Anti-HBcore screening of blood donors: pros and cons

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Transfusion Transmitted Infections
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Disclosure of interests of Hans Zaaijer

- No consultancy, no advisory boards, no shares,
  or other interests in companies.
- Sometimes I am paid for lectures by non-profit organizations.
- My lectures for commercial organizations are always unpaid.

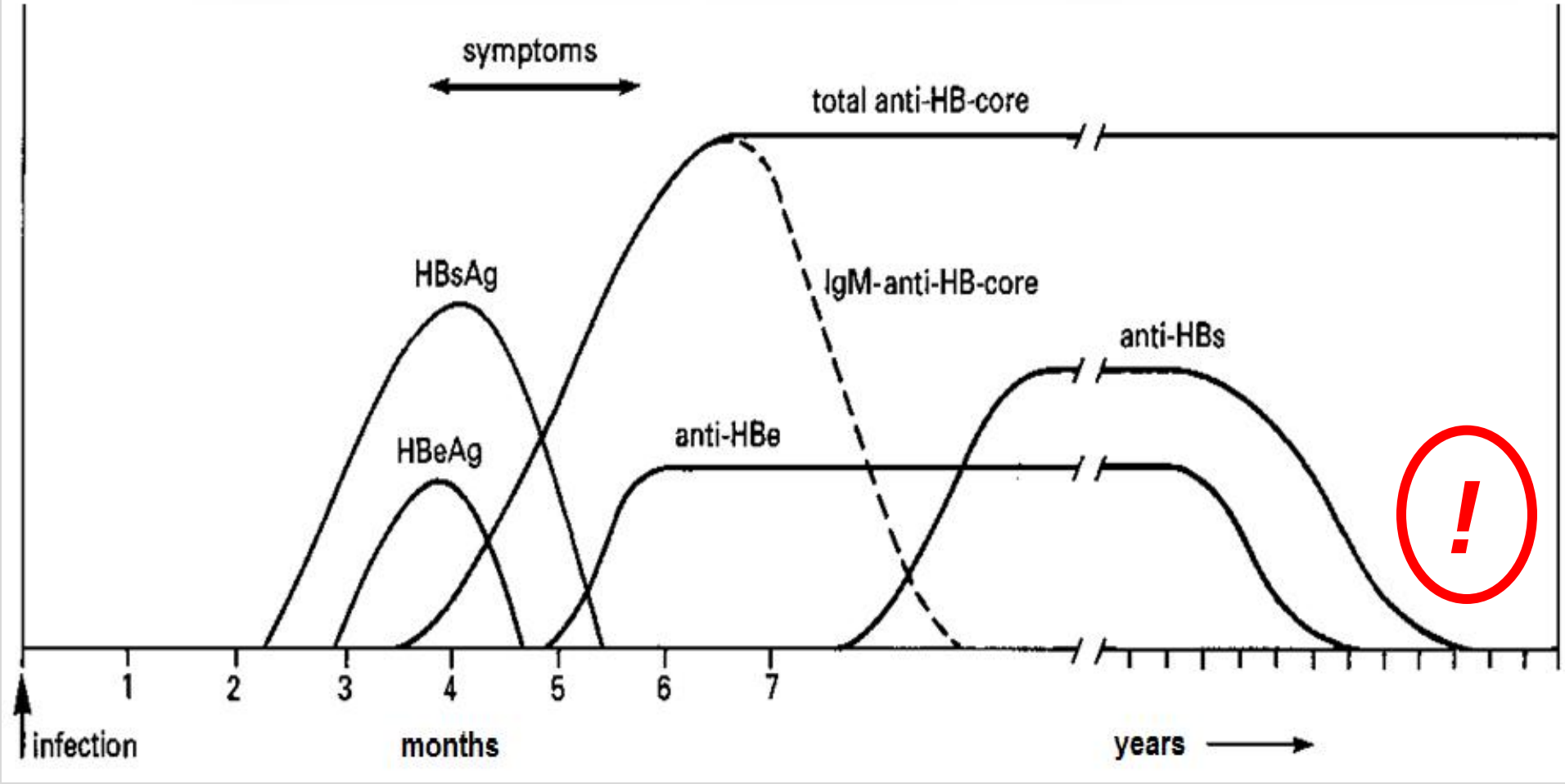
Overview of my lecture

1) Brush up your hepatitis B:
   - HBV serology.
   - Latent (occult) HBV infection.

2) HBV-DNA and anti-HBcore donor screening in Holland.

