

Estimating transient HBV infection duration using donation intervals

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Study aim

From literature:

- $\pm 10\%$ of individuals do not clear HBV infection^[1]
- Acute (transient) infection is detectable with a serology based test for ± 77 days^[1] and with HBV NAT for ± 90 days^[2]

Can these numbers be re-evaluated / confirmed using routinely collected data on infected donors?

[1] Seed CR, Cheng A, Ismay SL, et al. Transfusion 2002 42:1365-1372

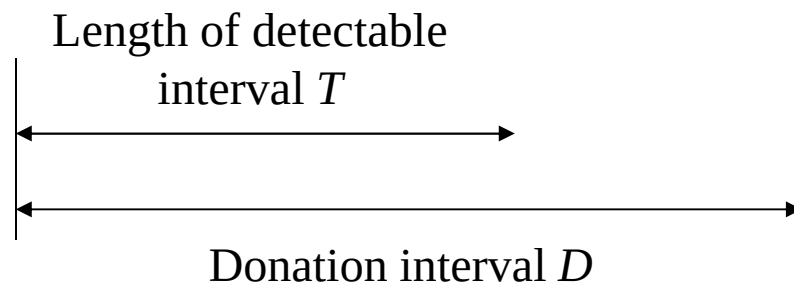
[2] Assal A, Barlet V, Deschaseaux M, et al.: Transfusion 2009 49: 301-310

Yes we can!

- Information on the proportion of infections cleared and the length of the detection interval are captured within routinely collected data!
- and can be derived from the donation intervals of infected (and uninfected) donors.

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Probability of detection is proportional to the length of T relative to D

How?

o Necessary data

- Last donation intervals of all donors who test HBV positive
- A large sample of the donation intervals of all donors, with relevant background variables for these donors (to exclude confounding)

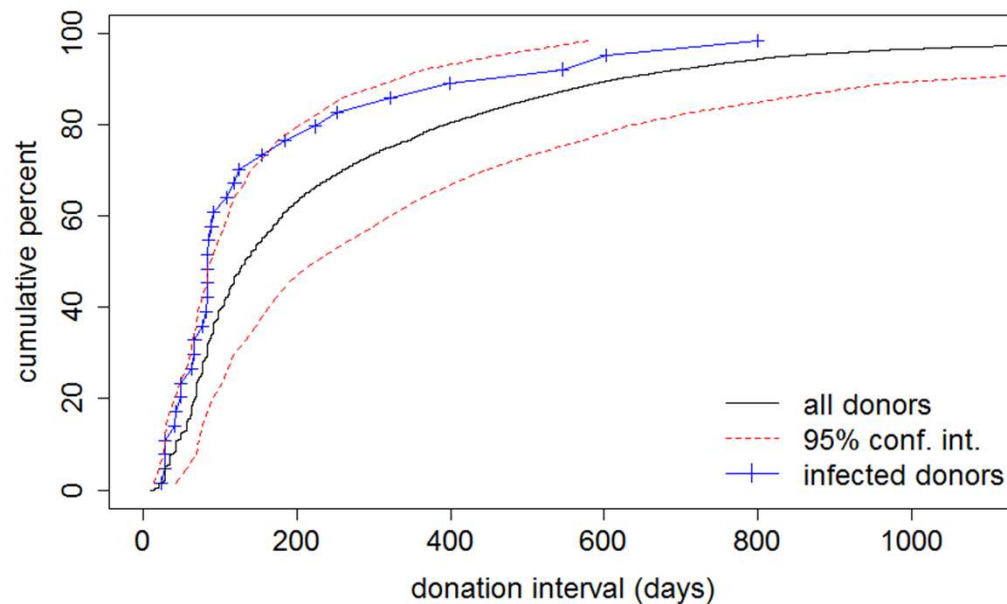
o Maximum likelihood method

- Donation intervals of uninfected donors are used to predict the distribution of donation intervals for infected donors
- Calculate the probability of the observed interval distribution of HBV positive donors under different assumptions and select the most likely solution

