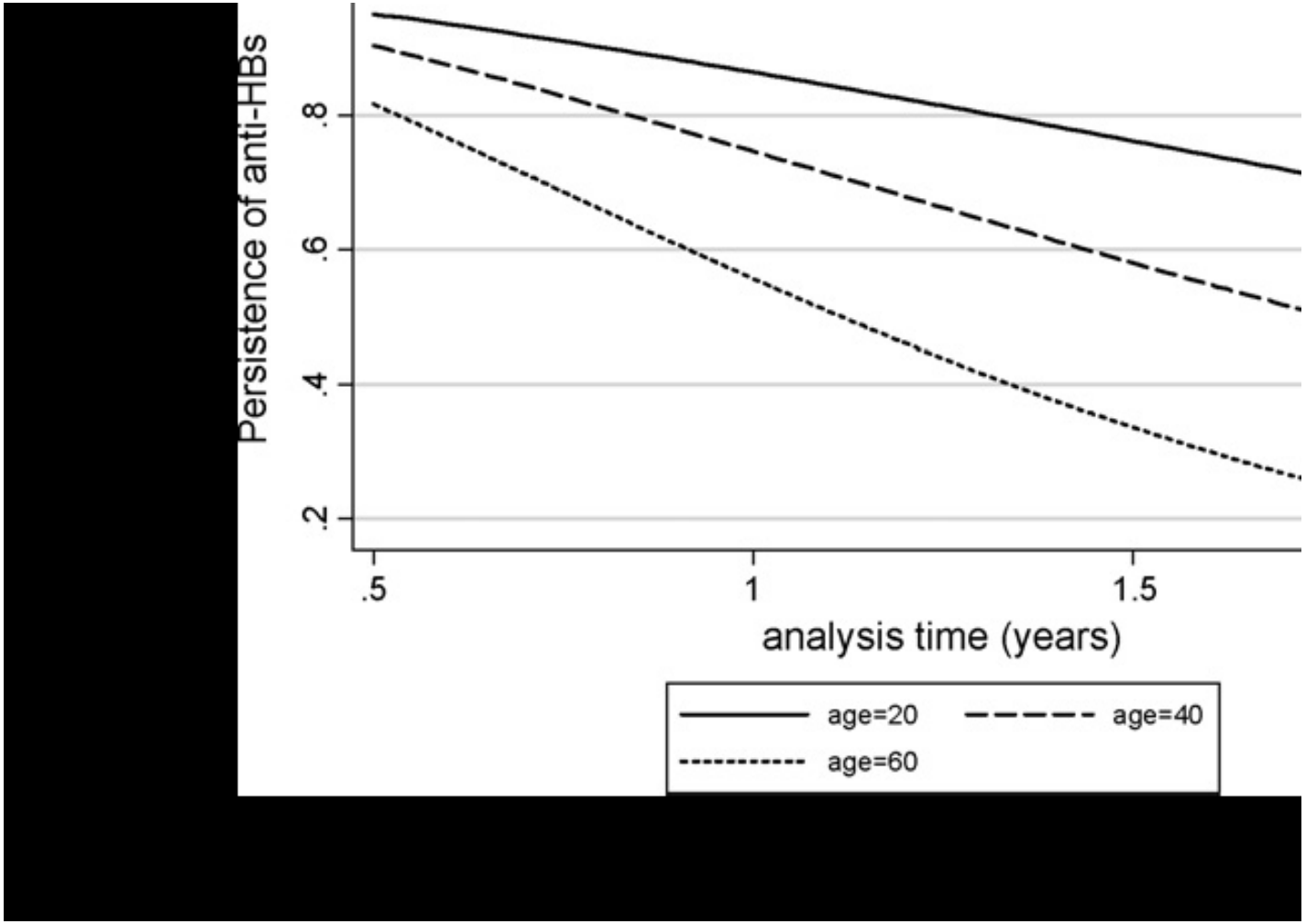


Fig. 3. Weibull regression showing persistence of the anti-HBs antibodies during the follow-up after a succesful HBV vaccination. Antibody titre is expressed as UI/L. In this regression analysis, the dependent variable was the time from seropositive status to seronegative reversion, whereas the explanatory variable was the antibody titre after the completion of the immunization process. This titre was preliminarly converted to its decimal logarithm. The group of low antibody producers after the immunization procedure completion loses the antibodies in an accelerated way, and this difference was statistically significant ($p < 0.0001$).