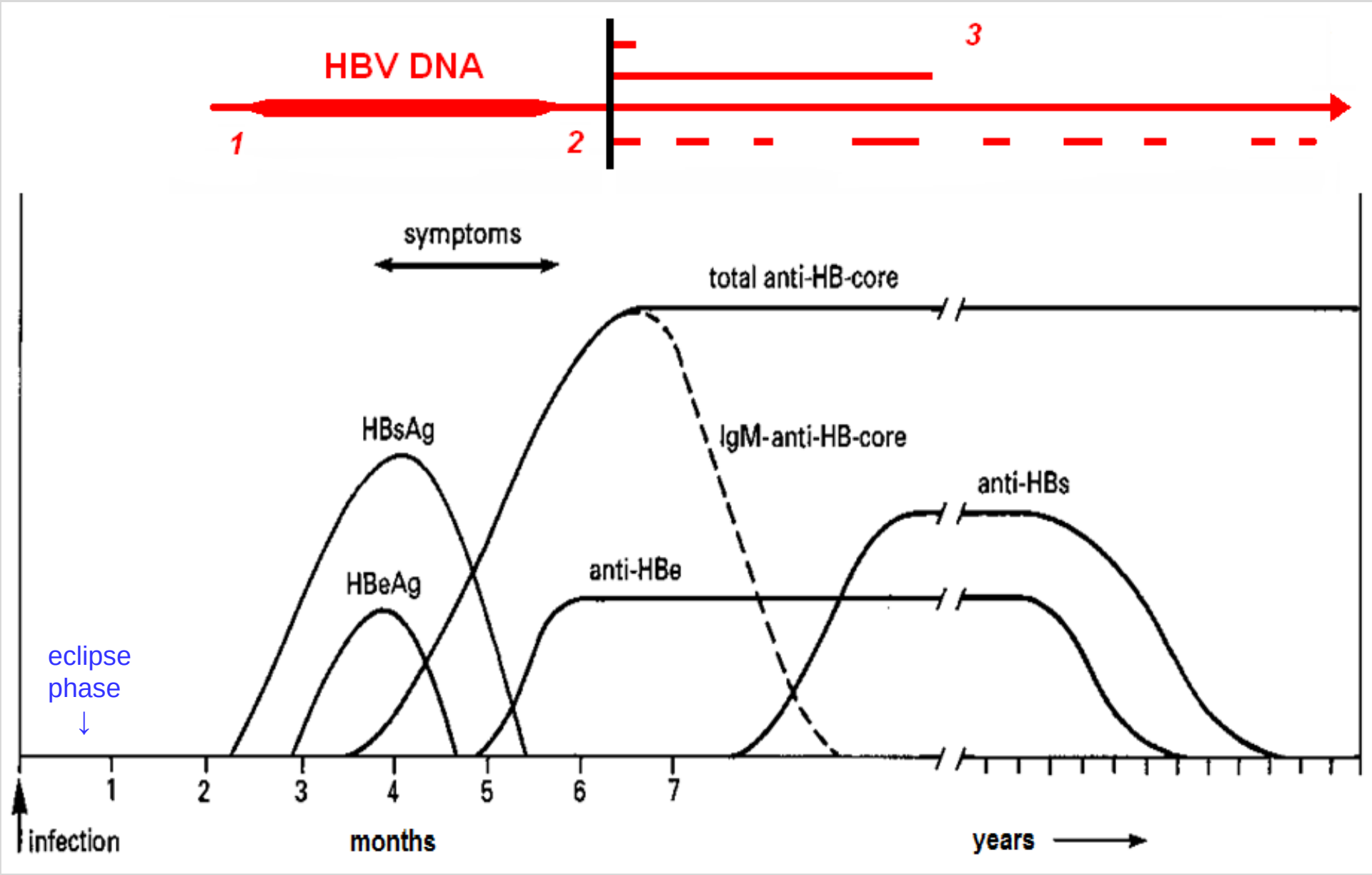
3) Conclusion, (dis)advantages of anti-HBcore donor screening.

HBV serology in acute, resolving infection



1,2,3: HBV DNA = pos and HBsAg = neg

3 = latent / occult HBV infection



After resolved hep.B, 3 possibilities:

1) Truly cleared infection

No HBV genomes left in the liver.

2a) Latent infection

HBsAg and HBV-DNA = negative

but some hepatocytes contain HBV genomes

(latent infection)

2b) Occult infection

HBsAg = neg. (≥ 6 months) and HBV-DNA = pos.

depends on sensitivity of your HBV PCR.

Detection of stages of HBV infection

	HBV PCR	HBsAg	a-core
eclipse phase	–	–	–
very early acute infection	+	–	–
acute infection	+	+	–/+
late acute infection	+	–	+
latent/occult infection	–/+	–	+
chronic HBV infection	+	+	+
vaccine suppressed infection	+	–	–

Detection of stages of HBV infection

	HBV PCR	HBsAg	a-core
eclipse phase	–	–	–
very early acute infection	+	–	–
acute infection	+	+	–/+
late acute infection	+	–	+
latent/occult infection	–/+	–	+
chronic HBV infection	+	+	+
vaccine suppressed infection	+	–	–

we all screen donations for HBsAg,

if you add anti-HBcore donor screening:

- you prevent all HBV transmissions by 'occult' donors.
  Higher yield if many donors had HBV infection in the past.
  ▸estimate yield from acore+ prevalence in donor population.

if you add HBV PCR donor screening:

- you prevent part of HBV transmissions by occult donors (NAT pool size!)
- you detect vaccine suppressed HBV infections.
  ▸how many donors are vaccinated? how many encounter HBV?
- you detect earlier stage of HBV infection.
  ▸what is incidence of acute hep.B in your donor population?

Estimate costs and benefits, otherwise maybe: safety ↑ , costs ↑↑↑

Donor loss by anti-HBcore screening

"More HBV in your population → more donor loss".
More transmissions prevented by aHBcore screening!

in my opinion, donor 'loss' is limited to:

1) False-positive aHBcore reactivity: low, fixed % of donorpop.
2) True aHBcore-positive donors with anti-HBs <200 IU/L (or 100?)

The majority of truly aHBcore-positive donors have high levels of anti-HBs and can donate safely, they are not lost.

By the way, I propose:
defer donors who (truly) seroconvert for aHBcore during their donor career, independent of aHBs. Risky behavior! Next time it may be HIV or HCV.

HBV screening of blood donors in Holland

1973 - HBsAg

2008 - HBV-DNA (2006: plasma pools)

2011 - anti-HBcore

What is the yield of HBV-DNA screening? (without anti-core screening)

Surface antigen-negative hepatitis B virus infection in Dutch blood donors

R. W. Lieshout-Krikke · M. W. A. Molenaar-de Backer · P. van Swieten · H. L. Zaaijer

Eur J Clin Microbiol Infect Dis

July 2006 – June 2011 in the Netherlands

4.400.000 donations screened for HBV-DNA,

23 donors: HBsAg-neg & HBV-DNA pos:

15 donors with chronic occult HBV infection.

Low HBV DNA loads: 9x pos <15 IU/mL, 2x pos <20 IU/mL,
20, 23, 33, 220 (8 days after index) IU/mL.

anti-HBs: 8x neg and 7x 10-100 IU/L: 13, 14, 23, 31, 32, 65, 86 IU/L.

> Occult HBV DNA loads are very low, NAT misses many occult infections.

4 donors with early infection, pre-seroconversion.