o Assumptions

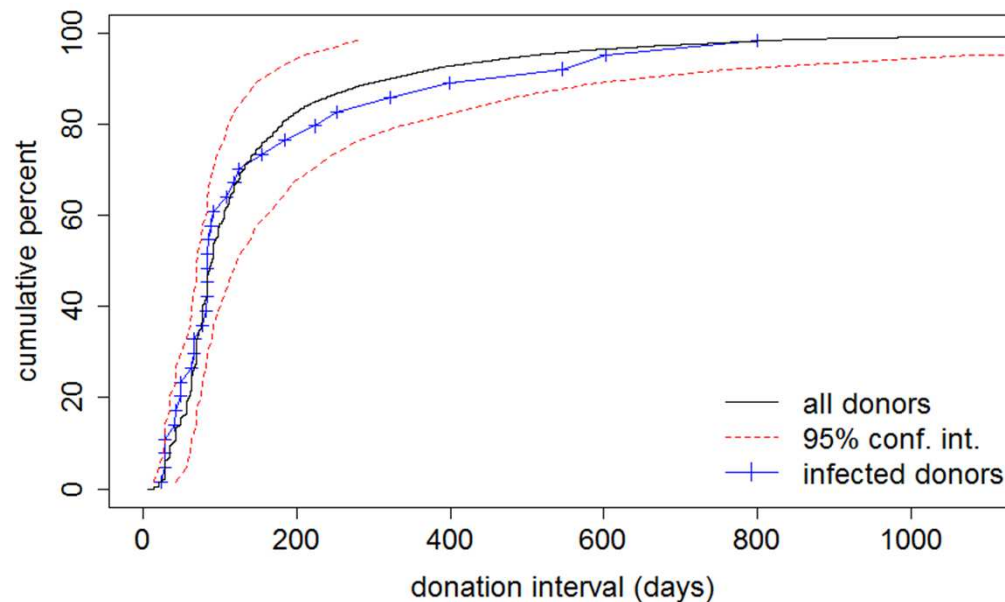
- No interaction between donation interval and infectious status

The distribution of donation intervals of infected donors with its expected distribution



The distribution of donation intervals of the Dutch HBV positive donors as compared to the expected interval distribution of all Dutch donors **when assuming HBV infections do not clear.**

The distribution of donation intervals of infected donors with its expected distribution



The distribution of donation intervals of the Dutch HBV positive donors as compared to the expected interval distribution of all Dutch donors **when presuming that 10% do not clear the infection, and that remaining donors test positive for 77 days.**

Data and results so far

	Number of HbsAg+	Number DNA+
Sanquin, The Netherlands	32	-
Eugene Zhiburt, Russia	18 (confirmed cases only)	-
Gilles Delage, Héma-Québec	4	2
Diana Teo, Singapore	-	11
Syria Laperche, France	6	12
Sheila Obrien, Canada	2	-

Pooling the Dutch, Russian and Quebec serology cases (N=54) the maximum likelihood estimation shows:

- proportion not clearing = 20% (95% CI: 0-75%)
- detectible period = 91 days (95% CI: 20-330)

Power

HBV infections and donations were simulated:

- Simulated donation intervals from the observed Dutch donation interval distribution.
- 10% of simulated donors never cleared HBV, remaining donors cleared at 70 days.

Simulated number of HBV infected donors	95% interval of the detection interval
34	10-180
54	10-140
102	15-130
338	45-95
1015	60-90

Conclusion

- 1) Method works, but ***much*** more data is required....
- 2) We may extend the model to incorporate all observed test outcomes.
This allows estimating model parameters as well as confirming test outcomes found in various settings.
- 3) There is a lot of data out there, let's use it!

**Thanks to the collaborating
SRAP colleagues**