Persistence of anti-HBs
.2
.4
.6
.8
.5
1
1.5
analysis time (years)
age=20
age=40
age=60

Anti-HBs response rate at Follow-up

Responders (58)

- 1 yr FU: 41/58 (70.6%);
- 2 yrs FU: 19/58 (32.7%)

All evaluable (65)

- 1 yr FU: 41/65 (63.0 %)
- 2 yrs FU: 19/65 (29.3 %)

HIV/AIDS INVITED ARTICLE

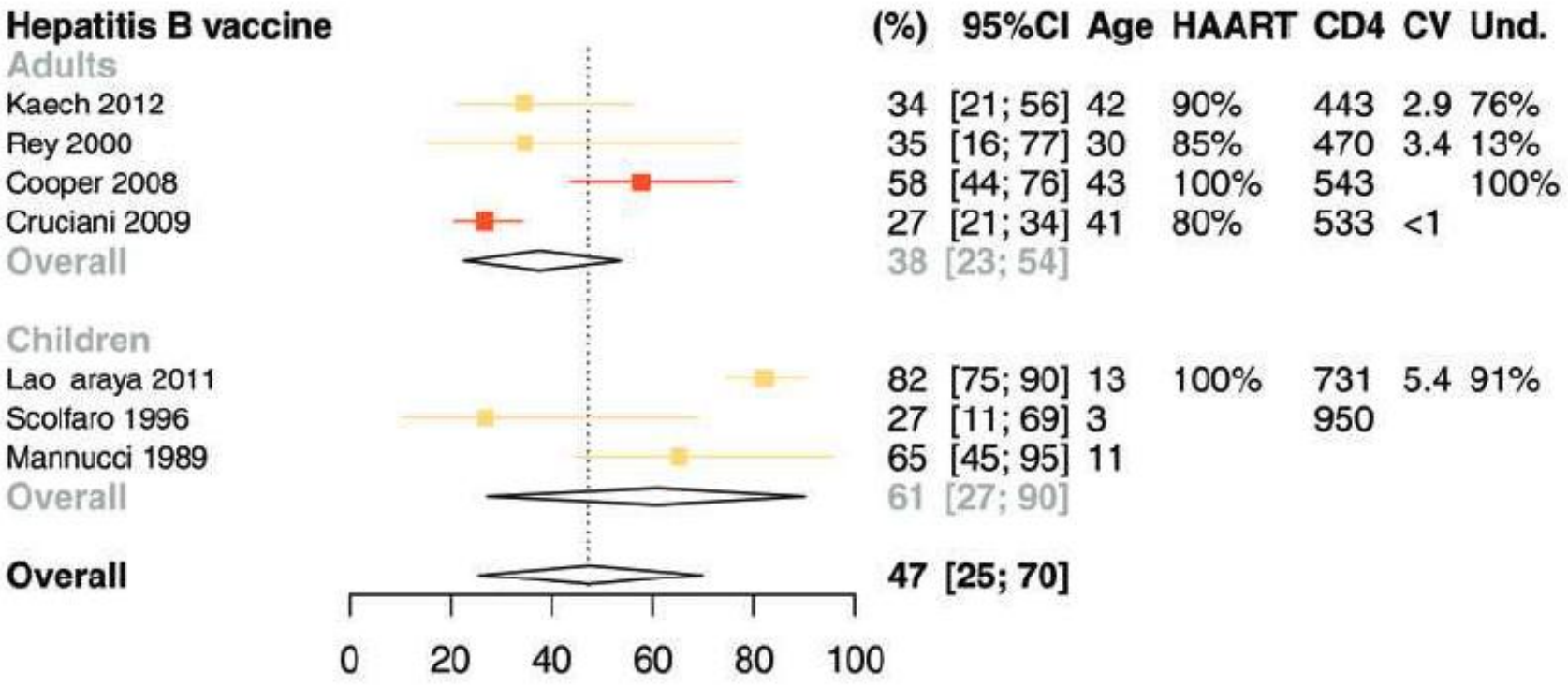
Kenneth H. Mayer, Section Editor

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]

Clinical Infectious Diseases 2014;58(8):1130–9

Percentage of Seroprotection at 2 yrs FU (Kerneis et al, CID 2014)



IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

Lorry G. Rubin,[1] Myron J. Levin,[2] Per Ljungman,[3,4] E. Graham Davies,[5] Robin Avery,[6] Marcie Tomblyn,[7] Athos Bousvaros,[8] Shireesha Dhanireddy,[9] Lillian Sung,[10] Harry Keyserling,[11] and Insoo Kang[12]