3 donors with vaccine suppressed infection.

intermezzo

1 donor with HBV genotype G

HBsAg-negative mono-infection with hepatitis B virus genotype G

H. L. Zaaijer,[1,2] H. J. Boot,[3] P. van Swieten,[4] M. H. G. M. Koppelman[5] and H. T. M. Cuypers[4]
[1]Department of Blood-borne Infections, Sanquin, Amsterdam; [2]Clinical Virology (CINIMA), Academic Medical Center, Amsterdam; [3]Laboratory for Infectious Disease and Screening, National Institute for Public Health and the Environment (RIVM), Bilthoven; [4]Virology Department, Sanquin, Amsterdam; and [5]National Screening Laboratory, Sanquin, Amsterdam, the Netherlands

Journal of Viral Hepatitis, 2011

Intermezzo: ‘vaccine break through'

I think HBV vaccination protects via 2 mechanisms:

1) Initially, as long as anti-HBs is ++ :
incoming viruses are neutralised before they can infect hepatocytes.

2) When anti-HBs has waned: incoming viruses infect some hepatocytes. Replication starts.
Immune system is activated, infected cells are cleared, HBV infection is aborted.
(serology: HBsAg= neg; HBV-DNA = pos; anti-core conversion, and anti-s ↑).
This should be called 'vaccine suppressed infection', not 'vaccine break through'.

All follow-up studies of HBV-vaccinated populations show silent anti-core conversions. No disease or secundary transmission.

HBV vaccination protects against disease, seks. transmission, and chronic infection; not against silent HBV infection.

'vaccine failure' = *clinical* hep.B after vaccination. Very rare.

How infectious are occult donations?

Rare transmission of hepatitis B virus by Dutch donors with occult infection

Ryanne W. Lieshout-Krikke,[1] Marian G.J. van Kraaij,[2] Fikreta Danovic,[2] and Hans L. Zaaijer[1]

Transfusion 2016; 56(3): 691-8

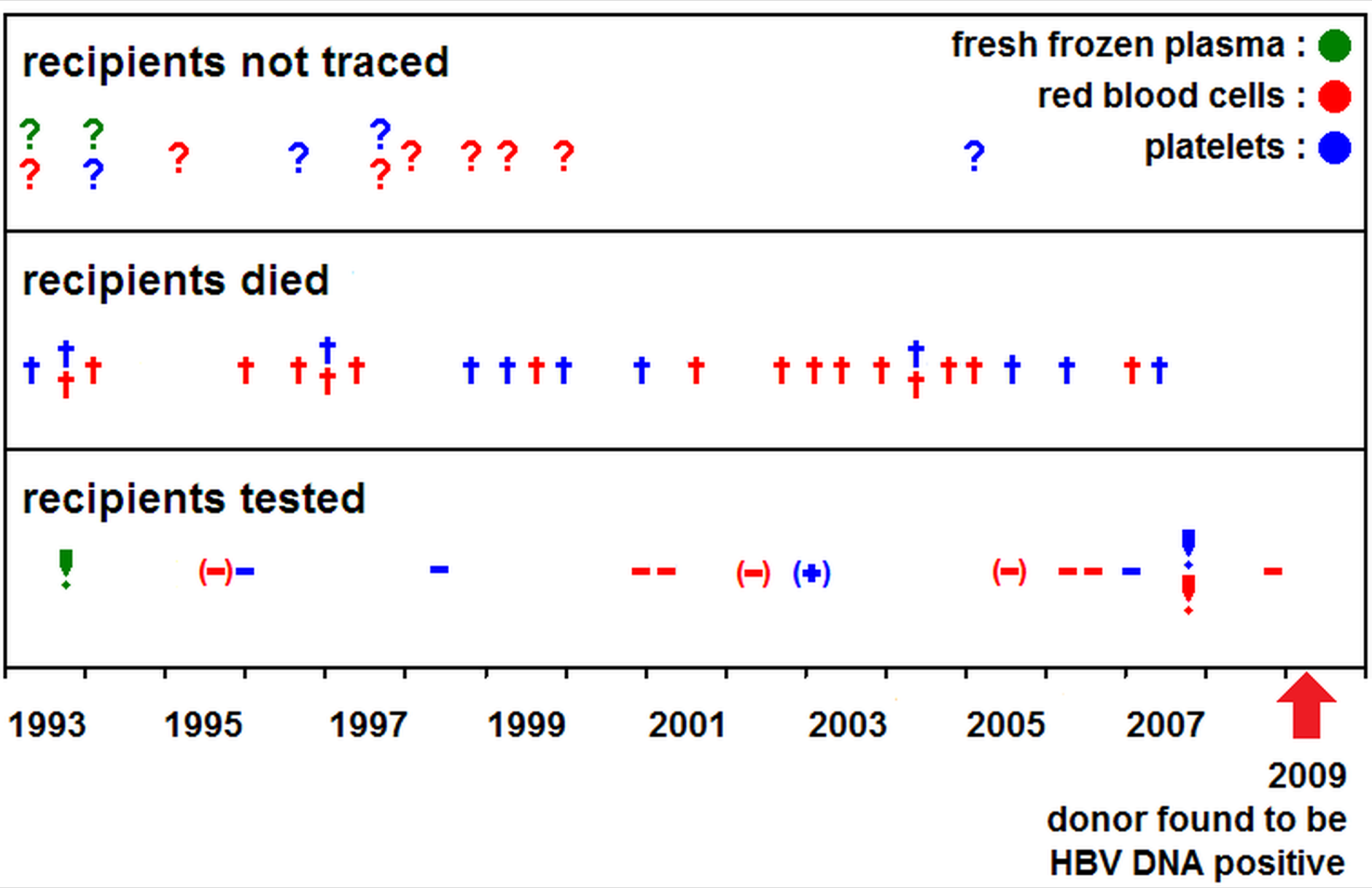
HBV status of 80 transfusion recipients of 14 OBI donors (Occult hepB infection)

74 recipients testing negative		6 recipients with current or past HBV infection	
no present HBV infection (HBsAg neg)	74/74	4 present infection	**3 associated with same donor** 1 infected before transfusion
no past infection	**52/74 a-HBc neg** 21/74 a-HBc status unknown	2 past infection	**1 associated with a donor** 1 other risk factors

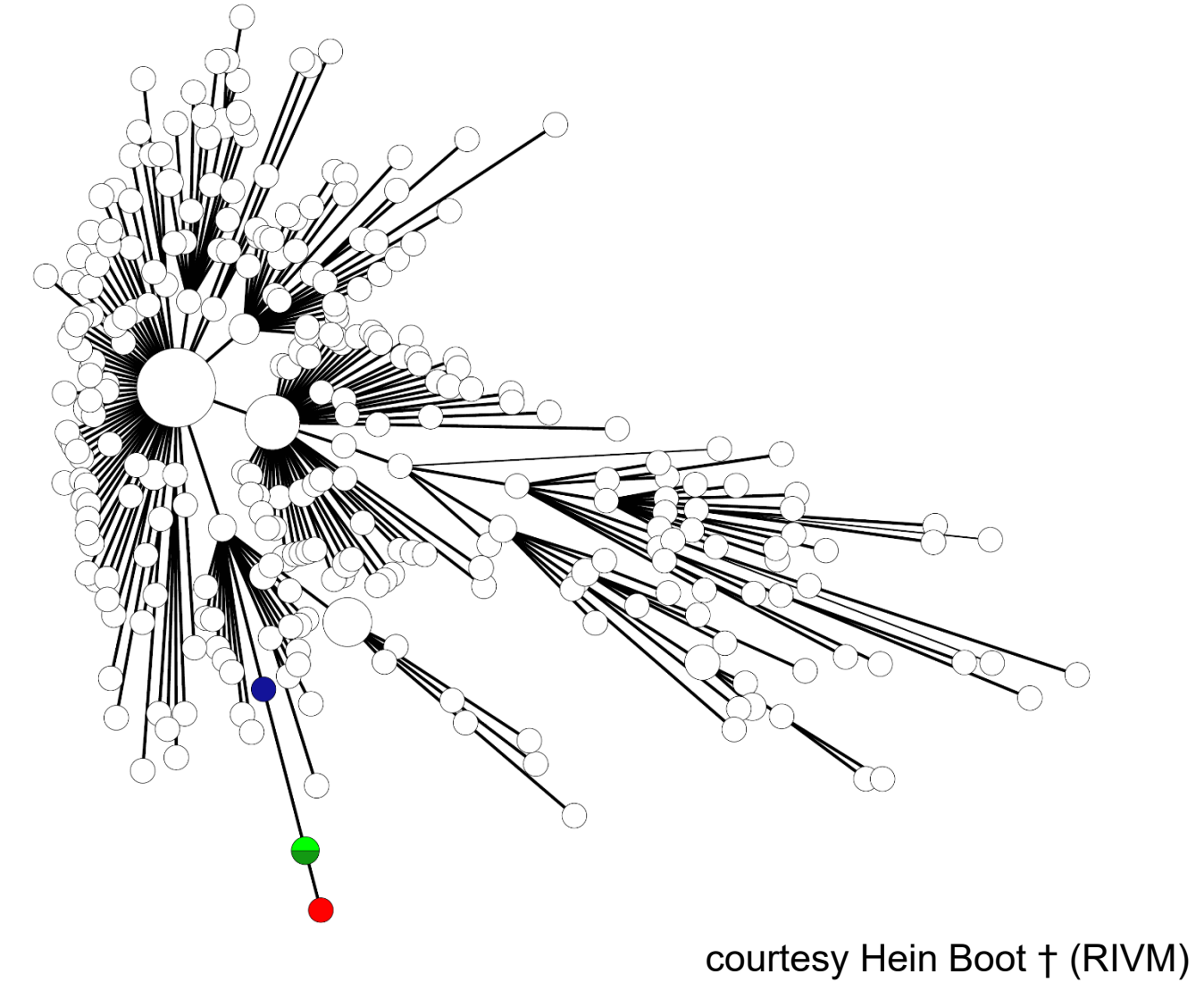
5% (4/80) of OBI exposed patients were infected.

we assume: occult donors are not infectious if their anti-HBs ≥ 200 IU/L

3 recipients HBV infected by 1 occult donor



Minimum spanning tree, showing HBV surface gene sequences of donor X (red), patient A, patient B, and patient C (blue); and 375 contemporary Dutch cases of hepatitis B (RIVM State Institute)