IDSA guidelines 2013: Hep B vaccine in HIV infected

59. HIV-infected patients should receive the HepB vaccine series (strong, moderate), with consideration of high-dose HepB vaccine (40 μg/dose) for adults (weak, moderate) and adolescents* (weak, low). One to 2 months after completion, patients should be tested for anti-HBs (antibodies to HepB surface antigen; strong, low). If a postvaccination anti-HB concentration of ≥10 mIU/mL is not attained, a second 3-dose series of HepB vaccine (strong, low; alternative: 1 dose of HepB vaccine after which anti-HBs is tested*), using standard dose (strong, moderate) or high dose (40 μg*; weak, low) for children and high dose for adolescents* and adults (strong, low), should be administered.

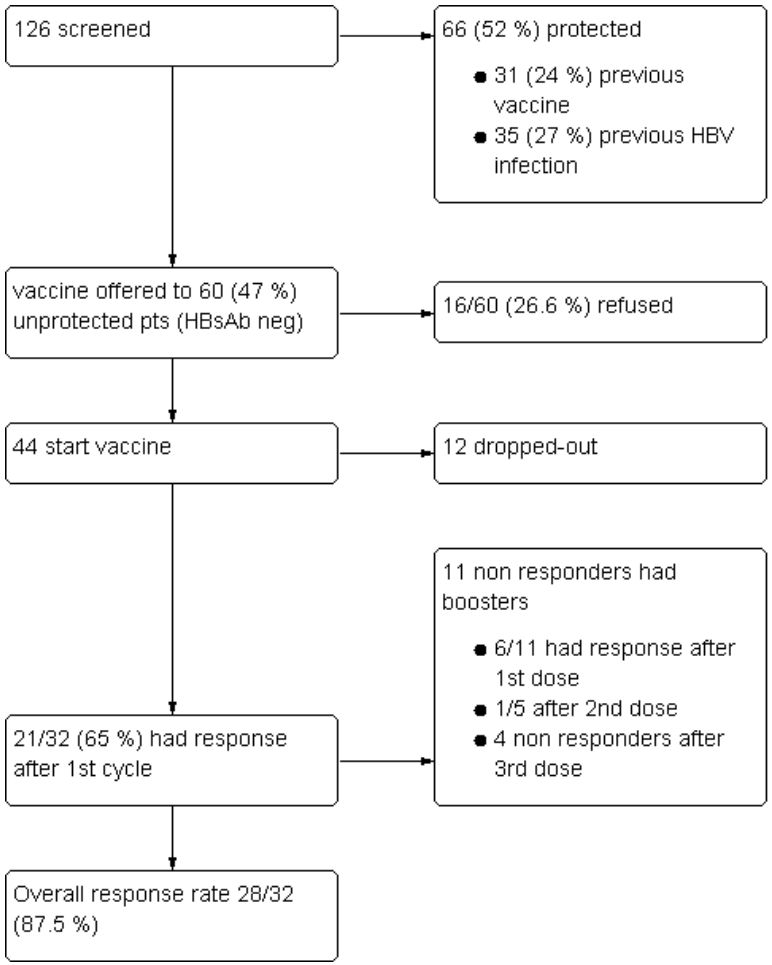
Conclusions. HBV vaccine in HIV pts.

- Role of high dose vaccine need to be confirmed in well designed RCTs.
- Booster doses increase significantly response rate
- Duration of anti-HBs response strongly correlates with anti-HBs titers at the end of vaccine cycle(s)

2. HBV vaccine in the Verona drug addiction service: a 2009-2010 cohort study

- A prospective cohort study among problem drug (PWID and PWUD) users followed at the DAS
- Only HIV-negative patients included
- Standard (HBVAXPRO 10 mcg/ml), accellerated (0, 1 & 2 m.) schedule.
- Boosters (1-3) in non responders

Flow diagram of the vaccine study in a cohort of Problem drug users in Verona Drug Addiction Service



Conclusion. HBV vaccine in PDU

- **50 % Problem Drug Users in DAS at risk for HBV**
- **Screening and Vaccine protocols still important in Italy (and elsewhere)**
- **Rate of response after a standard vaccine schedule ~ 65 %.**
- **1 additional booster dose increases consistently response rate (~10 % of total population; 50 % of non responders to standard cycle)**