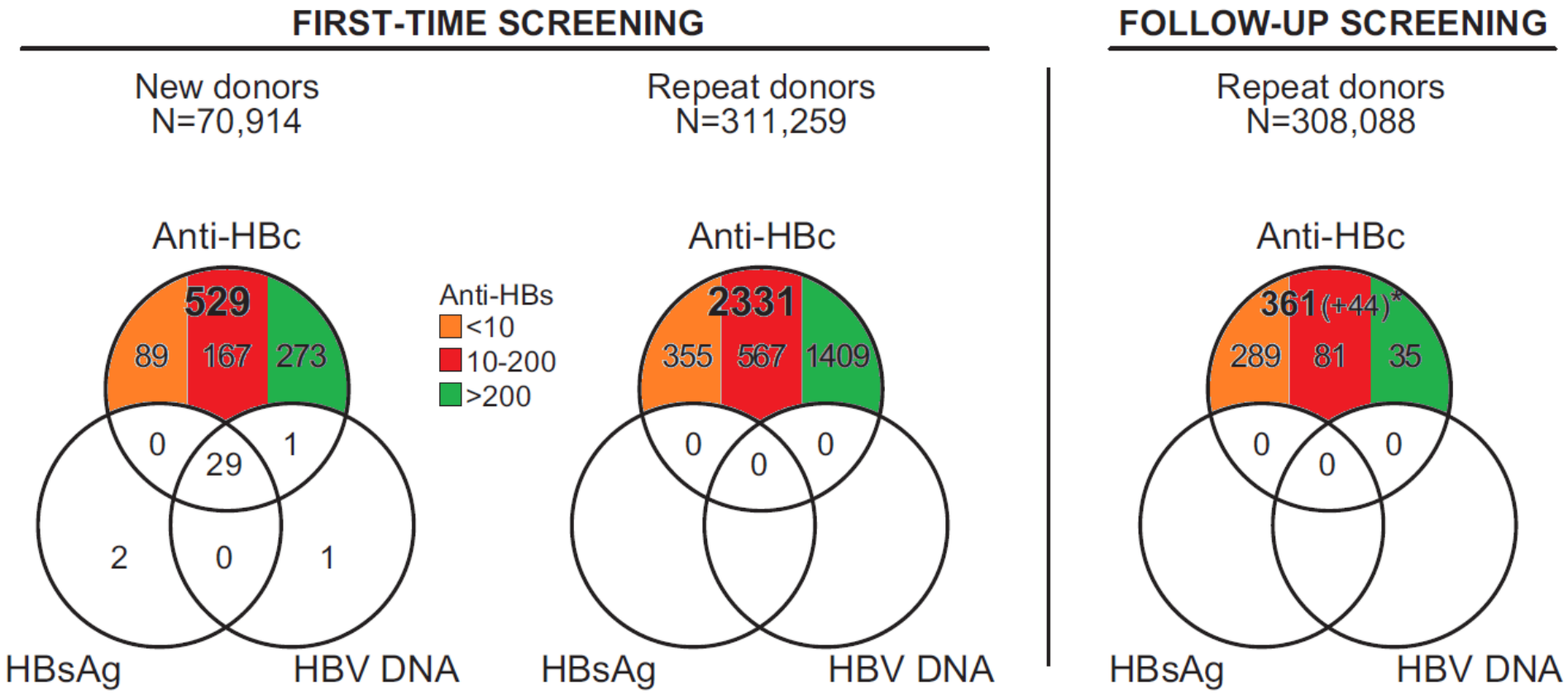
for detection of occult HBV donations,
anti-HBcore screening is more sensitive than HBV NAT.

but:

How many donors do you loose
by anti-HBcore screening?

in the Netherlands, overall:
2,1 % anti-core positive; 0,2% HBsAg positive

anti-HBcore screening in NL, July 2011 – July 2013

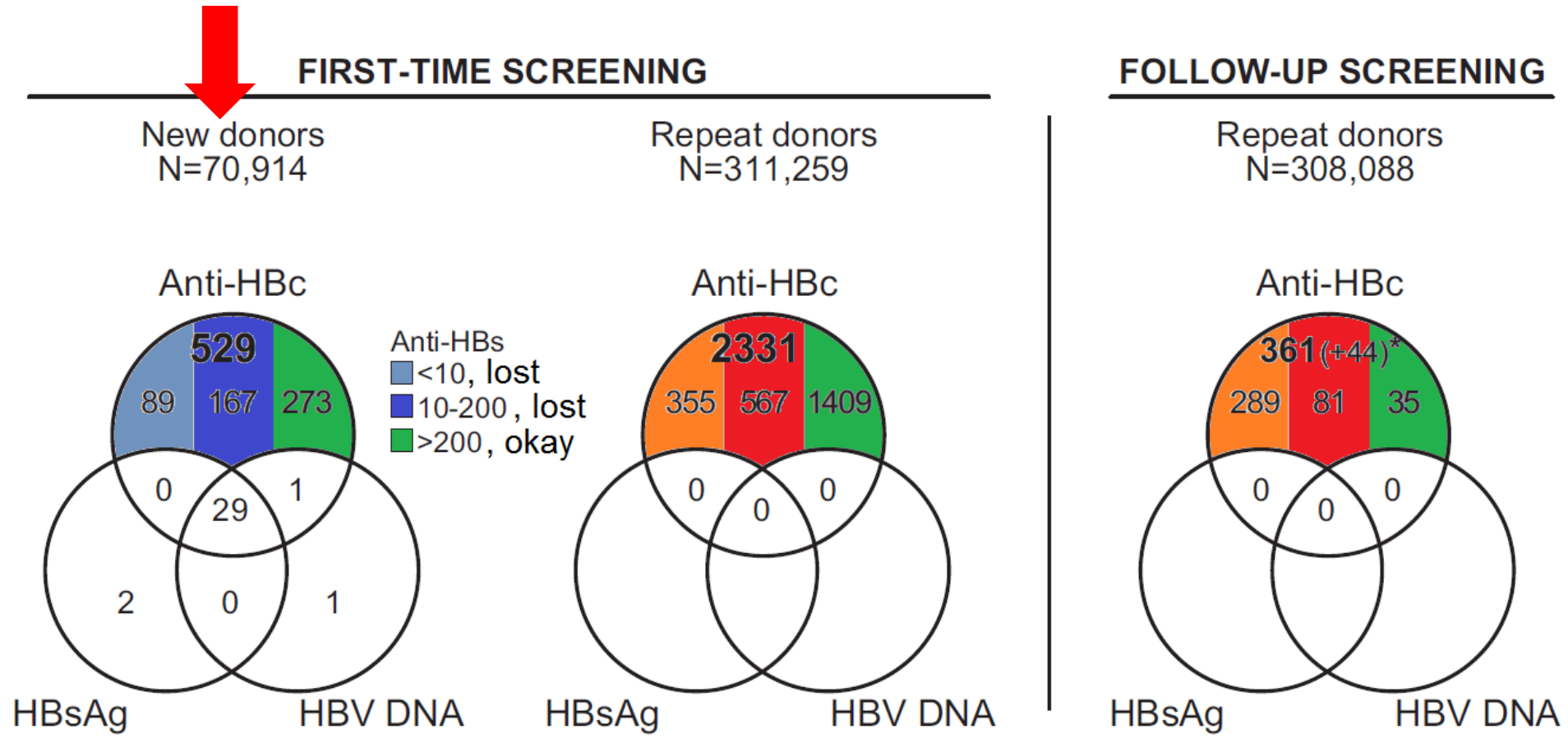


The yield of universal antibody to hepatitis B core antigen donor screening in the Netherlands, a hepatitis B virus low-endemic country

Thijs J. van de Laar,[1,2] Tanneke Marijt-van der Kreek,[3] Marijke W. Molenaar-de Backer,[1,2] Boris M. Hogema,[1,2] and Hans L. Zaaijer[1,4]

Transfusion 2015, 55(6): 1206-13

anti-HBcore screening in NL, July 2011 – July 2013

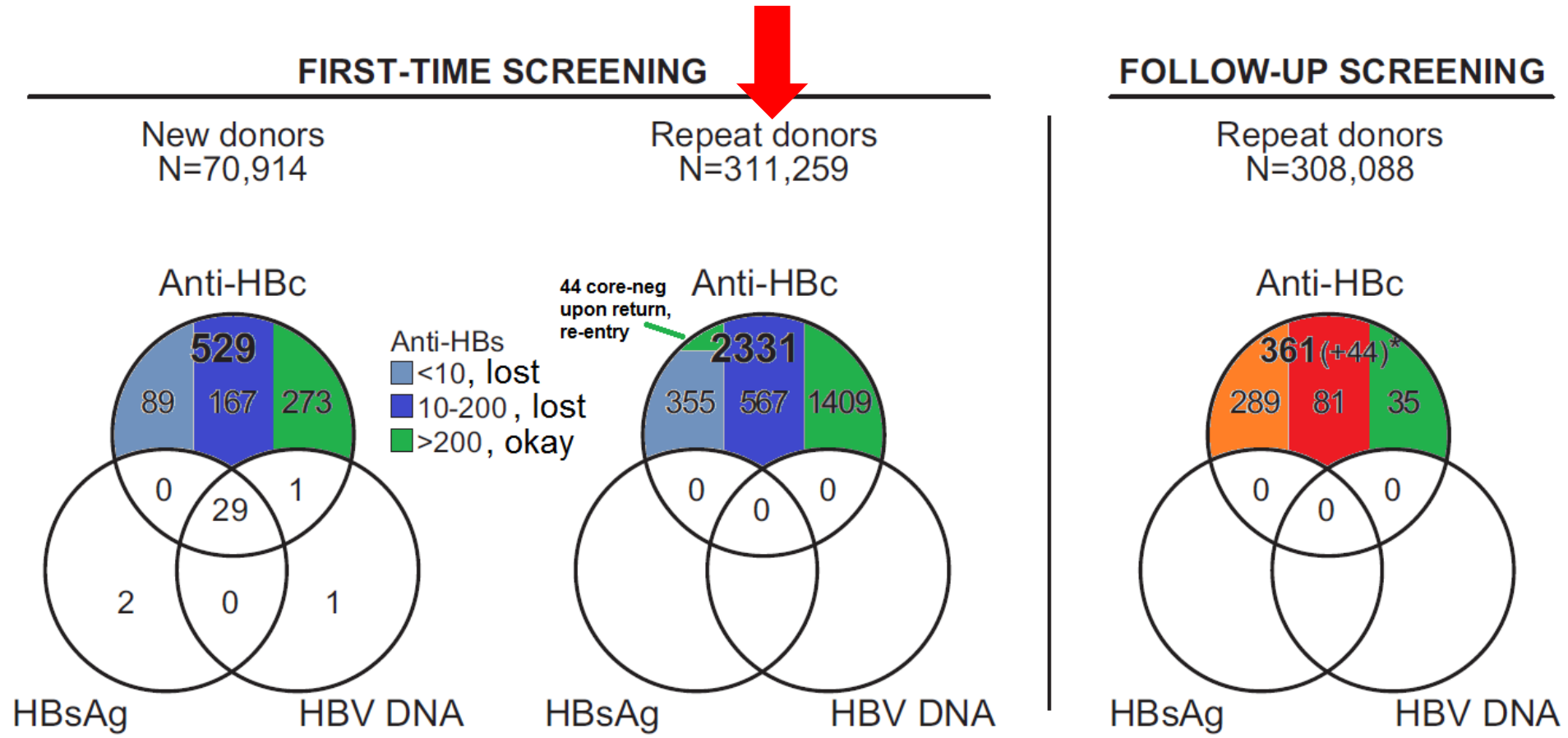


screening of 70,914 new donors: 0,36% deferred

(89 + 167 = 256)

stable over time: 0,24 – 0,43% per trimester

anti-HBcore screening in NL, July 2011 – July 2013

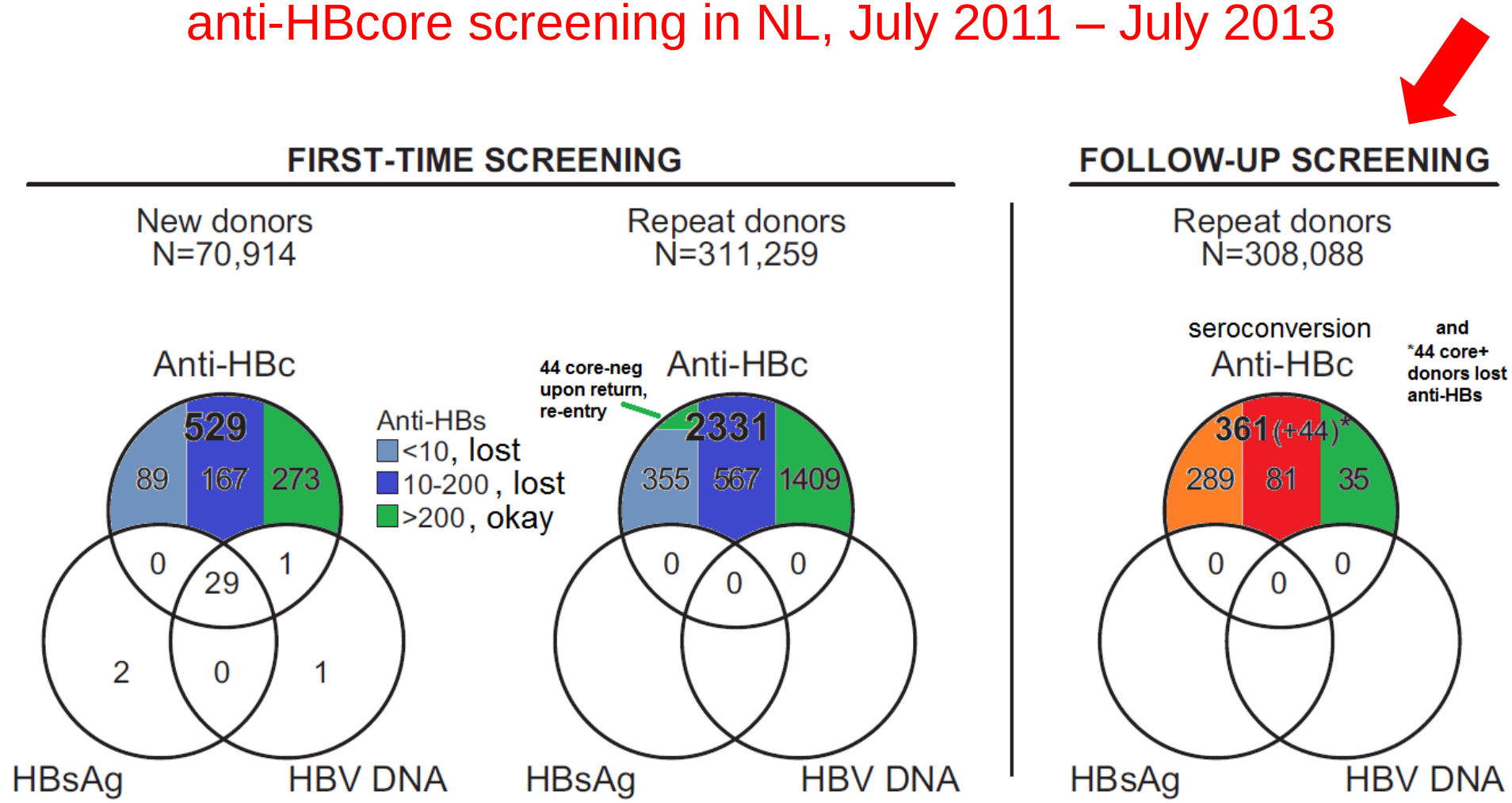


first-time screening of 311,259 repeat donors: 0,30% deferred

(567 + (355-44) = 878)

355 anti-s neg: 71 no return; 239 again core+, 1 recent inf, 44 core neg → re-entry

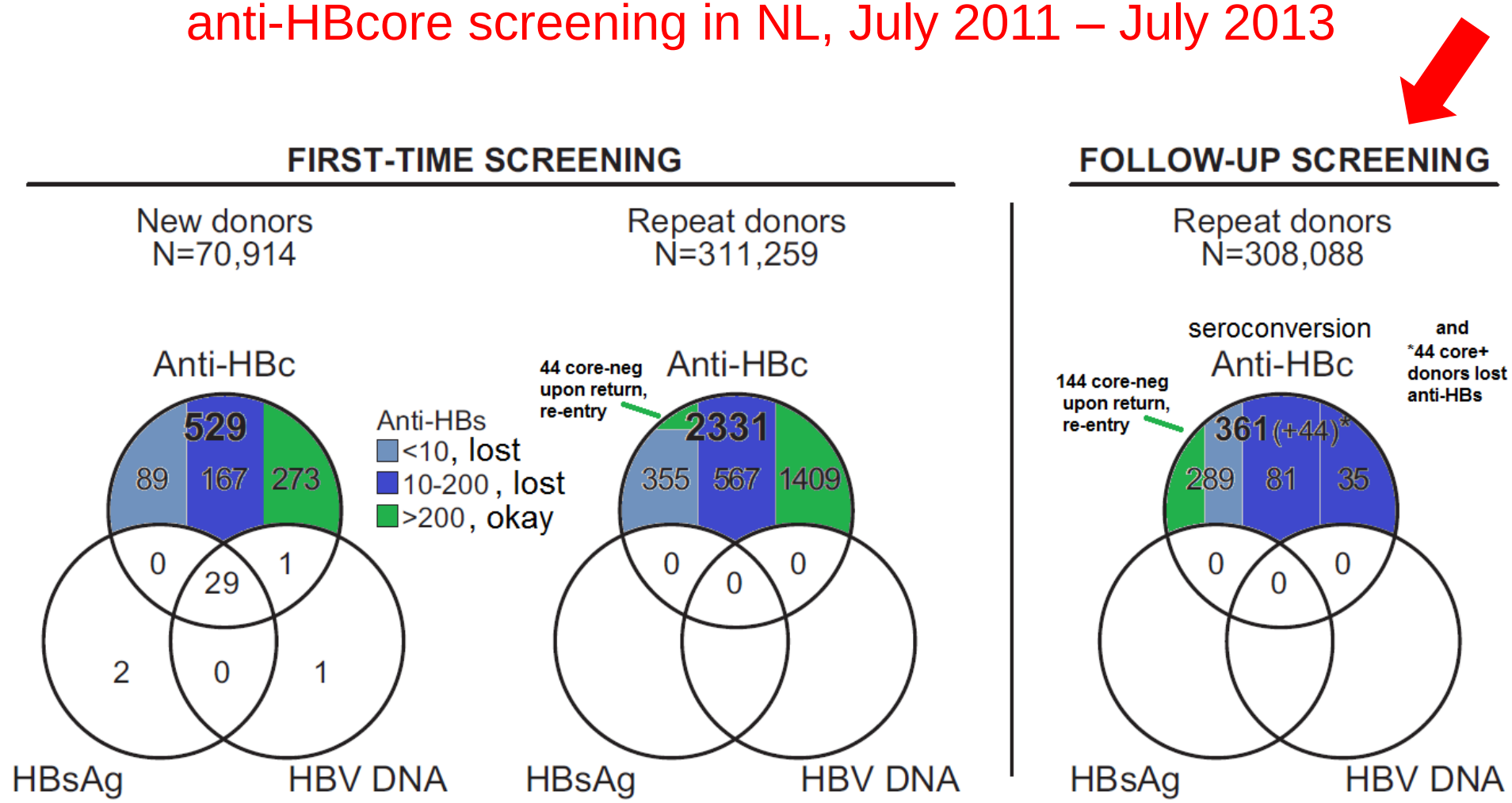
anti-HBcore screening in NL, July 2011 – July 2013



2 year follow up of 308,088 repeat donors:

361 anti-core seroconversions (0,12%); and 44 core+ donors lost a-HBs (< 200 IU/L)

anti-HBcore screening in NL, July 2011 – July 2013



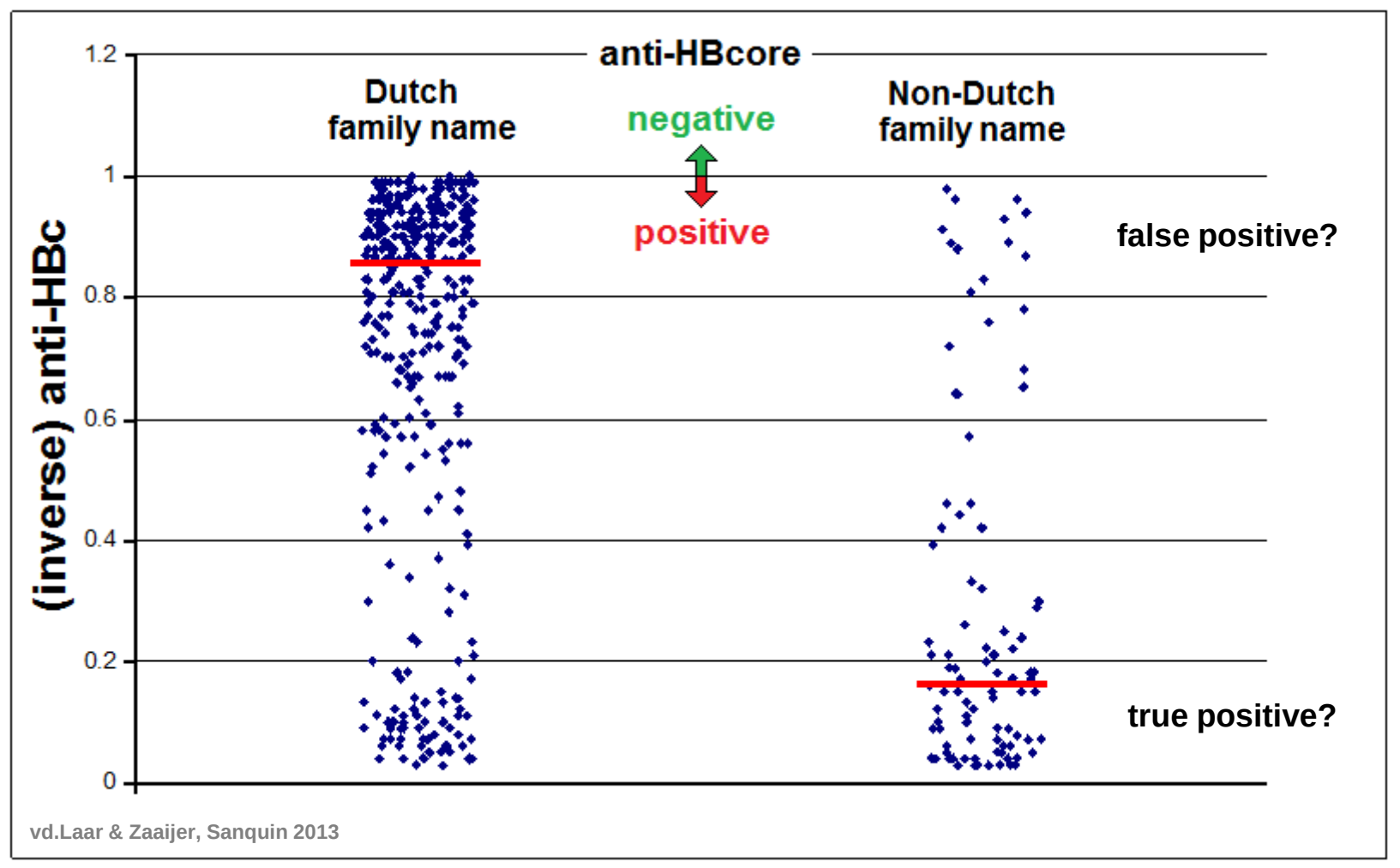
continued screening of 308,088 repeat donors: 0,1% deferred.

361 'seroconverting' donors: 81+35+(289-144)= 261 + 44 lost-antiHBs deferred

289 anti-s neg: 62 no return; 83 again core+ (3 anti-s+,1 recent inf), 144 core neg→re-entry

Loss due to false-positivity: < (62+(83-4)) = < 0,05%

Distribution of 'core-only' signals in Dutch donors



2013-2017: 170.879 new donors tested for anti-core: 1167 = 0,68% pos.
if we assume that weak and intermediate positive = false positive:
306 = 0,18% of new donors anti-core false positive.

Conclusion: pros and cons of anti-HBcore screening

For detection of OBI anti-core is more sensitive than HBV NAT.

advantage:
Prevention of (some) transfusion transmitted HBV infections.

disadvantages:
- Donor loss by false positive anti-HBcore results.
  Donor loss can be limited by:
  - no deferral if sufficient level of concurrent anti-HBs.
  - re-entry of donors with temporary anti-HBcore reactivity.

- OBI-donor is not very infectious. Is aHBcore cost-effective?
For example: estimate number of your true aHBcore+ and aHBs<100 donors, and assume 5% transmission from this group.

a ‘con’ that is a ‘pro’ ?
More HBV in your population → more donor loss?
More transmissions prevented by aHBcore screening!

Thank you